THE EFFECTS OF ARTERIAL OCCLUSION IN THE CHICKEN

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ABSTRACT

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by Charles Henry McGinnis, Jr.

One area of research in the physiology of birds which has not received adequate study is blood pressure regulation. It was considered that since the well-known carotid sinus and aortic baroreceptors are important as immediate blood pressure regulators in mammals, a determination of functional baroreceptor areas in the chicken should be basic to a study of blood pressure regulation in this species.

Commercial Leghorn-type hens (approximately 12 months of age) were used throughout this study. All birds were anesthetized with 130 mg. of sodium phenobarbital per kg. body weight prior to surgery. Blood pressure, when measured, was obtained by direct means from a carotid or ischiatic artery. Blood pressure measurement was accomplished utilizing a Statham pressure transducer and either a Brush analyzer and pen recorder or a Grass Model 5 Polygraph.

Carotid and vertebral arteries were permanently ligated in the thoracic cavity of Leghorn-type hens. The birds were then kept for a period of two weeks. At the end of this time they were sacrificed and body and heart weights measured. No significant differences were found in body weights or heart weights. All birds with either the carotid or vertebral arteries ligated survived, while only 75 percent of those with both vertebral and carotid arteries ligated survived. The great tolerance shown by most hens to ligation of both carotid and vertebral arteries indicated the presence of considerable collateral

circulation to the head and raised the question of whether or not a well-developed baroreceptor mechanism is needed to protect the cerebral circulation in the chicken.

Systemic blood pressure and cerebral blood pressure (determined by cannulating a carotid artery craniad) were measured in hens during vertebral and carotid occlusion at the carotid-vertebral bifurcation. Occlusion of the carotid arteries produced a small, highly significant increase in systemic blood pressure, a highly significant decrease in heart rate and a moderate, highly significant decrease in cerebral blood pressure. Occlusion of both the carotids and vertebrals produced a large, highly significant increase in systemic blood pressure which appeared immediately subsequent to a large, highly significant decrease in cerebral pressure. A small increase in heart rate and a moderate, highly significant decrease in respiratory rate were also obtained. Analysis of the data indicated that systemic blood pressure response did not begin to appear until arterial occlusion caused cerebral perfusion pressure to decrease to approximately 45 to 53 mm. Hg. These results demonstrated a lack of baroreceptor reflex response to either bilateral carotid or vertebral artery occlusion. The large increase in systemic blood pressure and the decrease in respiratory rate obtained with occlusion of both carotid and vertebral arteries were attributed to cerebral ischemia. The intracarotid injection of small quantities of hypercapnic blood into hens produced the same pattern of response obtained with occlusion of both carotids and vertebrals, thus, adding support to the concept of cerebral ischemia.

The direct application of high, pulsatile arterial pressure into one carotid of hens produced no reflex effect on systemic blood

pressure or heart rate. This indicated a lack of intracranial baroreceptors.

To test for pressoreceptor reflexes from the area of the carotid artery homologous to the mammalian carotid sinus, unilateral brachiocephalic artery occlusion with contralateral vagotomy was accomplished. Occluding a brachiocephalic artery removed approximately 75 percent of the arterial pressure from the area of the ipsilateral carotid artery homologous to the mammalian carotid sinus (this area located caudal to the carotid-vertebral bifurcation and cranial to the root of the subclavian artery). Sectioning the contralateral vagus removed the primary innervation of the carotid sinus homologue and carotid body on that side; thus, only the single innervated carotid artery was subjected to pressure change. This procedure was accomplished with each carotid artery. No apparent baroreceptor reflex responses resulted when pressure was altered in the innervated carotid. The carotid sinus homologue in the Leghorn-type hen did not appear to be a functional baroreceptor region.

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INTRODUCTION

Sturkie, in a 1958 review paper concerning avian physiology, reiterated a statement originally made in the preface of his book, Avian Physiology: "Knowledge in certain areas of avian physiology is limited, fragmentary and often confused, and little or no research is being conducted". One of these little investigated areas in the physiology of birds is blood pressure regulation.

It was considered that since the most important immediate blood pressure regulators in mammals are the well-known baroreceptors and chemoreceptors located in the areas of the carotid sinus and aortic arch, a determination of functional baroreceptor areas in the chicken should be basic to a study of blood pressure regulation in this species. Essentially nothing is known about baroreception and chemoreception in birds. Our knowledge in this regard is probably equivalent to what it was in the mammal in 1920 or earlier.

This study is an attempt to clarify some of the factors involved in blood pressure regulation in the chicken. The importance of the carotid and vertebral blood supply and the existence of functional baroreceptor areas in the head and neck were of particular concern.

REVIEW OF LITERATURE

I. Introduction

The discovery of the systemic circulation by William Harvey (1628) was indeed the beginning of cardiovascular research. This is certainly reflected in this statement by Harvey: "I was almost tempted to think with Francastorius that the motion of the heart was only to be comprehended by God". The subsequent measurement of blood pressure for the first time by Stephen Hales (1733) added further impetus to the study of circulation. Arterial blood pressure was then measured with a mercury manometer by Poiseuille (1828) and recorded graphically by Ludwig (1847). After these and other observations, the physiologists concluded that arterial blood pressure must be controlled by regulatory mechanisms (Heymans, 1957).

II. Circulatory Homeostasis

A. General

Circulatory homeostasis refers to the maintenance of constant conditions with regard to circulation; that is, the tendency of the body toward constancy of blood pressure, blood volume, and blood flow.

The three basic mechanisms responsible for the control of arterial blood pressure are the capillary fluid shift mechanism, renal regulation, and neural control (Guyton, 1961). Since blood pressure per se is the result of cardiac output and peripheral resistance, it can be seen that varying either or both of these factors can, in turn, alter blood pressure (Guyton, 1961; Ruch and Fulton, 1961). Regulation of arterial blood pressure is, in fact, accomplished by the alteration

of cardiac output and peripheral resistance. Of the three basic pressure control mechanisms probably the most important is the regulation imposed by the nervous system. Neural regulatory mechanisms are capable of compensating for changes in blood pressure within seconds while other mechanisms may require minutes to days to effect compensatory changes (Guyton, 1961).

The medulla oblongata is the portion of the central nervous system which is of prime importance in circulatory homeostasis. Here are found the cardioaccelerator center, cardioinhibitor center and vasoconstrictor center (Guyton, 1961; Ruch and Fulton, 1961). The term, center, does not imply a discrete anatomical area of the medulla but rather a functional unit (Ruch and Fulton, 1961) made up of various loci which produce a particular physiological effect upon stimulation. Pressor center is the term applied to the loci distributed throughout the lateral reticular formation in the rostral two-thirds of the medulla which are responsible for vasoconstriction and cardioacceleration (Ruch and Fulton, 1961). The loci responsible for decreased vasoconstriction and cardioinhibition are found primarily in the reticular formation in the caudal half of the medulla and are referred to as the depressor center (Ruch and Fulton, 1961). The pressor and depressor regions are collectively termed the vasomotor center. The latter is a reflex center which responds to afferent impulses from baroreceptors, chemoreceptors, higher brain centers, and to the concentrations of oxygen, carbon dioxide, and hydrogen ions in the blood perfusing the medulla (Guyton, 1961; Ruch and Fulton, 1961). Pressor action is characterized by increased sympathetic

activity and decreased vagal activity while the reverse occurs in the case of depressor action; furthermore, there is reciprocal inhibition between the two components of the vasomotor center (Guyton, 1961; Ruch and Fulton, 1961).

Physiological research concerning the factors regulating blood pressure in mammals has shown that baroreceptors and chemoreceptors are of prime importance in this regard (Heymans, 1957; Neil, 1960). These receptors are nerve endings sensitive to changes in blood pressure and blood chemistry respectively. The baroreceptors are found in the walls of the heart and blood vessels while chemoreceptors are found in tissue adjacent to the aorta and carotid arteries. The receptors transmit afferent impulses to the vasomotor center which then reflexly sends corrective impulses to the blood vessels and heart.

B. Baroreceptors in Mammals

1. Carotid sinus receptors

One of the most important systemic baroreceptor areas is found in the walls of the dilated region situated at the bifurcation of the common carotid into the internal and external carotid arteries. The dilation, or carotid sinus, is located at the origin of the internal carotid artery (Heymans and Neil, 1958). This structure was considered to be pathological until Schafer (1877) and Binswanger (1879) both showed the carotid sinus to be a normal occurrence in adult cadavers.

The carotid sinus is present in all mammals except the ruminants (Heymans and Neil, 1958) where extensive baroreceptor innervation is

found at the origin of the occipital artery (De Castro, 1928). The functional significance of the carotid sinus was not realized until Hering (1923) showed that increased pressure on the carotid bifurcation produced a reflex bradycardia and hypotension. He found that the reflex originated with the carotid sinus and that it was mediated by the sinus nerve, a branch of the glossopharyngeal (Hering, 1924a,b).

The innervation of the carotid bifurcation and the adjacent carotid body was described in dogs, cats and man by Gerard and Billingsley (1923). De Castro (1926, 1928) demonstrated the extensive sensory innervation of the carotid sinus and described two types of sensory endings found in the adventitia. Sunder-Plassman (1930), in a similar study, also described two types of sensory endings, those with fine arborizations and those with coarse arborizations.

Probably the first indication of systemic baroreceptor control, which was not understood at the time, was the finding of Cooper (1836) that compression of both carotid arteries produced a rise in systemic blood pressure and an accelerated heart rate. This was confirmed by Magendie in 1838.

Siciliano (1900) observed that bilateral occlusion of the common carotid arteries resulted in tachycardia and hypertension, while occluding only the external and internal carotids and occipitals did not produce the same effects. He found that when only the internal carotids were occluded that bradycardia and hypotension were obtained. Pagano (1900) stated that a decrease in heart rate and blood pressure is obtained by increasing the pressure in the common carotid artery. He concluded that these results were produced by a common carotid reflex

mechanism and not by direct stimulation of cardiovascular centers by blood pressure. In addition, he stated that the most sensitive reflexogenic site was located close to the carotid bifurcation. Both Siciliano and Pagano concluded that reflex actions on the cardiovascular centers resulted from the effect of blood pressure on receptors in the common carotid artery. However, the view was still held that blood pressure had a direct effect on the brain centers (Eyster and Hooker, 1908) and work rejecting the hypothesis of Siciliano and Pagano was published by Kaufmann (1912) and Kisch and Sakai (1923).

Sollman and Brown (1912) found that traction on the cephalic end of the carotid artery caused a fall in blood pressure, but they could not determine the nervous pathways involved in this reflex. Conclusive proof of the existence of the carotid sinus reflex was provided by Hering (1923, 1924a,b). He demonstrated the afferent role of the sinus nerve and that pressure on the carotid sinus decreased both heart rate and blood pressure (Heymans and Neil, 1958). Thus, the original concept of Pagano and Siciliano was verified.

Bronk and Stella (1932) recorded afferent impulses in the carotid sinus nerve from one or more pressure receptors in the carotid sinus of the rabbit. Impulse activity was measured simultaneously with arterial blood pressure. A discharge of impulses was found to occur at all blood pressures found in the living animal and the degree of activity of the sinus receptors was found to vary with the blood pressure. Maximum impulse frequency from a single receptor occurred during systole and minimum frequency during diastole. An increasing number of sinus receptors came into play as mean blood pressure was elevated. It was

concluded that the reflex effects of the carotid sinus on blood pressure are based on the fact that increased arterial pressure causes an increasing number of afferent impulses in the sinus nerve which act on the regulatory centers. The maximum frequency observed from a single receptor was 120-140 impulses per second.

Impulse records from single pressure receptors in the isolated, perfused carotid sinus of the rabbit have shown that steady pressure produces a regular train of impulses which continues indefinitely (Bronk and Stella, 1935). Thus, these pressure receptors showed little adaptation. A drop in pressure in the sinus caused a cessation of impulses, but after some seconds impulses were again discharged at a frequency characteristic of the new pressure. A wide variation in the threshold was found for individual receptors in the sinus.

Ead et al. (1952) recorded impulse activity of the carotid sinus in the cat during pulsatile and non-pulsatile blood flow. Pulsatile flow produced bursts of impulses occurring during systole and early diastole while non-pulsatile flow resulted in a steady impulse discharge. Pulsatile flow through the sinus produced greater impulse frequencies than non-pulsatile flow. Non-pulsatile flow in vagotomized cats caused a higher systemic blood pressure than pulsatile flow; thus, indicating greater influence of the latter on the medullary regulatory centers.

The sinus nerve of the cat has been reported to contain 650 to 700 medullated fibers with 3.5 percent being 6-8 μ in diameter, 17.5 percent less than 3 μ in diameter and 79 percent 3-5 μ in diameter (De Castro, 1951). Douglas and Ritchie (1956) observed that the carotid sinus nerve of the rabbit contained a large group of small non-medullated afferent fibers (C fibers)with reflex depressor activity in addition to the

medullated A fibers known to be present. Evidence was also presented indicating the presence of C fibers in the sinus nerve of the cat.

Landgren (1952a) showed that the carotid sinus baroreceptors in the cat respond to a pressure rise with an increased frequency of discharge within certain limits of pressure. This pressure region was called "the recording range of the receptor". The recording range of the large baroreceptor fibers was found to be from 30 to 200 mm.Hg while the threshold pressure for a steady discharge varied from 80 to 120 mm.Hg. The small baroreceptor fibers showed a higher recording range and a threshold of steady discharge at 120 to 150 mm.Hg. During pressure decreases in the sinus, a minimum impulse discharge was found between 50 to 60 mm.Hg. An increased discharge occurred as pressure dropped to 0 mm.Hg, but this was attributed to deformation of the sinus wall.

Landgren (1952b) also advanced the hypothesis that large baroreceptor spikes in an electroneurogram of the sinus nerve of the cat are elicited from stretch receptors which act in parallel with the contractile elements of the sinus wall while small spikes come from stretch receptors acting in series with the contractile elements. He stated that another possible explanation for the small spikes is that they result from nerve endings squeezed between the smooth muscle fibers in the media during distention of the wall as well as during contraction of the muscle fibers.

Neurograms of the carotid sinus nerve in normotensive and chronic renal hypertensive dogs have shown a considerable difference in the threshold of response in the sinus receptors of the two types of dogs (McCubbin et al., 1956). Impulse activity commenced at higher pressure levels in hypertensive dogs than in normotensive animals. The baroreceptor

mechanism appeared to be reset to a higher blood pressure level in the hypertensive dogs since buffer action was retained. The baroreceptors tended to maintain rather than inhibit the high levels of blood pressure in the hypertensive animals. Kezdi (1962) demonstrated that if the carotid sinus of the dog is prevented from being exposed to the high systemic pressure of experimental renal hypertension, the sinus baroreceptors do not undergo a "higher set". Apparently hypertensive levels of blood pressure have a direct effect on the walls of the sinus.

It should be recognized that electrical stimulation of the carotid sinus nerve in an animal may not produce the expected depressor response under certain conditions of anesthesia. Douglas et al. (1948) found that additional Nembutal given to cats previously anesthetized with an intraperitoneal injection of 40 mg. of Nembutal per kg. of body weight can reverse the depressor response of sinus nerve stimulation to one of pressor action. Neil et al. (1949a) reported that intravenous injections of chloralose into cats previously anesthetized with Nembutal or chloral hydrate reversed the depressor response of sinus nerve stimulation to one of pressor action. These authors attributed the pressor action to stimulation of afferent chemoreceptor fibers and to the depression of sinus baroreceptors and the vasomotor center by chloralose. However, Neil et al. (1949b) observed that chloralose injected into Nembutalized rabbits and dogs did not reverse the depressor action of sinus nerve stimulation.

Schmidt (1932) reported that in perfusion experiments with dogs, cats, and rabbits a rise in carotid sinus pressure caused respiratory depression or apnea while a fall in pressure resulted in hyperpnea. Winder (1938)

embolized the carotid body of the dog and similarly observed a depression of respiration with a rise in sinus pressure. Heymans and Pannier (1945) eliminated the carotid body from the carotid sinus circulation in the dog and found that increased pressure in the sinus inhibited respiration while decreased pressure resulted in reflex hyperpnea. Thus, the carotid sinus baroreceptors have a definite effect on respiration (Heymans and Neil, 1958; Heymans, 1963).

Palme (1943) first observed that the topical administration of adrenaline to the wall of the carotid sinus caused a depression of systemic blood pressure. He attributed this effect to a direct action of the drug on the baroreceptors. Since this time the topical application of various vasoconstrictor drugs to the carotid sinus of dogs and cats has verified Palme's results (Heymans and van den Heuvel-Heymans, 1950, 1951; Heymans et al., 1951; Landgren et al., 1952; Heymans et al., 1953; Heymans and Delaunois, 1955; Matton, 1957; Green et al., 1958). The application of vasodilator drugs on the carotid sinus has been found to produce a reflex hypertension (Heymans and van den Heuvel-Heymans, 1950; Landgren et al., 1952) while the administration of adrenolytic agents blocked or reversed the effect of topical adrenaline or noradrenaline (Heymans and van den Heuvel-Heymans, 1951; Heymans et al., 1951). Sectioning of the sinus nerve eliminated the depressor response to local application of adrenaline or noradrenaline on the carotid sinus (Heymans and van den Heuvel-Heymans, 1951) while cold blockade abolished all drug response (Landgren et al., 1952). Green et al., (1958) believed that the effects of the various drugs on the impulse activity of the baroreceptors are the result of deformation or distortion of the nerve endings occasioned

by contraction or relaxation of the muscular elements of the arterial wall.

Holt et al., (1946) reported that stimulation of the carotid sinus nerve in the dog produced, on the average, a decrease in cardiac output. Brind et al., (1956) observed no change in cardiac output in the dog when bilateral carotid occlusion was accomplished. Kenney et al., (1951) found no change in the cardiac output of the dog when either stimulation of the sinus nerve or bilateral common carotid occlusion was carried out. Heymans and Neil (1958) reviewed the work dealing with the influence of the carotid sinus reflexes on cardiac output and pointed out the general lack of agreement in this area of research. Polosa and Rossi (1961) reported that bilateral carotid occlusion in the dog resulted in a reflex increase in vasomotor tone but no change in cardiac output.

2. Common carotid receptors

Green (1953) described for the first time a new baroreceptor area found in the walls of both common carotid arteries of the cat. Baroreceptor innervation was found about 2 cm. below the carotid sinus in the region of the origin of the ramus muscularis dorsalis artery. The afferent nerve innervating this area courses to the nodose ganglion of the vagus and has been termed "the common carotid baroreceptor nerve". Electroneurographic studies of this nerve have shown its activity to be comparable to that of the sinus and aortic baroreceptor nerves. No chemoreceptor activity was detected. Gann and Barter (1959) reported a similar baroreceptor area located at the thyrocarotid arterial junction in the dog. Additional baroreceptor areas were found in the cat in the walls of the right common carotid artery (Green, 1954). One area is located 4 cm. proximal to the superior thyroid artery while another is situated

1-1/2 to 2 cm. proximal to the same artery. Boss and Green (1954) indicated a third baroreceptor area found only in the right common carotid. This one is located at a point immediately distal to the well-known baroreceptor area found at the root of the right subclavian artery. These three additional receptor regions were found to be innervated by nerves which contribute to the right aortic nerve. Thus, a total of five new baroreceptor areas were discovered in the cat, four in the right common carotid and one in the left (Boss and Green, 1956). In each area myelinated fibers of the baroreceptor nerves ramify in the adventitia and appear as fibrillar structures (Boss and Green, 1956).

3. Aortic and right subclavian arterial receptors

In 1866 Cyon and Ludwig demonstrated that by stimulating the central end of a small nerve in the neck, which they called the depressor nerve, heart rate and blood pressure were inhibited reflexly. In addition, they reported that the hypotensive effect of depressor nerve stimulation was the result of vasodilation confined primarily to the region supplied by the splanchnic nerves (Ludwig and Cyon, 1866). Since sectioning of both depressor nerves did not result in a rise of arterial pressure, Ludwig did not believe that these nerves were tonically active (Neil, 1962). Marey (1876-8) stated that blood pressure regulates heart rate reflexly with the depressor nerve serving as the afferent pathway.

Bayliss (1893) reported that stimulation of the central end of the depressor nerve resulted in vasodilation in the kidneys, intestines, limbs, head and neck. He also observed that the fall in blood pressure remains constant regardless of how long the depressor nerve is stimulated and that usually stimulation of both depressors produces more of an effect

than if just one is stimulated.

Koster and Tschermak (1902 a,b) demonstrated that the sensory endings of the depressor nerve are found in the aortic arch. Tello (1924) observed that the left depressor nerve in the mouse embryo innervated the aortic arch while the right depressor innervated the right subclavian-carotid angle and part of the brachiocephalic artery. Similar findings were reported for the rabbit, cat and guinea pig by Nonidez (1935 b). Histological studies show that the sensory endings of the sinus nerve and the depressor nerve may be quite variable in form and that the important point to be noted in the case of both is the richness of their sensory innervation (Heymans and Neil, 1958). Boss and Green (1956) indicated that the barosensory nerve endings found in the adventitia of the carotid sinus and subclavian areas exemplify forms found in all baroreceptor areas.

Eyster and Hooker (1908) observed that increased pressure in an isolated portion of the thoracic aorta produced a reflex slowing of the heart. Osborne (1920) found that when aortic pressure was increased in the dog, impulses were set up in depressor nerve fibers. When aortic pressure was decreased, impulse traffic decreased and no additional nerve impulses were detected. Thus, it was determined that there were not two sets of fibers in the depressor nerve which reacted differently to aortic pressure changes. Increasing or decreasing aortic pressure merely increased or decreased the stimulation of the depressor nerve. On this basis Osborne believed that the self-adjusting mechanism of the depressor is constantly in action. Daly and Verney (1926) reported that when cerebral pressure is kept constant in the dog, a rise in aortic pressure

causes a reflex slowing of the heart.

Green (1954) and Neil (1956 a) have both confirmed the presence of baroreceptor innervation at the junction of the right subclavian and common carotid arteries in the cat. Neil (1956 a) found electroneurographic records of the depressor nerve to show that the response of the baroreceptors to changes of pulse pressure is similar to that of the baroreceptor fibers in the carotid sinus nerve. Altering the pressure in a perfused, innervated carotid-subclavian segment produced reflex responses similar to those obtained from a perfused carotid sinus. That is, a reflex hypotension and reduction in breathing.

