Effect of Catecholamines on Plasma Free Fatty Acids and Blood Sugar in Birds* (33966)

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Elevation of plasma FFA levels following injection of catecholamines has been well documented in several mammalian species (1, 2), but there is little information about the effect of these hormones on fat mobilization in birds (3). Carlson *et al.* (4) reported that infusion of norepinephrine does not affect plasma FFA concentration in the domestic fowl. Norepinephrine does not stimulate *in vitro* the lipolytic activity of chicken adipose tissue (4), but epinephrine stimulates lipolysis in the adipose tissue of pigeons (5). Because catecholamines are considered to play an important role in the process of fat mobilization (1, 6, 7) it is of interest to investigate their effects in other avian species. A study of the effects of epinephrine and norepinephrine on the plasma FFA and blood sugar of geese, turkeys, and ducks is reported here.

Methods. Experimental animals and analytical methods were as previously described (8). Anesthesia was induced with sodium pentobarbital[1] (35 mg/kg, ⅔ iv, ⅓ im). Infusions were made through a P.E. 90-gauge catheter inserted into a wing vein, using a continuous infusion pump.[2] Infusion rates were 3.06 ml/hr for geese and 1.20 ml/hr for ducks.

Food was removed from the cages 16–18 hr before the beginning of the experiments. One hr was allowed between the induction of anesthesia and the first control blood sample taken 30 min before administration of the catecholamine. Appropriate dilutions of epinephrine,[3] and norepinephrine[4] in 0.9% NaCl were prepared daily, immediately before use. Control animals were infused with 0.9% NaCl solution.

Results. Injection of epinephrine in geese (Table I). Intravenous injection of 10.0 μg of epinephrine/kg caused in unanesthetized geese an elevation of plasma FFA, of borderline statistical significance, 15–45 min after injection. The same dose of epinephrine caused a sharp and significant drop of plasma FFA at 5 min, but no other significant FFA change, when injected to the same geese anesthetized with sodium pentobarbital.

Injection of norepinephrine in geese and turkeys (Table II). No significant change of plasma FFA was observed after intravenous injection of 10.0 μg of norepinephrine/kg in nonanesthetized geese, but 20.0 μg of norepinephrine/ kg caused significant elevation of FFA 5 and 15 min after injection. The latter dose had no significant effect on the plasma FFA of turkeys.

Infusion of epinephrine and norepinephrine, for 2 hr, in anesthetized geese (Table III). Continuous infusion of epinephrine (2.5 μg/kg/min) caused progressive decrease of plasma FFA. In contrast, norepinephrine infused at the same rate caused significant elevation of plasma FFA sustained throughout the infusion period. No FFA change was observed in control animals infused with saline solution.

Infusion of epinephrine and norepinephrine in ducks. Epinephrine and norepinephrine (0.5 μg/kg/min) were infused, each to a group of 6 mallard male ducks, for 2 hr. No elevation of plasma FFA was detected with either of the two catecholamines. At the

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[1] Diabutal, Diamond Laboratories Inc., Des Moines, Iowa.

[2] Model 600-910, Harvard Apparatus Co. Dover, Mass.

[3] Adrenalin chloride, Parke, Davis Co., Detroit, Mich.

[4] Levophed, Whinthrop Laboratories, New York, N. Y.

TABLE I. Effect of a Single Epinephrine Injection (10.0 μg/kg, iv) on Plasma FFA (meq/liter) of 7 Geese without Anesthesia and when Anesthetized with Sodium Pentobarbital.[a]

			After injection (min)				
	C1[b]	C2[c]	5	15	30	45	60
Nonanesthetized	1.10	1.16	1.07	1.45	1.56	1.46	1.45
	±0.10	±0.09	±0.16	±0.10	±0.17	±0.11	±0.15
Difference: sample—mean control			−0.06	0.32	0.43	0.33	0.32
			±0.11	±0.13	±0.16	±0.12	±0.15
			$p = 0.7$	0.05	0.04	0.04	0.07
Anesthetized	0.99	1.01	0.65	1.08	1.06	1.10	1.05
	±0.08	±0.07	±0.06	±0.08	±0.07	±0.08	±0.06
Difference: sample—mean control			−0.35	0.08	0.06	0.10	0.05
			±0.08	±0.04	±0.05	±0.05	±0.05
			$p = 0.006$	0.10	0.23	0.10	0.35

