Beta-Receptor Activity in Aorta

VARIATIONS WITH AGE AND SPECIES

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ABSTRACT

Helically cut thoracic aortic strips (from rats, rabbits, and guinea pigs) in a state of low to moderate tone and under the influence of alpha-receptor blockade relaxed in response to isoproterenol. Propranolol blocked these relaxations. Helically cut thoracic aortic strips from cats and abdominal aortic strips from rats, rabbits, and cats were not relaxed by isoproterenol. In addition, aortic beta-receptor activity of rats and rabbits decreased with increasing age. The ability of thoracic aortas to be relaxed by isoproterenol was lost when rats were 90 days old and when rabbits were 2 years old. Significant loss of beta-receptor activity was not evident in rat trachea and stomach. Sodium nitrite completely relaxed thoracic and abdominal aortas from all species including thoracic aortas from old rats and rabbits. We conclude: (1) there are species differences in the response of thoracic aortic strips to beta-receptor stimulation; (2) a gradient in beta-receptor activity exists in the aorta with greater activity in the thoracic aorta and a relatively small amount of activity in the abdominal aorta; and (3) aortic beta-receptor activity decreases with increasing age.

ADDITIONAL KEY WORDS isoproterenol trachea stomach thoracic aorta abdominal aorta cat guinea pig rat.

Marked species and age differences in the response to drugs are well known (1-4). Although variations in rates of drug metabolism may account for many of these differences, little is known about species and age differences at the receptor level. The presence or absence of specific drug receptors in certain organ systems might be the major or a contributory factor underlying species and age differences.

This paper compares beta-receptor activity in aortic strips from various laboratory animals. The results show that beta-receptor activity is present in thoracic aortas of guinea pigs, rabbits, and rats but is absent in those of cats. Furthermore, in rabbits and rats the activity of beta receptors in the thoracic aorta is greater than in the corresponding abdominal region. In addition, the results indicate that during the aging process, the thoracic aorta loses its ability to relax in response to beta-receptor stimulation but does not lose its ability to relax in response to NaNO₃ though it becomes less sensitive to this drug.

Methods and Materials

Animals of either sex were used. Guinea pigs (NIH strain) weighed 400 to 800 g, rabbits (New Zealand) 1.5 to 3.3 kg; rats (Sprague-Dawley) 150 to 550 g, and cats 1.2 to 4 kg. Rats and guinea pigs were killed by a blow on the head and rabbits by the injection of 20 ml of air into the marginal ear vein. Tissues were removed from cats anesthetized with either ether or pentobarbital sodium (25 mg/kg).

Aortic Strip Preparations

Helically cut thoracic and abdominal aortic strips were prepared by the method of Furchgott and Bhadrakom (5). Each strip (about 3.5 cm long) was suspended in a 10 ml isolated organ bath (NIH design) containing a modified Krebs bicarbonate solution of the following composition in mmoles/liter: KCl, 4.6; CaCl₂·2H₂O, 2.5;
The strips were oxygenated with a mixture of 95% O₂ and 5% CO₂ and temperature was maintained at 37.5°C with a Haake constant-temperature circulating unit. Contractions were measured isometrically with a Grass FT03 force-displacement transducer and recorded on a Grass polygraph as changes in grams of tension. Aortic strips of guinea pigs and rats were subjected to an initial tension of 1 g and those of rabbits and cats to 2 g. The stretching procedure introduced by Wurzel et al. (6) was used whenever necessary to ensure a stable baseline. The strip was placed in the isolated organ bath for 1 to 2 hours before drugs were tested. Drugs were made up for each experiment in Krebs bicarbonate solution. All drugs were added to the 10-ml bath in volumes of 0.1 to 0.3 ml, so that dilution was not a factor.

Activity of beta receptors in aortic strips was measured from the responses to isoproterenol after blockade of alpha receptors by phentolamine, as suggested by Furchgott (7). Preliminary experiments showed that the concentration of phentolamine used in all experiments was adequate to block most of the contractile action of high concentrations of isoproterenol which stimulated alpha receptors in addition to beta receptors. Phentolamine was kept in contact with the tissue for at least 45 minutes before testing for beta-receptor activity. Phentolamine alone neither contracted nor relaxed the aorta.