Neil et al., (1949 c) observed that stimulation of the left or right aortic (depressor) nerve in rabbits and cats produced a fall of arterial pressure. Douglas and Schaumann (1956) reported that stimulation of the aortic nerve in the cat with a low intensity stimulus caused a substantial depressor effect accompanied by little change in respiration. Stronger stimulation resulted in pressor effects and respiratory excitation. Still stronger stimulation produced a reappearance of depressor effects with no further change in respiration. These effects were interpreted to indicate the presence in the aortic nerve of large depressor fibers, small pressor fibers and smaller depressor fibers.

Douglas and Ritchie (1956) and Douglas et al., (1956 a) found that aortic nerves in the rabbit contain a large group of small non-medullated afferent fibers (C fibers) in addition to the large medullated fibers (A fibers) known to be present. The C fibers were found to have a powerful depressor effect and to produce this effect at lower frequencies of stimulation than the A fibers. Stimulation of the non-medullated afferents

produced slight bradycardia but no apparent respiratory effect. Douglas et al., (1956 b) indicated that the greater depressor response of pulsatile pressure changes in the great vessels as compared to non-pulsatile pressure is not due to the pattern of impulses set up by pulsation but is the result of the recruitment of fibers.

Agostoni et al. (1957) reported that the aortic nerve of the cat contains 450 fibers of which two-thirds are myelinated. The myelinated fibers were found to have a bimodal distribution with the peaks falling into the 2-4 and 8-10 μ diameter groups. Paintal (1953 c) determined the conduction velocity of depressor fibers in the vagus nerve of the cat to be 33 m./sec.

As was found with the carotid sinus reflex, a dosage of Nembutal beyond the normal anesthetic dose in cats produced a reversal of the depressor effect upon central vagus nerve stimulation (Douglas et al., 1948). Reversal of the depressor effect upon stimulation of the aortic nerve in the cat anesthetized with chloralose has also been reported (Neil et al., 1949 c).

4. Cardiac receptors

Bainbridge (1915) reported that increased venous filling of the heart leads to a rise in venous pressure and to acceleration of the heart rate. This effect has been termed the Bainbridge reflex. Bainbridge claimed that the reflex acceleration of the heart when venous inflow is increased is caused by impulses arising within the heart. Nonidez (1937) found baroreceptor nerve endings in the intrapericardial portions of the venae cavae and the pulmonary veins of the cat, dog and rabbit. Afferent arborizations were also discovered in the wall of the coronary sinus near

its entrance into the right atrium. Two types of nerve endings were found: subendothelial terminations and perimuscular arborizations. The subendothelial endings occurred in all the veins entering the heart and were considered by Nonidez to be the receptors for the Bainbridge reflex.

Whitteridge (1948) observed that a number of fibers in the cervical vagus of the cat show activity corresponding to cardiac rhythm. These fibers were separate from aortic depressor fibers and pulmonary stretch fibers. Evidence was presented that some of these fibers arise from endings on the roots of the great veins or on the right atrium. It was stated that occasionally fibers may be found which arise from the pulmonary veins or left atrium.

Jarisch and Zotterman (1948) studied the afferent impulse traffic in cardiac branches of the vagus on both sides in the cat while simultaneously recording an electrocardiogram or pressure changes in the auricles. They recorded impulses in fibers with a diameter of 2.8 to 7 μ which were stimulated by endings around the orifices of the caval veins and from the auricular septum of the right side as well as around the orifices of the pulmonary veins in the left auricle. Stimulation of the receptors was caused by distention resulting from increased pressure and by the mechanical events of the heart. Besides large spike potentials originating in the auricles, very small spikes were obtained. These were considered to come from very thin afferent fibers which were strongly stimulated by pinching the ventricles. It was concluded that the afferent heart fibers responsible for a depressor reflex were very thin fibers ending in the auricles and ventricles. The function of the large afferent fibers ending only in the auricles was not determined.

Dickinson (1950) found a linear relationship between venous pressure

and frequency of discharge in fibers from the right atrium of the cat. Aviado et al., (1951) reported that increased pressure in the right side of the heart of the dog caused reflex bradycardia and peripheral vasodilation due to receptors in the right auricle. This view opposes that of Bainbridge (1915).

Paintal (1953 a) described afferent nerve fibers in the vagus of the cat which end in the atria but do not show bursts of impulse activity during the a wave of the venous pulse. He names these type B receptors and those that are active during the a wave type A receptors (Paintal, 1953 b). It was concluded that the type B right and left atrial receptors do not respond to intra-atrial pressure changes as do the type A, but are stretch receptors which respond to changes in atrial filling. The conduction velocity of fibers from right atrial type A receptors was found to be 20 m./sec.; from left atrial type B receptors, 20 m./sec.; and from right atrial type B receptors, 13 m./sec. (Paintal, 1953 c).

Paintal (1955) reported the discovery of right and left ventricular receptors in the cat which respond to changes in ventricular pressure. Fibers from these receptors belong to the A group of medullated fibers and their conduction velocity lies between 10 and 20 m./sec. Aviado and Schmidt (1959) observed bradycardia and inhibition of respiration and vasomotor activity during increased inflow of blood into the left side of the heart in the dog. They attributed these results to left ventricular pressoreceptors.

Henry and Pearce (1956) described afferent vagal fibers from the left atrium of the dog with discharge characteristics similar to the atrial stretch receptors found in the cat. They suggested that since

certain maneuvers which cause diuresis in the anesthetized animal also stimulate these atrial receptors, cardiac atrial stretch receptors may serve as a sensory mechanism in the reflex regulation of blood volume by control of urine output.

Neil (1960) ascribed two roles to the atrial receptors; a rapid reflex adjustment of the circulation to overloading of the heart, and a possibly more important long-term role as guardians to adjustment of the blood volume. He also indicated the normal role of receptors in the ventricles to be as proprioreceptors of the circulation.

5. Pulmonary receptors

Brodie and Russell (1900) observed that stimulation of the central end of the pulmonary fibers of the vagus in the dog caused reflex inhibition of the heart, apnea and a depression of blood pressure. Schwiegk (1935) found that increasing the pressure in the pulmonary artery of one lung in the dog resulted in a fall of systemic blood pressure and cardiac slowing. However, changes in the pulmonary circulation of the cat were rarely found to affect systemic pressure and heart rate (Schweitzer, 1936). On the other hand, histological examination of the pulmonary artery in the cat revealed the presence of afferent nerve endings similar to those of the carotid sinus and aorta. Both Schwiegk and Schweitzer found the pulmonary reflexes to depend on the integrity of the vagus. Aviado et al., (1951) demonstrated that increased pressure in the pulmonary circulation of the dog caused reflex peripheral dilation and rapid shallow breathing. Bradycardia occurred with increased pressure at the pulmonary arterial bifurcation. All of the pressoreceptors were reported to be innervated by the vagus.

Coleridge and Kidd (1959, 1960) recorded afferent impulses from single fiber preparations of the cervical vagus in the dog. Activity in these fibers ceased with occlusion of the pulmonary artery at its junction with the right ventricle, while activity increased when the artery was occluded at the lung roots. Receptors were located in the main right and left pulmonary arteries proximal to the origins of the lobar branches and near the main bifurcation of the pulmonary artery. The main pulmonary arterial trunk was shown to contain no receptors. The thresholds of ten pulmonary arterial baroreceptors were found to be within the range 16-25/7-13 mm.Hg (Coleridge and Kidd, 1961). An increase in pulmonary arterial pressure caused an increase in the frequency of discharge to 200-300 per second with pressures of about 45-50/20-25 mm.Hg. Pulsatile pressure was a more effective stimulus than steady pressure. If pressures of from 20 to 60 mm.Hg were applied to the pulmonary artery of the dog, hypotension and sometimes bradycardia were obtained (Coleridge and Kidd, 1963). Pressures above 80 mm.Hg produced hypertension. The hypotension and bradycardia were attributed to pulmonary baroreceptors, while the hypertensive reaction remains unexplained.

6. Intracranial receptors

As early as 1900 Pagano believed that blood pressure affected a common carotid reflex mechanism and did not have a direct effect on the brain centers. In 1908 Eyster and Hooker stated that heart rate changes are believed by most workers to be the result of a direct effect of arterial pressure on the cardioinhibitor center. It was not until the work of Hering in 1923 that it was realized that many effects thought to be caused by the direct effect of blood pressure on the brain were actually

a result of the carotid sinus reflex. However, Nash (1926) reported that without a doubt a rise of blood pressure in the head causes a slowing of the heart and a fall of blood pressure in the body even with the carotid sinus denervated. Anrep and Segall (1926) also reported that a rise in cerebral blood pressure in the dog caused a slowing of the heart rate even when the sinus area was destroyed. These latter two reports are, of course, suggestive of baroreceptor activity in blood vessels of the head.

Taylor and Page (1951 b) obtained no changes in systemic blood pressure while perfusing the brain of the dog under pressure. They concluded that no cerebral baroreceptors were present. However, Rodbard and Stone (1955) studied intracranial compression in the dog and hypothesized an intracranial baroreceptor mechanism. Heymans and Neil (1958) did not agree with this hypothesis. Aviado and Schmidt (1955) stated that pressoreflexes from the cerebral vessels are difficult to interpret. They argue that circulatory responses obtained when blood flow is increased to an isolated head may be the result of a change in the chemical composition of the blood reaching and leaving the medullary centers rather than a true pressoreflex. It was concluded that the acceptance of the presence of cerebral pressoreceptors is not justified until something is known about the sensory innervation of these receptors.

Booth et al., (1960) indicated the presence of cephalic baroreceptors in swine since pressor responses were still obtained from bilateral carotid occlusion even after complete vagotomy and carotid sinus denervation. However, Downing et al., (1963) reported a lack of cranial baroreceptor activity in the dog. It was observed, in perfusion experiments, that ischemia, hypoxia or hypercapnia of the CNS resulted in an elevation

of systemic blood pressure. If the blood perfusing the CNS was well oxygenated, the pressure could be reduced to 35 mm.Hg without eliciting any systemic response; thus, indicating no baroreceptor activity.

7. Abdominal and thoracic receptors

Gammon and Bronk (1935) found that impulses originating from Pacinian corpuscles in the mesentery of the cat could be measured at the peripheral ends of the splanchnic and mesenteric nerves. Perfusion of the mesenteric circulation under pressure stimulated the corpuscles. However, no effect on general blood pressure could be obtained by perfusing the superior mesenteric artery either before or after section of the aortic and carotid sinus nerves.

Sarnoff and Yamada (1959) reported that combined occlusion of the celiac, superior and inferior mesenteric arteries in the cat produced a large pressor response. Occlusion of the pancreatic arteries produced pressor responses two-thirds to three-fourths the response obtained by total visceral artery occlusion. The response to either visceral or pancreatic hypotension was usually greater than that obtained by bilateral carotid occlusion. It was suggested that in the cat the reflex influence of the carotid sinus and aortic arch receptors is dominated by the abdominal receptor system. This was based on the fact that intact carotid sinus and aortic receptors permitted the elevation of blood pressure during visceral hypotension. Selkurt and Rothe (1960) studied splanchnic baroreceptors in the dog and cat. They found that in the cat occlusion of the celiac and superior mesenteric arteries produced a large pressor response which exceeded that of bilateral carotid occlusion; thus, confirming the work of Sarnoff and Yamada. However, similar occlusions

in the dog showed the pressor response of bilateral carotid occlusion to be greater than that resulting from splanchnic hypotension. Carotid sinus denervation increased the response to splanchnic hypotension; therefore, it was concluded that abdominal arterial responses are strongly held in check by the more dominant carotid baroreceptors in the dog.

Gruhzit et al., (1954) reported that vasodilation of the femoral vessels of the dog following epinephrine injection was, in part, the result of a previously undescribed reflex. After the elimination of various other known reflex systems, femoral dilation still was found to occur with the administration of epinephrine. The source of the reflex was localized to the descending thoracic aorta. It was postulated that mechanoreceptors along the course of the thoracic aorta, activated by the inotropic cardiac action of epinephrine, may be the afferent source of this reflex.

C. Chemoreceptors in Mammals

1. Carotid bodies

Adams (1958) expressed little doubt that A. Haller originally discovered the carotid body in the human in 1742. However, he further indicated that the first published account of this structure was by H. W. L. Taube (1743) and the first suggestion that it may serve a sensory function was made by Druner (1925) while proof of this function came from De Castro (1928).

In man, there is a pair of carotid bodies with one member located at the bifurcation of each common carotid artery (Adams, 1958). Each body is generally described as being ovoid or fusiform in shape with its long axis situated vertically; however, the literature reviewed by Adams shows that

both the shape and size may vary considerably. Lyonnet (1941) reported the human carotid body size to be 5 x 2.5-4 x 1.5 mm.

The carotid body is usually invested by a collagenous connective tissue capsule and supplied by a small artery (or arteries) from the carotid bifurcation (Adams, 1958). Innervation of the structure is reported to be primarily by medullated fibers from the glossopharyngeal nerve but also by medullated fibers from the vagus nerve and non-medullated fibers from the sympathetic system (primarily from the superior cervical ganglion).

Ham and Leeson (1961) described the structure of the carotid body as being similar to an endocrine gland in that the organ is composed of clumps and cords of epithelioid cells, and contains an abundant supply of sinusoidal capillaries. The epithelioid cells are richly supplied with nerve endings.

Comroe and Schmidt (1938) reported that hyperpnea caused by intra-carotid injection of lobeline or cyanide is caused by receptors in the carotid body and not in the sinus; in addition, pressure was found to have no effect on the carotid body in the dog. The carotid body was stimulated by either a reduction in oxygen or an increase in carbon dioxide content of the fluid perfusing it. Anoxia was found to have a greater hyperpneic effect than hypercapnia. It was concluded that the carotid body reflexes are an accessory mechanism reacting in emergencies to foreign chemicals, anoxemia and unusually great increases in carbon dioxide tension of the blood. Respiration was believed to normally be controlled by chemical stimuli (CO_2) acting on the cells of the respiratory center.

Landgren and Neil (1951) demonstrated a marked increase in carotid

chemoreceptor discharge following hemorrhage in the cat. During the period of spontaneous circulatory recovery or during ventilation with 100 percent oxygen, chemoreceptor discharge decreased considerably. Two explanations were advanced for the effect of hemorrhage on chemoreceptor activity: (1) impulse activity may increase due to the accumulation of normal anaerobic metabolites as a result of decreased blood flow through the carotid body; (2) or active vasoconstriction of the afferent arterioles of the carotid body may cause decreased blood flow through it which, in turn, could result in an increased rate of formation of anaerobic metabolites due to the low oxygen tension and, in addition, cause a decreased rate of removal of these metabolites.

Duke et al., (1952) observed that chemoreceptor discharge is not obtained in cats breathing small concentrations of carbon monoxide until failure of circulation and respiration occurs causing a reduction of blood oxygen tension. Chemoreceptors responded early to anoxic anoxia and stimulated the respiratory center. In carbon monoxide anoxia (anemic anoxia) the chemoreceptors were not stimulated until respiration began to fail. This demonstrated the importance of oxygen tension in the blood to chemoreceptor function.

Bernthal et al., (1951) reported that bradycardia resulted from hypoxia of the carotid chemoreceptors in dogs. It was concluded that the cardiac acceleration of systemic hypoxia does not arise chemoreflexly at the carotid bodies. Neil (1956 b) found that anoxic tachycardia developed in cats breathing 5 percent oxygen in nitrogen. Perfusion of the carotid bodies with oxygenated Ringer-Locke solution caused hypopnea and hypotension but did not affect the tachycardia. When anoxic blood flow was

resumed through the carotid bodies hyperpnea, hypertension and transient bradycardia were obtained. The bradycardia appeared to be a secondary effect of the reflex hyperpnea. The carotid chemoreceptor reflexes were considered to make no contribution to the tachycardia of systemic anoxia.

Daly and Scott (1958) observed that in the artificially ventilated dog bradycardia is obtained when the carotid body is perfused with hypoxic blood. In spontaneously breathing dogs stimulation of the carotid body caused an increase or no change in heart rate while respiration increased. The primary effects of hypoxic stimulation of the carotid bodies in the dog were believed to be bradycardia and vasoconstriction; however, these responses were throught to be partly or wholly masked by mechanisms arising secondarily as a result of the increase in respiratory minute volume (Daly and Scott, 1962). Downing and Siegel (1963) found no increase in cardiac sympathetic discharge during perfusion of the isolated carotid sinus of the cat with hypoxic blood. Systemic hypoxia, however, caused a marked increase in sympathetic discharge and a bradycardia which developed if the hypoxic condition was sustained for several minutes. Cardiac sympathetic discharge was also increased with systemic hypercapnia. It was concluded that in systemic hypoxia the chemoreceptors reflexly stimulate the sympathetic vasomotor centers and the parasympathetic cardioinhibitory centers but have little effect on the cardiac sympathetic centers. Increased cardiac sympathetic discharge occurring during systemic hypoxia or hypercapnia was believed to be the result of direct rather than reflex stimulation of the centers in the central nervous system.

Hornbein *et al.*, (1961) established that in the artificially ventilated cat carotid chemoreceptor activity was present at an arterial pO_2

of 100 mm.Hg and increased the most as the oxygen tension was lowered to 40 mm.Hg. A potentiation of hypoxia and increased $(H+)$-pCO_2 was demonstrated with regard to chemoreceptor activity. Hornbein and Roos (1963) reported that carbon dioxide acts as a carotid chemoreceptor stimulus in the cat only by virtue of its effect in altering $(H+)$. The previously mentioned potentiation between hypoxia and hypercapnia at the chemoreceptor level was believed to be due primarily to interaction between low oxygen tension and increased $(H+)$ independent of carbon dioxide.

2. Aortic bodies

Penitschka (1931) noted the presence of paraganglia located between the aortic arch and the pulmonary artery in the mammal. He called this structure the paraganglion aorticum supracardiale. Palme (1934) confirmed the earlier observation of Busachi (1912) that there are two groups of paraganglia, one located under the concavity of the aortic arch and the other near the left coronary artery. Palme termed these paragnaglia supracardiale superius et inferius. Heymans and Neil (1958, p. 121) state that Nonidez referred to paraganglionic tissue between the aortic arch and the pulmonary artery as the "aortic body", the site of this tissue corresponded to that of the paraganglion aorticum supracardiale of Penitschka. In addition, Nonidez (1935 b) described two more groups of cells which he referred to collectively as the glomus aorticum. The right glomus was found between the right subclavian and carotid arteries in the rabbit and cat or below the subclavian artery in the guinea pig. The left glomus was situated above the aortic arch and internal to the left subclavian artery. Both glomi were observed to be

richly innervated by nerve fibers arising from their respective aortic nerves. Since the structure of these glomi was similar to that of the carotid body, a chemoreceptor function was postulated for these structures.

Heymans and Heymans in 1927, were the first to discover peripheral chemoreflexogenic zones in the dog (Heymans and Neil, 1958). In cross-circulation experiments it was demonstrated that asphyxia, anoxia or hypercarbia would cause increased respiratory movements which could be eliminated by vagotomy. Further experimentation showed that the chemoreceptor activity originated in the cardio-aortic area.

Neil et al., (1949 c) presented evidence through intraventricular injection of nicotine or lobeline, that the aortic nerves of the cat, particularly the right nerve, contain chemoreceptor fibers from the aortic body. Stimulation of either the left or right aortic nerves produced a depression of blood pressure in Nembutalized cats. Reversal of the depressor effect was obtained after an additional dosage of chloralose was given.

Landgren and Neil (1951) found that, as with the carotid chemoreceptors, there was a marked increase in aortic nerve impulse activity following hemorrhage in the cat. During the period of spontaneous circulatory recovery or during ventilation with 100 percent oxygen, chemoreceptor discharge decreased considerably. Kenney and Neil (1951) reported that in cats and dogs suffering from hemorrhage, cold block of the vagus caused a fall in blood pressure. If the aortic chemoreceptors were inactivated by intraventricular or intra-aortic injection of acetic acid, the depression of blood pressure by cold block of the

vagus was abolished.

Howe (1956) described the aortic bodies in the cat. He found four groups of glomus tissue which received their sensory innervation from the aortic depressor nerves and were embedded in the connective tissue around the major arteries. The glomus tissue was classified as follows: group 1, found on the ventral surface of the root of the right subclavian artery; group 2, found on the ventral surface of the root of the left subclavian artery; group 3, found on the ventral surface of the aortic arch superior to the ductus arteriosus and inferior to group 2; group 4, found in the connective tissue deep between the aortic arch and the pulmonary arterial trunk. The arterial supply of the aortic bodies was derived from the aorta or its main branches while the venous drainage was either directly into the superior vena cava or via the left costo-cervical vein. No connection with the pulmonary circulation was found. No obvious differences were found between the various groups of aortic bodies with regard to nervous innervation, vasculature or morphology. It appeared likely that all the aortic bodies would possess a chemo-receptor function.

Diamond and Howe (1955, 1956) indicated that evidence showing a chemoreceptor function for the aortic bodies is satisfactory for only one cell group, the one that corresponds with Penitschka's paraganglion aorticum supracardiale. Thus, to determine if other aortic bodies are chemosensory, afferent impulses were measured in a branch of the left aortic nerve in the cat. Activity increased in the nerve when either oxygen content of the ventilating gas was decreased or the blood pressure was lowered. Impulse activity resulting from low blood pressure could be

decreased by ventilating the animal with 100 percent oxygen. In each experiment the nerve from which the activity was being measured was traced down to one or two aortic bodies near the root of the left subclavian artery. It was concluded that these aortic bodies were the site of discharge of the chemoreceptor impulses.

Paintal (1953 c) measured the conduction velocity of chemoreceptor fibers in the vagus of the cat and found it to be 10 m./sec.

Heymans and Neil (1958) indicated that when chemoreceptors have been inactivated, the systemic response to carbon dioxide is almost unchanged; however, there is evidence that these receptors do function somewhat in response to blood carbon dioxide tension in eupneic conditions. The primary importance of the chemoreflex to the animal lies in the response to anoxia. After chemoreceptor denervation, anoxia causes only a depression of respiration and circulation. This is, of course, quite opposite to the anoxic response obtained with intact chemoreceptors.

