Many avian species demonstrate systolic and diastolic blood pressures (BP) higher than those of most mammals. However, neural and humoral control of BP in birds is not well understood. BP varies with strain, age, sex, and environment. Moreover, naturally occurring atherosclerosis has been noted in the aorta, coronary, and other major arteries in turkeys, chickens, pigeons, and various wild birds, whereas arteriosclerosis in the resistance vessels appears to be absent.

It is presumed that both birds and mammals phylogenetically evolved from primitive reptiles. However, the bird kidney appears to be a transitional form, intermediate between reptiles and mammals, which possesses a macula densa of the juxtaglomerular apparatus, reptilian-type and mammalian-type nephrons, and autonomic innervation of the blood vessels. Thus, the birds may provide a useful model with which to study the evolution of the role of the renin-angiotensin and adrenergic nervous systems in the control of cardiovascular function.

The chemical structure of chicken angiotensin I ([Asp\(^1\), Val\(^6\), Ser\(^7\)]AI) has been determined by Nakayama et al. Recently, we developed an antibody to synthetic chicken AI in the goat using human immunoglobulin as a conjugate. Thus, plasma renin activity (PRA) can be measured with radioimmunoassay (RIA) of fowl AI by repeatedly collecting small blood samples from the same animal. In the present investigation, we studied the effects of an angiotensin-converting enzyme inhibitor, an angiotensin II (AI) antagonist, and a beta-adrenergic blocking drug on the BP, PRA, and plasma catecholamine concentrations in chronically cannulated, conscious chickens to determine whether the renin-angiotensin and the adrenergic nervous system have a role in the control of BP in birds.
Methods

Animals

Female white leghorn chickens, Gallus gallus, 25 wks of age, were purchased from a local breeder. Chickens were initially kept in groups in large indoor cages, and were transferred to individual cages (12 in. W × 18 in. D × 18 in. H) 3 weeks prior to cannulation. Photoperiod (12-hr light-dark cycle) and temperature (23 ± 1°C) were controlled. Chickens were fed laboratory chow (Wayne 15% Egg Ration; Allied Mills) containing NaCl (0.03–0.12 mEq/g), and tap water was allowed ad libitum. The average age and weight of the chickens (n = 45) at the beginning of the experiment was 32.0 ± 0.8 weeks and 1.54 ± 0.03 kg respectively.

Surgical Preparation

Chickens were lightly anesthetized with 75 mg/kg (i.m.) of ketamine (Bristol-Myers) supported by a local anesthetic (2% Lidocaine; Eikins-Sinn). The thigh muscles were dissected from the lateral side, and a clear vinyl expanded catheter (Dural Plastics and Engineering, Australia) was chronically implanted in the abdominal aorta by insertion through the left ischiac artery. The other end of the catheter was tunneled through the subcutaneous space to a point of exteriorization on the head of the chicken; this catheter was used for measuring BP and collecting blood samples. Another catheter was inserted into the vena cava through the left external iliac vein for drug infusion. Catheters were flushed daily with small amounts of heparin (100 U/ml)-saline (0.9% NaCl) solution, and the tips of the catheters were closed with polished stainless steel plugs (0.8 mm o.d.).

Drugs and Hormones

[Asp₁, Val₆, Ser⁴]AII, [Asp₁, Val₆]AII, and [Sar₁, Ile⁶]AII were kindly provided by Dr. Mahesh C. Khosla, Cleveland Clinic Foundation, Cleveland, Ohio. Propranolol HCl (dl, Ayerst Labs) and SQ 14,225 (Captopril, Squibb) were gifts from the respective companies. Reserpine (Serpasil; CIBA), [¹²⁵I]Na (Union Carbide), lactoperoxidase/glucose-oxidase reagent (Bio-Rad Lab), glutathione (Sigma), and ethyleneglycol-bis-(β-amino-ethyl ether) N,N'-tetracetic acid (EGTA, Sigma) were purchased commercially.