According to the Ahlquist classification of adrenotropic receptors (8), stimulation of alpha receptors in vascular smooth muscle causes contraction and stimulation of beta receptors causes relaxation (inhibition). The activity of beta receptors is demonstrated in a preparation that is made to contract (5). In the present study, histamine and serotonin were generally used to contract the aortic strip. Relaxant responses were plotted as percent of the maximal possible relaxation, that is, relaxation of the contracted strip back to the baseline. Technical difficulties prevented us from examining the response of the abdominal aortic strip of the guinea pig. To obtain significant reproducible results from helically cut aortic strips, the aorta must be separated from the connective tissue and fat surrounding it. Several abdominal aortas from guinea pigs fragmented during this procedure and had to be discarded. Excellent results, however, were obtained with abdominal aortic strips from rabbits, rats, and cats.

PREPARATIONS OF RAT TRACHEA AND RAT STOMACH STRIP

Helically cut tracheal strips were prepared by the method of Constantine (9). Strips of rat stomach fundus were prepared by the method of Vane (10). Responses of these smooth-muscle preparations were recorded as described for the aortic strip. The initial tension was 1 g for the trachea and 2 g for the stomach. Before testing for beta-receptor activity, both muscles were made to contract with an appropriate concentration of acetylcholine.

The following drugs were used: NaNO₂ (J. T. Baker, reagent grade); phentolamine methanesulfonate; propranolol HCl; serotonin creatinine sulfate H₂O (Mann); acetylcholine chloride (Aldrich); histamine dihydrochloride (Mann); l-isoproterenol d-bitartrate dihydrate (Sterling-Winthrop); and pentobarbital sodium (Nembutal, Abbott). Concentrations of isoproterenol, histamine, serotonin, and acetylcholine are expressed in terms of the free base. The concentrations of all other drugs are expressed in terms of the salt.

Figure 1

Left: Relaxation of a histamine-contracted guinea pig thoracic aortic strip by isoproterenol in the presence of alpha-receptor blockade by phentolamine (1 μg/ml). Right: Inhibition of the isoproterenol relaxation by a beta-receptor blocking agent (propranolol, 0.03 μg/ml).

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Results

I. SPECIES DIFFERENCES IN BETA-RECEPTOR ACTIVITY

Thoracic Aortic Strips of Guinea Pigs, Rabbits, Rats, and Cats.—Figure 1 shows a large response to isoproterenol (0.3 μg/ml) of a thoracic aortic strip from a guinea pig in the presence of phentolamine (1 μg/ml). Isoproterenol promptly produced a marked relaxation of the contraction produced by histamine, 0.3 μg/ml (Fig. 1, left). The relaxation was completely blocked by exposing the tissue to propranolol, a beta-receptor blocking agent, for 1 hour, 0.03 μg/ml (Fig. 1, right). Propranolol neither contracted nor relaxed the aorta. The relaxation produced by isoproterenol was thus a beta-receptor response.

Isoproterenol also relaxed the thoracic aorta from young rats 6 to 10 weeks old and rabbits 8 to 12 weeks old (Fig. 2). As with guinea pig aorta, this relaxation was blocked by propranolol. Aortic strips from rabbits were made to contract with either serotonin or histamine. Those from rats were made to contract only with serotonin since histamine does not contract the rat aorta. All experiments were run in the presence of phentolamine (rabbit, 1 μg/ml; rat, 0.3 μg/ml). The dose range of isoproterenol required to elicit a relaxation was about the same in the three species, that is, 1 to 3 ng/ml was usually the threshold concentration whereas 0.1 to 0.3 μg/ml produced the maximal response. Higher concentrations of isoproterenol (1.0 μg/ml and larger) produced submaximal responses. This suggests that the alpha-receptor effect of these high concentrations of isoproterenol mani-
fested itself despite the presence of phentola-
mime. The guinea pig aortic strip was least
sensitive to relaxation produced by the beta-
receptor stimulant.

Figure 2 also shows that isoproterenol did
not relax the thoracic aorta of the cat. When
alpha-receptor blockade was induced by
phentolamine (1 μg/ml), concentrations of
isoproterenol up to 10 μg/ml failed to relax
cat thoracic aorta previously made to contract
with serotonin. In fact, this high concentration
actually increased the tone slightly, suggesting
an alpha-receptor effect.

Abdominal Aortic Strips of Rabbits, Rats,
and Cats.—Isoproterenol in the presence of
phentolamine did not appreciably relax heli-
cally cut strips of abdominal aortas from the
same rabbits and rats whose thoracic aortas
showed beta-receptor activity (Fig. 3). More-
over, the cat abdominal aorta likewise did not
respond to beta-receptor stimulation (Fig. 3).
One rat abdominal aorta of the eight tested
showed considerable beta-receptor activity.
The sensitivity of this particular tissue to
sodium nitrite was also enhanced.