3. Pulmonary chemoreceptors

Duke et al., (1963) reviewed the histological evidence for pulmonary chemoreceptor tissue and presented experimental evidence for the existence of such tissue in the cat and rabbit. The systemic circulation of the animal was perfused at a normal pressure and flow rate while an isolated pulmonary arterial segment was perfused separately at normal pressure and flow rate. When the pulmonary arterial segment was perfused with NaCN, increased vagal afferent activity was obtained. Anoxia or asphyxia of the pulmonary perfusate caused increased depth of respiration and increased sympathetic activity. Hypercapnia of the pulmonary blood flow had little effect in the presence of a high oxygen tension.

D. Baroreceptors and Chemoreceptors in Birds

1. Baroreceptors

A review of the literature indicates that no functional baroreceptor areas have as yet been identified in the chicken. Drugs inducing vasopression or vasodepression usually produced bradycardia and tachycardia respectively; thus indicating possible baroreceptor reflexes (Harvey et al., 1954; Durfee, 1964). The heart rate changes induced in this way were abolished after bilateral vagotomy, adding further support to this view (Durfee, 1964).

"Birds have no carotid sinus in the ordinary sense; nor has anything like a labyrinth been observed in the bird's carotid" (Adams, 1958; p. 171). The area considered to be the homologue of the carotid sinus of mammals is not to be found at the bifurcation of the common carotid into the internal and external carotid arteries, but is located along the common carotid just beyond the origin of the subclavian artery (Muratori, 1932, 1934; Nonidez, 1935 a; Chowdhary, 1953; Adams, 1958). Located adjacent to the sinus area are the carotid body and the nodose ganglion of the vagus which supplies the fibers that innervate this area (Nonidez, 1935 a; Chowdhary, 1953). The nerve endings form a band or girdle around the sinus region of the carotid and are not as complicated or elaborate as in the mammal (Adams, 1958). Chowdhary (1953) indicated that there are certain histological differences associated with this region. He found that over an area of 1-1.5 mm. on the lateral side of the carotid artery just above the origin of the artery to the carotid body, the adventitia is thicker and the entire media contains collections of specialized cells similar to the carotid body. The nerve endings from the nodose ganglion appear to be primarily associated with these specialized cells which are

not characteristic of the sinus region in mammals (Adams, 1958). Adams (1958), therefore, expressed doubt as to whether this area in birds can be considered exactly the same as the sinus region of mammals.

Jung (1934) and van der Linden (1934) both were unable to obtain any cardiac or vasomotor response from the area of the bifurcation of the common carotid into the internal and external carotids in birds. Van der Linden found that bilateral occlusion of the common carotids in the neck produced hypertension; however, this was attributed to cerebral anemia. The clamps were placed on the arteries rostral to the area homologous to the carotid sinus thus eliminating any reflexes from this region (Heymans and Neil, 1958). Stimulation of the carotid bifurcation also produced no cardiovascular effects while stimulation of the carotid sinus region in the thorax produced variable results (van der Linden, 1934). Ara (1934) claimed to have obtained carotid sinus reflex responses by occluding the common carotid artery caudal to the sinus area. Harvey et al., (1954) reported that during the course of pharmacological studies in chickens he had to use eleven birds before he found one that would produce a rise in blood pressure greater than 10 mm.Hg in response to bilateral carotid occlusion in the cervical area. Durfee (1964) found no pressure reflexogenic areas in association with the carotid arteries in the chicken. Rodbard and Saiki (1952) hypothesized an intracranial baroreceptor mechanism which may control cerebral blood flow in the chicken.

Nonidez (1935 a) reported that the chicken has only one depressor nerve, the right one. This nerve originates from the nodose ganglion of the right vagus and innervates the wall of the aorta above the opening of

the ductus arteriosus. Some of the fibers end as diffuse arborizations while others enter encapsulated corpuscles of various sizes containing epithelioid cells. No pressoreceptor function for this area has as yet been established.

2. Chemoreceptors

Kose (1902, 1904, 1907) was the first to make an intensive study of the carotid body in birds and to conclusively demonstrate that, as in mammals, the avian carotid body is an entirely independent structure. Chowdhary (1953) found only one carotid body on each side of the neck in the chicken. Apparently confusion concerning the number of carotid bodies in the bird can be attributed to the presence of paraganglionic masses in the vicinity of the true carotid body (Adams, 1958). According to Muratori (1933), one carotid body lies on each side at the base of the neck (thoracic inlet) beside the common carotid just beyond the origin of the subclavian artery. The carotid body is found lateral to the common carotid with the ganglion nodosum of the vagus nerve dorsolateral to it (Adams, 1958). The ganglion tends to separate the carotid body from the jugular vein. The body may retain a cellular connection with the carotid artery, as Kose found, and it may lie in close association with one of the parathyroids, as was found in the chicken by Chowdhary.

Chowdhary (1953) reported the size of the carotid body in the chicken to be approximately 0.8 x 0.5 x 0.5 mm. The arterial supply was found to be obtained from a small artery from the carotid while the venous drainage is by several veins, one of which empties into the internal jugular vein while the rest join veins from the parathyroids and

ultimobranchial body. The innervation of the carotid body was shown to be by a branch of the vagus which arises from the nodose ganglion.

Adams (1958) indicated that the carotid body in birds is surrounded by a dense connective tissue capsule and that the body itself is made up of lobules of epithelioid cells. The lobules are supplied by lobular arterioles and innervated by nerve fibers which enter the lobules and ramify among the epithelioid cells. These fibers are non-myelinated but are originally derived from a capsular plexus which is composed of thick, medullated fibers.

Fedde et al., (1963 b) provided some evidence that the carotid body of the chicken may not be sensitive to changes in the carbon dioxide tension of the blood. Durfee and Sturkie (1963) found that anoxic hypertension could not be obtained in the chicken. The immediate reaction to anoxia was hypotension; thus, it would appear that the carotid bodies or other chemoreceptors were not responsive to anoxia.

Hollenberg and Uvnas (1963) reported that submersion asphyxia in unanesthetized ducks produced bradycardia, increased blood pressure, decreased splanchnic and skin blood flow, and little change in skeletal muscle blood flow. These circulatory responses were abolished after denervation of the carotid bodies and baroreceptors. The net result of these circulatory responses in the diving duck was believed to be a decreased oxygen supply to areas of the body that can withstand an oxygen deficit for a limited period, while the available oxygen was conserved for tissues more sensitive to a lack of oxygen. Evidence was presented which indicated that stimulation of chemoreceptors is responsible for the circulatory changes observed in the diving duck.

Nonidez (1935 a) suggested that the encapsulated corpuscles located in the wall of the avian aorta (chick) may be homologous with the mammalian paraganglion aorticum supracardiale. Aortic bodies have since been described in the yellow-breasted bunting (Emberiza aureola) (Tcheng and Fu, 1962); the little bittern (Ixobrychus eurythmus) and the great reed warbler (Acrocephalus arundinaceus) (Fu et al., 1962); and the chicken (Tcheng et al., 1963). Aortic bodies were found in the connective tissue between the ascending aorta and the pulmonary artery in all of these birds. In this respect the birds were considered similar to mammals. In one newly-hatched chick that was studied, 25 aortic bodies were found primarily situated on the dorsal and lateral surfaces of the pulmonary arteries, brachiocephalic arteries and aorta. Aortic bodies in the birds studied were made up of epithelioid cells with sensory innervation from the vagus as determined by Tcheng and Fu (1962) in the yellow-breasted bunting. The smallest bodies found in the chicken were 20-30 μ in size. Tcheng et al., (1963) suggested a possible chemoreceptor or baroreceptor function for the aortic bodies in birds.

E. Summary

Aviado and Schmidt (1955, p. 248) provide an excellent summary for a discussion of reflexes involving the blood vessels.

a) "Nature of the experimental evidence required to identify and evaluate reflexes from blood vessels. To be complete this should include information on the location of the receptors, the nature of the effective stimulus, the identity and course of the nerve in which impulses are carried, the pattern of the reflex effect, and the physiological, pathological and pharmacological significance of the reflex system. The

latter is deduced from the effects of arousing it to increased activity and of inactivating it by blockade or section of the appropriate nerves.

b) Patterns of physiological responses to be expected. Only two have been clearly established, viz. The effects of stimulation of the pressoreceptors of the carotid sinuses and aortic arch, and the effects of stimulating the chemoreceptors of the carotid and aortic bodies. The former consists of bradycardia, decreased vasomotor tone and respiratory depression or apnea, the latter of tachycardia, increased vasomotor tone and hyperpnea. The two prototype patterns therefore are inhibition and stimulation, respectively, of the activity of the medullary centers which control circulation and respiration. Both patterns have been elicited in their entirety by physiological stimuli only from the carotid-aortic reflex zones though both can be produced by drugs in other regions. Parts of each pattern or mixtures of both have been reported from many sources."

OBJECTIVES

1. To determine the importance of the carotid and vertebral arterial blood supply to survival and the maintenance of normal cerebral function in the chicken.
2. To determine if there are functional baroreceptors in the carotid artery or in the head of the chicken which exert regulatory influences on systemic blood pressure.
3. To determine if the area in the chicken homologous to the mammalian carotid sinus has a blood pressure regulating function similar to that of the carotid sinus of mammals.

GENERAL PROCEDURE

I. Experimental Stock

The birds used in these experiments were Leghorn-type hens which were obtained commercially as chicks and reared at the Michigan State University Poultry Plant. Hens were transferred from the poultry plant to laying batteries in the laboratory when they were approximately one year of age. Water and a cage layer ration were supplied to all hens *ad libitum*. Lights were on at least 14 hours each day and the birds were exposed to normal room temperature variations.

II. Anesthesia

The hens were anesthetized with 130 mg. of sodium phenobarbital per kg. of body weight administered intravenously into the brachial vein. Under this plane of anesthesia the hen reacted to toe pinch with a slight withdrawal reflex while a definite shaking of the head resulted when the comb was pinched. Pinching the skin in the cervical and thoracic areas produced no reflex. Fedde *et al.*, (1963 a) consider birds under this level of anesthesia to be lightly anesthetized.

Sodium phenobarbital was chosen as the anesthetic for these experiments because of its long action and the margin of safety in dosage level as compared to sodium pentobarbital. Alpha-chloralose was considered for use as an anesthetic, but preliminary studies showed that spontaneous muscle spasms would often develop in the birds and cause erratic blood pressure fluctuations.

III. Surgical Procedure

Each hen was restrained in a supine position on an animal board. The legs and wings were tied down and a wire placed through the external nares

in the beak and then anchored to the board to limit movement of the head.

After anesthetization the vertebral and carotid artery bifurcations were exposed in the thoracic cavity to allow ligation or clamping, then the appropriate incisions were made for cannulations to record blood pressure.

The bifurcations of the carotid and vertebral arteries were exposed by making a mid-line incision on the ventral surface of the anterior thoracic area and proceeding via an intraclavicular approach to the bifurcations (Fig. 1). Connective tissue and adipose tissue were cleared from the arteries by blunt dissection to allow clamping or ligation.

IV. Blood Pressure Measurement

Blood pressure measurements were made by direct means from either a carotid artery or an ischiatic artery. In the case of the carotid artery, a longitudinal incision was made in the skin on the ventral surface of the upper cervical area. The carotid artery (or arteries) was then dissected free from the overlying connective tissue and M. longus colli at about the level of the third cervical vertebra. If the artery was to be cannulated for measurement of systemic blood pressure a permanent ligature was placed around the cranial end of the exposed portion of the carotid and a serrefine clamp placed on the caudal end. A nick was made in the isolated segment of the artery and a fluid-filled polyethylene cannula (P.E. 90, I.D. .034" x O.D. .050") introduced caudad into the carotid artery. The cannula was tied in place with another ligature and the clamp removed to allow the blood pressure to act against the fluid in the cannula. The cannula was filled with either a 5 or 10 percent sodium citrate solution to serve as an anticoagulant and was connected to a

P-23 AC Statham arterial pressure transducer. The transducer was, in turn, connected either to a Brush Analyzer model BL-320 and pen recorder or to a Grass Model 5 polygraph for recording purposes. Calibration of the recorders was accomplished using a pocket model aneroid sphygmomanometer to measure pressure applied directly on the transducer.

If the ischiatic artery was to be isolated for cannulation, an incision was made along the caudal edge of the thigh. The M. biceps femoris was then separated from the M. semimembranosus and M. semitendinosus which allowed easy access to the ischiatic artery. Cannulation was carried out in a manner similar to that described for the carotid artery.

Mean blood pressure was calculated as one-third the pulse pressure plus the diastolic pressure and was expressed in mm.Hg.

Cyclic variations in blood pressure due to respiration or other reasons were averaged to provide a better estimate of the blood pressure.

V. Heart Rate Measurement

Heart rate was obtained from the blood pressure record. Measurement was usually made over a ten second period and multiplied by six to provide a heart rate in beats per minute. In cases where rapid changes in heart rate were obtained over periods of time less than ten seconds, readings were made accordingly; thus larger multiplication factors were required. Record speed was maintained at 5 mm. per second.

VI. Respiratory Rate Measurement.

The rate of respiration was measured directly from the blood pressure record since artificial ventilation was not utilized in any of the experiments. The rate was usually measured over a 30 second period and

multiplied by two to provide respiration in cycles per minute. However, if obvious changes in rate occurred in shorter periods of time, they were measured accordingly and multiplied by a suitable factor.

VII. Statistical Analysis

Statistical analysis of the data was accomplished by the use of Student's t-test and the Analysis of Variance (Snedecor, 1956). Significance was indicated only when the probability was less than one percent.

VIII. Abbreviations Used

SP - Systolic pressure in mm.Hg.

DP - Diastolic pressure in mm.Hg.

PP - Pulse pressure in mm.Hg.

MSBP - Mean systemic blood pressure in mm.Hg.

MCBP - Mean cerebral blood pressure in mm.Hg.

HR - Heart rate in beats per minute.

RR - Respiratory rate in cycles per minute.

Fig. 1. A diagrammatic sketch of the ventral view of the major arteries of the cervical and thoracic area of the chicken.

ec - external carotid artery

ic - internal carotid artery

va - vertebral artery

thy - thyroid gland

sa - subclavian artery

bca - brachiocephalic artery

ao - aorta

pa - pulmonary artery

cc - common carotid artery

csh - area of the carotid sinus homologue

a - point of occlusion of the carotid artery

b - point of occlusion of the vertebral artery

c - point of occlusion of both carotid and vertebral arteries

d - point of occlusion of the brachiocephalic artery

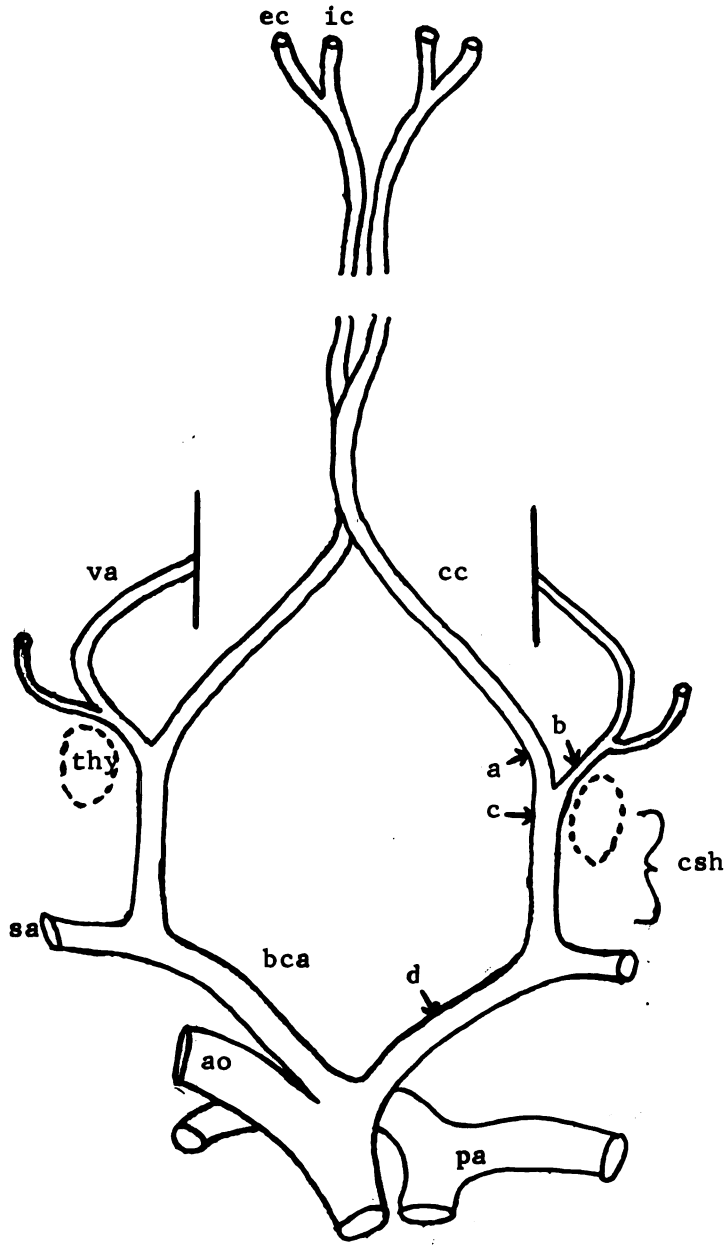

Figure 1.

RESULTS

Experiment I: The effect of ligation of the carotid and vertebral arteries in Leghorn-type hens on survival, heart weight, and body weight during a two-week period.

A total of 25 hens was utilized in this experiment. All birds were weighed, anesthetized and the carotid-vertebral bifurcations exposed as described previously. Ligation of the arteries was accomplished with nylon ligatures as follows: (1) bilateral vertebral artery ligation immediately above the bifurcation in five hens; (2) bilateral carotid artery ligation immediately above the bifurcation in five hens; (3) bilateral carotid artery ligation immediately below the bifurcation in ten hens, thus preventing blood flow through both the carotids and vertebrals; (4) and the surgical procedure without ligation in five hens which served as controls.

Following surgery the incisions were closed with wound clips and all birds were placed in a laying battery in the laboratory. Feed and water were supplied ad libitum, lights were on at least 14 hours a day and the birds were exposed to room temperature variation. The hens were kept for a period of two weeks. At the end of this time they were weighed, sacrificed, heart weights measured and ligatures examined to see if the occlusions had been maintained.

Heart weights were obtained as follows: (1) the pericardial sac was removed from the heart; (2) protruding vessels were trimmed down to the heart wall; (3) adipose tissue was trimmed from the outside of the heart; (4) the atria and ventricles were cut open and residual blood removed; (5) the heart was then rinsed in tap water, blotted on a paper

towel and weighed to four decimal places on a Mettler balance.

The results of this experiment are shown in Table 1. Analysis of Variance showed no significant differences ($P > .01$) among body weights at the beginning or end of the experiment, although the greatest change obtained was a loss of weight in the group of hens with both carotids and vertebrals ligated. No significant differences ($P > .01$) were found among heart weights expressed either as actual weight or on a per kg. body weight basis.

Mortality encountered during the experiment consisted of three birds in the group with both vertebral and carotid arteries occluded. One hen died in less than one hour after surgery, the second in less than six hours, and the third nine days after the operation.

A post-mortem examination of all the birds at the end of the experiment showed that a few ligatures had broken loose or were weak, but examination of the vessels with a dissecting microscope showed the arteries to be totally occluded by tissue growth in the lumen.

During the experimental period all the surviving hens appeared normal and many of them laid eggs (ranged 0 to 90 percent production). No differences in behavior could be seen between control birds and those that were ligated. A pupillary light reflex was observed in the ligated hens and they showed good balance when forced to perch.

It would appear from the results of this experiment that (1) no cardiac hypertrophy developed as a result of permanent occlusion of the carotid and vertebral arteries; (2) survival depended on collateral circulation to the head and was a function of each bird's individuality in the amount of collateral circulation available; (3) and no apparent

brain damage occurred from the ligations as evidenced by normal behavior and no significant loss of body weight.

Table 1. The effect of ligation of the carotid and vertebral arteries in Leghorn-type hens on survival, heart weight and body weight during a two-week period

No. of hens	Arteries ligated	Average body weight (gms.) Before ligation	Two weeks after lig.	Percent change	Average heart weight (gms.) Absolute	Per kg. body wt.	No. of hens dead
5	Left and right vertebrals	1838 ± 90[1]	1830 ± 74	0	6.18 ±0.12	3.40 ±0.16	0
5	Left and right common carotids	1844 ± 90	1846 ± 69	0	5.65 ±0.45	3.04 ±0.15	0
10	Left and right vertebrals and common carotids	1846 ±104	1774 ± 77	- 4	5.92 ±0.62	3.30 ±0.24	3[2]
5	Sham operated	1864 ± 74	1816 ± 82	- 3	5.56 ±0.25	3.06 ±0.06	0

[1] Standard error of the mean.

[2] Time of death after ligation: less than 1 hour, 5-1/2 hours, 9 days.

Experiment II: A. The effect of occluding the carotid and vertebral arteries in Leghorn-type hens on systemic blood pressure, heart rate and respiration. B. The effect of ligation of the carotid and vertebral arteries on survival, heart weight and body weight after direct blood pressure measurement.

A. A total of 17 hens was utilized in this experiment. All birds were weighed, anesthetized, and the carotid-vertebral bifurcations isolated. In the first five birds blood pressure was measured by direct means from an ischiatic artery as described previously. In the remaining 12 hens blood pressure was obtained by cannulation of the left common carotid. A Statham P-23 AC arterial transducer was used to pick up blood pressure changes and a Brush Analyzer and recorder were used to amplify and record the pressure. A loose ligature was placed around each bifurcation so the arteries could be lifted away from the surrounding tissue to facilitate occlusion. Serrefine clamps were used to occlude the various arteries.

The following occlusion procedure was used with the first five hens:

(1) clamp left and right vertebral arteries for approximately two minutes, remove clamps;

(2) allow five minute recovery period;

(3) clamp left and right carotid arteries for approximately two minutes, remove clamps;

(4) allow five minute recovery period;

(5) clamp below both bifurcations to occlude both vertebrals and carotids for approximately two minutes, remove clamps;

(6) allow at least a ten minute recovery period before starting with step (1) again.

This procedure was considered to be one occlusion series and was repeated three times in each bird.

The occlusion procedure used in the remaining 12 hens consisted of steps (3) through (6) of the above procedure. Only two occlusion series were accomplished in each of these birds. In step (3) it can be seen that since the left carotid artery was cannulated for blood pressure only the right carotid had to be clamped. In step (5) the right carotid was clamped below the bifurcation but only the left vertebral artery was clamped since the left carotid was cannulated.