[a] Means and SE.
[b] Control sample taken 30 min before injection.
[c] Control sample taken just before injection.

end of infusion plasma FFA levels were about 60% of the control value. Mean FFA decrease for the 6 ducks infused epinephrine was 0.62 meq/liter (SE ± 0.12), and that for the 6 ducks receiving norepinephrine 0.74 meq/liter (SE ± 0.19). Both decreases were significant ($p = 0.001$ and 0.008, respectively). No significant change of plasma FFA was observed in control ducks infused with saline solution. Higher doses of epinephrine (1.0, 2.0, and 3.0 μg/kg/min) were tested in single animals with results similar to those reported for the 0.5 μg/kg/min dose.

Blood sugar changes. Blood sugar of geese

TABLE II. Effect of a Single Norepinephrine Injection (iv) on Plasma FFA (meq/liter) of Nonanesthetized Geese and Turkeys.[a]

					After injection (min)				
Birds	No.	Dose (μg/kg)	C1[b]	C2[c]	5	15	30	45	60
Geese	8	10.0	1.11	1.12	1.25	1.20	1.19	1.10	1.10
			±0.16	±0.16	±0.17	±0.15	±0.15	±0.18	±0.14
Difference: sample—mean control					0.13[d]	0.08[d]	0.07[d]	−0.02[d]	−0.02[d]
					±0.12	±0.06	±0.04	±0.09	±0.06
	8	20.0	1.10	1.10	1.40	1.37	1.32	1.22	1.17
			±0.08	±0.08	±0.10	±0.13	±0.11	±0.09	±0.09
Difference: sample—mean control					0.30[e]	0.27[e]	0.22[f]	0.12[d]	0.07[d]
					±0.05	±0.08	±0.07	±0.08	±0.08
Turkeys	5	20.0	0.48	0.52	0.60	0.57	0.60	0.64	0.60
			±0.04	±0.05	±0.04	±0.04	±0.07	±0.06	±0.05
Difference: sample—mean control					0.10[d]	0.07[d]	0.10[d]	0.14[d]	0.10[d]
					±0.04	±0.04	±0.08	±0.07	±0.05

[a] Means and SE.
[b] Control sample taken 30 min before injection.
[c] Control sample taken just before injection.
[d] Not significant ($p > 0.05$).
[e] Significant ($p < 0.01$).
[f] $0.01 < p < 0.05$.

TABLE III. Effect of Intravenous Infusions of Epinephrine and Norepinephrine (2.5 μg/kg /min, each, for 2 hr) on Plasma FFA in Geese.[a]

	No. of birds	C1[b]	C2[c]	Time of infusion (min) 5	15	30	60	90	120
Epinephrine	8	1.16 ±0.13	1.12 ±0.11	0.84 ±0.09	0.83 ±0.10	0.74 ±0.09	0.66 ±0.10	0.69 ±0.12	0.64 ±0.09
Difference: sample—mean control				−0.30[d] ±0.04	−0.31[d] ±0.06	−0.40[d] ±0.09	−0.48[d] ±0.09	−0.45[d] ±0.09	−0.50[d] ±0.07
Norepinephrine	8	1.00 ±0.17	1.03 ±0.11	1.54 ±0.22	1.85 ±0.25	1.86 ±0.26	1.71 ±0.19	1.70 ±0.20	1.66 ±0.18
Difference: sample—mean control				0.52[d] ±0.15	0.83[d] ±0.17	0.84[d] ±0.19	0.69[d] ±0.12	0.68[d] ±0.16	0.64[d] ±0.14
Saline solution	2	0.94	0.94	0.89	0.95	0.94	1.01	0.84	0.92

[a] Means and SE (meq/liter).
[b] Control sample taken 30 min before infusion.
[c] Control sample taken just before starting infusion.
[d] Significant difference ($p < 0.01$).

showed a 20% elevation above preinjection level ($p<0.01$) 15 min after injection of 10.0 μg/kg of epinephrine. No difference in blood sugar change was observed between anesthetized and nonanesthetized geese. Only minimal changes of blood sugar were noted after injection of norepinephrine in geese and turkeys.