To rule out the possibility that the anesthet-
ic present in the cat aortic tissue interfered
with the response to isoproterenol, we tested
the thoracic aorta from a rabbit which had
been anesthetized with 35 mg/kg of pento-
obarbital sodium. Beta-receptor responses to
isoproterenol were as great as those of
thoracic aortas removed from rabbits killed by
an air embolism.

Four of the five cats used in the above study
weighed between 3 and 4 kg and were
approximately 1 to 2 years old. To evaluate
the effect of age on the vascular response to
drugs as noted in rabbits and rats (see
below), we examined the responses of a
thoracic and abdominal aorta from a 3-month-
old kitten (1.2 kg) to isoproterenol in the
presence of phentolamine. Again, no relaxa-
tion was produced in response to isoprote-
renol.
Effect of NaNO₂ on Thoracic and Abdominal Aortic Strips.—Since thoracic aortas from different mammalian species have different sensitivities to isoproterenol, it was important to test the innate ability of the tissue to relax in response to drugs, such as NaNO₂, a nonspecific smooth-muscle relaxant. All thoracic and abdominal aortas tested relaxed (Fig. 4). Both the thoracic and abdominal aortas from the rabbits were more responsive to NaNO₂ than those arteries from the rat. The guinea pig thoracic aorta was the least sensitive of the thoracic aortas from the three species. With three cat thoracic and abdominal aortas, 100 μg/ml of NaNO₂ produced relaxation comparable with that seen in the other three species (Fig. 4), even though cat aortas did not relax in response to isoproterenol.

Alpha Receptor Responses to Isoproterenol in Four Species.—Isoproterenol caused contraction of the thoracic aortas from all four mammalian species studied. As shown in Figure 5, the entire concentration ranges of the dose-response curves are similar, the ED₅₀ values lying between 5 and 15 μg/ml. These concentrations are approximately 500 to 1000 times greater than those necessary to produce relaxation. These experiments were performed without previous treatment with a beta-receptor blocking agent, which probably would have shifted the threshold concentrations somewhat to the left in the guinea pig, rabbit, and rat, since thoracic aortas from these species possess appreciable beta-receptor activity (see above). All abdominal aortas likewise contracted in the presence of these concentrations of isoproterenol. These contractile responses produced by isoproterenol must have been mediated by alpha receptors, because they were blocked by phentolamine and not by propranolol.

II. EFFECT OF AGE ON BETα-RECEPTOR ACTIVITY

A. Thoracic Aorta

Male Rats.—Figure 6 (top) compares the responses to NaNO₂ of thoracic aortic strips from male rats 41 to 60 and 78 to 90 days old. The aortas from older rats were less responsive to NaNO₂, particularly at lower concentrations, but relaxed completely at a concentration of 100 μg/ml. A full dose-response relationship to NaNO₂ was not obtained in thoracic aortas from rats 205 to 255 days old. Aortas from these animals, however, relaxed completely to 100 μg/ml of NaNO₂. Figure 6 (bottom) also compares the relaxation to isoproterenol after alpha-receptor sites had been blocked by phentolamine (0.3 μg/ml). The aortas from the younger group of animals (41 to 60 days old) showed the greatest response; those from the older group (78 to 90 days old) showed only a slight relaxation; aortas from animals 205 to 255 days old did not respond at all.

Female Rats.—The thoracic aortas from female rats 90 days old did not respond to isoproterenol (Table 1), although maximal relaxation was still produced by 100 μg/ml of NaNO₂. There was no statistical difference between the beta-receptor activities of thoracic aortic strips from male and female rats 41 to 60 days old (compare Fig. 6, and Table 1).

Male Rabbits.—Figure 7 shows the responses of thoracic aortas from male rabbits of various ages to NaNO₂ (top) and to isoproterenol in the presence of phentolamine, 1 μg/ml (bottom). The effect of NaNO₂ was almost identical in tissues from rabbits 56 to 70 and 120 to 155 days old, but the response to isoproterenol was markedly reduced in the older group. There was, however, still a substantial amount of beta-receptor activity remaining in aortas from rabbits 120 to 155 days old. In contrast, almost all beta-receptor activity in rat aortas was lost at approximately 90 days. Thoracic aortas from male rabbits 405 to 590 days old were somewhat less responsive to NaNO₂ than those of the two younger groups. Moreover, these aortas did not relax appreciably in response to isoproterenol. Thoracic aortas from rabbits 2 to 5 years old still responded maximally to NaNO₂, however, the ED₅₀ for the older rabbits was ten times that for the younger animals. Thoracic aortas from rabbits in this age group did not relax at all to isoproterenol.