Measurement of Blood Pressure and Collection of Blood Samples

The BP (electronically averaged mean aortic pressure) was measured with a strain gauge pressure transducer (Statham P23DC or Hewlett-Packard 1280C). Chickens were loosely tied by their legs, while the rest of the body remained unrestrained. The head was covered with a black plexiglass box to avoid stimulation from the environment. The room was kept dark and quiet. During measurement of BP for 15 minutes, the chickens showed no sign of excitement.

For measurement of PRA and plasma angiotensinogen level, blood samples (0.3 ml) were drawn from indwelling catheters into chilled capillary tubes, which were coated with ammonium EDTA and placed in a cooled chamber (2–4°C). For measurement of plasma catecholamines, 0.4 ml of blood was taken into a syringe moistened with a glutathione (60 mg/ml)-EGTA (90 mg/ml) mixture. The blood for plasma Na, K, and Cl measurement was withdrawn into hemocrit tubes (0.05 ml). Before the collection of blood samples, 0.2 ml of blood was taken to clear the dead space of the catheter. The blood collected initially was reinjected. If the chickens were excited before or during sample collection, the blood was redrawn the following day.

Protocol 1: Acute Treatment

The experiment began on the twelfth postsurgical day. After 15 minutes of BP recording (preinfusion period), a blood sample was collected. The efficient doses of the inhibitors were determined by testing their inhibitory potencies of respective agonist drugs in different groups of anesthetized and conscious birds. The drugs or hormones were infused or injected at the following rates:

1. [Asp₁, Val₆]AII, 100 ng/kg/min, for 10 minutes (n = 6)
2. [Sar₁, Ile⁶]AII, initial dose of 10 or 50 μg/kg followed by 1 or 5 μg/kg/min respectively for 15 minutes (n = 8). [Sar₁, Ile⁶]AII, 5μg/kg/min, abolished the pressor response to 1 μg/kg of [Asp₁, Val₆]AII.
3. Propranolol, initial doses of 0.5 or 1.0 mg/kg followed by 1 or 2 mg/kg/hr respectively for 15 minutes (n = 6). Propranolol, 0.4 mg/kg/hr, inhibited the vasodepressor response to 1 μg/kg of isoproterenol.
4. SQ 14,225, 1 to 2.5 mg/kg, waiting 15 minutes (n = 7). SQ 14,225, 1 mg/kg, completely inhibited the BP response to 200 ng/kg of [Asp₁, Val₆, Ser⁴]AII.
5. Reserpine (n = 5), 1 to 2 mg/kg/day or 0.9% NaCl (solvent), 0.4 ml/kg/day for 2 days.11

Blood samples were taken immediately after cessation of drug infusion. In reserpinized chickens, the blood samples were taken at 24 hours after the last injection. The same chickens were used repeatedly for different drug applications, with 2 to 3 day intervals, except for the reserpine experiment.

Protocol 2: Chronic Treatment

Control Period (1½ Weeks)

Starting at the fourth postsurgical day, BP measurement (3/wk) and blood sample collections (2/wk) were done as shown above. The BP was measured at 2
to 3 hours and blood samples were taken at 4 to 6 hours after the drug injection.

Experimental Period (2 Weeks)

Studies on the effect of SQ 14,225, propranolol, and saline were conducted in different groups in which chickens were distributed in such a manner so as to have a proportional number of birds in each group with high (above 150 mm Hg), middle (120-150 mm Hg), and low (below 120 mm Hg) BP. The following drugs were injected i.m. daily (half dose at 8:30 a.m., and half dose at 4:30 p.m.): Group 1 (n = 12): saline, 0.4-0.8 ml/kg/day for 2 weeks.

Group 2 (n = 14): propranolol, 4 or 8 mg/kg/day for 2 weeks; and Group 3 (n = 12): SQ 14,225, 10 or 20 mg/kg/day in the first week, and 20 or 40 mg/kg/day in the second week; Group 2 (n = 14): propranolol, 4 or 8 mg/kg/day for 2 weeks; and Group 3 (n = 12): saline, 0.4-0.8 ml/kg/day for 2 weeks.