Infusion of epinephrine (2.5 μg/kg/min) in geese caused progressive elevation of blood sugar reaching a maximum of 78% above control level at the end of the 2-hr infusion, ($p = 0.0008$). Norepinephrine infused at the same rate caused only a small transient increase of blood sugar, at 5 min (12% above control, $p = 0.006$).

Both epinephrine and norepinephrine infused at the rate of 0.5 μg/kg/min, caused elevations of blood sugar in ducks. Levels at 120 min of infusion were 40% above control, but only the elevation produced by norepinephrine was significant ($p = 0.003$).

Discussion. These results reveal some differences in the effect of the catecholamines on plasma FFA levels between the avian species studies. They also indicate that this effect is influenced by anesthesia.

In unanesthetized geese both catecholamines caused elevation of plasma FFA (Tables I and II), but epinephrine was more effective than norepinephrine. The effect of 10.0 μg/kg of epinephrine, although of borderline statistical significance, was roughly comparable to that of 20.0 μg/kg of norepinephrine, and 10.0 μg/kg of norepinephrine failed to produce any significant change of FFA.

The FFA response to epinephrine injection in unanesthetized geese compares, in absolute terms, with that observed in the anesthetized dog (6). Turkeys showed no change in plasma FFA when injected with 20.0 μg/kg of norepinephrine, thus suggesting that this species is less responsive to norepinephrine than the goose.

That anesthesia influences the effect of epinephrine on plasma FFA is shown by the data in Table I and by the fact that continuous infusion of epinephrine caused in anesthetized geese a progressive decrease of plasma FFA (Table III). No significant decrease of plasma FFA was observed when either catecholamine was injected to unanesthetized geese, but in anesthetized geese infusion of norepinephrine caused an elevation of plasma FFA and that of epinephrine caused FFA to decrease.

Continuous infusion of norepinephrine (2.5 μg/kg/min) caused significant elevation of plasma FFA throughout the infusion period in geese, in contrast with the lack of effect reported by Carlson *et al.* (4) in the domes-

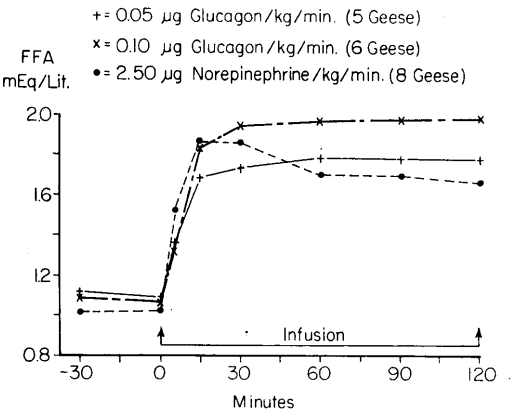

FIG. 1. A comparison of the effects of glucagon and norepinephrine infusions on the plasma FFA of anesthetized geese.

tic fowl. It is apparent that the effect observed in geese is smaller than that observed in the dog under comparable conditions. Thus, infusion of norepinephrine at the rates of 1.0 and 2.0 μg/kg/min produced 3- to 5-fold increases of plasma FFA concentration in anesthetized dogs (6, 9) whereas the infusion of 2.5 μg/kg/min of norepinephrine caused only a 1.8-fold increase of FFA in anesthetized geese.