Respiration, heart rate, and blood pressure were recorded continuously, while measurements were made before occlusion, during one minute after occlusion and at approximately two minutes after occlusion. The before occlusion measurements served as control readings while the values recorded for one minute after occlusion represented the changes that occurred during the first minute which were believed to be the primary effects of the occlusion. The two minute values were taken to show the trends of the various parameters. The observations taken within each hen were averaged for each parameter to provide one representative value for each bird under each condition of occlusion.

The results of this experiment are shown in Table 2. Statistical analysis was accomplished using a t-test of differences. Occlusion of the vertebral arteries caused a small, non-significant ($P > .01$) increase in mean blood pressure and a highly significant decrease in heart rate during one minute after occlusion. Occlusion of both common carotids,

however, produced a small, but highly significant increase in systolic pressure, diastolic pressure, and mean blood pressure while there was a highly significant decrease in heart rate (Fig. 2)[1].

Occlusion of both the carotids and vertebrals produced a very large and highly significant increase in systolic pressure, diastolic pressure, pulse pressure and mean blood pressure (Fig. 2). A highly significant decrease in respiratory rate was obtained while only a small, non-significant ($P > .01$) increase in heart rate was observed. The highly significant change in blood pressure from one to two minutes after occlusion indicates a notable transiency of the maximal blood pressure effects. These results are very suggestive of ischemic effects rather than a pressure reflex mechanism.

B. Twelve of the 17 hens utilized in this experiment were not sacrificed after the occlusion studies. These birds were used to repeat part of Experiment I. The incisions in six hens were closed with wound clips, leaving both vertebral arteries and the right carotid artery patent. The incisions in the remaining six birds were closed after permanently ligating the carotid arteries below the vertebral bifurcation. The birds were kept for two weeks in a laying battery in the laboratory. At the end of this time the hens were weighed, sacrificed and heart weights taken as described in Experiment I.

A statistical analysis (t-test) of the results shown in Table 3 indicated no significant differences ($P > .01$) between body weights or heart

[1] Experience has indicated that the results of occlusion of the vertebral arteries are usually similar in direction and magnitude to those obtained by occlusion of the carotids. The differences in significance noted in these results are, in all likelihood, a reflection of the difference in the number of animals subjected to each condition of occlusion.

weights; thus, these results are in agreement with those of Experiment I. It is found, as in Experiment I, that the greatest change in body weight was a loss obtained in the group with both vertebrals and carotids occluded.

Mortality consisted of the loss of one hen in the totally ligated group. This bird died ten days after ligation.

Table 4 shows a combination of the results of Experiments I and IIB. Only the results for the totally ligated birds and the control or sham operated birds are shown. No statistical differences ($P > .01$) were found between body weights or heart weights. The level of mortality shows a 75 percent survival rate in birds with their vertebral and carotid arteries occluded for two weeks.

Table 2. The effect of occluding the carotid and vertebral arteries in Leghorn-type hens on systemic blood pressure, heart rate and respiration

No. of hens	Arteries occluded	Parameter measured[1]	Before occlusion (control)	After occlusion 1 Min.	After occlusion 2 Min.	Change as % of control 1 Min.	Change as % of control 2 Min.	Change of % from 1 - 2 Min.
5	Left and right vertebrals	SP	117	120	119	+ 3	+ 2	- 1
		DP	99	101	101	+ 2	+ 2	0
		PP	18	19	18	+ 6	0	- 6
		MSBP	105 ± 4[2]	107 ± 7	107 ± 4	+ 2	+ 2	0
		HR	252 ±11	236 ±12	242 ± 9	- 6*	- 4	+ 2
		RR	25 ± 1	25 ± 1	25 ± 1	0	0	0
17	Left and right common carotids	SP	112	116	114	+ 4*	+ 2*	- 2
		DP	93	97	96	+ 3*	+ 3*	- 1
		PP	19	19	18	0	- 5	- 5
		MSBP	99 ± 4	103 ± 4	102 ± 4	+ 4*	+ 3*	- 1
		HR	248 ± 7	241 ± 7	243 ± 7	- 3*	- 3*	+ 1
		RR	27 ± 1	27 ± 2	27 ± 2	0	0	0
17	Left and right vertebrals and common carotids	SP	115	158	141	+37*	+23*	-14*
		DP	97	123	114	+27*	+18*	- 9*
		PP	18	35	27	+94*	+50*	-44*
		MSBP	103 ± 4	135 ± 6	123 ± 4	+31*	+19*	-12*
		HR	249 ± 7	270 ±11	251 ±10	+ 8	+ 1	- 7*
		RR	27 ± 1	21 ± 1	23 ± 1	-22*	-15*	+ 7

[1] Blood pressures given in mm.Hg; heart rate in beats per minute; respiration in cycles per minute.

[2] Standard error of the mean.

* Statistically significant at a probability of less than 1%.

Table 3. The effect of ligation of the carotid and vertebral arteries in Leghorn-type hens on survival, heart weight and body weight after direct blood pressure measurement

No. of hens	Arteries ligated	Average body weight (gms.) Before ligation	Two weeks after lig.	Percent change	Average heart weight (gms.) Absolute	Per kg. body wt.	No. of hens dead
6	Left common carotid[1]	1560 ± 69[2]	1587 ± 78	+ 2	4.85 ±0.26	3.08 ±0.18	0
6	Left and right vertebrals and common carotids	1770 ± 58	1598 ± 98	- 10	4.93 ±0.47	3.07 ±0.17	1[3]

[1] Left common carotid ligated due to prior blood pressure cannulation.

[2] Standard error of the mean.

[3] Time of death 10 days after ligation.

Table 4. Summary of the effect of carotid and vertebral artery ligation in Leghorn-type hens on body weight, heart weight and survival during a two-week period

No. of hens	Arteries ligated	Average body weight (gms.) Before ligation	Two weeks after lig.	Percent change	Average heart weight (gms.) Absolute	Per kg. body wt.	No. of hens dead
16	Left and right common carotids below vertebral	1814 ± 64[1]	1701 ± 64	- 6	5.51 ±0.42	3.21 ±0.15	4[2]
11	Left common carotid in 6. None in 5.	1698 ± 68	1691 ± 65	0	5.18 ±0.21	3.08 ±0.10	0

[1] Standard error of the mean.

[2] Time of death after ligation: less than 1 hour, 5-1/2 hours, 9 days, 10 days.

Fig. 2. The effect of bilateral occlusion of the carotid arteries and bilateral occlusion of both the carotid and vertebral arteries on systemic blood pressure and heart rate in the Leghorn-type hen. Left carotid artery cannulated for systemic blood pressure measurement and therefore occluded throughout the record. Heart rate shown above or below the blood pressure tracing.

A-1: right carotid artery occluded.

B-2: right carotid artery desoccluded 2 min. and 20 sec. after A-1.

C-3: right carotid artery occluded below carotid-vertebral bifurcation, left vertebral artery already occluded; thus, both carotids and vertebrals occluded at this point.

D-4: left vertebral artery desoccluded 2 min. and 25 sec. after C-3.

D-5: right carotid and vertebral arteries desoccluded.

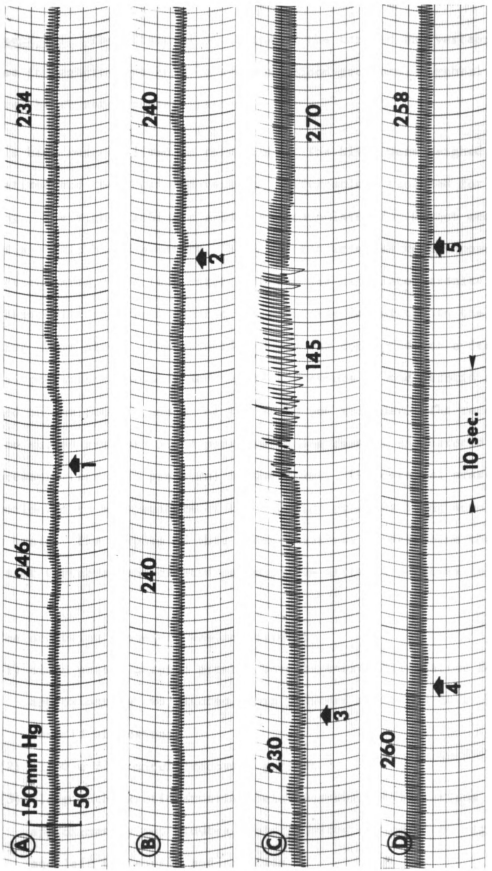
A
150 mm Hg
50
246
234
1
B
240
240
2
C
230
145
270
3
D
260
4
10 sec.
258
5

Figure 2.

Experiment III. The effect of occlusion of the carotid and vertebral arteries in Leghorn-type hens on systemic blood pressure, cerebral blood pressure, heart rate and respiration.

Six hens were utilized in this study. The birds were weighed, anesthetized and their carotid-vertebral bifurcations isolated for clamping. The right ischiatic artery was cannulated for direct measurement of systemic blood pressure. Both carotid arteries were exposed in the cervical area. The left carotid artery was cannulated craniad in three hens while the right carotid was similarly cannulated in the remaining three birds. The carotid cannula was connected to a Statham arterial pressure transducer and the back-pressure in the carotid artery recorded on the second channel of the Brush pen recorder. The record obtained showed systemic blood pressure on one channel and carotid back-pressure (cerebral pressure) on the other. The cerebral pressure was considered to be a measure of the arterial pressure being supplied to the brain. The purpose of this measurement was to determine the effects of vertebral and carotid occlusion on arterial pressure in the brain.

The occlusion procedure was as follows:

(1) clamp patent carotid artery above vertebral bifurcation for approximately two minutes, this provided right and left carotid occlusion;

(2) allow a five minute recovery period;

(3) clamp both carotid arteries below vertebral bifurcations for approximately two minutes, this provided occlusion of right and left vertebrals and carotids;

(4) allow a ten minute recovery period before repeating step (1). This procedure was carried out twice in each bird.

Blood pressure, heart rate and respiration were recorded continuously, while measurements were made before occlusion, during one minute after occlusion and two minutes after occlusion. As in Experiment II, the before occlusion values served as control readings while the one minute values represented the changes that occurred during the first minute after occlusion which were believed to be the primary effects of the occlusion. The two minute measurements were taken to indicate the trends of the various parameters. The measurements within each hen were averaged to provide representative values.

The results of this experiment are shown in Table 5. Statistical analysis of the data was accomplished using a t-test of differences. Occlusion of both carotid arteries produced a highly significant decrease in cerebral pressure at one and two minutes after occlusion (Fig. 3). A small, non-significant ($P > .01$) decrease in heart rate was obtained while little change was noted in any of the other parameters. Occlusion of both the carotids and vertebrals, however, resulted in a highly significant increase in systolic pressure, diastolic pressure and mean systemic blood pressure while highly significant decreases were obtained in mean cerebral pressure and respiration (Fig. 3). A small, non-significant ($P > .01$) rise in heart rate was also obtained.

Figure 4 shows the relationship of control systemic blood pressure and control cerebral blood pressure. These values were obtained from the six hens in this experiment in addition to two other hens in which these measurements were made. A highly significant linear relationship between

the two parameters indicated a dependency of cerebral pressure on systemic pressure.

Figure 5 is a scatter diagram showing the relationship between the initial change obtained in mean systemic blood pressure and that obtained in mean cerebral blood pressure during the first minute after occlusions of the carotids alone and the carotids and vertebrals. The points seem to indicate that a systemic response occurs when cerebral pressure decreases to below 35 mm.Hg.

These data appear to indicate that a systemic pressure response is obtained when occlusion of arteries to the head diminishes the blood supply to a certain critical level.

Table 5. The effect of occlusion of the carotid and vertebral arteries in Leghorn-type hens on systemic blood pressure, cerebral blood pressure, heart rate and respiration

No. of hens	Arteries occluded	Parameter measured[1]	Before occlusion (control)	After occlusion 1 Min.	After occlusion 2 Min.	Change as % of control 1 Min.	Change as % of control 2 Min.	Change of % from 1 - 2 Min.
6	Left and right common carotids	SP	125	125	123	0	- 2	- 2
		DP	98	99	98	+ 1	0	- 1
		PP	26	26	25	0	- 4	- 4
		MSBP	107 ± 6[2]	108 ± 6	106 ± 6	+ 1	- 1	- 2
		MCBP	71 ± 4	51 ± 5	61 ± 5	-28*	-14*	+14
		HR	257 ±13	242 ±13	252 ±13	- 6	- 2	+ 4
		RR	36 ± 3	35 ± 3	36 ± 2	- 3	0	+ 3
6	Left and right common carotids and vertebrals	SP	126	171	154	+36*	+22*	-14
		DP	99	131	121	+32*	+22	-10
		PP	27	40	33	+48	+22	-26
		MSBP	108 ± 6	144 ± 5	132 ± 3	+33*	+22*	-11
		MCBP	72 ± 4	26 ± 6	35 ± 4	-64*	-51*	+13*
		HR	260 ±14	274 ±16	254 ±16	+ 6	- 2	- 8
		RR	36 ± 2	27 ± 3	26 ± 3	-25	-28*	- 3

[1] Blood pressures given in mm.Hg; heart rate in beats per minute; respiration in cycles per minute.

[2] Standard error of the mean.

* Statistically significant at a probability of less than 1%.

Fig. 3. The effect of bilateral occlusion of the carotid arteries and bilateral occlusion of both the carotid and vertebral arteries on systemic blood pressure, cerebral blood pressure and heart rate in the Leghorn-type hen. Right ischiatic artery cannulated for systemic blood pressure measurement and left carotid cannulated craniad for measurement of cerebral pressure. Left carotid was therefore occluded throughout the record. Systemic blood pressure shown in top half of record while cerebral pressure shown in bottom half. Heart rate shown below systemic blood pressure tracing.

A-1: right carotid artery occluded.

B-2: right carotid artery desoccluded 2 min. 22 sec. after A-1.

C-3: right carotid artery occluded below carotid-vertebral bifurcation, left vertebral artery already occluded; thus, both carotids and vertebrals occluded at this point.

D-4: right carotid and vertebral arteries desoccluded 2 min. 26 sec. after C-3.

D-5: left vertebral artery desoccluded.

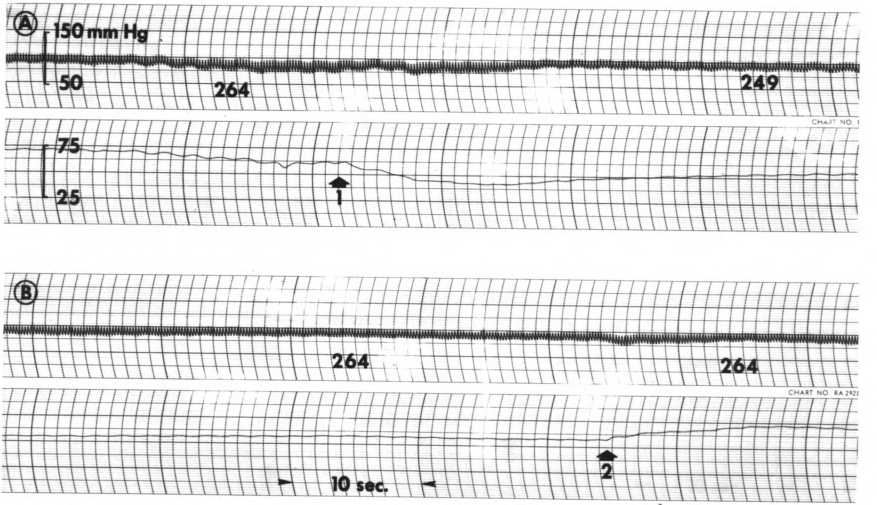
A
150 mm Hg
50
264
249
CHART NO. 1
75
25
1
B
264
264
CHART NO. RA 2921
10 sec.
2

Figure 3.

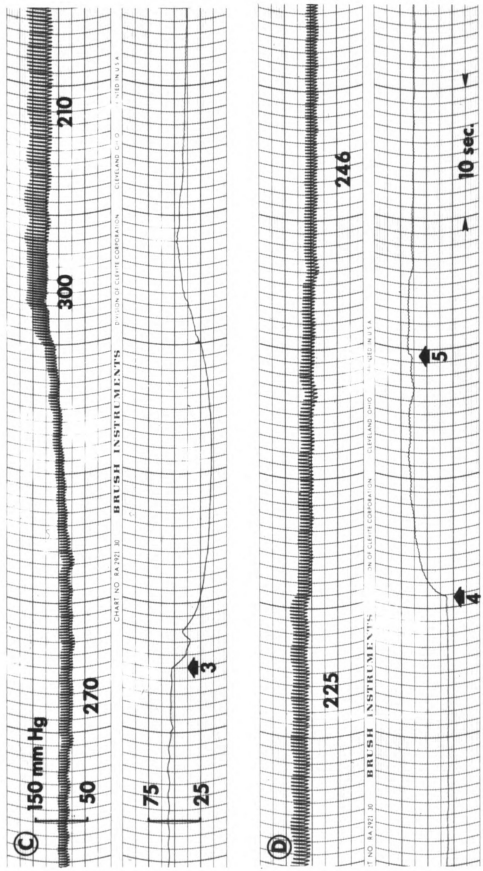

Figure 3 Continued.

Fig. 4. A graph showing the relationship of control cerebral blood pressure to control systemic blood pressure in eight Leghorn-type hens. Systemic blood pressure was measured from an ischiatic artery while cerebral blood pressure was measured by the craniad cannulation of a carotid artery. A highly significant linear relationship was found between these two parameters showing an apparent dependency of cerebral pressure on systemic pressure.

* Significant at a probability of less than 1%.

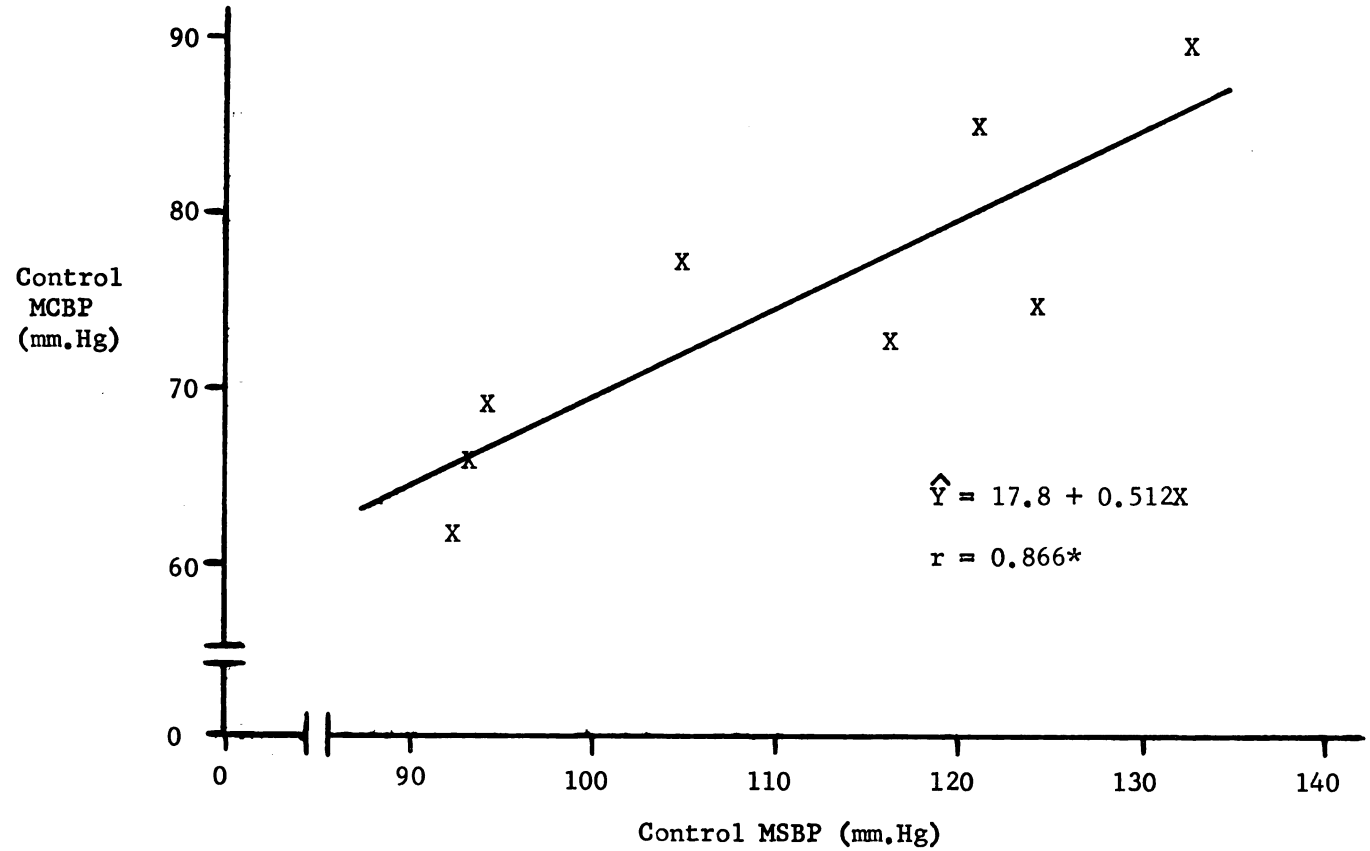
90
80
70
60
0
Control
MCBP
(mm.Hg)
X
X
X
X
X
X
X
$\hat{Y}$ = 17.8 + 0.512X
r = 0.866*
0
90
100
110
120
130
140
Control MSBP (mm.Hg)

Figure 4.

Fig. 5. A scatter diagram showing the relationship of the initial change in systemic blood pressure to the initial cerebral blood pressure effect obtained after bilateral occlusion of the carotid arteries and bilateral occlusion of both the carotid and vertebral arteries in six Leghorn-type hens. Note systemic pressure responses with cerebral pressures below 35 mm.Hg.

X = effect after bilateral carotid and vertebral artery occlusion.

● = effect after bilateral carotid artery occlusion.