Female Rabbits.—There was no statistically significant difference in the effects of isopro-
Dose-response curves for the relaxant effect of NaNO₂ (top) and isoproterenol (bottom) in helically cut thoracic aortic strips from male rats of varying ages. The strips were previously made to contract with serotonin after alpha-receptor sites had been blocked with phentolamine. Each point represents the mean ± se.

**TABLE 1**

**Relaxant Responses to Isoproterenol of Thoracic Aortas from Female Rats of Varying Ages**

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>0.01</th>
<th>0.1</th>
<th>1.0</th>
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<tr>
<td>47-56</td>
<td>43.2 ± 8.9 (8)</td>
<td>65.8 ± 8.1 (8)</td>
<td>54.5 ± 9.4 (8)</td>
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<td>84-90</td>
<td>0.0 ± 0.0* (3)</td>
<td>3.7 ± 2.0* (3)</td>
<td>0.0 ± 0.0* (3)</td>
</tr>
<tr>
<td>209-275</td>
<td>4.4 ± 4.4† (5)</td>
<td>12.8 ± 5.0* (5)</td>
<td>3.0 ± 2.0* (5)</td>
</tr>
</tbody>
</table>

Response to isoproterenol was obtained after a contraction produced by serotonin. Alpha-receptor sites had been blocked with phentolamine. The number of aortas is in parentheses. Values are means of % maximal relaxation ± se.

*P < 0.001 (Student's t-test).
†P < 0.01 (Student's t-test).

Isoproterenol and NaNO₂ on thoracic aortas from young male and female rabbits (compare Fig. 7, 56 to 70 days, with Fig. 8, 50 to 60 days). However, the female rabbit aortas showed a
lower threshold to NaNO₂. NaN₀₂ responses of thoracic aortas from female rabbits decreased with increasing age of the animals, but not as much nor as rapidly as did the isoproterenol responses (Fig. 8). It is of particular interest that beta-receptor activity disappeared more slowly in female aortas than in male aortas (Figs. 7 and 8).

B. Rat Trachea and Stomach

To determine if a similar age-dependent loss in beta-receptor activity occurs in other organs, we examined the responses of tracheal and stomach smooth muscle from young and old rats to isoproterenol. Only at an isoproterenol concentration of 30 μg/ml were the responses significantly decreased in trachea from old compared to younger rats (Table 2), and there was no dramatic decrease in beta-receptor activity with increasing age at any other isoproterenol concentration. Stomach beta-receptor activity was also apparently unaffected by the aging process (three experiments).

Discussion

We studied species and age variation in beta-receptor activity in vitro to circumvent a number of complications associated with in vivo studies. Previous work from this and other laboratories has demonstrated that...
Dose-response curves for the relaxant effect of NaNO₂ (top) and isoproterenol (bottom) in helically cut thoracic aortic strips from female rabbits of varying ages. The strips were previously made to contract with histamine after alpha-receptor sites had been blocked with phentolamine. Each point represents the mean ± se.

**TABLE 2**

<table>
<thead>
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<th>Age (days)</th>
<th>0.01</th>
<th>0.1</th>
<th>0.3</th>
<th>1.0</th>
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<tbody>
<tr>
<td>41-60</td>
<td>27.0 ± 3.0 (3)</td>
<td>40.2 ± 9.5 (6)</td>
<td>45.0 ± 5.4 (5)</td>
<td>39.6 ± 7.4 (5)</td>
</tr>
<tr>
<td>275-420</td>
<td>9.3 ± 2.0* (4)</td>
<td>43.0 ± 14.3 (4)</td>
<td>31.2 ± 6.0 (6)</td>
<td>22.3 ± 7.7 (3)</td>
</tr>
</tbody>
</table>

Response to isoproterenol was obtained after a contraction produced by acetylcholine. The number of tracheas is in parentheses. Values are means of % maximal relaxation ± se.

