The Effects of the Carotid Sinus Reflex on Cardiovascular Function

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THE EFFECTS OF THE CAROTID SINUS REFLEX
ON CARDIOVASCULAR FUNCTION

by

Thomas Kenny Akers

A Dissertation Submitted to the Faculty of the Graduate School
of Loyola University in Partial Fulfillment of
the Requirements for the Degree of
Master of Science

June
1959
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BIOGRAPHY

Thomas Kenny Akers was born in Brooklyn, New York, January 16, 1931.

He was graduated from Fenwick High School of Oak Park, Illinois in June, 1948. In September of the same year he entered DePaul University, Chicago, Illinois. He entered the United States Navy in March, 1951 and was released to the retired list in January, 1954. He resumed his studies at DePaul University and received the Degree of Bachelor of Science in June, 1956.

He entered the Graduate School of Loyola University of Chicago in September, 1956.
INTRODUCTION

The carotid sinus is a dilation of the internal carotid artery at its origin. It is found in all mammals with the exception of the ruminants. In the ruminants, a dilation at the origin of the occipital artery corresponds to the carotid sinus (1). Nerves from the bifurcation of the carotid artery run into the carotid plexus which receives contributions from the vagus and sympathetic trunks. A branch of the glossopharyngeal nerve enters the area of the carotid sinus.

That afferent impulses arose from the carotid sinus was noted by a number of investigators, but it was not until 1924 that Hering (10) demonstrated the importance of the carotid sinus in the regulation of systemic blood pressure. Since that time Heymans and Koch and their co-workers have extended our knowledge of its physiology (1,2,3,4,5,6,7,8,9).

In 1836 Astley Cooper noted that occlusion of the common carotid arteries induced a rise in systemic blood pressure. He felt that this response was due to cerebral anemia.

Czermak (11) in 1866 described what he called the "Vagusdruckversuch"; a test which is administered by placing the fingers on the neck and pressing firmly. The digital compression induces cardiac slowing. Czermak attributed the slowing of the heart to mechanical stimulation of the vagus nerve. In 1870, Concato (12) stated that pressure on the carotid sinus was more effective in producing bradycardia than pressure on the vagus.

1As cited by Heymans (1).
His experiments attracted no attention.

Hering had been interested in Czermak's work and performed the "Vagusdruckversuch" on many people. In one case only a very light pressure was necessary to elicit cardiac slowing. Such delicate pressure seemed inadequate to stimulate the vagus. In 1920, Hering (13) showed that mechanical stimulation of the vagus in rabbits would not produce bradycardia. By 1923, he had localized the reflex to the nerves ending in the region of the carotid sinus (14). By placing clips on the carotid sinus in the dog, Hering was able to show systemic hypotension as well as bradycardia. He further showed that these responses could be abolished by cutting the glossopharyngeal nerve (10).

In 1929, Hering demonstrated that injection of fluid into the isolated sinus caused bradycardia and hypotension and Heymans showed that changes in pressure in a sinus perfused by a donor animal produced reflex changes in the blood pressure of the recipient animal (1,10,15). Since that time much work has been done to demonstrate the importance of the reflex in the control of circulation. Most of this work has employed sinus perfusion methods and has been primarily concerned with the response to an increased pressure (16,17,18,19,20,21,22,23).

Common carotid occlusion causes a rise of systemic blood pressure. This—as Hering showed—is a reflex. If the aortic nerves, in the vagus, are cut, then carotid occlusion evokes an even greater rise in pressure (24,25). Apparently either the sinus nerves or the aortic nerves are capable of operating alone in controlling blood pressure.
In 1926, the innervation of the carotid sinus was extensively investigated by de Castro (29) and has since been studied by Heymans (1), Danielopolu (30) and others (31,32,33). They have concluded that the nerve described by Hering (10) is the most important and that the carotid sinus reflex maintains homeostasis of the circulation. When the common carotid artery is occluded and pulsatile pressure to the sinus is cut off, the tension receptors in the wall of the sinus decrease their frequency of impulses up the glossopharyngeal nerve to the brain stem. It is postulated that the decrease in impulses from this nerve releases the inhibition on the vasomotor center in the medulla oblongata, resulting in a greater degree of peripheral vasoconstriction and a concomitant rise in systemic blood pressure.