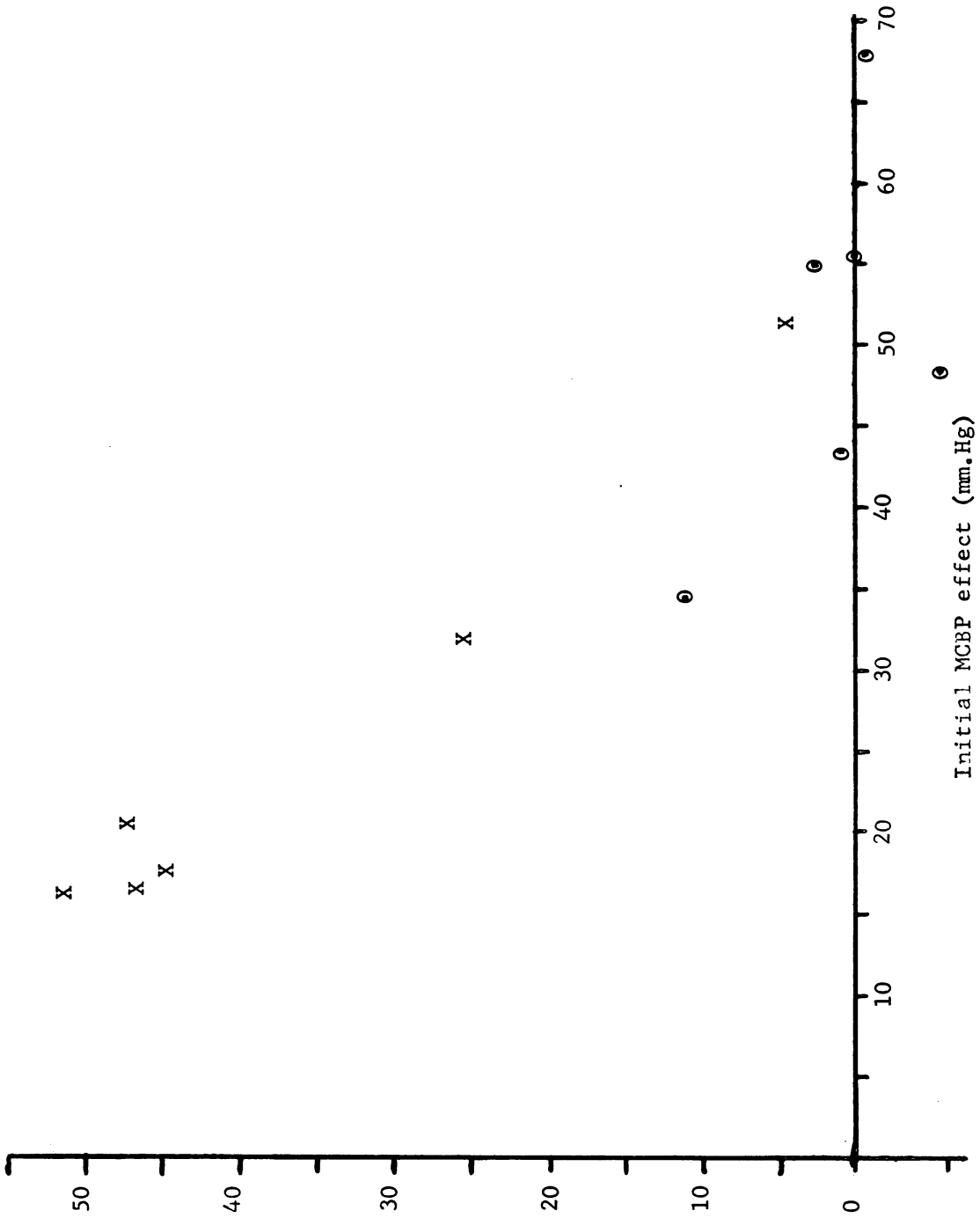
Initial change in MSBP (mm.Hg)
50
40
30
20
10
0
10
20
30
40
50
60
70
Initial MCBP effect (mm.Hg)

Figure 5.

Experiment IV. A. The effect of intracarotid injection of small quantities of hypercapnic and hyperoxygenated blood on systemic blood pressure, cerebral blood pressure, heart rate and respiration in Leghorn-type hens. B. The effect of rapid arterial pressure changes in the cerebral circulation.

A. Eight hens were utilized in this experiment. The birds were weighed, anesthetized and the carotid-vertebral bifurcations isolated in six of them. Both carotid arteries were exposed in the cervical area of all eight hens. The left carotid was cannulated caudad for the measurement of systemic blood pressure and cannulated craniad for the measurement of cerebral pressure. The right carotid was cannulated craniad to provide a route for injection and withdrawal of blood. In six birds the left vertebral artery was permanently ligated with a nylon ligature while the right vertebral artery was isolated for clamping during the experiment. Each hen was heparinized with 9 mg. of heparin to prevent blood clots from forming in the cannulas or cerebral vessels. Blood pressure was recorded with Brush equipment in two birds while a Grass Model 5 polygraph was utilized with the remaining six hens.

It was believed that, in the six hens with one patent vertebral artery, occlusion of this artery would reduce the cerebral pressure to such an extent to produce the usual transient systemic pressure response. In this condition, blood supply to the brain was considered to be marginal and a small quantity of hypercapnic or hyperoxygenated blood was expected to be effective in the presence of minimum dilution by collateral circulation.

In four hens, donor blood from another bird was used for injection

purposes while in the remaining four birds the hens' own blood was withdrawn through the injection cannula and reinjected after treatment. All blood was maintained at approximately 40° C. in a water bath. Hypercapnic blood was prepared by bubbling pure carbon dioxide through the blood until it appeared a dark purple color. Hyperoxygenated blood was prepared by bubbling pure oxygen through the blood until it was bright red in color. The blood was kept in a small Erlenmeyer flask in a water bath before injection. Slightly more than 2 cc. of blood were drawn up from the flask into a syringe in preparation for injection. The syringe was then fitted to a three-way valve connected to the injection cannula and the valve adjusted to permit injection of the blood into the cannula. The time for injection ranged from 7 to approximately 22 seconds. Injection times averaged about 12 seconds in duration.

The injection procedure was as follows:

(1) either donor blood or the birds' own blood (approximately 2.5 cc.) was placed in a small Erlenmeyer flask and prepared as described above;

(2) the right vertebral artery was then occluded in six of the hens and systemic blood pressure allowed to stabilize for two minutes;

(3) approximately 2.2 cc. of prepared blood were then drawn into a syringe and injected as previously discussed, usually hypercapnic blood was injected first;

(4) at least two minutes were allowed to pass after injection, then the clamp was removed from the right vertebral artery;

(5) a ten minute recovery period was allowed before the whole procedure was repeated using oxygenated blood.

This entire sequence for hypercapnic and hyperoxygenated blood was completed twice in seven of the hens and once in one. The two hens in which the vertebral arteries were not occluded were used with just the right and left carotids occluded by the cannulas.

Measurements of the various parameters were made before injection, during one minute after injection and two minutes after injection. The purpose of these measurements was the same as those described for the occlusion studies in Experiments II and III. The values for each parameter were averaged within each hen to provide a representative value.

The results of this experiment are shown in Table 6. Statistical analysis was accomplished using a t-test of differences. The injection of oxygenated blood had little over-all effect on the parameters measured; however, small but highly significant changes were obtained in systolic pressure, pulse pressure, cerebral pressure and heart rate (Fig. 6). The most notable of these changes was probably the highly significant decrease in heart rate. The injection of hypercapnic blood, however, produced a large and highly significant increase in systolic pressure, diastolic pressure, pulse pressure, mean systemic blood pressure and cerebral blood pressure (Fig. 6). A small, non-significant ($P > 0.01$) rise was obtained in heart rate. The pattern of the hypercapnic response was very similar to that obtained by carotid and vertebral occlusion in previous experiments.

It was noted during the course of the experiment that only two out of the six hens responded with a substantial increase in systemic blood pressure when the right vertebral artery was clamped. In four of these hens collateral circulation apparently provided enough blood to the head

so that cerebral pressure did not drop below a critical level when the right vertebral was occluded. Table 7 shows blood pressure, heart rate and respiration data for these six hens before and one minute after the right vertebral artery was occluded. The before occlusion values served as control readings and the one minute after occlusion values were the changes that occurred during the first minute which were believed to be the primary result of the occlusion. Statistical analysis of the data by a t-test of differences revealed a highly significant decrease in cerebral pressure while the changes in all other parameters measured were non-significant ($P > 0.01$).

A scatter diagram (Fig. 7) of the systemic blood pressure response versus the level to which the cerebral pressure dropped after occlusion in each of the six hens shows that a systemic response occurs at approximately a level of 30 mm.Hg of cerebral pressure. The scatter diagram of Experiment III (Fig. 5) was superimposed on that of this experiment (Fig. 7). The resulting diagram (Fig. 8) shows close agreement between the two sets of data and indicates that a systemic pressure response is usually obtained at a level of 30 to 35 mm.Hg of cerebral pressure.

B. During the injection experiment, high arterial pressure was supplied to the cerebral vessels of each hen by first withdrawing approximately 2 cc. of blood from the injection cannula (or in some cases using donor blood) and then immediately reinjecting the blood in pulses of high pressure. No systemic blood pressure or heart rate effects were observed as a result of this procedure. The level of pressure applied to the cerebral vessels via the right carotid cannula was measured by changes in cerebral pressure recorded from the left carotid cannula (Fig. 9).

Table 6. The effect of intracarotid injection of small quantities of hypercapnic and hyperoxygenated blood on systemic blood pressure, cerebral blood pressure, heart rate and respiration in the Leghorn-type hen

No. of hens	Arteries occluded	Parameter measured[1]	Before injection (control)	After injection 1 Min.	After injection 2 Min.	Change as % of control 1 Min.	Change as % of control 2 Min.	Change of % from 1-2 Min.
			Blood + O_2					
8	Left and right common carotids and vertebrals or left and right common carotids	SP	126	133	135	+ 6	+ 7*	+ 1
		DP	107	109	112	+ 2	+ 5	+ 3
		PP	19	24	23	+26*	+ 21*	- 5
		MSBP	113 ± 6[2]	117 ± 9	120 ± 7	+ 4	+ 6	+ 2
		MCBP	43 ± 5	47 ± 5	48 ± 6	+ 9	+ 12*	+ 3
		HR	270 ±15	253 ±14	256 ±15	- 6*	- 5*	+ 1
		RR	27 ± 3	25 ± 3	25 ± 3	- 7	- 7	0
			Blood + CO_2					
		SP	130	160	142	+23*	+ 9*	- 14*
		DP	110	131	118	+19*	+ 7	- 12*
		PP	20	29	24	+45*	+ 20	- 25
		MSBP	117 ± 7	141 ± 6	126 ± 5	+21*	+ 8	- 13*
		MCBP	45 ± 6	55 ± 6	50 ± 7	+22*	+ 11	- 11
		HR	267 ±15	282 ±15	267 ±14	+ 6	0	- 6
		RR	25 ± 2	23 ± 2	25 ± 2	- 8	0	+ 8

[1] Blood pressures given in mm.Hg; heart rate in beats per minute; respiration in cycles per minute.

[2] Standard error of the mean.

* Statistically significant at a probability of less than 1%.

Table 7. The effect of occluding the right vertebral artery in Leghorn-type hens, whose common carotid arteries and left vertebral artery had previously been permanently ligated, on blood pressure, heart rate and respiration

No. of hens	Arteries occluded	Parameter measured[1]	Before occlusion of right vertebral (control)	One minute following occlusion of right vertebral	Change as percent of control
6	Left and right vertebrals and common carotids	SP	133	146	+ 10
		DP	112	122	+ 9
		PP	21	24	+ 14
		MSBP	119 ± 3[2]	130 ± 7	+ 9
		MCBP	63 ± 5	36 ± 5	- 43*
		HR	271 ± 18	272 ± 19	0
		RR	29 ± 4	25 ± 4	- 14

[1] Blood pressures given in mm.Hg; heart rate in beats per minute; respiration in cycles per minute.

[2] Standard error of the mean.

* Statistically significant at a probability of less than 1%.

Fig. 6. The effect of the intracarotid injection of small quantities of hypercapnic and hyperoxygenated blood on systemic blood pressure, cerebral blood pressure and heart rate in the Leghorn-type hen. Systemic blood pressure obtained by caudad cannulation of left carotid artery and cerebral blood pressure measured by craniad cannulation of left carotid artery. Injection of blood made into right carotid artery via a cannula; thus, both carotids were occluded. The left vertebral artery was permanently ligated, the right vertebral artery was occluded at least 2 min. before injection; therefore, at time of injection both carotids and vertebrals were occluded. Cerebral pressure is shown in the top half of the record while systemic pressure is shown in the bottom half. Heart rate shown above systemic blood pressure tracing.

A-1 to A-2: injection of 2.2 cc. of hypercapnic donor blood.

B-3 to B-4: injection of 2.2 cc. of hyperoxygenated donor blood.

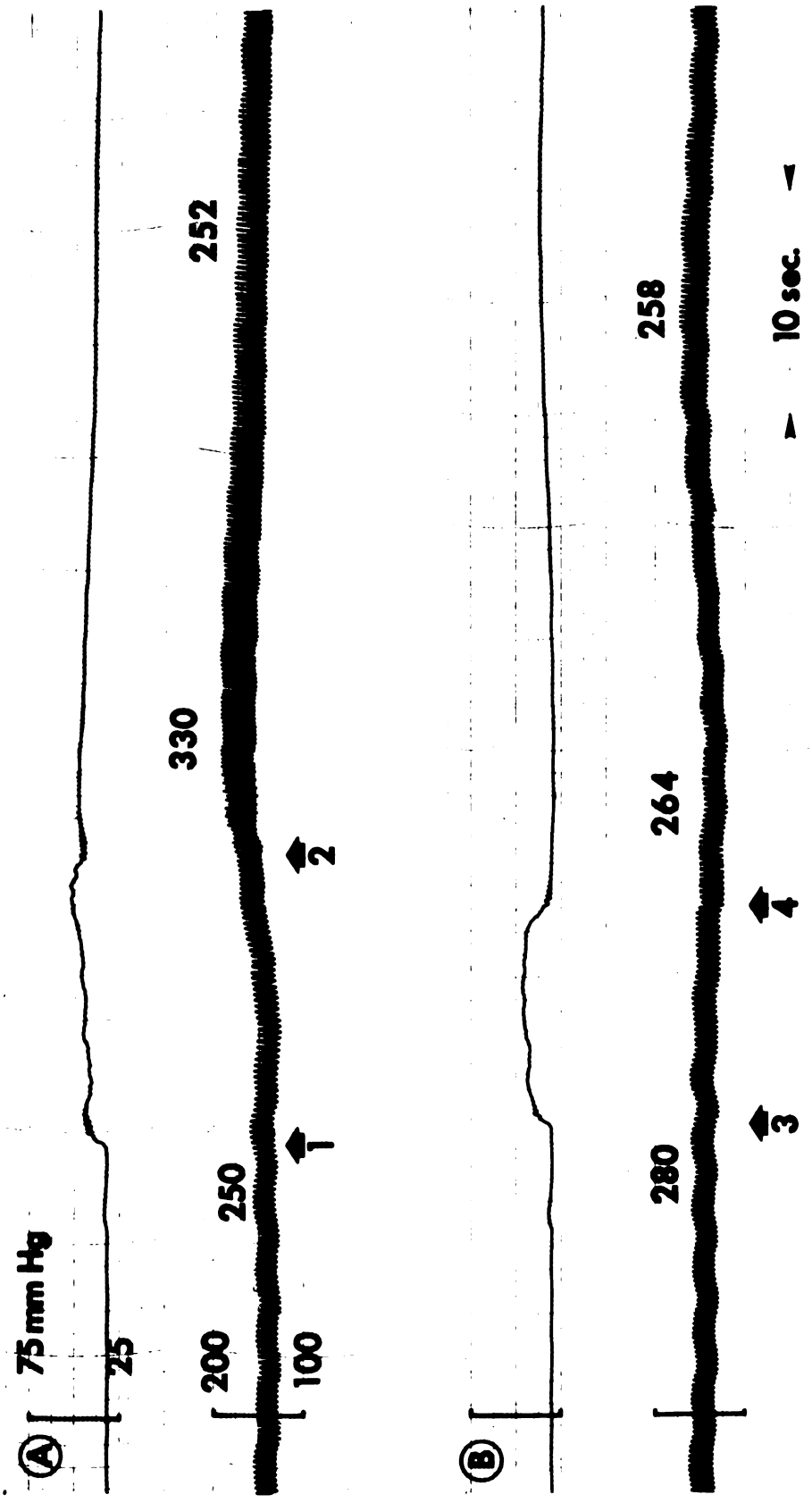

Figure 6.

Fig. 7. A scatter diagram showing the relationship of the initial change in systemic blood pressure to the initial cerebral blood pressure effect obtained after bilateral carotid and vertebral artery occlusion in six Leghorn-type hens. Note systemic pressure responses with cerebral pressures below 30 mm.Hg.

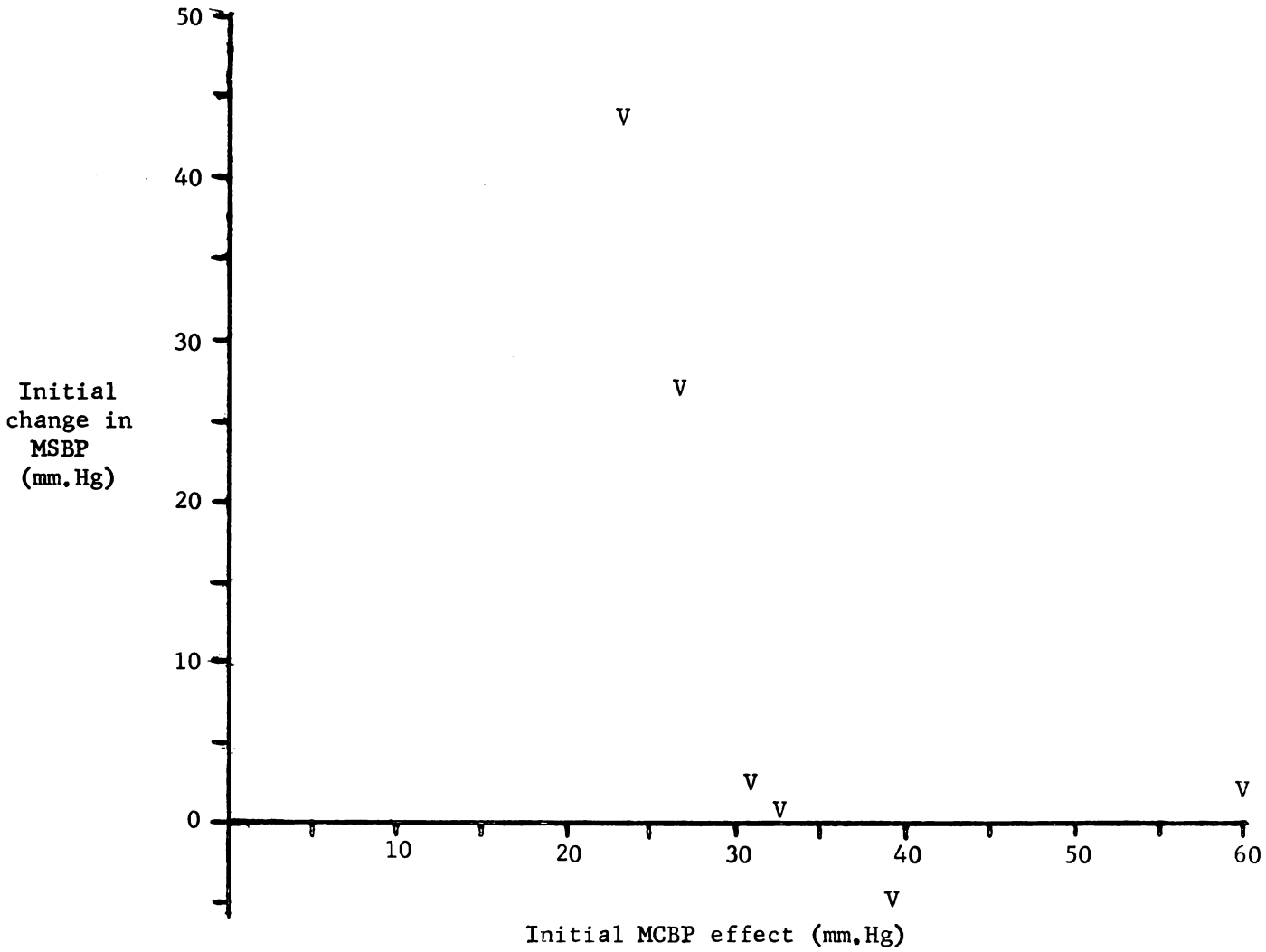
50
40
30
20
10
0
Initial change in MSBP (mm.Hg)
10
20
30
40
50
60
Initial MCBP effect (mm.Hg)

Figure 7.

Fig. 8. A scatter diagram combining the data of Figures 5 and 7 showing the relationship of the initial change in systemic blood pressure to the initial cerebral blood pressure effect obtained after bilateral occlusion of the carotid arteries and bilateral occlusion of both the carotid and vertebral arteries in Leghorn-type hens. Note systemic pressure responses with cerebral pressures below 35 mm.Hg.

X = effect after bilateral carotid and vertebral artery occlusion; Exp. III.

Θ = effect after bilateral carotid artery occlusion; Exp. III.

V = effect after bilateral carotid and vertebral artery occlusion; Exp. IV.