*P < 0.05 (Student's t-test).

species variation is commonly caused by differences in drug metabolism (2-4). The use of isolated preparations lessens this variable and also reduces the number of events between the administration of the drug and the actual receptor mechanism. Data obtained using isolated smooth muscles can be evaluated on the basis of observed responses. If a
response occurred, the drug must have united with its particular receptor substance and the complete chain of events connecting it to the contractile mechanism must be present and functional. On the other hand, if no response occurred and the tissue appeared to be operating normally in all other respects, we can presume that one or more of the components of the total receptor system were either absent or altered.

When helically cut thoracic aortic strips obtained from guinea pigs, rabbits, and rats were treated first with an alpha-receptor blocking agent and made to contract, they relaxed on addition of isoproterenol (Fig. 2). This relaxation was blocked by propranolol, a beta-receptor blocking agent. By contrast, relaxation could not be elicited by isoproterenol in thoracic aortas from cats (Fig. 2). On the other hand, thoracic aortas from all species relaxed in response to NaNO₂ (Fig. 4), indicating that these vessels have the ability to relax.

Comparison of the responses of thoracic aortas to isoproterenol and NaNO₂ (Figs. 2 and 4) show that the guinea pig was less sensitive to both of these agents than was the rabbit or the rat. NaNO₂ produced a greater response in rabbit aorta than in rat aorta, whereas the isoproterenol dose-response curves for rat and rabbit aortas overlapped.

Helically cut abdominal aortas from rabbits, rats, and cats exhibited little or no beta-receptor activity (Fig. 3). This is of particular interest in view of the results of Takenaka (11), Iwaki et al. (12), and Bevan and Osher (13) who showed that in an in-vitro system different blood vessels from the same animal differed in their sensitivity to alpha-receptor stimulants. In the present study, different segments of the same artery were shown to vary in their sensitivity to beta-receptor stimulants. Similar results were obtained by Zuberbuhler and Bohr (14) on the coronary vascular tree of the dog. In their study, small coronary vessels were uniformly relaxed by beta-receptor stimulants. On the other hand, large vessels contracted in response to catecholamines or relaxed after a transient contraction.

As indicated in results, one of eight rat abdominal aortas showed substantial beta-receptor activity while the others showed little activity. Since this segment of artery in the rat has a small lumen, it is difficult to prepare a helically cut strip; therefore, beta-receptor activity may have been masked in the other rat abdominal aortas for technical reasons. On the other hand, beta-receptor activity in the abdominal aorta may vary greatly from rat to rat. In all probability beta receptors are present to some degree in the abdominal aorta of the rat. Altura and Zweifach (15) have presented evidence that such sites exist in the rat mesenteric microvasculature. Helically cut abdominal aortas from rabbits and cats, however, are easily prepared and they showed no beta-receptor activity (Fig. 3). Therefore, species difference may occur in beta-receptor activity of abdominal aortas.

Bolton and Bowman (16) recently described the functional nature of adrenoreceptors in the cardiovascular system of the domestic fowl. Helically cut strips from the abdominal aorta of adult fowls relaxed in response to isoproterenol, indicating the existence of beta-receptor sites in this nonmammalian species. However, not all nonmammalian species possess beta-receptor sites in the large blood vessels. Burnstock and Kirby (17) have shown that helically cut strips from both right and left systemic arteries of the sleepy lizard or the toad and from the ventral aorta of the trout and eel contain no catecholamine receptors which mediate relaxation.

In the present study, all thoracic and abdominal aortas contracted in the presence of high concentrations of isoproterenol (Fig. 5). This shows that an alpha-receptor effect could be elicited by this agent in these vascular strips from all species and that the species variation described in this communication is confined to the beta-receptor component of this type of stimulation. Furthermore, the species variation exists at the receptor level. In addition, the present study has shown...
that a gradient in beta-receptor activity exists in the aorta, with a greater activity in the thoracic aorta and only a relatively small amount of activity in the corresponding abdominal segment.

This study also presents pharmacologic evidence that the thoracic aorta undergoes functional changes in addition to the well-known structural alterations that take place during the aging process (18, 19). These changes result in an impaired ability to relax in response to drugs. Thus, the thoracic aorta from older rats and rabbits relaxed maximally to NaNO₂, though somewhat higher concentrations were required than those needed to produce similar responses in younger animals. Even though thoracic aortas from all ages of animals relaxed completely to NaNO₂, those from older animals had lost their ability to relax in response to isoproterenol.