All of these workers measured the blood pressure response by means of mercury manometers and therefore could not faithfully reproduce changes in pulse pressure denoting changes in the dynamics of myocardial contraction (33).

Many investigators have found that activation of the sympathetic outflow to the heart by sympathetic trunk stimulation, lower brain stem stimulation or by hypothalamic stimulation results in an augmentation of the force of myocardial contraction (34,35,37,38,39,40). These data stress the significance of the role of the nervous system in the control of myocardial contraction.

Since the earlier studies, it has been demonstrated that certain augmentor pathways exist in the hypothalamus and lower brainstem which
pass down the cord to the heart (38,39,40).

Heymans states that chloralose and pentothal when administered in ordinary anesthetic doses to dogs do not reduce the cardiovascular responses to the carotid sinus reflex. Chloralose causes a curious irresponsiveness of the vasomotor center to baroreceptor stimulation in the cat (1).

There is a great deal of literature concerning the effects of anesthetics on the response of the reflex. Gellhorn (39) has shown that changes in the blood pressure through the injection of drugs alters the responsiveness of the hypothalamus. These effects were abolished by denervation of the sino-aortic area. He was able to demonstrate an increase of discharging neurons in the posterior hypothalamus during and after the recovery of the blood pressure from drug induced hypotension. McDowall (15) and Winder (26) have found that this is not always the case. In cats, they have found that barbiturates are more depressant than chloralose and recommend the use of chloralose so as not to depress the sympathetic nervous system. Other workers confirm this (27,28). Manning (38) has found that barbiturates depress the augmentor response of the hypothalamus to electrical stimulation.

In the literature there exists no clear cut evidence that the augmentor pathways described above participate in the carotid sinus reflex. Therefore it is the purpose of this thesis to determine whether augmentor responses are involved in the carotid sinus reflex and to determine the area in the brain in which they are integrated. By the accurate recording of the arterial pressure pulse, alterations in the dynamics of myocardial contraction may be interpreted from changes in the pressure pulse.
It is further proposed to show the effects of different anesthetics upon the central integration of the augmentor response of the carotid sinus reflex.
MATERIALS AND METHODS

1. Transaction Technique

Transactions of the brain stem were performed in two ways in this study. In the early experiments a surgical method was employed; however there was generally a large blood loss with this method and therefore an electrolytic method was employed.

A constant current apparatus as described by Fleming (41) was used. This apparatus is so constructed that the current does not vary despite changes in tissue resistance and electrode polarization. The current intensity may be continuously and accurately varied from 0--10 milliamperes, and an automatic timer provides control of the duration of current flow. In order to prevent gross motor movements, the circuit provides an additional control which regulates the rate of rise to the desired current intensity.

The parameters of electrolytic ablation employed were ten milliamperes and forty-five seconds with a ten second rise time.

The procedure involved was as follows. With the animal prone, a sagittal incision was made in the skin on the superior surface of skull and the skin retracted. Periosteal levers were used to elevate ear muscle attachments on the parietal bones of the skull. After muscle attachments were cleared a hole was drilled on each side with a one inch trephine in the center of the origin of the muscle. A rongeur was used to remove the bone between the two holes. The dura mater lying beneath was cut.
with a sharp scalpel, care being taken not to damage the superior sagittal sinus. The electrodes were then inserted with a slight forward angle. Usually the tentorium could be felt via the electrodes. If this occurred they were withdrawn and reinserted a little more anteriorly. The electrode carrier was clamped in a stand and each electrode adjusted vertically until resistance was felt.

Histological sections showed that the area of ablation lies just anterior to the superior colliculii (see figure 1).
FIGURE 1

A schematic mid-sagittal section through the dog's brain showing the electrode pathway and area of ablation.

CA--Commissura anterior
CH--Optic chiasma
MI--Massa intermedia

Mm--Corpus Mamillare
Fo--Pons
Ce--Cerebellum
2. **Stimulation Technique**

Carotid occlusion was accomplished by clamping, with bulldog clamps, both common carotid arteries in the neck below the level of the hyoid cartilage of the trachea. Carotid occlusion is known to cause a rise in systemic blood pressure.