Recovery Period (1 1/2 Weeks)

The BP (3/wk) and blood sample collection (2/wk) were performed as above.

Radioimmunoassay of Chicken Angiotensin I

An antibody to [Asp1, Val5, Ser8]AI was made by immunizing a goat with a conjugate of human immunoglobulin and fowl AI. The same analog, [Asp1, Val5, Ser8] AI, was labelled with [125I]Na (Union Carbide) using the lactoperoxidase technique. The antiserum at a final dilution of 1:200,000 and [125I]fowl AI, purified by DEAE cellulose and Sephadex G-25 column chromatography, were used for the RIA of fowl AI. Natural fowl AI measured by RIA was nearly equal to that measured by the rat vasopressor bioassay.

Plasma Renin Activity and Plasma Angiotensinogen Level

The PRA was measured as the rate of fowl AI generation. Plasma (50 µl), 2 M ammonium acetate buffer (pH 5.5, 5 µl), 1% neomycin sulfate (Upjohn)-1% thimerosal (Merthiolate, Lilly) solution (pH 5.5, 5 µl), 3.8% ammonium EDTA (pH 5.5, 5 µl), and phenylmethylsulfonylfluoride (PMSF, Sigma, 12.5 mg/ml, 2 µl) were incubated at 37°C for 2 or 3 hours (duplicate determination). The formation of fowl AI in conscious chicken plasma is linearly related to the duration of incubation for 3 hours. Generated AI was determined by RIA, mentioned above. The mixture without incubation, but otherwise treated similarly, was used as control. Generation of AI in this control mixture was negligible.

Plasma (10 µl), 2 M ammonium acetate buffer (pH 7.4, 92 µl), 1% neomycin-1% thimerosal solution (pH 7.4, 20 µl), 3.8% ammonium EDTA solution (pH 7.4, 20 µl), and PMSF (25 mg/ml, 8 µl) were incubated at 37°C for 40 minutes with an excess amount of renin (50 µl of kidney extract, dialyzed against disodium EDTA, acid-treated and readjusted to pH 7.4). Plasma angiotensinogen levels were expressed as the maximum amount of AI formed from 1 ml of plasma.

Plasma Catecholamines and Plasma Electrolytes

Plasma concentrations of norepinephrine and epinephrine were measured by minor modifications of the radioenzymatic method described by DaPrada and Zürcher. The tritiated normetanephrine and metanephrine formed by incubation of plasma with catechol-0-methyl transferase and 3H-S-adenosylmethionine were separated either by thin layer chromatography or by reverse-phase high pressure liquid chromatography prior to liquid scintillation counting.

Plasma Na and K levels were measured with a flame photometer (Instrumentation Laboratories) with a lithium internal standard. Plasma chloride was measured by coulometric titration (Buchler digital chloridometer).

Analysis of Response

In acute studies, values during the preinfusion (or preinjection) period were compared with those during or after infusion (or injection) by a paired t test. In chronic studies, mean values during the control period were calculated for individual animals. The differences between mean control values and those obtained during each experimental and recovery period were then analyzed by a paired t test. The natural log-transformed data were used for statistical analysis of PRA to correct for heterogeneity.

Results

Control Values

The mean control levels of chronically cannulated conscious female chickens (n = 45) were as follows: BP (mean aortic pressure) = 137.6 ± 2.0 mm Hg; heart rate = 295 ± 4 beats/min; PRA = 3.55 ± 0.31 ng/ml/hr; angiotensinogen = 1229 ± 66 ng/ml; plasma norepinephrine = 370.3 ± 56.3 pg/ml; plasma epinephrine = 106.2 ± 25.2 pg/ml; plasma Na+ = 156.0 ± 0.9 mEq/liter; K+ = 3.80 ± 0.05 mEq/liter; and hematocrit = 24.4 ± 0.3%. The distribution of BP range among 45 female chickens is shown in figure 1.

