suggesting that the high ratio may be of peripheral events. This concept is supported by the facts, such as lowering of the plasma T_3/T_4 ratio by cholestyramine feeding in the germfree rat (table 1), and better intestinal absorption of T_3 than T_4 observed in the conventional rat[17]. The reabsorption of T_3 is thought to be enhanced by an increase of intestinal bile concentration[7], which is higher in the germfree rat[9,18].

To elucidate the mechanism of the high T_3/T_4 ratio in germfree rat plasma, further studies would be necessary on the thyroidal release of T_3, the hepatic conversion[19] from T_4, a prohormone[20], to T_3 and the biliary excretion or intestinal reabsorption of T_3 in germfree rats. However, our present study suggests that the enterohepatic circulation of thyroid hormones may have more significance in regulating the plasma T_3/T_4 ratio in the germfree rat than in the conventional. In addition, we assume that the high plasma T_3 level in the germfree rat may be a result of adaptation.

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Effect of adrenaline and adrenergic active drugs on growth hormone secretion in immature cockerels

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Summary. In immature cockerels adrenaline administration lowered the levels of plasma growth hormone. Both alpha and beta adrenergic receptor agonists also depressed the circulating growth hormone levels. In the presence of beta blockade, the suppressive effect of adrenaline on growth hormone secretion was not observed.

In primates there is considerable evidence that adrenergic pathways are involved in the control of growth hormone secretion[1-4]. In particular it is known that many of the stimuli that cause growth hormone release (e.g. insulin hypoglycaemia, exercise, arginine) act via dual adrenergic mechanisms; being suppressed by alpha blockade and enhanced by beta blockade[4]. Large doses of adrenaline itself have also been found to stimulate growth hormone secretion in the monkey[5] although in man a stimulatory effect of adrenaline on growth hormone secretion is only seen in the presence of beta blockade[6], an effect which is blocked by alpha blockade[7]. In contrast, adrenaline has been found to inhibit growth hormone secretion in the rat and this effect is not influenced by alpha or beta adrenergic blockade[8]. Adrenaline has also been found to inhibit growth hormone release in sheep[9] and mice[10] although it has no effect in pigs[11] and cattle[12]. In birds very little is known of the factors controlling growth hormone secretion and the possibility that adrenaline or adrenergic mechanisms might affect the circulating levels of plasma growth hormone has not been assessed. However, in the domestic fowl growth hormone secretion is affected in some stressful conditions[13] when endogenous adrenaline might be expected to be released. Therefore the aim of the present communication was to investigate the effect of adrenaline and adrenergic agents on the levels of plasma growth hormone in the domestic fowl.

Materials and methods. All the birds used in this study were 6-8-week-old cockerels (Thornber 909's). They were bled by brachial vein venipuncture and 1-1.5 ml blood taken. The needle was left in situ and the test substances i.v. injected. A 2nd blood sample was taken 20 min later. In 1 experiment groups of 8-week-old cockerels were i.v. injected with adrenaline (L-epinephrine, Sigma Chemical Co. Ltd.) at doses of 0-10 mg/kg b.wt in a volume of 1 ml/kg. Subsequently groups of 6-week-old cockerels were treated with freshly dissolved adrenaline (1 mg/kg), alone or together with various adrenergic receptor-active drugs: phentolamine mesylate (Ciba Ltd) an alpha blocker, 1 mg/kg; L-phenylephrine hydrochloride (Sigma Chemical Co. Ltd) an alpha stimulator, 1 mg/kg; DL-propranolol hydrochloride (Sigma Chemical Co. Ltd) a beta blocker, 1 mg/kg and DL-isoproterenol hydrochloride (Sigma

Table 1. Effect of adrenaline on the levels of plasma growth hormone in immature cockerels

Dose of adrenaline	Plasma growth hormone (ng/ml ± SEM, N = 5)		% Pretreatment level (means ± SEM, N = 5)
	Pretreatment level	Posttreatment level	
0	55 ± 12	63 ± 13	127 ± 24
0.01	44 ± 5	47 ± 12	111 ± 29
0.10	91 ± 19	34 ± 8*	37 ± 9**
1.00	58 ± 15	18 ± 1*	41 ± 10**
10.00	63 ± 16	16 ± 1*	23 ± 4***

Significantly different from pretreatment level, *$p < 0.05$ (paired t-test). Significantly different from saline controls, **$p < 0.01$; ***$p < 0.001$ (ANOVA analysis of variance).