However the effects of common carotid occlusion should not be simply interpreted as being due to complete withdrawal of sinus baroreceptor impulses. Schmidt (48) found that occlusion of the common carotid artery caused a fall of 36% of the initial pressure measured in the carotid sinus. But the pressure recovered to within 19% of its control level. This indicates considerable backflow of blood via anastomotic vessels. Recently Chungcharoen and his group (43, 44) and Wang and his group (15) reinvestigated this problem and found that unilateral occlusion of the common carotid artery decreased the sinus pressure by 50%; however within 30 seconds the sinus pressure was within 10-35% of its initial value. If both carotids were occluded the fall of sinus pressure was even greater but it still recovered to within 10-35% of the initial value in 30 seconds. These workers showed by an elaborate series of experiments that the recovery was due to the backflow of blood from the vertebral arteries via the circle of Willis. It was found that the anastomotic vessel, joining the orbital branch of the internal maxillary artery to the internal carotid, is sometimes as large as the internal carotid. Therefore, not too much attention should be paid to the level of the mean pressure in the sinus. Had, Green and Neil (46) demonstrated that a pulsatile pressure
has a greater effect, reflexogenically, than a steady pressure of the same mean value as far as the response of systemic blood pressure is concerned. In 1932, Bronk and Stella showed that baroreceptors respond to rate of change of pressure (47). Therefore even though the level of sinus pressure recovers within 30 seconds of occlusion the reflexogenic effects of the occlusion are manifest due to the lack of pulsatile pressure.

Hence it follows that this technique is adequate to initiate the reflex rise in blood pressure.
3. Recording Techniques

Records of the pressure pulse in the femoral artery were obtained by means of a Sanborn Electromanometer adapted to drive a Sanborn E.C.G. optical galvanometer. A light beam was reflected from the galvanometer mirror and focused on moving photosensitive paper to give a photokymographic record of the pressure pulse curve. Some of the earlier records were obtained by means of a Sanborn Electromanometer coupled with a Sanborn Polyviso recorder (Model 64). In this case the pressure pulse curves were recorded on moving heat sensitive paper with a heated stylus attached to the galvanometer of the Polyviso.

The general principle of operation is as follows. A closed fluid system is continuous with, in this case, the arterial blood of the femoral artery and the transducer. The pressure and any alterations in pressure in the fluid system is transmitted to the transducer. The transducer is a microphone condenser type and the diaphragm in contact with fluid column acts as one plate of the condenser. The transducer condenser is the variable component of an alternating current bridge circuit. When the transducer is activated by the pressure, the bridge is unbalanced and the output voltage is in proportion to the magnitude of change occurring in the variable component.

The output voltage of the electromanometer is then suitably amplified to drive the optical galvanometer or the polyviso galvanometer. For the optical system a modified Sanborn Model 126 general purpose DC amplifier was used in this stage of the circuit. The modification is necessary to
obtain a critically damped galvanometer response to a square wave signal input.

An integrating cardiottachometer (48) was added to the system at this point. The input to the tachometer was taken from the oscilloscope output of the DC amplifier. The output of the tachometer was connected to a Howell Reflecting galvanometer.

The photokymograph consisted of a modified Phipps and Bird model 70-140 kymograph housed in a light tight metal box. The modification was as follows. A Bodine electric motor type M38-11K was mounted outside of the metal box and flexibly coupled with a brass shaft mounted on the bearings of the original motor. The speed of the external drive motor was controlled by a Superior Electric Powerstat and operated on DC current. This modification allowed paper speeds to be changed rapidly. The light tight metal box was provided with a slit $\frac{1}{2}$ inch wide and 14 inches long through which the light beams reflected from the galvanometers could pass. With a suitable lens system the light beams from the pressure galvanometer, tachometer galvanometer, the timer and the signal magnet were focused upon the photosensitive paper. (see Figure 2).

The recording techniques used in this study are capable of faithfully reproducing events occurring in the pulse pressure curve to the tenth harmonic if the frequency of the heart doesn't exceed four beats per second.
6. Experimental Procedure

This study was carried out on 16 young adult mongrel dogs. Half of the dogs were anesthetized with 50 mg/kg of pentobarbital sodium in a

Animals were ventilated by ventilating the respiratory system by the common carotid arteries and cannulated and the entire head of the animal removed. The head was first perfused with saline to remove the blood in its vessels and then perfused with formalin to preserve the tissue. The brain was removed for histological workup. This was done to verify the level of electrolytic transection.