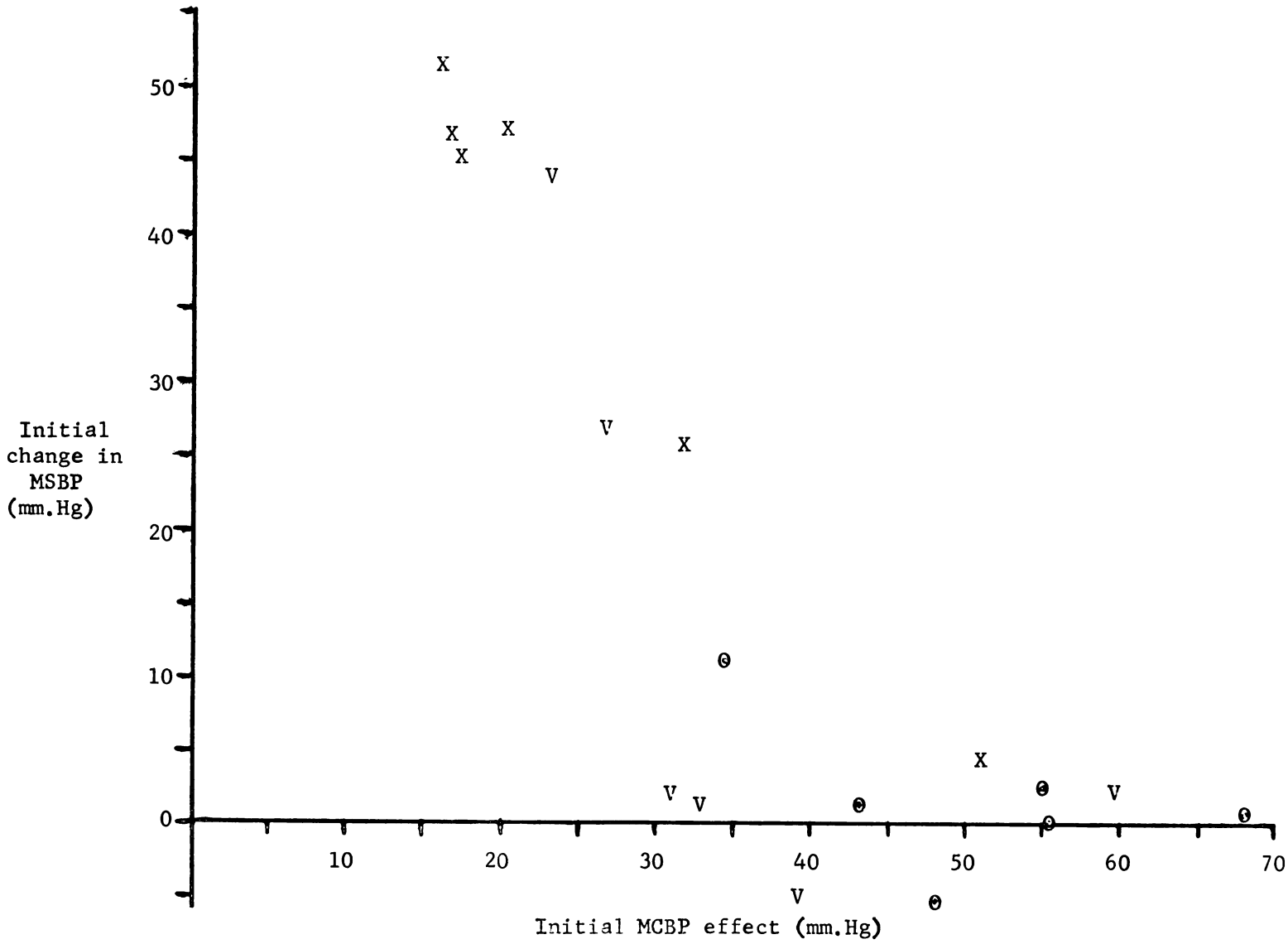
Initial change in MSBP (mm.Hg)
50
40
30
20
10
0
10
20
30
40
50
60
70
Initial MCBP effect (mm.Hg)

Figure 8.

Fig. 9. The effect of increased cerebral arterial pressure on systemic blood pressure and heart rate in the Leghorn-type hen. Cerebral blood pressure measured by craniad cannulation of the left carotid artery and systemic blood pressure measured by caudad cannulation of the left carotid artery. The left vertebral artery was permanently ligated. Cerebral pressure was increased by injection of blood into a cannula in the right carotid artery. Cerebral blood pressure is shown in the top half of the record while systemic blood pressure is shown in the bottom half. Heart rate is indicated above the systemic pressure tracing.

A: 2.1 cc. of bird's own blood injected under pulsatile pressure.

B: same hen as A. Right vertebral artery was occluded before pressure application, thus in this case both carotids and vertebrals were occluded. Pressure was applied by forcing blood back and forth in the carotid cannula.

C: different hen than B. Two cc. of bird's own blood injected under pulsatile pressure.

D: different hen than B or C. Two cc. of bird's own blood injected under pulsatile pressure.

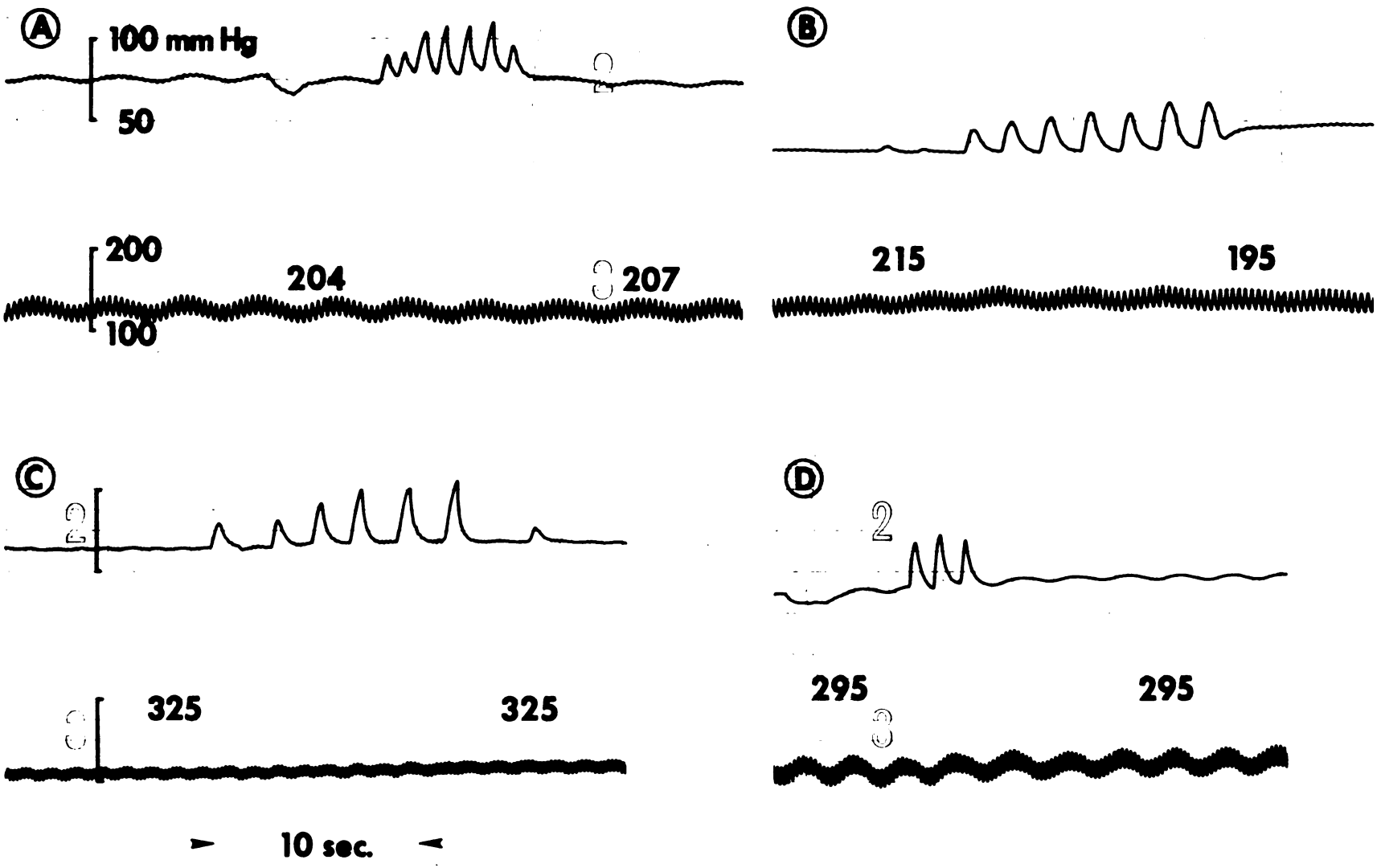

Figure 9.

Experiment V: The effect of unilateral vagotomy and brachiocephalic artery occlusion in Leghorn-type hens on systemic blood pressure, heart rate and respiration.

This experiment was carried out using six hens. The birds were weighed, anesthetized and the brachiocephalic arteries exposed in the thoracic cavity. Exposure was accomplished by providing an opening in the intraclavicular space large enough to pass a small serrefine clamp through it, using a pair of long forceps. Little dissection had to be done since the brachiocephalic arteries are not surrounded by adipose or connective tissue to any great extent and are quite prominent. The right ischiatic artery was cannulated to record systemic blood pressure changes in all the hens. The left carotid artery and right vagus nerve were isolated in the cervical area of three birds while the right carotid and left vagus were isolated in the remaining three. The carotid arteries were cannulated caudad to record control carotid blood pressure and the vagi were isolated for subsequent unilateral vagotomy. A Grass Model 5 polygraph was used to record the two blood pressures.

In the three birds with the left carotid artery cannulated, the left brachiocephalic artery was clamped twice, each occlusion period averaged 54 seconds in length. The right vagus was then sectioned and the left brachiocephalic clamped two more times for an average of 56 seconds. At least ten minutes were allowed for recovery between each clamping and between vagotomy and clamping.

The same procedure was carried out on the three hens with the right carotid cannulated, except that the right brachiocephalic artery was clamped and the left vagus sectioned. Average occlusion time before vagotomy was 76 seconds and after vagotomy 83 seconds.

The purpose of brachiocephalic occlusion was to reduce ipsilateral carotid pressure and thus severely reduce pressure in the area of the carotid sinus homologue. Sectioning the contralateral vagus eliminated the primary nervous innervation of the carotid sinus homologue on that side. It was expected that by reducing pressure in the innervated carotid, a systemic blood pressure and heart rate response would be obtained if the sinus homologue were pressure sensitive. In this experiment, both carotids were tested for pressure reflexes.

Carotid and ischiatic artery pressures were recorded continuously, while measurements were made before occlusion, during occlusion and one minute after occlusion. Carotid pressure was indicative of the pressure in the area of the sinus homologue while ischiatic pressure showed systemic responses. Measurement was made of the highest level of systemic blood pressure obtained during occlusion in addition to the level of pressure just before desocclusion.

The results of occlusion in each set of three hens are shown in Table 8A while a summary of all the results is shown in Table 8B. Statistical analysis was computed only for the data in Table 8B. A t-test of differences was used to determine significance. It is seen in Table 8A that the largest mean systemic blood pressure response (+ 27 mm.Hg) due to occlusion was obtained in the birds with right vagotomy; however, it is also seen that right vagotomy reduced respiration by more than 50 percent. In any case, blood pressure returned to control levels before desocclusion (Fig. 10). Left vagotomy reduced respiratory rate by approximately 17 percent; thus, there was a considerable difference in the effects of unilateral vagotomy on respiratory rate.

Table 8B shows only one highly significant difference in systemic blood pressure, and this was obtained before vagotomy. Systemic blood pressure at one minute after occlusion dropped to a level highly significantly less than control pressure. No significant changes were obtained in heart or respiration rate with brachiocephalic occlusion before or after vagotomy. No statistical analysis was accomplished on the carotid pressure data since the magnitude of change with occlusion was obviously significant. These results seem to indicate the lack of a pressure reflex mechanism associated with the carotid sinus homologue in the hen.

Table 8A. The effect of unilateral vagotomy and brachiocephalic artery occlusion in Leghorn-type hens on systemic blood pressure, heart rate and respiration

No. of hens	Experimental condition	Parameter measured[1]	Carotid artery pressure			Right ischiatic artery			
			Before occlusion	During occlusion	1 Min. after desocclusion	Before occlusion	During occlusion: Highest level	During occlusion: Level at desocclusion	1 Min. after desocclusion
3	LBCA[2]	SP	129	--	122	130	138	127	123
	occlusion	DP	105	--	96	106	114	101	98
	(Av. occlusion	PP	24	--	26	24	24	26	25
	time = 54 sec.)	MSBP	113	26	104	114	122	110	106
		HR	--	--	--	249	242	247	256
		RR	--	--	--	32	32	31	31
	LBCA	SP	118	--	124	122	151	126	128
	occlusion and	DP	89	--	95	90	119	90	96
	right vagotomy	PP	29	--	29	32	32	36	32
	(Av. occlusion	MSBP	100	23	105	102	129	102	106
	time = 56 sec.)	HR	--	--	--	246	248	251	240
		RR	--	--	--	15	15	14	16
3	RBCA	SP	123	--	114	129	134	125	118
	occlusion	DP	91	--	84	94	98	91	85
	(Av. occlusion	PP	32	--	30	35	42	34	33
	time = 76 sec.)	MSBP	102	23	94	105	110	102	96
		HR	--	--	--	298	301	306	309
		RR	--	--	--	29	29	29	29
	RBCA	SP	138	--	116	141	144	129	121
	occlusion and	DP	103	--	86	102	107	94	86
	left vagotomy	PP	35	--	30	39	37	35	35
	(Av. occlusion	MSBP	115	26	96	115	119	106	98
	time = 83 sec.)	HR	--	--	--	297	289	301	310
		RR	--	--	--	24	23	21	23

[1] Blood pressures given in mm.Hg; heart rate in beats per minute; respiration in cycles per minute.

[2] LBCA - left brachiocephalic artery; RBCA - right brachiocephalic artery.

Table 8B. Summary of the effect of unilateral vagotomy and brachiocephalic artery occlusion in Leghorn-type hens on systemic blood pressure, heart rate and respiration

No. of hens	Experimental condition	Parameter measured[1]	Carotid artery pressure			Right ischiatic artery			
			Before occlusion	During occlusion	1 Min. after desocclusion	Before occlusion	During occlusion: Highest level	During occlusion: Level at desocclusion	1 Min. after desocclusion
6	RBCA or LBCA[2] occlusion (Av. occlusion time = 65 sec.)	SP	126	--	118	129	136	126	120
		DP	98	--	90	100	106	96	91
		PP	28	--	28	29	30	30	29
		MSBP	107 ± 6[3]	25 ± 3	99 ± 7	110 ± 6	116 ± 5	106 ± 3	101 ± 7*
		HR	--	--	--	273 ±24	271 ±22	276 ±20	282 ±24
		RR	--	--	--	30 ± 2	31 ± 2	30 ± 1	30 ± 2
	RBCA or LBCA occlusion + left or right vagotomy (Av. occlusion time = 69 sec.)	SP	128	--	120	131	148	128	125
		DP	96	--	91	96	113	92	91
		PP	32	--	29	35	35	36	34
		MSBP	108 ± 6	25 ± 4	100 ± 6	108 ± 7	124 ± 6	104 ± 5	102 ± 6
		HR	--	--	--	271 ±24	268 ±22	276 ±22	275 ±25
		RR	--	--	--	20 ± 2	19 ± 3	17 ± 2	19 ± 2

[1] Blood pressures given in mm.Hg; heart rate in beats per minute; respiration in cycles per minute.

[2] LBCA - left brachiocephalic artery; RBCA - right brachiocephalic artery.

[3] Standard error of the mean.

* Statistically significant at a probability of less than 1%.

Fig. 10. The effect of unilateral occlusion of the brachiocephalic arteries with and without contralateral vagotomy on systemic blood pressure and heart rate in the Leghorn-type hen. Systemic blood pressure measured from right ischiatic artery, carotid blood pressure in area of carotid sinus homologue measured by caudad cannulation of carotid artery. Top half of record is carotid pressure and bottom half ischiatic pressure. Heart rate shown above ischiatic pressure tracing.

A-1: occlusion of right brachiocephalic artery.

A-2: desocclusion of right brachiocephalic 71 sec. after A-1.

B-3: occlusion of right brachiocephalic artery 14 min. 25 sec. after left vagotomy.

B-4: desocclusion of right brachiocephalic 93 sec. after B-3.

C-5: different hen from that in A and B. Occlusion of left brachiocephalic artery.

C-6: desocclusion of left brachiocephalic 77 sec. after C-5.

D-7: occlusion of left brachiocephalic artery 18 min. 53 sec. after right vagotomy.

D-8: desocclusion of left brachiocephalic 65 sec. after D-7.

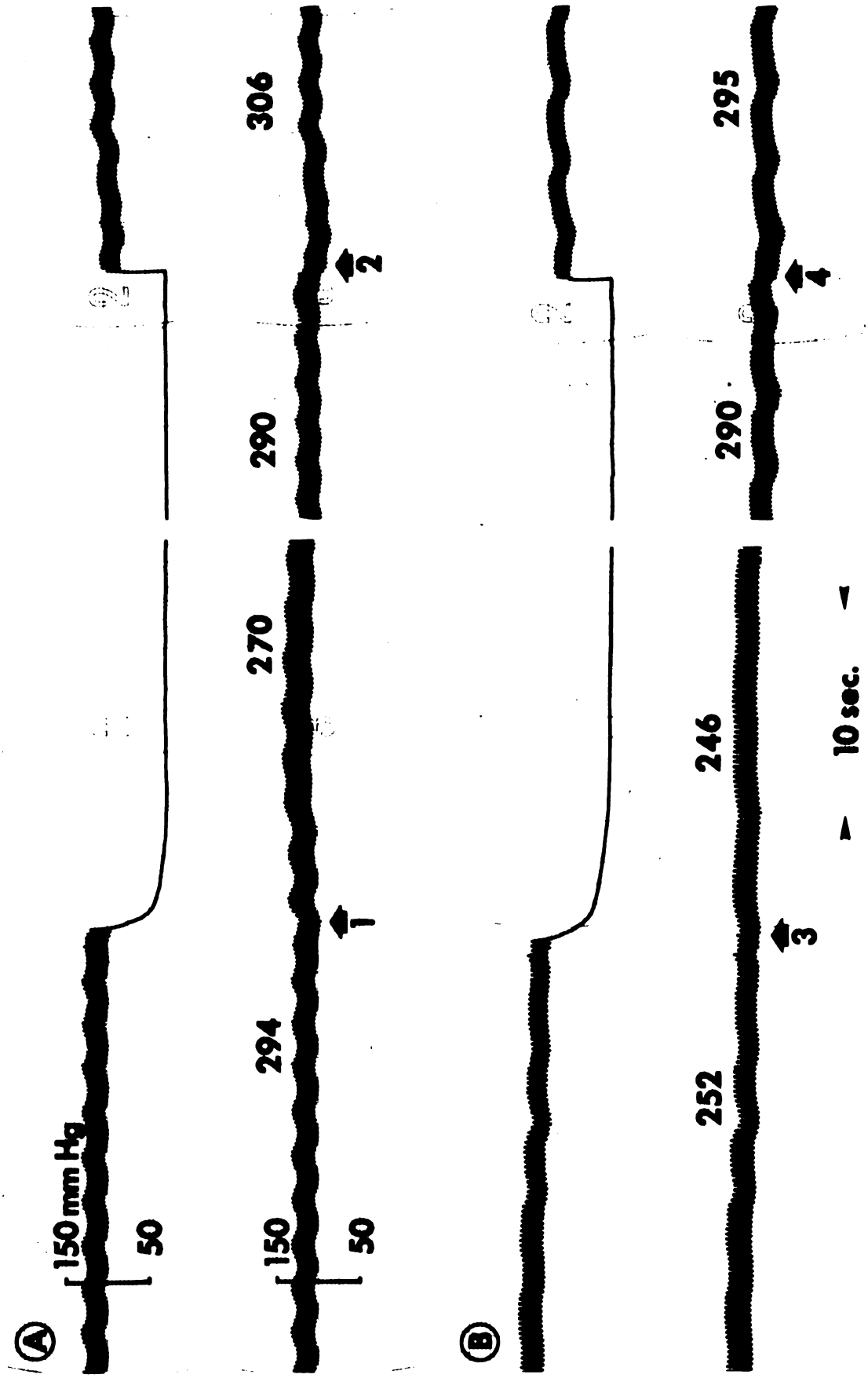

Figure 10.

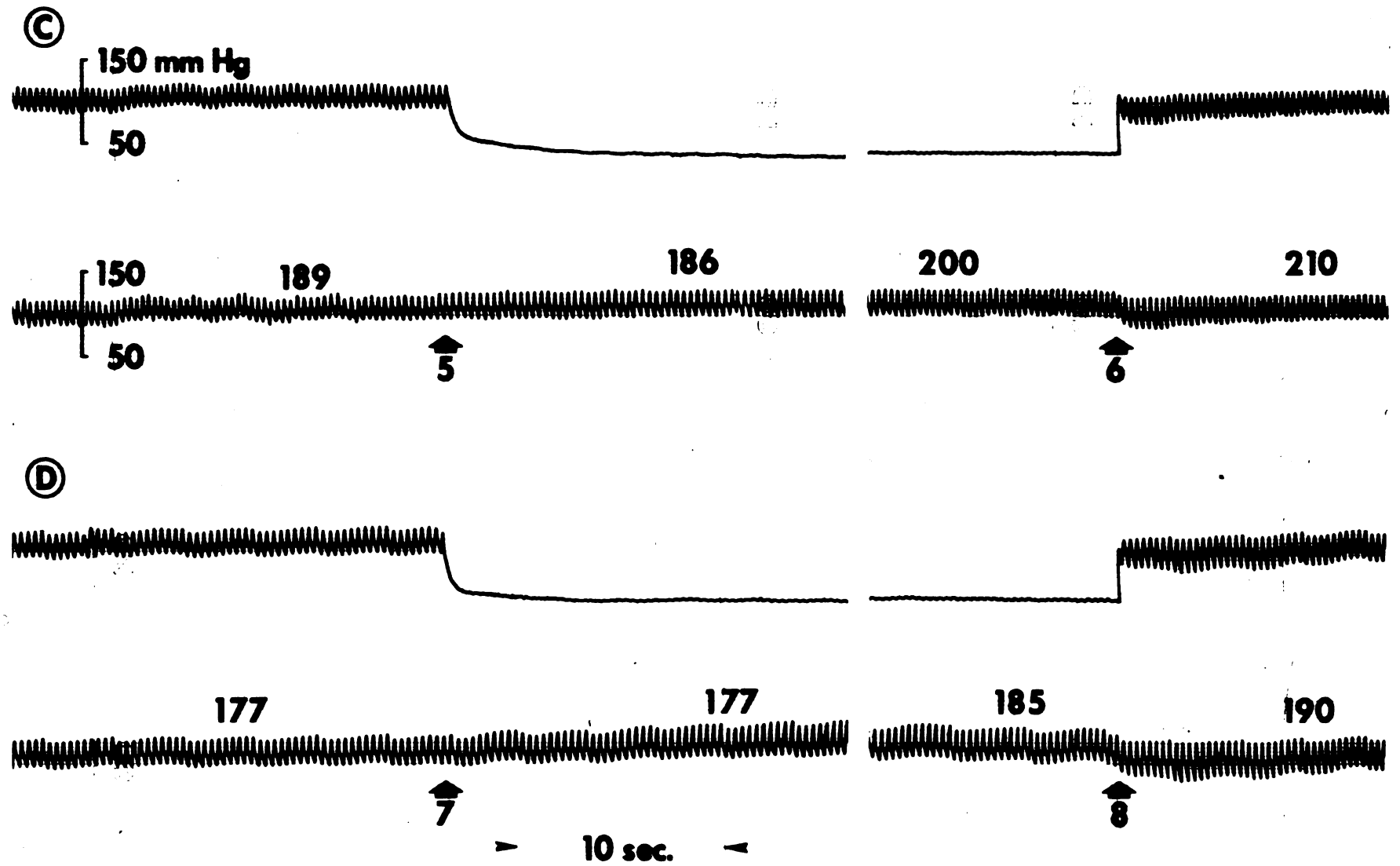

Figure 10 Continued.