Acute Treatment

[Asp1, Val5]AII and [Sar1, Ile8]AII

Infusion of [Asp1, Val5]AII produced a biphasic response; an initial depressor (7.4 ± 1.6 mm Hg) was quickly followed by a pressor (11.6 ± 3.2 mm Hg) response (fig. 2). Plasma norepinephrine levels increased in all animals examined (fig. 3). Plasma epinephrine also increased in four of six animals, but the increases were smaller than those of norepinephrine. [Sar1, Ile8]AII increased BP transiently (7.9 ± 3.0 mm Hg). Plasma norepinephrine increased slightly, whereas no consistent change was noted in plasma epinephrine levels (fig. 3). Hematocrit increased
Propranolol, Reserpine, and SQ 14,225

Immediately after the start of propranolol infusion, the BP and heart rate decreased 13.1 ± 3.7 mm Hg and 100 ± 9 beats/min respectively (fig. 2). Chickens became slightly lethargic. Lower doses of propranolol (0.2 mg/kg/hr) were also effective. Acute infusion of propranolol increased both plasma norepinephrine and epinephrine levels (fig. 3) and slightly increased hematocrit (p < 0.05). Reserpine treatment decreased the BP and heart rate but PRA did not change (table 1). Since resting BP of this group was low, the experiment was repeated in another group of chickens (n = 10). The BP also decreased from 146.7 ± 6.2 to 127.9 ± 8.1 mm Hg. In the control saline-treated group, the BP and heart rate did not change but PRA decreased slightly (table 1). A single injection of SQ 14,225 did not change the BP, heart rate, PRA, plasma catecholamines, electrolytes, or hematocrit (figs. 2 and 3).

Table 1. Effect of Reserpine on Blood Pressure, Heart Rate, and Plasma Renin

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Blood pressure</th>
<th>Heart rate</th>
<th>Plasma renin activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>Reserpine (n = 5)</td>
<td>129.8</td>
<td>98.8</td>
<td>272</td>
</tr>
<tr>
<td></td>
<td>± 3.5</td>
<td>± 4.3</td>
<td>± 25</td>
</tr>
<tr>
<td>Saline (n = 5)</td>
<td>128.5</td>
<td>128.8</td>
<td>262</td>
</tr>
<tr>
<td></td>
<td>± 2.5</td>
<td>± 3.6</td>
<td>± 12</td>
</tr>
</tbody>
</table>

Statistical analysis was done between pre- and post-treatment levels by a paired t test. Heart rate was taken in four birds. Pre and Post indicate before and after treatment.

* p < 0.05.
† p < 0.01.
Chronic Treatment

Propranolol

The BP and heart rate decreased 19.1 ± 3.0 mm Hg and 76 ± 6 beats/min, respectively, at 48 hours after the start of the treatment (BP not measured before 48 hours), and maintained approximately the same levels throughout the experiment (fig. 4). To determine the BP variation in relation to injection time (twice daily), we measured the BP and heart rate at 2 and 8 hours after the first daily injection. At 8 hours (immediately before the second daily injection), the BP (120.2 ± 5.1 mm Hg) and HR (283 ± 9 beats/min) were slightly higher than those measured at two hours (BP: 112.0 ± 6.1 mm Hg, HR: 235 ± 13.5 beats/min), but still much lower than those during the control period. After cessation of propranolol treatment, both BP and HR returned to the pretreatment levels. The PRA during propranolol treatment was not significantly different from the mean PRA of the control period, although PRA in the second experimental week was lower than that of the first experimental week (fig. 5). The plasma sodium (Na) concentration showed a tendency to increase during the second experimental week and the recovery period (table 2). Plasma catecholamines increased during the first and second experimental weeks and returned toward control values during the recovery period (table 3).