Wilens and Sprouls (19) studied the histopathology of the rat extensively and concluded that "with advancing age the aorta developed only relatively mild [histological] changes." It is not surprising, therefore, that the aortas from older animals were still able to relax completely to NaNO₂. The loss in beta-receptor activity may be due to a defect in the beta-receptor system. Although the data obtained in this study do not pinpoint the exact nature of the lesion, the area can be narrowed considerably. Since NaNO₂ produced maximal relaxation in aortas from both young and old animals, the contractile mechanism and especially those components needed to complete the relaxation process were intact and functional. Therefore, the inability of isoproterenol to relax aortas from older animals must be due either to a change in the beta receptors, so that they no longer unite with beta-receptor stimulants, or to an alteration of one of the steps in the chain of events that links the receptor to the contractile mechanism.

Biochemical changes with age in the aorta have been reported by Kirk (20), who showed that with increasing age the activities of various enzymes in human aortic tissue decreased, some did not change, and some increased and then decreased. Since activities of the enzymes in aorta may change with increasing age, it seems reasonable to postulate that a receptor-linked enzymic process has been altered by aging, resulting in a decreased biologic activity.

Another example of a beta-receptor function that decreases with increasing age is the calorigenic effect of norepinephrine (21). Privitera et al. (22) recently reported that circulatory alpha- and beta-receptor systems in the newborn dog are quantitatively similar to those in the adult dog. Their experiments measured the total circulatory response to the intravenous administration of various biogenic amines and did not make use of the responses of isolated segments of the vascular tree to beta-receptor stimulation in the presence of alpha-receptor blockade and vice versa. Using the isolated abdominal aorta of the rat as an indicator of vascular reactivity, Tuttle (23) showed that aortas from rats 1 year old contracted more forcefully in the presence of norepinephrine than did aortas from rats 100 days old. The response of aortas from rats 2 years old, however, was considerably depressed. Siro-Brigiani and Chieppa (24) examined the responses of the coronary vessels of young and old oxen and horses to sympathetic stimulation. In young oxen tyramine, an indirectly acting sympathomimetic amine, caused a spasm followed by a prolonged relaxation. In adult oxen, relaxation did not follow the spasm induced by tyramine. These investigators also showed that isoproterenol caused relaxation in the coronary vessels of young horses but not in those of adult horses. Unfortunately, they did not test the effects of a nonspecific smooth-muscle relaxant such as NaNO₂ to determine the extent of structural changes which might have impaired relaxation. Nevertheless, their results are in accord with ours in the present study.

The change with age in beta-receptor activity in the vascular system suggested the possibility of similar effects of aging on pharmacologic receptor activity in other organ systems. We have shown that tracheas from young rats do not exhibit much alpha-receptor activity, whereas tracheas from older rats...
show prominent alpha-receptor effects when stimulated by norepinephrine (25). The present study shows that the responses of the stomach and trachea to beta-receptor stimulation were not significantly decreased in older animals. This was not surprising in view of the extremely large number of beta receptors in these organs. Even if the activity of a substantial number of beta receptors was lost, there would still be enough present to permit a full relaxation.

We do not know the full significance of the decrease in beta-receptor activity of thoracic aortas of older animals. The most obvious consequence of a loss in beta-receptor activity of the vascular system would be an increase in the arterial blood pressure. Although the aorta does not exert much effect on the total peripheral resistance, which is the major factor controlling the mean arterial blood pressure, the fact that loss of beta-receptor activity occurs in one segment of the vascular tree suggests that a similar loss may occur in the smaller vascular beds. Okamoto and Aoki (26) showed that systolic blood pressure of normotensive rats increased sharply from age 5 to 10 weeks and then leveled off. Since beta-receptor activity in the aorta had decreased markedly by 12 weeks, it was tempting to speculate that a cause-and-effect relationship exists. With this in mind, we examined the responses of thoracic aortas from a strain of genetically hypertensive rats and found that these aortas had significant beta-receptor activity (27). Since hypertension may occur despite the presence of appreciable beta-receptor activity, the loss of beta-receptor activity of certain vascular smooth muscle with age may be a normal occurrence and not pathologic.

In accord with this view Trcka and Fleisch (unpublished observations) recently found that beta-receptor activity in the ventral tail artery of the rat decreased at an earlier stage of development than that reported for the aorta.

Further studies are necessary to establish the presence or absence of a relationship between a loss in vascular beta-receptor activity and arterial blood pressure.

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