Alterations in Carotid Sinus Reflex Control of Arterial Hemodynamics Associated with Experimental Hyperlipemia in the Racing Greyhound

ROBERT H. COX, ROGER J. BAGSHAW, AND DAVID K. DETWEILER

SUMMARY We administered a high cholesterol diet to racing greyhounds and studied its effects on the characteristics of carotid sinus reflex control of arterial pressure-flow relations. Dogs were anesthetized with halothane, and pressure and flow were simultaneously measured in the ascending aorta and the celiac, mesenteric, renal, and iliac arteries. The carotid sinuses were isolated bilaterally and perfused with a physiological salt solution under controlled conditions. The variation of regional pressure-flow relations and regional vascular resistance was assessed as a function of mean carotid sinus pressure (MCSP) with the vagi bilaterally sectioned to eliminate aortic arch afferents. Some differences were found in set point (i.e., MCSP = mean arterial pressure) values of hemodynamic variables; cardiac output and renal and iliac flows were significantly lower. Control and set point values of mean arterial pressure were not significantly different between the two groups. The variation of every hemodynamic variable with the exception of heart rate with carotid sinus pressure was attenuated markedly in the diet-treated dogs. Substantial lesions were found involving the entire carotid sinus region of every diet-fed animal. These results suggest that pathological alterations in the carotid sinus region are at least in part responsible for a reduction in the sensitivity of carotid sinus baroreflexes associated with atherosclerosis.


Based on indirect studies, it generally is considered that a decrease in the sensitivity of arterial baroreceptors occurs with aging and hypertension (Vlachakis et al., 1976; Gribben et al., 1971; Korner et al., 1974; Bristow et al., 1969). Both age and high blood pressure have been implicated as independent contributors to this general decline in baroreceptor sensitivity with advanced age (Vlachakis et al., 1976; Gribben et al., 1971). It has been suggested that atherosclerotic change in the carotid sinus is one of the factors contributing to this reduced reflex sensitivity (Vlachakis et al., 1976; Bristow et al., 1969; Randall et al., 1976). Both morphological and mechanical studies of the carotid sinus in human autopsy samples have indicated atherosclerotic involvement of that anatomical site (Winson et al., 1974; Heath et al., 1973) as well as an increase in the wall stiffness of the carotid sinus (Heaton and Heath, 1976; Angell-James and Lumley, 1974).

Relatively few studies have attempted to define the effects of atherosclerosis on the reflex control of peripheral arterial hemodynamics in terms of direct measurements, of either pressure, flow, or resistance in the arterial system (Rothbaum et al., 1974). Angell-James has performed two studies in rabbits in an attempt to define some of the changes associated with experimental pathophysiology of the aortic arch. In one study, changes in the characteristics of afferent aortic arch baroreceptor mechanisms were found to be associated with vitamin D sclerosis and hypertension in the rabbit (Angell-James, 1974a). These changes consisted of a reduction in afferent nerve activity at a given level of distending pressure in the isolated artificially perfused aortic arch. Also, the sensitivity of afferent nerve discharge with changes in perfusion pressure (i.e., the slope) was reduced in the treated animals. In a subsequent study on effects of long-term high lipid intake, she found similar alterations in aortic arch baroreceptor properties (Angell-James, 1974b).

It has been known for some time that the carotid sinus reflex undergoes resetting in experimental hypertension (McCubbin et al., 1956). That is, a given level of afferent nerve activity is generated at a higher arterial blood pressure in hypertensive compared to normotensive animals. The overall capacity for adaptation and resetting in the carotid sinus reflex is relatively large and can occur both at the efferent and afferent ends of the reflex arc as well as in the central nervous system (Peterson, 1966; Johansson, 1974). The studies to date concerned with changes in carotid sinus baroreflexes associated with atherosclerosis have not adequately tested the possibility of baroreceptor resetting. In addition, to our knowledge no studies of changes in the overall characteristics of the carotid sinus reflex...
associated with experimental atherosclerosis have been attempted in the dog.

Accordingly, it was the objective of these studies to evaluate the changes in carotid sinus reflex control of arterial hemodynamics in the racing greyhound associated with a prolonged intake of high cholesterol diet. Specifically, we evaluated the carotid sinus reflex control of regional pressure-flow relations in a number of different vascular beds as well as in the entire systemic circulation.