DISCUSSION

Effect of Carotid and Vertebral Artery Ligation on Survival, Heart Weight and Body Weight.

The data in Tables 1, 3 and 4 show that ligation of the carotid and vertebral arteries in Leghorn-type hens for two weeks had no significant effect on body weight or heart weight. The hens with both carotids and vertebrals ligated showed a 75 percent survival rate while all other experimental birds showed a 100 percent survival rate. These results indicate that most Leghorn-type hens must have a sufficient and readily available system of collateral circulation to the brain. The extensiveness of the collateral circulation in all probability varies with the individual, and it is this variability that may account for the inability of certain hens to survive ligation.

A comparison of these results with those obtained in experiments with other animals shows considerable differences. Linzell and Waites (1957) found that after tying off both carotid and vertebral arteries in anesthetized goats or sheep the caridac, vasomotor and respiratory centers remained functional only up to one hour. Taylor and Page (1951 a), however, reported that out of eleven dogs in which the vertebral and carotid arteries were ligated, ten lived. They described the dogs as acting stupidly for several days after ligation. The dogs appeared dazed, listless and often not interested in food or drink during this period. It appears, therefore, that the hen is quite tolerant to vertebral and carotid ligation when compared to the sheep, goat and dog. In contrast with the results of Taylor and Page, the hens that underwent carotid and vertebral ligation could not be differentiated from the sham operated birds on the basis of behavior.

If the importance of maintaining a sufficient and constant blood flow to the brain is considered in the light of the fact that 75 percent of the hens with their carotid and vertebral arteries ligated survived for two weeks, the question may be raised as to the necessity for the chicken to have a well-developed carotid pressure regulating system to control cerebral circulation. It would appear that if most hens can survive and undergo normal activity for at least two weeks with the major arteries to the head ligated, the normal hen with all channels of circulation open should certainly be capable of supplying sufficient blood to the brain under almost any condition. Dickinson and McCubbin (1963) add support to this concept since they pointed out that severe cerebral ischemia can occur in man, but in animals other than the giraffe spontaneous cerebral infarction does not commonly occur.

Best and Taylor (1961) indicated that any factor increasing outflow resistance to the heart is capable of causing cardiac hypertrophy. They reported that, based on heart weight to body weight ratios, cardiac hypertrophy has been produced in rats in two days and in dogs in two to three weeks. No cardiac hypertrophy based either on absolute heart weights or per kg. body weight was detected in the experimental hens over a two-week period. This would seem to indicate that the resistance to flow offered by the occluded arteries and the collateral circulation did not present any great stress to the heart. Any neurogenic or central ischemic hypertension which may have resulted from the occlusion apparently did not last long enough to produce cardiac hypertrophy. These results provide further evidence that most hens readily adapt to the loss of the carotid and vertebral blood supply.

Effect of Carotid and Vertebral Artery Occlusion on Blood Pressure, Heart Rate and Respiration.

The results of Experiment IIA shown in Table 2 indicate no great effect on blood pressure, heart rate or respiration upon bilateral occlusion of either the carotid or vertebral arteries in Leghorn-type hens. Occlusion of the carotids produced a small, highly significant increase in systolic, diastolic and mean blood pressures; however, this rise was probably mechanical in nature. Heymans and Neil (1958) pointed out that when the common carotid arteries are occluded after sinus denervation, there is often a rise of a few mm.Hg of mean systemic pressure which is attributed to a reduction in the capacity of the cardiovascular system. In conjunction with the rise in blood pressure a small and highly significant decrease in heart rate was obtained. This may very well have been a baroreceptor effect in response to the mechanical rise of blood pressure. Vertebral artery occlusion usually produced results similar to carotid occlusion. The results in Table 2 show the trends of the various parameters to be in the same direction with either carotid or vertebral occlusion. The differences in statistical significance can be attributed to the difference in the number of birds in each category.

Harvey et al., (1954) reported that the chicken responds poorly to carotid occlusion. They found that only one out of eleven chickens tested produced a blood pressure response greater than 10 mm.Hg with bilateral occlusion of the carotids. These results are in agreement with the findings of this study. The lack of blood pressure response to bilateral carotid occlusion in the chicken is in marked contrast to the usual increase of 20 or more mm.Hg found in mammals under similar

conditions. The difference in response is, of course, due to the carotid sinus reflex in the mammal. The sinus homologue in the chicken is reportedly located in the thoracic cavity (Adams, 1958). Harvey et al. occluded the carotids mid-cervically while occlusion in this study was accomplished at a point considered to be immediately cranial to the area of the sinus homologue. Under these conditions of occlusion the sinus homologue was not tested for a pressure function, but it appeared that from the level of the carotid and vertebral bifurcation up to and including the head there were no functional baroreceptors present.

Occlusion of both the carotids and vertebrals, however, produced a large and highly significant increase in systolic, diastolic, pulse and mean blood pressures. In addition, there was a small, non-significant increase in heart rate and a highly significant decrease in respiration. These results show increased sympathetic activity produced by the occlusion. The maximal blood pressure effects were transient in nature and showed a highly significant decrease from one to two minutes after occlusion, although the two minute levels of blood pressure were still highly significantly greater than contol values. A highly significant decrease in heart rate was also observed from one to two minutes after occlusion. The blood pressure and heart rate changes appear to represent a decrease in sympathetic activity.

The blood pressure effects observed with carotid and vertebral occlusion were believed to be caused by cerebral ischemia. The transiency of the maximal effects was probably the result of the increased systemic blood pressure forcing blood through collateral channels to the head and relieving the ischemia. The time delay between occlusion and the

maximum blood pressure effect may indicate a period of accumulating effects of ischemia (Fig. 2). The slowing of the heart rate observed in Figure 2 at the peak of the blood pressure rise may be indicative of a baroreceptor response initiated from some area located caudal to the clamps. This type of response was not infrequently obtained.

The slowing of respiratory rate with carotid and vertebral occlusion adds further evidence to the belief that ischemia is responsible for the blood pressure effects. Sturkie (1954) and Fedde et al., (1963 b) report the fact that increased carbon dioxide tension in the blood of the chicken results in decreased rate of respiration. This response is opposite to the hyperpnea normally obtained in the mammal.

The measurement of cerebral pressure by the craniad cannulation of a carotid artery provided an indication of the effect of carotid and vertebral occlusion on cerebral perfusion pressure. The results of Experiment III shown in Table 5 again indicate a decrease in heart rate and little effect on blood pressure with bilateral carotid occlusion; however, there was a highly significant decrease of 28 percent in cerebral pressure during the first minute after occlusion. It would appear that if there were any functional baroreceptors in the head or at the bifurcation of the carotid into the internal and external carotids, a sympathetic response should have occurred with a drop in cerebral pressure of this magnitude. Occlusion of both carotids and vertebrals resulted in a large and highly significant increase in systolic, diastolic and mean systemic blood pressures. There was a highly significant decrease of 64 percent in cerebral pressure and a highly significant decrease in respiratory rate. A 64 percent decrease in cerebral pressure should certainly be indicative of decreased cerebral

blood flow, although this could only be verified by measurement with a flowmeter. Cerebral ischemia probably resulted and caused the sympathetic response in blood pressure. The increased systemic pressure must have provided more blood to the head via collateral circulation since cerebral pressure increased 13 percent by two minutes after occlusion; thus, the ischemia would have been partially relieved and this allowed the systemic blood pressure to decrease by 11 percent at two minutes after occlusion.

Rodbard and Saiki (1952) hypothesized baroreceptors in the head of the chicken which respond not only to blood pressure but also to intracranial pressure. They said that the baroreceptors would operate as differential manometers and respond to variations in the difference between intracranial and arterial pressures. They indicated that these receptors are probably similar in structure and function to the pressoreceptors of the carotid sinus and when intracranial pressure is raised the greater pressure acting outside the arterial wall of the baroreceptor would produce the same effect as if the blood pressure had been reduced. Impulses from the baroreceptor would then pass to the vasomotor center and be interpreted as a fall in blood pressure. It would appear, however, that if increased intracranial pressure acted on the outside of the arterial wall of the hypothetical baroreceptor there would be a deformation of the wall rather than a uniform reduction in the vessel diameter. Such a deformation of the arterial wall would be expected to result in a stimulation of the baroreceptors and cause a reflex reduction in systemic pressure rather than a rise. The results of the experiments presently being reported do not support the hypothesis of Rodbard and Saiki since no indication of intracranial baroreceptor activity

was found.

Table 6 (Experiment IV) shows the results of the intracarotid injection of hypercapnic and hyperoxygenated blood. A small, non-significant rise in systemic blood pressure occurred with the injection of oxygenated blood. This was accompanied by a highly significant decrease in heart rate which may have been the result of peripheral baroreceptor activity responding to the small blood pressure rise. The injection of hypercapnic blood produced large and highly significant increases in systolic, diastolic, pulse and mean systemic pressures. The pattern of response was very similar to that obtained by occlusion of the carotid and vertebral arteries. This provided further support for the concept that cerebral ischemia was responsible for the sympathetic responses obtained with occlusion of the carotid and vertebral arteries. It is seen in these results that cerebral pressure appeared to vary directly with systemic blood pressure; thus, the results obtained with the injection of hypercapnic blood were not associated with a decrease in cerebral pressure as was the case during occlusion of the carotids and vertebrals.

The data in Table 7 (Experiment IV) show that hens with both carotid arteries and the left vertebral artery ligated at the beginning of experimentation did not, on the average, show a great blood pressure response when occlusion of the right vertebral artery was accomplished. These results were in contrast to the usual results previously obtained when both vertebrals and carotids were periodically occluded in hens. The fact that cerebral pressure decreased only to an average of 36 mm.Hg after right vertebral artery occlusion indicated that collateral circulation apparently was supplying blood to the head. This probably resulted

from leaving both carotids and one vertebral artery ligated from the beginning to the end of each experiment. The data shown in Table 5 indicate that a cerebral pressure of approximately 26 mm.Hg was necessary to produce the large blood pressure response obtained in Experiment III. Although occlusion of the right vertebral artery produced a highly significant decrease of 43 percent in cerebral pressure in Experiment IV, no significant change in systemic blood pressure resulted. A consideration of the cerebral pressure data obtained in Experiments III and IV seemed to indicate that the systemic blood pressure response to carotid and vertebral occlusion depended on the level to which the cerebral pressure dropped rather than on how much it dropped. When the individual data of these two experiments were plotted on a scatter diagram (Fig. 8) it appeared that a systemic blood pressure response began to occur when cerebral pressure decreased to approximately 30 to 35 mm.Hg. If the data of Table 5 are considered again, it is seen that control cerebral pressure is approximately 66 percent of control systemic blood pressure. Thus, if cerebral pressure varies directly with systemic pressure, as is indicated in Figure 4, it may be assumed that 30 to 35 mm.Hg of cerebral pressure are approximately equal to cerebral perfusion pressures of 45 to 53 mm.Hg. Guyton (1961) indicated that decreasing arterial pressure to as low as 60 mm.Hg does not normally decrease cerebral blood flow because of local autoregulation; however, he further indicated that if arterial pressure falls below 60 mm.Hg and especially below 30 to 50 mm.Hg, the cerebral tissues become ischemic and the central nervous system ischemic reflex occurs. The computed values of cerebral perfusion pressure at which a systemic blood pressure response was obtained in the chicken agree very nicely with the levels

reported by Guyton which produce an ischemic response in the mammal. These data provide strong evidence that blood pressure responses obtained by vertebral and carotid occlusion in the hen are the result of cerebral ischemia and not pressure reflexes from the head or bifurcation of the internal and external carotid arteries.

Further support for the lack of baroreceptor activity in the head or carotid bifurcation is found in Figure 9. The application of high levels of pulsatile arterial pressure to the head via the carotid artery produced no apparent reflex baroreceptor effects on systemic blood pressure. The pressure applied was measured by a cranial cannulation of the contralateral carotid artery; thus, considering the previous discussion, it can be seen that the pressure level measured was probably only about 66 percent of the actual pressure applied to the head.

Effect of Unilateral Vagotomy and Brachiocephalic Artery Occlusion on Blood Pressure, Heart Rate and Respiration.

The results of Experiment V shown in Tables 8A and 8B indicate that unilateral brachiocephalic artery occlusion with or without contralateral vagotomy has little effect on systemic blood pressure (Fig. 10). If the carotid sinus homologue and carotid bodies of the chicken are innervated by the vagus nerve, as is reported in the literature (Adams, 1958), the results of this study appear to demonstrate a lack of a carotid sinus reflex in the hen. Central cannulation of the carotid artery on the side in which the carotid sinus was to be tested provided a measurement of intrasinus pressure. Sectioning the contralateral vagus denervated the carotid sinus and carotid body of that side. Occlusion of the brachiocephalic artery on the innervated side decreased the intrasinus pressure more than 75 percent of control systemic pressure

while normal blood pressure was maintained through the denervated carotid. In all cases it was found that regardless of which vagus was cut or which brachiocephalic occluded, blood pressure usually increased several mm.Hg but always returned to near control values before desocclusion of the arteries. Occlusion of the brachiocephalic arteries produced no significant changes in any parameter measured. An intrasinus pressure decrease of more than 75 percent of the control for a period of time averaging more than a minute in length would certainly be expected to produce a significant effect on systemic blood pressure and heart rate if a pressure reflex mechanism were active in the area of the sinus homologue. The fact that systemic pressure returned to near control values before the clamp was removed from the brachiocephalic artery lends further support to this view. It would also appear that if the carotid body in the chicken were an active chemoreceptor, it would have produced a systemic pressure response as a result of the drastically reduced blood flow resulting from brachiocephalic occlusion. The results of this study agree with those of Durfee (1964) in that no pressure reflexogenic areas were found associated with the carotid artery in the chicken.

SUMMARY

1. Permanent ligation of the carotid, vertebral and carotid and vertebral arteries in Leghorn-type hens for a period of two weeks produced no significant differences in body weight or heart weight. A 100 percent survival rate was obtained in all hens except those in which both the carotids and vertebrals were ligated. In this group 75 percent of the birds survived. These results appeared to indicate that (1) no cardiac hypertrophy developed as a result of the ligations; (2) survival depended on collateral circulation to the head and was a function of the individuality of each bird in the amount of collateral circulation available; (3) and no apparent brain damage occurred from the ligation as evidenced by normal behavior and no significant loss of body weight in the survivors. These data show that most hens can survive and undergo normal activity for at least two weeks with the major arteries to the head ligated. In view of these results, a well-developed carotid pressure regulating system to protect cerebral circulation would not seem to be mandatory in the chicken. The ability of most hens to adapt to the loss of the carotid and vertebral blood supply indicated that the patency of these vessels is not an absolute necessity for survival or the maintenance of normal cerebral function.

2. Bilateral occlusion of the carotid arteries at the carotid-vertebral bifurcation in Leghorn-type hens produced a small, highly significant increase of 4 percent in systemic blood pressure and a highly significant decrease of 3 percent in heart rate. Occlusion of both the carotids and vertebrals produced a large, highly significant increase of 31 percent in systemic blood pressure, a non-significant increase of 8 percent in heart rate and a highly significant decrease of 22 percent

in respiration.

Cerebral blood pressure was measured in hens by cannulating a carotid artery craniad. It was found that bilateral carotid occlusion produced a highly significant decrease of 28 percent in cerebral pressure while only a small, non-significant rise of 1 percent in systemic blood pressure was obtained. Occlusion of both vertebrals and carotids produced a highly significant decrease of 64 percent in cerebral pressure immediately followed by a highly significant increase of 33 percent in systemic blood pressure and a highly significant decrease of 25 percent in respiratory rate. These data seem to indicate a lack of baroreceptor activity in the hen from the level of the carotid-vertebral bifurcation up to and including the head. The large systemic blood pressure response obtained with carotid and vertebral occlusion was attributed to cerebral ischemia. Analysis of individual data indicated that systemic blood pressure responses began to occur only when cerebral perfusion pressure was decreased to 45 to 53 mm.Hg by arterial occlusion. This is considerably lower than control systemic arterial blood pressure.

The direct application of high, pulsatile arterial pressure into one carotid of hens produced no reflex effect on systemic blood pressure or heart rate. This indicated a lack of intracranial baroreceptors. The intracarotid injection of small quantities of hypercapnic blood produced a pattern of response similar to that obtained with carotid and vertebral occlusion. This provided further support to the concept of cerebral ischemia.

The results of these experiments indicated a lack of reflex baroreceptor activity in the head or in the carotid artery cranial to the

carotid-vertebral bifurcation.

3. Unilateral brachiocephalic artery occlusion with contralateral vagotomy was accomplished to test for pressoreceptor reflexes from the area of the carotid artery homologous to the mammalian carotid sinus. Occluding a brachiocephalic artery removed approximately 75 percent of the arterial pressure from the area of the ipsilateral carotid artery homologous to the mammalian sinus. This pressure change was measured by cannulating the carotid artery centrally in the cervical region. Sectioning the contralateral vagus removed the primary innervation of the carotid sinus homologue and carotid body on that side; thus, only the single innervated carotid artery was subjected to pressure change. This procedure was accomplished with each carotid artery. No significant effects on systemic blood pressure, heart rate or respiration were obtained as a result of brachiocephalic occlusion either before or after vagotomy.

The carotid sinus homologue in the Leghorn-type hen did not appear to possess a baroreceptor function; therefore, it is doubtful that this structure functions in blood pressure regulation as does the carotid sinus in mammals.

LITERATURE CITED

Adams, W. E., 1958. The Comparative Morphology of The Carotid Body and Carotid Sinus. C. C. Thomas, Springfield, Illinois.

Agostoni, E., J. E. Chinnock, M. de Burgh Daly and J. G. Murray, 1957. Functional and histological studies of the vagus nerve and its branches to the heart, lungs and abdominal viscera in the cat. J. Physiol. 135:182-205.

Anrep, G. V., and H. N. Segall, 1926. The central and reflex regulation of the heart rate. J. Physiol. 61:215-231.

Ara, G., 1934. Arch Fisiol. 33:332. (as cited by Heymans and Neil, 1958).

Aviado, D. M., Jr., T. H. Li, W. Kalow, C. F. Schmidt, G. L. Turnbull, G. W. Peskin, M. E. Hess and A. J. Weiss, 1951. Respiratory and circulatory reflexes from the perfused heart and pulmonary circulation of the dog. Am. J. Physiol. 165:261-277.

Aviado, D. M., Jr., and C. F. Schmidt, 1955. Reflexes from stretch receptors in blood vessels, heart and lungs. Physiol. Rev. 35:247-300.

Aviado, D. M., Jr., C. F. Schmidt, 1959. Cardiovascular and respiratory reflexes from the left side of the heart. Am. J. Physiol. 196:726-730.

Bainbridge, F. A., 1915. The influence of venous filling upon the rate of the heart. J. Physiol. 50:65-84.

Bayliss, W. M., 1893. On the physiology of the depressor nerve. J. Physiol. 14:303-325.

Bernthal, T., W. Greene, Jr. and A. M. Revzin, 1951. Role of carotid chemoreceptors in hypoxic cardiac acceleration. Proc. Soc. Exp. Biol. Med. 76:121-124.

Best, C. H., and N. B. Taylor, 1961. The Physiological Basis of Medical Practice. The Williams and Wilkins Co., Baltimore.

Binswanger, O., 1879. Anatomische Untersuchungen über die Ursprungsstelle und den Anfangstheil der Carotis interna. Arch. Psychiat. Nervenkr. 9:351-368. (as cited by Heymans and Neil, 1958).

Booth, N. H., H. E. Bredeck and R. A. Herin, 1960. Baroceptor reflex mechanisms in swine. Am. J. Physiol. 199:1189-1191.

Boss, J., and J. H. Green, 1954. Nervous structures in recently described baroceptor areas of the right common carotid artery in the cat. J. Physiol. 124:43P-44P.

Boss, J., and J. H. Green, 1956. The histology of the common carotid baroreceptor areas of the cat. Circ. Res. 4:12-17.

Brind, S. H., J. R. Bianchine and M. N. Levy, 1956. Effect of bilateral carotid occlusion of common carotid arteries on cardiac output and oxygen content of arterial and venous blood in the anesthetized dog. Am. J. Physiol. 185:483-486.

Brodie, T. G., and A. E. Russell, 1900. On reflex cardiac inhibition. J. Physiol. 26:92-106.

Bronk, D. W., and G. Stella, 1932. Afferent impulses in the carotid sinus nerve. I. The relation of the discharge from single end organs to arterial blood pressure. J. Cell. Comp. Physiol. 1:113-130.

Bronk, D. W., and G. Stella, 1935. The response to steady pressures of single end organs in the isolated carotid sinus. Am. J. Physiol. 110:708-714.

Busachi, P., 1912. Arch. ital. Anat. Embriol. 11:352. (as cited by Heymans and Neil, 1958).

Chowdhary, D. S., 1953. A Comparative Study of the Carotid Body and Carotid Sinus of Vertebrates. II. The carotid body and "carotid sinus" of the fowl (Gallus domesticus). Doctorate thesis, Edinburgh. 58 pp.

Coleridge, J. C. G., and C. Kidd, 1959. Receptors in the pulmonary artery. J. Physiol. 147:20P.

Coleridge, J. C. G., and C. Kidd, 1960. Electrophysiological evidence of baroreceptors in the pulmonary artery of the dog. J. Physiol. 150:319-331.

Coleridge, J. C. G., and C. Kidd, 1961. Relationship between pulmonary arterial pressure and impulse activity in pulmonary arterial baroreceptor fibers. J. Physiol. 158:197-205.