FIGURE 2
The experimental setup.
4. **Experimental Procedure**

This study was carried out on 18 young adult mongrel dogs. Half of the dogs were anesthetized with 32.5mg/kg of pentobarbital sodium in saline and the other half were anesthetized with 100mg/kg of chloralose in carbowax. The trachea was cannulated and artificial respiration was instituted. The common carotid arteries and vagi were exposed and loose ligatures placed around them. The femoral artery was isolated and cannulated with a 25 gauge 3/4 inch blunt end needle. The needle and the three-way adapter valve, connected to the fluid system of the electromanometer, were filled with heparin solution. The following procedures were then employed:

1. A blood pressure recording was made and both common carotids were clamped with bulldog clamps for 15 seconds. After the blood pressure returned to pre-experimental levels, the kymograph was stopped.

2. The animal was bilaterally vagotomized and procedure 1 was repeated.

3. The animal was transected and the blood pressure was allowed to stabilize for one hour. Procedure 1 was then repeated.

Animals were sacrificed by disconnecting the respirator. One of the common carotid arteries was cannulated and the entire head of the animal removed. The head was first perfused with saline to remove the blood in its vessels and then perfused with formalin to preserve the brain. The next day the brains were removed for histological workup. This was done to verify the level of electrolytic transection.
5. **Analysis of Data**

In the normal situation the dynamic equilibrium of the arterial system is such that the stroke volume of the heart equals the outflow from the arteries into the capillaries. If however this equilibrium is altered in any way, such as changes in heart rate, changes in stroke volume, or changes in peripheral resistance, the stroke volume is disproportionate to the peripheral outflow until a new state of dynamic equilibrium exists.

Wiggers (35) studied this problem in an artificial circulation model in which each of the factors could be regulated separately. Such studies showed that an increase in heart rate caused a greater rise in diastolic pressure than in systolic pressure, thus reducing pulse pressure. Increase in peripheral resistance elevates diastolic pressure more than systolic pressure until systolic distensibility begins to diminish drastically; then systolic pressure rises progressively faster than diastolic until the pulse pressure exceeds normal. Increase in stroke volume raises systolic pressure more than diastolic, thereby increasing the pulse pressure above normal.

Keeping in mind that in the intact animal the situation is much more complex and the majority of cardiovascular changes obtained are mixed responses, the dynamics of the artificial circulation model are applicable.

In this study, the pressure pulse curves from the photokymograms were analysed in following manner. An increase in pulse pressure obtained primarily by a rise in systolic pressure was interpreted as an increase
in the force of myocardial contraction while a rise in blood pressure with a concomitant rise in diastolic pressure with little or no change in pulse pressure was interpreted as a vasoconstrictor response.

Changes in heart rate were determined by direct inspection of the photokymograph record of the integrating cardiotachometer.

The changes in cardiovascular function described above have been supported in general by the investigations of Cotten (34), Randall (49), and Rushmer (40).
EXPERIMENTAL RESULTS


In the following figures, the markings of the time line are spaced at ten second intervals. The onset and duration of occlusion is indicated by perpendicular lines. The period of occlusion varied from 20 to 60 seconds. These figures are graphic representatives of the original photokymograms which could not be reproduced photographically for this thesis.

Figure 5 depicts the effect of bilateral common carotid occlusion in an intact animal. The control pulse pressure was 25 mm. Hg. with a systolic pressure of 125 mm. Hg. and a diastolic pressure of 100 mm. Hg. The heart rate was 210 beats per minute. Within seven seconds of the onset of occlusion the systolic pressure had risen to 130 mm. Hg. while the diastolic pressure remained at control level. After 10 seconds of occlusion the diastolic pressure began to rise faster than the systolic rise so that after 20 seconds the pulse pressure was only 20 mm. Hg., a twenty percent decrease from the control level. The heart rate increased 6 beats per minute during the first 5 seconds.