Methods

We studied 15 healthy, young adult, racing greyhounds, all approximately 18 months old at the beginning of the experiment. Prior to the study, a complete medical evaluation showed the dogs to be healthy and free of infection and parasites. Five of these greyhounds were maintained for 1 year on a modification of the Malmros-Sternby diet (Malmros and Sternby, 1968), a semisynthetic diet containing 5% cholesterol and hydrogenated coconut oil. Control dogs were maintained on a commercial dog chow (Wayne dog food, Allied Mills). Periodically, the dogs were subjected to routine clinical evaluation, including electrocardiography, blood pressure determinations by direct arterial puncture, cholesterol and triglyceride determinations, and blood chemistry to check their general state of health. At the end of 1 year, the diet-fed dogs and their control counterparts were used in these experiments as a terminal procedure.

The control dogs averaged 29 ± 4 (mean ± sd) and those that were diet-fed averaged 27 ± 2 kg in body weight. The animals were sedated lightly by premedication with morphine sulfate (0.4 mg/kg, im) and atropine sulfate (0.5 mg, im), and anesthesia was induced with sodium thiamylal, 8-10 mg/kg, iv. The trachea was intubated and the dog ventilated with a constant volume respirator. Halothane was subsequently administered, in oxygen, at a concentration equivalent to 1+ minimum alveolar concentration (MAC) (0.7-0.9%). Periodically during the course of the experiment, arterial blood samples were removed and PC02, PO2, and pH measured using the appropriate electrodes (Instrumentation Laboratories, model 213). Any metabolic acidosis was corrected with intravenous sodium bicarbonate. Minute ventilation was adjusted to maintain PC02 within normal limits (Feigl and d’Alecy, 1972). The dog was placed in the right lateral decubitus position and a left thoracotomy performed at the 3rd intercostal space. The pericardium was opened and the ascending aorta exposed. A cuff-type electromagnetic flow probe (Statham type Q) was placed on the ascending aorta. The chest was closed in layers and the pneumothorax reduced via chest tube. The dog then was turned to the supine position and remained that way during the remainder of the experiment.

A midline laparotomy was performed, and the celiac, superior mesenteric, left renal, and right iliac arteries were exposed by blunt dissection. Cuff-type electromagnetic flow probes (Statham type Q) of appropriate size were placed at these various arterial sites. Pneumatic occlusion cuffs were placed on each artery distal to the flow probe to provide a measure of zero flow. Polyethylene catheters were inserted into a branch of the superior mesenteric artery, the thoracoabdominal artery, and a branch of the femoral artery. These polyethylene catheters were of 0.044 inch internal diameter and 20 cm long. They were connected to transducers (Statham P23Db or Gb) to measure arterial blood pressure.

While the laparotomy was being performed, the carotid sinuses were isolated and prepared for perfusion as previously described in detail (Bagshaw et al., 1971; Cox and Bagshaw, 1975). The isolation consisted of exposing the sinuses and ligating all visible macroscopic branches of the common and external carotids in the vicinity of the carotid sinuses. The external carotids were ligated and catheters passed retrograde toward the sinuses to carry the perfusate from the sinuses. The right carotid artery was cannulated using polyethylene tubing which was advanced into the ascending aorta to the position at which blood flow was measured. At the same time, another polyethylene catheter was passed down the jugular vein to the superior vena cava at the level of the right atrium. These catheters also were coupled to transducers for blood pressure measurement.

Before the isolation of the carotid sinuses was completed, we made control recordings of arterial pressures and flows at each of five sites (see Table 1), as well as venous pressure. These control measurements were recorded on analog magnetic tape along with appropriate baselines.

After the control measurements, the isolation of the carotid sinuses was completed as previously described (Cox and Bagshaw, 1975). Perfusion at constant flow was performed using a physiological salt solution (PSS) (Cox and Bagshaw, 1975). The temperature of the PSS was controlled by a heat exchanger at 38 ± 1°C. Perfusion pressure was set initially to approximately the initial mean control pressure (Table 1) of the dog and maintained for a period of at least 30 minutes to allow for stabilization. A sinusoidal pressure component was superimposed on the mean carotid sinus perfusion pressure which was approximately 40 ± 10 mm Hg peak to peak with a frequency of 70/min. The vago was cut bilaterally at the cervical level. This was done to eliminate the buffering effects of the aortic arch baroreceptors and other vagal afferents.