SQ 14,225

The BP was reduced 11.3 ± 2.6 mm Hg at 48 hours after start of treatment (BP was not determined before 48 hours), but it returned toward the control level at the end of the first experimental week (fig. 4). Increased doses of SQ 14,225 decreased the BP, and BP remained low, whereas the heart rate tended to rise. After cessation of the drug, the heart rate dropped immediately, but the BP remained low for 4 days. The PRA increased 5- to 6-fold during the experimental period, and returned to control level after cessation of the drug (fig. 5). No consistent change was observed in the levels of plasma angiotensinogen or catecholamines (table 3). Plasma Na concentration showed a gradual increase at the end of the experimental and recovery periods (table 2).

Figure 3. Plasma norepinephrine (upper) and epinephrine (lower) levels before and after infusion (or injection) of [Asp₁, VaP₁]All₁, [Sar¹, Ile⁶]All₁, propranolol, or SQ 14,225. Mean and se of catecholamine levels before and after drug applications were shown by open circles and vertical bars. Statistical analysis of the difference was done by a paired t test (log transformed). *p < 0.05; **p < 0.01.
Saline

Both the BP and heart rate remained relatively stable throughout the saline (solvent control) injection and recovery periods (fig. 4). However, PRA tended to decrease, whereas plasma Na increased, in the second week of the experimental and recovery periods (fig. 5, table 2).

Discussion

It has been reported that the BP of the birds increases with age, and is higher in males and in those fed a high Na diet. Of the various avian species, turkeys show a systolic BP over 200 mm Hg and diastolic BP over 150 mm Hg, but the BP and plasma Na concentrations were lower in turkeys kept in the field (105 to 110 mm Hg; n = 3) than in captive birds. These findings suggest that the BP of the birds is influenced by the environment. Indeed, we noted that excitement produces transitional increases of BP and heart rate.

Therefore, in the present investigation we measured the BP of chronically cannulated conscious chickens under conditions that would minimize the possible stress of restraint, light, noise, or handling. Yet, the BP (mean aortic pressure) varied within a wide range of 105 to 175 mm Hg, suggesting that birds may have a mechanism for regulating BP in addition to the response to environmental stress.
In spite of elevated BP, the intact conscious chickens showed a PRA comparable to, or higher than, those of man or dog. The PRA reported in the turkey (0.04-0.4 ng/ml/hr) was low. This is presumably due to the heterologous antibody (human AI antibody) used for measurement. Native AI ([Asp1, Val3, Ser7] AI) from chickens, close relatives of the turkey, does not cross-react with human [His8]AI antibody. Plasma angiotensinogen levels (angiotensin equivalent) were nearly 100 times higher than the angiotensin generated during 3 hours of incubation. Plasma norepinephrine concentrations in conscious chickens were comparable to those found in man, but epinephrine levels were higher than those reported in man and other mammals, suggesting that sympathoadrenal activity is high in the chicken. Plasma Na and Cl concentrations were similar to those reported for the same species, but higher than those for mammals. However, there was no correlation between plasma Na and BP levels during either the control or experimental periods of the present study.

The mechanism of the hypotensive effect of propranolol in mammals is not completely understood. Decrease in cardiac output, suppression of renin release, and action on the central nervous system have been suggested. Differing from the onset of the hypotensive effect of propranolol in mammals, which usually takes 1 to 3 days, the BP-lowering and bradycardic effects in conscious chickens were noted immediately after initiation of propranolol infusion. This quick onset suggests that hypotension after propranolol may be ascribed to a decrease in cardiac output.