The overall increase in blood pressure with the greater increase in diastolic than in systolic pressure is most likely due to vasoconstriction and possibly adrenal activation through the carotid sinus reflex. The slight increase in pulse pressure within the first seven seconds of the occlusion is best explained by increased myocardial contraction mediated in the brain stem (36). The effect of adrenal secretion may be
ruled out in this early phase, since the response was more rapid than the
circulation time of the animal. The heart rate increase during the early
phase must be attributed to a nervous reflex arc rather than a response
to adrenal secretion.

Figure 4 represents the same animal that is depicted in figure 3
except that in this case both vagi have been severed. In the vagotomised
animal the increase in pulse pressure is greater than in the intact animal.
In this case the systolic pressure rose from 80 mm. Hg. to 100 mm. Hg.
within the first 7 seconds of occlusion while the diastolic rose from
70 mm. Hg. to 80 mm. Hg., with a pulse pressure increase of 10 mm. Hg.
After 25 seconds the systolic pressure had reached 120 mm. Hg. and the di-
astolic pressure 100 mm. Hg. The pulse pressure remained 20 mm. Hg.
which was obtained during the first 7 seconds. Here again the long range
increase in diastolic pressure may be ascribed to a combination of neural
and hormonal vasoconstriction. The pulse pressure and heart rate increas-
es again occurred within 7 seconds.

Figure 5 is the same animal as above after midcollicular transection
(histologically verified). Under these conditions the systolic and dia-
stolic pressure increased, but with a slight decrease in pulse pressure.
Systolic pressure rose from 110 mm. Hg. to 152 mm. Hg. and diastolic
pressure rose from 80 mm. Hg. to 124 mm. Hg. The heart rate increased
moderately during the first 7 seconds. The overall increase in pressure
may be ascribed to the neural vasoconstriction set into operation by the
carotid sinus reflex. But in this case the augmentation of pulse pres-
sure indicative of increased myocardial contraction is missing.
Nembutalized intact animal.

The onset of occlusion is indicated by perpendicular lines.

The open circles represent the heart rate.

The closed circles represent the level of systolic and diastolic pressure measured every 2.5 seconds on the original photokymograph.
FIGURE 4

Nembutalised vagotomized animal.

Legend as in Figure 3.
FIGURE 5

Nembutalised transected animal.

Legend as in Figure 3.
2. **Cardiovascular Responses in Chloralosed Animals.**

The following figures depict the effect of bilateral common carotid occlusion on blood pressure in an animal under chloralose anesthesia. Figure 6 represents one of the typical animals in this series. The vagi are intact. The control level of blood pressure was 200 mm. Hg. systolic and 140 mm. Hg. diastolic pressure, with a pulse pressure of 60 mm. Hg. The control heart rate was 80 beats per minute. Seven seconds after the onset of occlusion the systolic pressure was 210 mm. Hg. and the diastolic pressure was 150 mm. Hg. The pulse pressure remained the same in this time. The heart rate had increased to 100 beats per minute. The intact animal under chloralose responded to carotid occlusion in the same manner as the nembutalized animal. However the responses in the chloralosed animals were greater.

The lack of pulse pressure rise is possibly due to an increased heart rate and to the intact baroreceptors of the aortic arch. The increase in heart rate may be classically explained on the basis of vagal inhibition and sympathetic activation. The diastolic pressure rise is probably due to vasoconstriction.

The animal in figure 7 was the same as the animal in figure 6 except that it had been bilaterally vagotomized. The pulse pressure increased during the first 7 seconds of occlusion from 50 mm. Hg. to a maximum of 80 mm. Hg. Heart rate increased from a control value of 135 per minute to 165 per minute. The latency of onset was less than 7 seconds. Within 10 seconds after cessation of occlusion heart rate and pulse pressure
had returned to preocclusion levels. Under these conditions the pulse pressure responses were greater than those found in nembutalised animals under similar experimental conditions. The good augmentation response is probably the result of the removal of aortic arch effects. The heart rate increase in this case can only be due to sympathetic activation.

Figure 8 illustrates the effect of carotid occlusion in the same animal as above, except that electrolytic transection at the midcollieular level had been performed 1 hour earlier. After occlusion there is no change in pulse pressure and heart rate due to occlusion of the carotid artery. There is a rise in mean pressure which is probably the result of vasoconstriction.
Figure 6

Chloralosed intact animal.

Legend as in Figure 5.
**FIGURE 7**

Chloralosed vagotomized animal.