Mean carotid sinus perfusion pressure was varied from about 40 to 200 mm Hg in steps of about 30 mm Hg. At each step, recordings of systemic hemodynamic variables were made following the achievement of a steady state. No attempt was made to measure or record the transient responses. Subsequently, mean perfusion pressure was lowered in steps back to 40 mm Hg. At the end of the
### Table 1: Comparison of Initial Hemodynamic Values and Values of Operating Point and Operating Point Sensitivities of Hemodynamic Variables in Control and Diet-Fed Greyhounds

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 10)</th>
<th>Diet (n = 5)</th>
<th>Control</th>
<th>Diet</th>
<th>Control</th>
<th>Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP</td>
<td>100 ± 6</td>
<td>99 ± 6</td>
<td>104 ± 4</td>
<td>98 ± 10</td>
<td>-0.87 ± 0.12</td>
<td>-0.17 ± 0.05*</td>
</tr>
<tr>
<td>CO</td>
<td>2,349 ± 231</td>
<td>1,575 ± 216</td>
<td>2,454 ± 317</td>
<td>1,513 ± 301</td>
<td>-0.32 ± 0.16</td>
<td>-0.05 ± 0.02*</td>
</tr>
<tr>
<td>HR</td>
<td>142 ± 5</td>
<td>138 ± 12</td>
<td>140 ± 12</td>
<td>141 ± 4</td>
<td>-0.09 ± 0.17</td>
<td>-0.06 ± 0.03</td>
</tr>
<tr>
<td>Ri</td>
<td>4,250 ± 613</td>
<td>5,431 ± 498</td>
<td>3,865 ± 4,111</td>
<td>5,990 ± 1,256*</td>
<td>-0.56 ± 0.18</td>
<td>-0.13 ± 0.07*</td>
</tr>
<tr>
<td>Re</td>
<td>42,620 ± 5,675</td>
<td>30,064 ± 4,143</td>
<td>38,917 ± 3,102</td>
<td>29,422 ± 3,110</td>
<td>-0.44 ± 0.14</td>
<td>-0.04 ± 0.02*</td>
</tr>
<tr>
<td>Rr</td>
<td>29,910 ± 3,758</td>
<td>24,842 ± 3,494</td>
<td>29,925 ± 2,132</td>
<td>28,238 ± 3,186</td>
<td>-0.80 ± 0.20</td>
<td>-0.09 ± 0.03*</td>
</tr>
<tr>
<td>Rm</td>
<td>32,192 ± 5,664</td>
<td>50,152 ± 12,523</td>
<td>28,833 ± 2,137</td>
<td>44,557 ± 5,361*</td>
<td>-0.90 ± 0.15</td>
<td>-0.12 ± 0.05*</td>
</tr>
<tr>
<td>Qi</td>
<td>62,245 ± 15,014</td>
<td>64,929 ± 13,675</td>
<td>52,568 ± 5,075</td>
<td>81,154 ± 9,262*</td>
<td>-1.26 ± 0.26</td>
<td>-0.20 ± 0.14*</td>
</tr>
<tr>
<td>Qr</td>
<td>203 ± 33</td>
<td>283 ± 42</td>
<td>203 ± 38</td>
<td>292 ± 46</td>
<td>-0.43 ± 0.21</td>
<td>-0.13 ± 0.06*</td>
</tr>
<tr>
<td>Qc</td>
<td>264 ± 38</td>
<td>406 ± 61</td>
<td>264 ± 28</td>
<td>358 ± 51</td>
<td>-0.06 ± 0.04</td>
<td>-0.08 ± 0.03*</td>
</tr>
<tr>
<td>Qo</td>
<td>278 ± 49</td>
<td>158 ± 31</td>
<td>274 ± 51</td>
<td>158 ± 26*</td>
<td>0.03 ± 0.08</td>
<td>-0.05 ± 0.02*</td>
</tr>
<tr>
<td>Qo</td>
<td>155 ± 28</td>
<td>102 ± 16</td>
<td>150 ± 30</td>
<td>90 ± 19*</td>
<td>0.38 ± 0.18</td>
<td>0.02 ± 0.03*</td>
</tr>
</tbody>
</table>

Data are mean ± 1 SEM. Legend: MAP = mean arterial pressure (mm Hg); CO = cardiac output (ml/min); HR = heart rate (beats/min); Ri = regional resistance (dyn-s/cm²); Q = regional flow (ml/min); a = aorta; c = carotid; m = mesenteric; r = renal; i = iliac; n = number of greyhounds.