### Table 2. Plasma Electrolyte Concentrations During Chronic Treatment with Propranolol, SQ 14,225, or Saline

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Electrolyte</th>
<th>Control*</th>
<th>Week 1*</th>
<th>Week 2</th>
<th>Recovery*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>Na</td>
<td>153.4 ± 1.1</td>
<td>154.3 ± 1.0</td>
<td>153.1 ± 1.3</td>
<td>160.1 ± 2.6</td>
</tr>
<tr>
<td>(n = 14)</td>
<td>K</td>
<td>3.85 ± 0.08</td>
<td>4.00 ± 0.10</td>
<td>4.04 ± 0.11</td>
<td>4.14 ± 0.14</td>
</tr>
<tr>
<td></td>
<td>Cl</td>
<td>128.9 ± 0.8</td>
<td>129.0 ± 1.1</td>
<td>127.1 ± 1.3</td>
<td>127.3 ± 1.5</td>
</tr>
<tr>
<td>SQ 14,225</td>
<td>Na</td>
<td>153.0 ± 1.5</td>
<td>154.3 ± 1.1</td>
<td>153.6 ± 1.6</td>
<td>160.6 ± 2.6</td>
</tr>
<tr>
<td>(n = 12)</td>
<td>K</td>
<td>3.77 ± 0.10</td>
<td>3.91 ± 0.07</td>
<td>3.90 ± 0.09</td>
<td>4.05 ± 0.19</td>
</tr>
<tr>
<td></td>
<td>Cl</td>
<td>126.3 ± 0.6</td>
<td>129.0 ± 0.9</td>
<td>127.9 ± 0.7</td>
<td>129.9 ± 0.7</td>
</tr>
<tr>
<td>Saline</td>
<td>Na</td>
<td>154.6 ± 1.2</td>
<td>153.1 ± 0.9</td>
<td>152.6 ± 0.8</td>
<td>160.2 ± 1.2</td>
</tr>
<tr>
<td>(n = 12)</td>
<td>K</td>
<td>3.76 ± 0.08</td>
<td>3.74 ± 0.08</td>
<td>3.89 ± 0.09</td>
<td>3.95 ± 0.17</td>
</tr>
<tr>
<td></td>
<td>Cl</td>
<td>127.9 ± 0.7</td>
<td>126.8 ± 0.9</td>
<td>124.9 ± 1.7</td>
<td>129.0 ± 1.4</td>
</tr>
</tbody>
</table>

*Mean value of two blood samples taken on different days was calculated for individual chickens, and then the mean ± SE (mEq/liter) of 12 to 14 birds was determined.

Statistical analysis was performed between control value and the values at each experimental and recovery period by a paired t test.

| Table 3. Plasma Catecholamine and Angiotensinogen Levels During Chronic Treatment with Propranolol, SQ 14,225, or Saline

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>NE</td>
<td>354 ± 62</td>
<td>510 ± 69</td>
<td>976 ± 166</td>
</tr>
<tr>
<td>(n = 10)</td>
<td>E</td>
<td>113 ± 27</td>
<td>101 ± 22</td>
<td>124 ± 28</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>1,129 ± 66</td>
<td>1,278 ± 110*</td>
<td>1,401 ± 127*</td>
</tr>
<tr>
<td>SQ 14,225</td>
<td>NE</td>
<td>456 ± 79</td>
<td>473 ± 95</td>
<td>482 ± 103</td>
</tr>
<tr>
<td>(n = 10)</td>
<td>E</td>
<td>216 ± 80</td>
<td>170 ± 71</td>
<td>160 ± 38</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>1,390 ± 155</td>
<td>1,246 ± 160</td>
<td>1,323 ± 217</td>
</tr>
<tr>
<td>Saline</td>
<td>NE</td>
<td>438 ± 43</td>
<td>349 ± 50*</td>
<td>358 ± 68</td>
</tr>
<tr>
<td>(n = 10)</td>
<td>E</td>
<td>190 ± 62</td>
<td>114 ± 25</td>
<td>103 ± 44</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>1,158 ± 86</td>
<td>1,179 ± 90</td>
<td>1,382 ± 130*</td>
</tr>
</tbody>
</table>

Mean value of two blood samples taken on different days of each period (control, experimental, and recovery) were calculated for individual chickens, and then the mean ± SE of 10 birds was determined. NE = plasma norepinephrine (pg/ml); E = plasma epinephrine (pg/ml); A = plasma angiotensinogen (ng/ml).

Statistical analysis was performed between mean control value and the values during each experimental and recovery period by a paired t test.