Table 2. Effect of adrenaline and adrenergic drugs on plasma growth hormone levels in immature cockerels

Treatment	Plasma growth hormone (ng/ml ± SEM, N = 5) Pretreatment level	Posttreatment level	% Pretreatment level (means ± SEM, N = 5)
Saline (1 ml/kg)	95 ± 7	85 ± 6	101 ± 5[f]
Adrenaline (1 mg/kg)	116 ± 14	63 ± 15[a]	42 ± 9[c]
Phentolamine (1 mg/kg)	72 ± 17	84 ± 26	127 ± 26[f]
Propranolol (1 mg/kg)	86 ± 20	116 ± 26	149 ± 23[c,f]
Isoproterenol (1 mg/kg)	123 ± 24	45 ± 9[b]	36 ± 6[d]
Phenylephrine (1 mg/kg)	140 ± 15	71 ± 7[a]	54 ± 9[c]
Adrenaline (1 mg/kg) + phentolamine (1 mg/kg)	91 ± 7	32 ± 7[a]	36 ± 10[d]
Adrenaline (1 mg/kg) + propranolol (1 mg/kg)	119 ± 46	72 ± 15	92 ± 22[f]
Adrenaline (1 mg/kg) + isoproterenol (1 mg/kg)	51 ± 17	36 ± 17[a]	44 ± 11[d]
Adrenaline (1 mg/kg) + phenylephrine (1 mg/kg)	112 ± 28	30 ± 13[b]	23 ± 7[e]

Significantly different from pretreatment level, [a]$p < 0.01$; [b]$p < 0.001$ (paired t-test). Significantly different from saline controls, [c]$p < 0.05$; [d]$p < 0.01$; [e]$p < 0.001$ (ANOVA analysis of variance). Significantly different from adrenaline treated birds, [f]$p < 0.05$ (ANOVA analysis of variance).

Chemical Co. Ltd) a beta stimulator, 1 mg/kg. Controls received 0.9% saline, 1 ml/kg. The concentrations of plasma growth hormone were determined using a specific radioimmunoassay[14]. Each plasma sample was assayed in duplicate at 2 dilutions and all plasmas from 1 experiment were assayed together to eliminate interassay variation. The results were analysed for statistical differences by Student's paired t-test and by ANOVA analysis of variance.

Results and discussion. It can be seen from table 1 that the basal (pretreatment) levels of plasma growth hormone were quite variable, as was observed in a previous study[15]. It is also evident from table 1 that the administration of saline to the control birds had little effect on the levels of plasma growth hormone. In marked contrast adrenaline administration had a dramatic effect on growth hormone secretion, with doses of 0.1, 1.0 and 10 mg/kg strikingly lowering the circulating growth hormone levels. Following adrenaline administration the maximum fall in the concentration of plasma growth hormone was roughly consistent with the known disappearance rate of growth hormone in plasma[16].

The effect of administering adrenaline to 6-week-old cockerels, alone or together with adrenergic receptor agonists and antagonists is shown in table 2. Adrenaline again lowered the levels of plasma growth hormone when injected alone, as did phenylephrine and isoproterenol. When adrenaline was injected together with these adrenergic receptor agonists, the inhibition of growth hormone secretion (expressed as a percentage of the pretreatment level) was not significantly greater than when either was administered alone. A fall in the levels of plasma growth hormone was also observed when adrenaline was simultaneously injected with the alpha blocker (phentolamine), but not when injected with the beta blocker (propranolol). Indeed, the post-treatment levels of plasma growth hormone in the birds injected with propranolol alone were higher than in birds treated with saline or adrenaline alone. In addition, when adrenaline and propranolol were injected together, the levels of plasma growth hormone were higher than in birds treated with adrenaline alone. Thus it would appear that the effect of adrenaline on growth hormone secretion is mediated via beta adrenergic receptors.

The results of the effects of adrenaline on growth hormone secretion in the domestic fowl are, therefore, apparently different from those in primates[5-7]. In the chicken the present results clearly demonstrate that peripherally administered adrenaline markedly lowers the levels of plasma growth hormone and provides evidence of an adrenergic control mechanism in the regulation of growth hormone secretion. Moreover, as adrenaline does not appreciably cross the blood brain barrier[17], the present results may also indicate the presence of adrenergic sites controlling growth hormone release outside the brain. Furthermore, unlike man[18], growth hormone secretion in the fowl is not regulated by negative feedback control from circulating glucose levels[19,20] and therefore the adrenaline induced suppression of growth hormone secretion in the chicken is unlikely to be due to the hyperglycaemia which follows adrenaline administration[21,22].

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