* Statistically significant, *P* < 0.05.

## Results

Substantial increases in serum cholesterol and triglycerides were found in all diet-fed dogs. Mean values of serum cholesterol averaged 186 ± 10 (mean ± SEM) mg/100 ml in control and 782 ± 57 in treated dogs. Serum triglycerides averaged 52 ± 4 mg/100 ml in control and 226 ± 25 in treated.

Examples of on-line recordings from representative control and diet-fed dogs are shown in Figure 1 at different values of mean carotid sinus pressure. Variation of carotid sinus pressure in the control greyhound produced large hemodynamic changes. On the other hand, similar variations in the diet-fed dog produced only minimal to negligible hysteresis effects.

A summary of values of various hemodynamic variables at the operating point pressure is given in Table 1 for the control and diet-fed dogs. Operating point sensitivities were all significantly lower in the diet-fed group. Consequently, values of vascular resistance at these sites were significantly lower in the diet-fed group.
increased. Very substantial differences existed in the variation of these hemodynamic variables with carotid sinus perfusion pressure variations about the operating point, i.e., operating point sensitivities. These values also are given in Table 1. All of these hemodynamic variables exhibited a reduced sensitivity to variations in carotid sinus perfusion pressure. This result indicates a generalized reduction in baroreflex sensitivity based on all hemodynamic variables.

A summary of the carotid sinus reflex control of systemic arterial hemodynamics is given in Figure 2. There is the expected inverse relationship between mean arterial pressure and mean carotid sinus perfusion pressure in both groups. However, the variation in the diet-fed dogs is much smaller than in the untreated animals. As indicated by the data in Figure 2, the major component of this variation was the result of changes in peripheral resistance. At the operating point in the control group, approximately two-thirds of the open-loop gain was due to the variation in peripheral resistance with carotid sinus pressure and approximately one-third due to the variation in cardiac output. In the case of the treated dogs, virtually no change in cardiac output was observed with carotid sinus perfusion pressure so that the entire change in open-loop reflex characteristics was the result of change in peripheral resistance.

Figure 3 shows a summary of the variation of regional resistance with mean carotid sinus perfusion pressure at the four peripheral sites for the two groups. For the control dogs, an inverse relationship between regional resistance and mean carotid sinus perfusion pressures was found at all four sites. The relative magnitude of the changes in bed resistance with mean carotid sinus perfusion pressure varied among the sites. There was a consistent attenuation in the variation of regional resistance with mean carotid sinus perfusion pressure in the diet-fed animals. The reduced sensitivity of regional resistance to changes in carotid sinus perfusion pressure is amplified further in Figure 4. In the case of the untreated control dogs, there was a substantial variation in sensitivity of regional resistance to carotid sinus perfusion pressure which was approximately symmetrical about the normal operating point value. In contrast, a large attenuation of sensitivity of regional resistance was seen in the treated group of greyhounds.

In all of the diet-fed animals, macroscopically visible lesions could be observed in both carotid sinuses. Figure 5 shows photomicrographs of sections of the carotid sinus from control and diet-fed dogs. These lesions were characterized by the loss of the internal elastic lamina. Intimal thickening was present and resulted from collagen fibers, smooth muscle cells, foam cells, cholesterol clefts and crystals, and a large number of extravascular red blood cells and fibrin. The extracellular space
in many areas appeared empty, probably as a result of the removal of glycosaminoglycans. Similar changes extended into the entire media in some places. The medial elastic lamella also were broken, discontinuous, and condensed and stained darker than normal. The lumen was intact but constricted by the severe intimal thickening. An endothelial lining was observed in some parts of the intima. The remainder of the endothelium may have been removed by the experimental procedures. These lesions had all the characteristics of a complicated atheroma and possessed many characteristics common to human lesions. In general, the lesions were nonuniformly distributed in the arterial system of the diet-fed dogs. Significant pathology was observed in the small- and medium-sized arteries of the coronary, the cerebral, and the mesenteric circulations in particular. The iliac artery was also a site usually demonstrating significant (intimal) lesion development.
DISCUSSION