Coleridge, J. C. G., and C. Kidd, 1963. Reflex effects of stimulating baroreceptors in the pulmonary artery. J. Physiol. 166:197-210.

Comroe, J. H., Jr., and C. F. Schmidt, 1938. The part played by reflexes from the carotid body in the chemical regulation of respiration in the dog. Am. J. Physiol. 121:75-97.

Cooper, A. P., 1836. Guy's Hosp. Rep. 1:457. (as cited by Heymans, 1957).

Cyon, E. V., and C. F. Ludwig, 1866. Arb. Physiol. Inst. Leipzig 1:128. (as cited by Heymans, 1957).

Daly, M. de Burgh, and M. J. Scott, 1958. The effects of stimulation of the carotid body chemoreceptors on heart rate in the dog. J. Physiol. 144:148-166.

Daly, M. de Burgh, and M. J. Scott, 1962. An analysis of the primary cardiovascular reflex effects of stimulation of the carotid body chemoreceptors in the dog. J. Physiol. 162:555-575.

Daly, I. de Burgh, and E. B. Verney, 1926. Cardiovascular reflexes. J. Physiol. 61:268-274.

De Castro, F., 1926. Trab. lab. Invest. biol. Univ. Madrid 24:365. (as cited by Heymans and Neil, 1958).

De Castro, F., 1928. Trab. lab. Invest. biol. Univ. Madrid 25:331. (as cited by Heymans and Neil, 1958).

De Castro, F., 1951. Acta physiol. Scand. 22:14. (as cited by Heymans and Neil, 1958).

Diamond, J., and A. Howe, 1955. A study of certain aortic bodies in the cat. J. Physiol. 128:76P-77P.

Diamond, J., and A. Howe, 1956. Chemoreceptor activity in the aortic bodies of the cat. J. Physiol. 134:319-326.

Dickinson, C. J., 1950. Afferent nerves from the heart region. J. Physiol. 111:399-407.

Dickinson, C. J., and J. W. McCubbin, 1963. Pressor effect of increased cerebrospinal fluid pressure and vertebral artery occlusion with and without anesthesia. Circ. Res. 12:190-202.

Douglas, W. W., I. R. Innes and H. W. Kosterlitz, 1948. Pressor responses caused by electrical stimulation of the vagus and sinus nerves in the cat anesthetized with Nembutal. J. Physiol. 107:48P.

Douglas, W. W., and J. M. Ritchie, 1956. Cardiovascular reflexes produced by electrical excitation of non-medullated afferents in the vagus, carotid sinus and aortic nerves. J. Physiol. 134:167-168.

Douglas, W. W., J. M. Ritchie and W. Schaumann, 1956 a. Depressor reflexes from medullated and non-medullated fibres in the rabbits aortic nerve. J. Physiol. 132:187-198.

Douglas, W. W., J. M. Ritchie and W. Schaumann, 1956 b. A study of the effect of the pattern of electrical stimulation of the aortic nerve of the reflex depressor responses. J. Physiol. 133:232-242.

Douglas, W. W., and W. Schaumann, 1956. A study of the depressor and pressor components of the cat's carotid sinus and aortic nerves using electrical stimuli of different intensities and frequencies. J. Physiol. 132:173-186.

Downing, S. E., J. H. Mitchell and A. G. Wallace, 1963. Cardiovascular responses to ischemia, hypoxia, and hypercapnia of the central nervous system. Am. J. Physiol. 204:881-887.

Downing, S. E., and J. H. Siegel, 1963. Baroreceptor and chemoreceptor influences on sympathetic discharge to the heart. Am. J. Physiol. 204:471-479.

Drüner, L., 1925. Ueber die anatomischen Unterlagen der Sinusreflexe Herings. Dtsch. med. Wschr. 51:559-560. (as cited by Adams, 1958).

Duke, H. N., J. H. Green, P. F. Heffron and V. W. J. Stubbens, 1963. Pulmonary chemoreceptors. Quart. J. Exp. Physiol. 48:164-175.

Duke, H. N., J. H. Green and E. Neil, 1952. Carotid chemoceptor impulse activity during inhalation of carbon monoxide mixtures. J. Physiol. 118:520-527.

Durfee, W. K., 1964. Cardiovascular reflex mechanisms in the fowl. Diss. Abst. 24:2966.

Durfee, W. K., and P. D. Sturkie, 1963. Some cardiovascular responses to anoxia in the fowl. Fed. Proc. 22:182. (abs.)

Ead, H. W., J. H. Green and E. Neil, 1952. A comparison of the effects of pulsatile and non-pulsatile blood flow through the carotid sinus on the reflexogenic activity of the sinus baroceptors in the cat. J. Physiol. 118:509-519.

Eyster, A. E., and D. R. Hooker, 1908. Direct and reflex response of the cardio-inhibitory centre to increased blood pressure. Am J. Physiol. 21:373-399.

Fedde, M. R., R. E. Burger and R. L. Kitchell, 1963 a. The effect of anesthesia and age on respiration following bilateral, cervical vagotomy in the fowl. Poultry Sci. 42:1212-1223.

Fedde, M. R., R. E. Burger and R. L. Kitchell, 1963 b. Localization of vagal afferents involved in the maintenance of normal avian respiration. Poultry Sci. 42:1224-1236.

Fu, S. K., T. Y. Chen and K. T. Tcheng, 1962. Studies on the glomera aortica of the great reed warbler and the von Schrenck's little bittern. Acta Zool. Sinica 13:297. (as cited by Tcheng and Fu, 1963).

Gammon, G. D., and D. W. Bronk, 1935. The discharge of impulses from Pacinian corpuscles in the mesentery and its relation to vascular changes. Am. J. Physiol. 114:77-84.

Gann, D. S., and F. C. Barter, 1959. Buffer function of the nerves arising at the thyrocarotid arterial junction in the dog. Am. J. Physiol. 197:1229-1232.

Gerard, M. W., and P. R. Billingsley, 1923. Anat. Rec. 25:391. (as cited by Heymans and Neil, 1958).

Green, J. H., 1953. A new baroceptor area in the cat. J. Physiol. 122:70P.

Green, J. H., 1954. Further baroceptor areas associated with the right common carotid artery in the cat. J. Physiol. 123:41P-42P.

Green, J. H., C. Heymans and E. Neil, 1958. The effects of topical application of drugs to the wall of the empty carotid sinus on baroreceptor impulse activity. J. Physiol. 142:59P.

Gruhzit, C. C., W. A. Freyburger and G. K. Moe, 1954. The nature of the reflex vasodilatation induced by epinephrine. J. Pharmacol. Exp. Therap. 112:138-150.

Guyton, A. C., 1961. Textbook of Medical Physiology. W. B. Saunders Company, Philadelphia and London.

Hales, S., 1733. An account of some hydraulic and hydrostatical experiments made on the blood and blood vessels of animals. In F. A. Willius and T. E. Keys, Classics of Cardiology. Henry Schuman, Inc., Dover Publications, Inc., New York, 1961.

Ham, A. W., and T. S. Leeson, 1961. Histology. J. B. Lippincott Company Philadelphia and Montreal.

Harvey, S. C., E. G. Copen, D. W. Eskelson, S. R. Graff, L. D. Poulsen and D. L. Rasmussen, 1954. Autonomic pharmacology of the chicken with particular reference to adrenergic blockade. J. Pharmacol. Exp. Therap. 112:8-22.

Harvey, W., 1628. Exercitatio anatomica de motu cordis et sanguinis in animalibus. In F. A. Willius and T. E. Keys, Classics of Cardiology. Translated by R. Willis, 1847. Henry Schuman, Inc., Dover Publications, Inc., New York, 1961.

Henry, J. P., and J. W. Pearce, 1956. The possible role of cardiac atrial stretch receptors in the induction of changes in urine flow. J. Physiol. 131:572-585.

Hering, H. E., 1923. Der Karotisdruckversuch. Münch. med. Wschr. 70:1287-1290. (as cited by Adams, 1958).

Hering, H. E., 1924 a. Der Sinus caroticus an der Ursprungsstelle der Carotis interna als Ausgangsort eines hemmenden Herzeflexes und eines depressorischen Gefässreflexes. Münch. med. Wschr. 71:701-704. (as cited by Adams, 1958).

Hering, H. E., 1924 b. Die Sinusreflexe vom Sinus caroticus werden durch einen Nerven (Sinusnerv) vermittelt, der ein Ast des Nervus glossopharyngeus ist. Münch. med. Wschr. 71:1265-1266. (as cited by Adams, 1958).

Heymans, C., 1957. Baroreceptors and blood pressure homeostasis. In J. McMichael (ed.), Circulation, A Symposium, II. Hameodynamics, pp. 116-124. C. C. Thomas, Springfield, Illinois.

Heymans, C., 1963. A look at an old but still current problem. Ann. Rev. Physiol. 25:1-14.

Heymans, C., and A. L. Delaunois, 1955. Action of nor-epinephrine on carotid sinus arterial walls and blood pressure. Proc. Soc. Exp. Biol. Med. 89:597-598.

Heymans, C., A. L. Delaunois and G. van den Heuvel-Heymans, 1953. Tension and distensibility of carotid sinus wall, pressoreceptors and blood pressure regulation. Circ. Res. 1:3-7.

Heymans, C., G. R. de Vleeschhouwer and G. van den Heuvel-Heymans, 1951. Adrenolytic drug and action of adrenaline and noradrenaline on carotid sinus. Arch. int. Pharmacodyn. 85:188-193.

Heymans, C., and E. Neil, 1958. Reflexogenic Areas of the Cardiovascular System. J. and A. Churchill Ltd., London.

Heymans, C., and R. Pannier, 1945. Presso-receptors of the carotid sinus and respiration. J. Physiol. 104:40P-41P.

Heymans, C., and G. van den Heuvel-Heymans, 1950. Action of drugs on arterial wall of carotid sinus and blood pressure. Arch. int. Pharmacodyn. 83:520-528.

Heymans, C., and G. van den Heuvel-Heymans, 1951. New aspects of blood pressure regulation. Circ. 4:581-586.

Hollenberg, N. K., and B. Uvnäs, 1963. The role of the cardiovascular response in the resistance to asphyxia of avian divers. Acta physiol. Scand. 58:150-161.

Holt, J. P., W. J. Rashkind, R. Bernstein and J. C. Greisen, 1946. The regulation of arterial blood pressure. Am. J. Physiol. 146:410-421.

Hornbein, T. F., Z. J. Griffo and A. Roos, 1961. Quantitation of chemoreceptor activity: The interrelation of hypoxia and hypercapnia. J. Neurophysiol. 24:561-568.

Hornbein, T. F., and A. Roos, 1963. Specificity of H ion concentration as a carotid chemoreceptor stimulus. J. Appl. Physiol. 18:580-584.

Howe, A., 1956. The vasculature of the aortic bodies in the cat. J. Physiol. 134:311-318.

Jarisch, A., and Y. Zotterman, 1948. Depressor reflexes from the heart. Acta physiol. Scand. 16:31-51.

Jung, F., 1934. Physiologische Versuche über Pressorezeptoren an der Karotisteilungsstelle bei Vögeln. Z. Kreislaufforsch 26:328-334. (as cited by Adams, 1958).

Kaufmann, P., 1912. Pflüg. Arch. ges. Physiol. 146:231; 147:35. (as cited by Heymans, 1957).

Kenney, R. A., and E. Neil, 1951. The contribution of aortic chemoceptor mechanisms to the maintenance of arterial blood pressure of cats and dogs after haemorrhage. J. Physiol. 112:223-228.

Kenney, R. A., E. Neil and A. Schweitzer, 1951. Carotid sinus reflexes and cardiac output in dogs. J. Physiol. 114:27-40.

Kezdi, P., 1962. Mechanism of the carotid sinus in experimental hypertension. Circ. Res. 11:145-152.

Kisch, B., and S. Sakai, 1923. Pflüg. Arch. ges. Physiol. 198:65,86. (as cited by Heymans, 1957).

Kose, W., 1902. Ueber das Vorkommen einer "Carotisdrüse" und der "chromaffinen Zellen" bei Vögeln. Nebst Bemerkungen über die Kiemenspaltenderivate. Anat. Anz. 22:162-170. (as cited by Adams, 1958).

Kose, W., 1904. Ueber die "Carotisdrüse" und das "chromaffine Gewebe" der Vögel. Anat. Anz. 25:609-617. (as cited by Adams, 1958).

Kose, W., 1907. Die Paraganglien bei den Vögeln. Zweiter Teil. Arch. mikr. Anat. 69:665-790. (as cited by Adams, 1958).

Köster, G., and A. Tschermak, 1902 a. Archiv für Anatomie und Physiologie, Anatomische Abtheilung, Supplement, p. 255. (as cited by Eyster and Hooker, 1908).

Köster, G., and A. Tschermak, 1902 b. Archiv für die gesammte Physiologie. XCiii:24-38. (as cited by Eyster and Hooker, 1908).

Landgren, S., 1952 a. On the excitation mechanism of the carotid baroceptors. Acta physiol. Scand. 26:1-34.

Landgren, S., 1952 b. The baroreceptor activity in the carotid sinus nerve and the distensibility of the sinus wall. Acta physiol. Scand. 26:35-56.

Landgren, S., and E. Neil, 1951. Chemoreceptor impulse activity following haemorrhage. Acta physiol. Scand. 23:158-167.

Landgren, S., E. Neil and Y. Zotterman, 1952. The response of the carotid baroreceptors to the local administration of drugs. Acta physiol. Scand. 25:24-37.

Linzell, J. L., and G. M. H. Waites, 1957. The effects of occluding the carotid and vertebral arteries in sheep and goats. J. Physiol. 138:20P.

Ludwig, C., 1847. Beitrage zur Kenntnis des Einflusses der Respirations Bewegung auf den Blutlauf im Aortensystem. Arch. Anat. Physiol., Leipzig, p. 242. (as cited by Neil, 1962).

Ludwig, C. F., and E. V. Cyon, 1866. Die Reflexe eines der sensiblen Nerven des Herzens auf die motorischen Nerven der Blutgefässe. Ber. der Sächs. Ges. der Wissenshaften. (as cited by Bayliss, 1893).

Lyonnet, J. H., 1941. Corpusculo carotideo. Contribución a su estudio anatómico, anátomotopográfico y quirúrgico. Arch. Soc. argent. Anat. 3:125-138. (as cited by Adams, 1958).

Magendie, F., 1838. Lecons sur les phénomènes physiques de la vie, Vol. 3. Brussels. (as cited by Heymans, 1957).

Marey, E. J., 1876-8. La circulation du sang. Paris: Masson. (as cited by Heymans, 1957).

Matton, G., 1957. Pharmacological actions on the carotid sinus baro-receptors in arterial hypertension. Arch. int. Pharmacodyn. 110:472-491.

McCubbin, J. W., J. H. Green and I. H. Page, 1956. Baroceptor function in chronic renal hypertension. Circ. Res. 4:205-210.

Muratori, G., 1932. Contributo all'innervazione del tessuto paragangliare annesso al sistema del vago (glomo carotico, paragangli estravagali ed intravagali) e all'innervazione del seno carotideo. Anat. Anz. 75:115-123. (as cited by Adams, 1958).

Muratori, G., 1933. Ricerche istologiche sull'innervazione del glomo carotico. Arch. ital. Anat. Embiol. 30:573-602. (as cited by Adams, 1958).

Muratori, G., 1934. Contributo istologico all'innervazione della zona arteriosa glomo-carotidea. Arch. ital. Anat. Embriol. 33:421-442. (as cited by Adams, 1958).

Nash, R. A., 1926. Concerning the part played by the sinus caroticus in the central regulation of the circulation. J. Physiol. 61:28P.

Neil, E., 1956 a. Reflex responses elicited in the cat by perfusion of the root of the right subclavian artery. Arch. int. Pharmacodyn. 105:468-476.

Neil, E., 1956 b. Influence of the carotid chemoreceptor reflexes on the heart rate in systemic anoxia. Arch. int. Pharmacodyn. 105: 477-488.

Neil, E., 1960. Afferent impulse activity in cardiovascular receptor fibers. Proc. of Symp. on Central Nervous System Control of Circulation. Amer. Physiol. Soc., Physiol. Rev. Sup. No. 4.

Neil, E., 1962. Neural factors responsible for cardiovascular regulation. Circ. Res. 11:137-143.

Neil, E., C. R. M. Redwood and A. Schweitzer, 1949 a. Pressor responses to electrical stimulation of the carotid sinus nerve in cats. J. Physiol. 109:259-271.

Neil, E., C. R. M. Redwood and A. Schweitzer, 1949 b. Blood pressure responses to electrical stimulation of the carotid sinus nerve in dogs and rabbits. J. Physiol. 109:281-287.

Neil, E., C. R. M. Redwood and A. Schweitzer, 1949 c. Effects of electrical stimulation of the aortic nerve on blood pressure and respiration in cats and rabbits under chloralose and Nembutal anesthesia. J. Physiol. 109:392-401.

Nonidez, J. F., 1935 a. The presence of depressor nerves in the aorta and carotid of birds. Anat. Rec. 62:47-66.

Nonidez, J. F., 1935 b. The aortic (depressor) nerve and its associated epithelioid body, the glomus aorticum. Am. J. Anat. 57:259-302.

Nonidez, J. F., 1937. Identification of the receptor areas in the venae cavae and pulmonary veins which initiate reflex cardiac acceleration (Bainbridge's reflex). Am. J. Anat. 61:203-232.

Osborne, W. A., 1920. Self-adjustment of blood pressure. J. Physiol. 54:c.

Pagano, G., 1900. Arch. ital. Biol. 23:1. (as cited by Heymans, 1957).

Paintal, A. S., 1953 a. Another atrial receptor. J. Physiol. 119:10P-11P.

Paintal, A. S., 1953 b. A study of right and left atrial receptors. J. Physiol. 120:596-610.

Paintal, A. S., 1953 c. The conduction velocities of respiratory and cardiovascular afferent fibres in the vagus nerve. J. Physiol. 121:341-359.

Paintal, A. S., 1955. A study of ventricular pressure receptors and their role in the Bezold reflex. Quart. J. Exp. Physiol. 40:348-363.

Palme, F., 1934. Z. mikr.-anat. Forsch. 36:391. (as cited by Heymans and Neil, 1958).

Palme, F., 1943. Z. ges. exp. Med. 113:415. (as cited by Landgren et al., 1952).

Penitschka, W., 1931. Z. mikr.-anat. Forsch. 24:24-37. (as cited by Heymans and Neil, 1958).

Poiseuille, J. L., 1828. Recherches sur la Force du Coeur Aortique (thèse). Paris, p. 23. (as cited by Neil, 1962).

Polosa, C., and G. Rossi, 1961. Cardiac output and peripheral blood flow during occlusion of carotid arteries. Am. J. Physiol. 200:1185-1190.

Rodbard, S., and H. Saiki, 1952. Mechanism of the pressor response to increased intracranial pressure. Am. J. Physiol. 163:234-244.

Rodbard, S., and W. Stone, 1955. Pressor mechanisms induced by intracranial compression. Circ. 12:883-890.

Ruch, T. C., and J. F. Fulton (eds.), 1961. Medical Physiology and Biophysics. W. B. Saunders Company, Philadelphia and London.

Sarnoff, S. J., and S. I. Yamada, 1959. Evidence for reflex control of arterial pressure from abdominal receptors with special reference to the pancreas. Circ. Res. 7:325-335.

Schmidt, C. F., 1932. Carotid sinus reflexes to the respiratory center. I. Identification. Am. J. Physiol. 102:94-118.

Schweitzer, A., 1936. Vascular reflexes from the lung. J. Physiol. 87:46P-48P.

Schwiegk, H., 1935. Pflügers Arch. 236:206. (as cited by Schweitzer, 1936).

Selkurt, E. E., and C. F. Rothe, 1960. Splanchnic baroreceptors in the dog. Am. J. Physiol. 199:335-340.

Shäfer, 1877. Ueber die aneurysmatische Erweiterung der Carotis interna an ihrem Ursprung. Allg. Z. Psychiat. 34:438-451. (as cited by Heymans and Neil, 1958).

Siciliano, L., 1900. Arch. ital. Biol. 23:338. (as cited by Heymans, 1957).

Snedecor, G. W., 1956. Statistical Methods. The Iowa State College Press, Ames, Iowa.

Sollman, T., and E. D. Brown, 1912. The blood pressure fall produced by traction on the carotid artery. Am. J. Physiol. 30:88-104.

Sturkie, P. D., 1954. Avian Physiology. Comstock Publishing Associates, A Division of Cornell University Press, Ithaca, New York.

Sturkie, P. D., 1958. A survey of recent advances in poultry physiology. Poultry Sci. 37:495-509.

Sunder-Plassmann, P., 1930. Z. ges. Anat. I. Z. Anat. Entwgesch. 93:567. (as cited by Heymans and Neil, 1958).

Taube, H. W. L., 1743. De Vera Nervi Intercostalia Origine. Inaug. Diss., Gottingae. Gottingae: A. Vandenhoeck. 20 pp. (as cited by Adams, 1958).

Taylor, R. D., and I. H. Page, 1951 a. Production of prolonged arterial hypertension in dogs by chronic stimulation of the nervous system. Exploration of the mechanism of hypertension accompanying increased intracranial pressure. Circ. 3:551-557.

Taylor, R. D., and I. H. Page, 1951 b. Peripheral vasomotor effects of adrenaline and noradrenaline acting upon the isolated perfused central nervous system. Circ. 4:563-575.

Tcheng, K. T., and S. K. Fu, 1962. The structure and innervation of the aortic body of the yellow-breasted bunting. Scientia Sinica 11:221-232.

Tcheng, K. T., S. K. Fu and T. Y. Chen, 1963. Supracardial encapsulated receptors of the aorta and the pulmonary artery in birds. Scientia Sinica 12:73-81.

Tello, J. F., 1924. Trab. lab. Invest. biol., Univ. Madrid 22:295. (as cited by Heymans and Neil, 1958).

van der Linden, P., 1934. Arch. int. Physiol. 40:59. (as cited by Heymans and Neil, 1958).

Whitteridge, D., 1948. Afferent nerve fibres from the heart and lungs in the cervical vagus. J. Physiol. 107:496-512.

Winder, C. V., 1938. Isolation of the carotid sinus pressoreceptive respiratory reflex. Am. J. Physiol. 122:306-318.