*p < 0.05.

|p < 0.01. |
output caused by blockade of the cardiac β1-receptor. It has been shown that the chicken heart receives dual innervation, stimulatory sympathetic nerves, and inhibitory parasympathetic (vagus) nerves. In mammals, a fall in the cardiac output is usually accompanied by an increase in the peripheral resistance, and thus BP does not decrease. It is possible that in chickens this neural reflex mechanism is poor. Furthermore, propranolol may exert a peripheral vasodilatory action in chickens.

Simpson et al. reported that both practolol, a relatively cardioselective blocking agent, and propranolol decreased both systolic and diastolic BP and β-aminopropionitrile-induced aortic ruptures in turkeys. The effect of propranolol was slightly more potent than that of practolol. In addition, fragmentation of elastic fibers of the aorta was prevented by propranolol.

The PRA in the second propranolol-treatment week was slightly lower than that of the first treatment week. However, since a similar change was observed in the PRA of the saline-treatment group, this decrease in PRA is presumably ascribed to saline (solvent) effect. The increase in plasma catecholamines after propranolol may be a response to acute reduction of BP or may be due to a release of catecholamines, as has been suggested in some mammals.

Furthermore, the fact that reserpine treatment decreased BP supports the concept that the adrenergic nervous system is important for maintaining BP in chickens. Heart rate also decreased after reserpine administration in all birds tested (n = 4), but due to the large variation of decrease, it was not statistically significant by a paired t test.

Repeated injection of SQ 14,225 decreased the BP in chickens. However, the hypotensive effect was not as marked as that caused by propranolol. Furthermore, BP returned to its original level unless a higher dose was given. A similar "escape" phenomenon has been noted in mammals. It is not clear whether the hypotensive effect of SQ 14,225 is due to its converting enzyme inhibiting action, since a much lower dose (1 mg/kg) of this drug is sufficient to inhibit pressor action of AI in chickens. The PRA increased during treatment with SQ 14,225 presumably because endogenous AII, which usually suppresses renin release, was reduced.

Saline treatment did not alter the BP or heart rate but decreased PRA, which may be the consequence of an increase in Na level in plasma and possibly in urine. The amount of saline used for solvent for the drugs is small, but we flushed the catheters daily after measurement of BP or blood collection with 0.3 ml of heparin-saline, which may promote Na accumulation. It appears that chickens are poor in excreting an excess amount of salt. In spite of the low NaCl content in the laboratory chow (approximate intake: 10 to 20 mEq/day), the plasma Na level is higher than that of man and other mammals. Avian kidneys are composed of a mixture of short reptilian-type nephrons, which do not possess a loop of Henle, and long mammalian-type nephrons. Thus, birds can produce a urine hyperosmotic to their plasma. However, the concentrating ability of avian kidneys is limited; maximum urine osmolality is 400 to 600 mOsm in chickens. In addition, chickens do not possess a functioning nasal gland for excreting Na. Since the primitive macula densa structure evolved in birds, the increase in Na delivery to the macula densa area may have suppressed renin release. The relationship among BP, mineralocorticoids, and renal handling of Na in chickens remains to be determined. The slight increases in plasma angiotensinogen levels noted in the propranolol- and saline-treated groups are presumably the consequence of decreased PRA.

Angiotensin II, in contrast to its exclusive vasopressor effect in mammals, has a dual action when administered to chickens; the vasopressor action of AII is primarily due to release of catecholamines, whereas the vasodepressor effect may possibly be a direct vasodilation or may, in part, be due to release of a depressor substance. The plasma norepinephrine concentrations after acute infusion of [Asp1, Val2]Angiotensin II shown in this study support the concept that the vasopressor action of angiotensin may be indirect, due to release of catecholamines. It is not clear, however, whether angiotensin regulates catecholamine release in vivo as well. The failure of SQ 14,225 or AI antagonist to cause a sustained lowering of BP or a decrease in plasma catecholamines appears to suggest that the renin-angiotensin system does not have a primary role in maintaining the BP in chickens.

**Acknowledgments**

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