Most previous studies of alterations in the characteristics of carotid sinus baroreflex control of the cardiovascular system in human and experimental atherosclerosis have been indirect or incomplete. Several investigators have studied the above using the heart period-systolic pressure changes which occur after the intravenous injection of phenylephrine, angiotensin, or trimethaphan (Smyth et al., 1969). The slope of heart period-systolic pressure curve for this condition decreased in human subjects with both increased age and arterial blood pressure (Vlachakis et al., 1976; Gribben et al., 1971; Korner et al., 1974; Bristow et al., 1969; Randall et al., 1976). These changes were interpreted as being the result of a decreased baroreceptor sensitivity secondary to atherosclerotic lesions in the arterial baroreceptor regions. This explanation was not verified in these studies. Rothbaum et al. (1974) found similar results associated with aging in the rat using phenylephrine injections but made no mention of the presence or absence of atherosclerosis. Thus, the changes found in such responses with age may not necessarily be related to atherosclerosis per se but may be the result of altered neural reflex control of heart rate with aging.

Angell-James has studied changes in afferent components of baroreflex mechanisms associated with experimental atherosclerosis (Angell-James, 1974b) and vitamin D sclerosis (Angell-James, 1974a) in the rabbit. The relation between perfusion pressure in the isolated aortic arch and afferent aortic nerve activity was employed as a measure of baroreceptor sensitivity. The latter was diminished in both studies. This approach examines only one portion of the overall baroreflex loop, however. It does not include potential effects of central or efferent resetting on baroreceptor reflexes (McCubbin et al., 1956; Folkow et al., 1973).

In the course of our experiments, some small variations in pulse pressure occasionally occurred. This usually consisted of an increase in pulse pressure amplitude with the increase in mean carotid sinus pressure. This variation usually did not exceed ±10 mm Hg of the 40 mm Hg amplitude targeted. This occurred as a result of limitation in the pressure bottle system used to modulate pulse pressure in the experimental apparatus. Although carotid sinus nerve activity is influenced by pressure pulsations in the carotid sinus, we do not consider these likely to influence the conclusions of our study for several reasons. First, the changes in pulse pressure were small and occurred gradually over a wide range of mean pressure variations. Second, similar changes occurred in both groups of animals. Third, most of the effects of pulse pressure on the systemic circulation occur with pulse pressure amplitude changes from 0 to 40 mm Hg with little effect above 40 mm Hg (Schmidt et al., 1972). Finally, most of the change in pulse pressure occurred for mean pressures over 120 mm Hg where the influence of pulse pressure is small.

The fact that these experiments were conducted under halothane anesthesia deserves some comment. Halothane has been reported to exert profound cardiovascular effects, including a depression of neural reflex mechanisms (Price, 1960; Skovsted et al., 1970). However, the results of these studies are subject to criticism for a variety of reasons. In many of these studies, halothane was superimposed on a (different) basal anesthetic, the animals were acutely prepared for study, minute ventilation was not controlled, appropriate control data were not obtained, and/or excessive levels of anesthesia were used. All of these factors would be expected to influence strongly the results published for the effects of halothane per se.

The dogs used in this study were lightly premedicated with a combination of morphine and atropine. The dose of each agent employed is unlikely to exert any profound influence on the results of these experiments. The small quantity of atropine...
(about 0.02 mg/kg) was included to offset the parasympathomimetic actions of morphine as well as to decrease respiratory tract secretions. Also, as the actual data acquisition was not performed until about 6 hours after premedication, it is unlikely that atropine, in particular, had any effect on the results presented here.

Recently we reported on studies of the carotid sinus control of regional arterial pressure-flow relations in halothane-anesthetized dogs (Bagshaw and Cox, 1977). We concluded that baroreceptor control of the peripheral circulation was as well preserved under halothane as with other anesthetic agents. This conclusion was based primarily on values of reflex gain and the overall range of baroreceptor control. In view of this fact, and as both groups of dogs were treated in a similar manner with regard to anesthesia, we feel that the use of halothane as the anesthetic agent is not of itself the cause for the differences reported here between the control and hyperlipemic animals.

The results of these experiments indicate significant differences in the carotid sinus control of arterial pressure/flow relations in racing greyhound dogs fed a high cholesterol diet. All measures of carotid sinus sensitivity showed a reduction in the diet-fed group. This suggests that some common denominator is responsible for the changes.