Legend as in Figure 3.
FIGURE 6

Chloralosed transected animal.

Legend as in Figure 3.
3. **Summary of Results.**

Table number I is a summary of the results from 15 animals which were subjected to bilateral common carotid occlusion with the vagi intact. In all cases there was an increase in both the diastolic and systolic pressures. Also in all but two of the cases there was an increase in heart rate. In 4 of the nembutalized animals the diastolic pressure increased as much as the systolic pressure so that the pulse pressure remained the same. Only 3 of the nembutalised animals and all of the chloralosed animals responded to the occlusion with a modest rise in pulse pressure. This rise was only 10-25 millimeters of mercury. The mean increase in pulse pressure over control levels was higher in the animals under chloralose anesthesia than it was in the animals under nembutal anesthesia (see figure 9).

When the animals were vagotomized there was a much greater change in pulse pressure. Table II summarizes the results of 9 animals. With the exception of 2 nembutalised animals, all animals responded to the occlusion with an increase in pulse pressure. The animals were much more reactive to carotid occlusion after vagotomy. The mean increase in pulse pressure over control levels was greater in the chloralosed animals than it was in the nembutalised animals (see fig. 9).

Eleven animals survived the transection procedure. After the blood pressure in these animals had stabilized (usually 1 hour post-operative) the occlusion stimulus was applied. Not one of the animals responded with an increase in pulse pressure. However 10 of the animals responded with
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**Code**

S---Systolic Pressure

D---Diastolic Pressure

P---Pulse Pressure

HR---Heart Rate/Min.

Pressure in MM. Hg.
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Abbreviations same as in Table I.
### TABLE III

 Transected Animals

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Code as in Table I.
an increase in mean arterial pressure. The heart rate did not change in
4 of the animals and only slightly in the rest (see Table III and Fig. 10).

Figure 9 is a summary of all of the experiments. The bars indicate
the average rise (in mm. Hg.) above the control level of pulse pressure.
The chloralose animals and the nembutal animals are grouped separately
under each procedure. The rise in pulse pressure over control values
for each animal is represented by a dot.

The heart rate responses to carotid occlusion in the various groups
of animals are difficult to evaluate. Figure 10 depicts the heart rate
in all of the animals in there various groups. The open bar represents
the control heart rate and the solid bar represents the heart rate during
carotid occlusion. In general, the heart rate of the nembutalized animals
was higher during the control period than the heart rate of the animals under
chloralose anesthesia. However the heart rates of both sets of animals
were about the same during occlusion. After transection the heart rates
of all the animals did not change markedly following carotid occlusion.
The chloralose animals in the post-transection state had lower heart rates
in general than the nembutalized group.
RISE IN PULSE PRESSURE ABOVE CONTROL LEVELS

FIGURE 9

The bars indicate the average rise.
The circles indicate the increase for each animal.
N--Nembutalized animals.
C--Chloralosed animals.
FIGURE 10

Open bars represent the control heart rate.

Solid bars represent the heart rate during occlusion.
4. **Drug Effects on Vasomotor Responses.**

It was noted that in all the animals anesthetized with 32.5 mg/kg. of Sodium pentobarbital (Nembutal), the rise of pulse pressure above control levels was less than the rise in pulse pressure in chloralosed animals. To test the depressant action of Nembutal upon the pulse pressure response, the following experiments were performed. Five dogs were prepared in usual manner using chloralose as an anesthetic and cutting the vagi to insure maximum response. Occlusion of both carotid arteries produced cardiovascular changes similar to those described for figure 8. Small doses of Nembutal 2.5-10 mg/kg., were administered intravenously by way of the femoral vein. The carotid arteries were again ocluded and the degree of depression measured. It was found that 5 mg/kg. of Nembutal i.v. was capable of depressing almost completely the augmentor response. An example of this phenomenon is illustrated in Figure (11). During the control occlusion, indicated by the first set of perpendicular lines, the systolic and diastolic pressure rose with a large augmentation of the pulse. At the large arrow a 5 mg/kg. dose of Nembutal was given intravenously by way of the femoral vein. A second occlusion of the carotid arteries was done 3 minutes following the injection. This resulted in a small presser response with little if any augmentation in the pulse pressure. The rise in heart rate was reduced (approximately 50%) by the Nembutal.
FIGURE 11

Legend as in Figure 5.