Since glucagon causes marked elevations of plasma FFA in birds (8) it is of interest to compare the effects of catecholamines and glucagon in geese. In unanesthetized geese single injection of epinephrine (10.0 μg/kg) produced elevations of plasma FFA somewhat greater than those produced by injection of 0.5 μg/kg of glucagon, but smaller than those observed when 1.0 μg/kg of glucagon was injected (8). The FFA response to the infusion of 2.5 μg/kg/min of norepinephrine is comparable to that obtained by infusion of 0.05 μg/kg/min of glucagon (10) as shown in Fig. 1.

It appears therefore, that, in terms of weight, glucagon is roughly 50 times more effective than norepinephrine in raising the plasma FFA when infused into anesthetized geese. Since the molecular weight of glucagon is about 20 times greater than that of norepinephrine this would indicate that on a molecular basis glucagon is about 1000 times more effective than norepinephrine.

The blood sugar changes were consistent with the concept that norepinephrine has a weaker glycogenolytic effect than epinephrine (11), except in the anesthetized ducks. The catecholamine effects on the blood sugar were not modified by anesthesia.

The elevations of blood sugar induced by epinephrine were much smaller than those produced by similar doses of glucagon (8, 10) and this is in agreement with observations in mammals showing that glucagon has greater and more persistent effects on liver glycogen and blood sugar than epinephrine (12).

Summary. Intravenous injection of epinephrine (10.0 μg/kg) caused elevation of plasma FFA in unanesthetized, but not in anesthetized geese. Norepinephrine injection (20.0 μg/kg) caused elevation of plasma FFA in geese but not in turkeys (both unanesthetized). In anesthetized geese infusion of epinephrine (2.5 μg/kg/min) caused progressive decrease of plasma FFA. Norepinephrine infused at the same rate caused a sustained elevation of plasma FFA. The FFA response to norepinephrine infusion in geese was smaller than that reported in dogs under comparable conditions. In anesthetized ducks both epinephrine and norepinephrine infused at the rate of 0.5 μg/kg/min caused progressive decrease of plasma FFA. The elevations of plasma FFA and blood sugar produced by catecholamines in geese are considerably smaller than those produced by glucagon.

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Comparison in Conscious Goats of the Effects of Epinephrine, Norepinephrine, and Tyramine on Blood Pressure* (33967)

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There are certain advantages to the use of the goat in experimental studies. The goat offers some advantages in bridging the gap between laboratory animals and higher primates because its neuromuscular coordination is of a superior type, it has a life span of about 10 years, and it is easy to condition to accept experimental procedures. They are also inexpensive and easy to maintain. Fletcher (1) in a report containing a comprehensive list of references, discussed the use of the goat in research. To date, specific detailed information on drug responses of the cardiovascular system of the goat is limited, particularly in conscious animals.

Rangsit (2) reported a marked increase in arterial blood pressure in unanesthetized sheep when given 1–3.5 ml of a 1:10,000 solution of epinephrine intravenously. Halmagyi (3), in normotensive sheep, found that norepinephrine infusion produced a statistically significant rise in systemic arterial pressure from 102 to 123 mm Hg.

The present report describes the results obtained when epinephrine,[1] norepinephrine,[1] and tyramine were administered to conscious goats.

Methods and Materials. Five sexually mature male goats (Spanish type) weighing between 21 and 45 kg were used for this study. They were previously surgically prepared with unilateral exteriorized carotid artery loops [Flournoy *et al.* (4)] and were drug free for at least 3 weeks prior to the initiation of the study. To record blood pressure from an exteriorized carotid artery, an 18-gauge silicon coated needle attached to silicone coated polyvinyl tubing was inserted into the carotid. Heparin (2000 units/100 ml of saline) was used to prevent clotting in the tube leading to the blood pressure transducer. Arterial blood pressure was recorded with a P-1000 Linear Core transducer used in conjunction with a Physiograph Four. A jugular vein was catheterized for the intravenous injections. All injections of pressor compounds were administered in single doses to individual goats and a minimum of 5 min of steady blood pressure recordings were obtained between injections. Each goat served as its own control. A regression analysis was used to establish the nature of the pressor responses and duration of action to the different injections.

Results. The dose–response relationships of the pressor responses to tyramine, epineph-

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