As suggested by a number of authors, the presence of macroscopic lesions in the carotid sinus could produce substantial reductions in the distensibility of the structure (Winson et al., 1974; Heath et al., 1973; Healeton and Heath, 1976; Angell-James and Lumley, 1974). As a result, normal systemic arterial pressures would produce significantly smaller changes in afferent nerve activity. Therefore, the presence of such lesions, if they substantially altered carotid sinus distensibility, could be responsible for the reduced sensitivity of the carotid sinus baroreceptor reflex shown in this study.

Postmortem examination of the test dogs also indicated significant pathology in the arterial circulation to the brain, especially the middle cerebral artery. It is possible that compromise of brain circulation also could be responsible for the generalized reduction in baroreceptor sensitivity.

The possibility exists that the reduction in carotid sinus sensitivity could be related to pathology in vascular smooth muscle; that is, a generalized reduction in smooth muscle contractility in terms of its ability to respond to efferent sympathetic nerve activity could exist secondary to the diet-induced lesions. Studies of isolated blood vessels from control and diet-fed animals (Cox and Detweiler, 1979) have shown substantial changes in the diet-treated animals that were regionally variable. There was an increase in the passive stiffness of arteries (no smooth muscle tone) in the diet-fed dogs. The maximum isometric force developed by smooth muscle in the iliac artery was reduced in the diet-fed animals; that of the carotid was unchanged. However, the ability of smooth muscle to produce shortening or constriction of the lumen was not significantly different in either the carotid or the iliac artery of diet-fed compared to control animal groups. The shortening characteristics of smooth muscle are more closely related to the neural control of peripheral resistance than is isometric force development.

This suggests that, although pathology may influence biophysical properties of arteries in these diet-fed animals, it may not be responsible for the decrease in baroreceptor sensitivity described in this study. It seems, therefore, that the most likely cause of reduced sensitivity is an alteration in carotid sinus mechanical properties which changes afferent nerve activity.

References


Quantitative Studies on Plasmalemmal Folds and Caveolae of Rabbit Ventricular Myocardial Cells

KATHERINE ROSCOE LEVIN AND ERNEST PAGE

SUMMARY Plasmalemmal folds and caveolae were investigated by qualitative and quantitative analysis of electron micrographs obtained by freeze fracture and transmission electron microscopy (TEM) of rabbit right ventricular papillary muscles whose mean sarcomere lengths ranged from 1.64 to 2.28 μm. In passively extended muscles, folds were observed at sarcomere lengths of 2.3 μm and could be shown by extrapolation to become completely extended at a maximum sarcomere length of 2.8 μm. It was concluded that the plasmalemma does not contribute to resting tension in the physiological range of sarcomere lengths. Caveolae are present in both the external plasmalemmal envelope and T-tubular plasmalemma. They show no preferential distribution with respect to underlying myofibrillar striations or membrane folds and are nearly devoid of membrane particles in freeze-fractured material. The surface density of caveolar necks (4.0/μm² apparent plasmalemmal area) is only 16–20% of that reported for frog skeletal muscle. Caveolae augment plasmalemmal area by 21–32%, assuming two or three caveolae per neck, respectively. Caveolar membrane does not serve as a reservoir of membrane to be recruited into external plasmalemma, at least over the physiological range of sarcomere lengths. In heart muscle they do not account for the T-tubular access resistance, and their function in this tissue remains unknown. Circ Res 46: 244–255, 1980

The existence of caveolae raises questions about the extent to which these structures contribute to plasmalemmal membrane area and, in particular, to specific membrane capacity, specific ion conductances, and ion fluxes per unit of membrane area. In this paper we have investigated these problems by means of measurements made on freeze-fractured membrane replicas and transmission electron micrographs of rabbit right ventricular papillary muscle. Our measurements were prompted by an extensive study of plasmalemmal folds and caveolae in frog skeletal muscle recently published by Dulhunty and Franzini-Armstrong (1975).

Portions of this work have previously appeared in abstract form (Levin and Page, 1977).

Methods

Preparative Methods for Transmission Electron Microscopy and Freeze Fracture

Experiments were performed on New Zealand White female rabbits (body weight 3.0–4.5 kg). After
Alterations in carotid sinus reflex control of arterial hemodynamics associated with experimental hyperlipemia in the racing greyhound.

R H Cox, R J Bagshaw and D K Detweiler

Circ Res. 1980;46:237-244
doi: 10.1161/01.RES.46.2.237

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1980 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/46/2/237

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/