At the large arrow a small (5 mg/kg.) dose of Nembutal was given intravenously.
DISCUSSION

Previous investigators have reported the cardiovascular responses to bilateral carotid artery occlusion. Their interpretations of the responses were limited chiefly by the recording techniques employed and the anesthetics used. This study demonstrates conclusively that increased myocardial contraction is a significant component of the carotid sinus reflex.

The increased force of myocardial contraction is the result of activation of the sympathetic outflow to the heart and is not due to increased adrenal medulla output. The latter possibility is eliminated positively by the short (3-7 seconds) latency of the response.

Upon examination of the augmentor responses in the intact animal (see figure 9) it is noted that the average rise in pulse pressure above the control level is greater in the animals under chloralose anesthesia than in the animals under nembutal. It has been shown by a number of investigators that nembutal depresses the higher centers and there is the possibility that nembutal depresses the baroreceptors themselves. This can account for the findings in the intact animals.

After vagotomy the augmentor response is greater in both the nembutalized and chloralosed animals than in the intact animals. This may be accounted for by that fact that the afferent fibers from the aortic baroreceptors have been removed by vagisecion. In this case the chloralosed animals responded to a greater degree than the animals under nembutal.
The explanation of this is as above.

After midcollicular transection there was no increase in pulse pressure in response to bilateral common carotid occlusion. Recent studies of Manning (38) have shown that there are specific areas in the posterior hypothalamus of the cat, which when stimulated electrically produce large augmentor responses. From the foregoing it may be concluded that the augmentor reflex is mediated at levels of the brain above the colliculi and is probably mediated in the hypothalamus.

All of the animals with a single exception of 18 in the transected state responded to the occlusion with an increase in diastolic pressure. The increase in diastolic pressure was taken to indicate vasoconstriction. The vasoconstriction occurred even after medullicular transection. This data supports the classical concept that the vasomotor center is medullary.

In general, most of the heart rate increases are lost when transection is done (see figure 10). Since the heart rate increased even in the vagotomized animals, it is therefore probable that the sympathetic heart rate increase is also mediated primarily at higher levels of the central nervous system (50).

The size of the augmentor response to carotid occlusion is relatively small when compared to the augmentor responses elicited by direct stimulation of various areas of the reflex pathway. When the left stellate ganglion is stimulated, cardioaugmentor responses with large increases in systolic pressure are recorded, while diastolic pressure and heart rate remain relatively unchanged. Peiss (36) has reported similar responses
during stimulation of the brain stem reticular formation. He feels that these are probably afferent pathways in part. Hypothalamic stimulation yields huge augmentor responses (38). These responses are sometimes 200 or 300 percent of the control levels. This study indicates that most of the ability to increase the force of myocardial contraction exists in pathways not activated by the mechanism controlling the regulation of blood pressure.
SUMMARY

1. Cardiovascular responses elicited by bilateral common carotid oclusion have been studied in intact bilaterally vagotomized or midecol-
licular transected dogs under sodium pentobarbital and alpha-chloralose anesthesia.

2. In the intact and the vagotomized animals, augmentation is the most common response. It is associated with increased heart rate and vasoconstriction.

3. In the midcollicular transected animals there was no augmentation and relatively little change in heart rate. The vasoconstriction was still present.

4. In general the augmentor responses in the nembutalized animals were much less pronounced than in the chloralosed animals. Minute doses of nembutal administered intravenously depressed almost completely the augmentor response in chloralosed vagotomized dogs.

5. It is concluded that the augmentor reflex is mediated above the level of transection. This study indicates that most of the ability to increase the force of myocardial contraction exist in pathways not activated by the mechanism controlling the regulation of blood pressure.
BIBLIOGRAPHY


APPROVAL SHEET

The dissertation submitted by Thomas Kenny Akers has been read and approved by three members of the faculty of the Graduate School.

The final copies have been examined by the director of the dissertation and the signature which appears below verifies the fact that any necessary changes have been incorporated, and that the dissertation is now given final approval with reference to content, form, and mechanical accuracy.

The dissertation is therefore accepted in partial fulfillment of the requirements for the Degree of Master of Science.

May 26, 1959

Date

Signature of Adviser