glycerol levels during ACTH stimulation was not affected by the doses of indomethacin and corticosteroids used, indicating that the anti-inflammatory drugs did not reduce lipolysis.

When the chopped fat tissue was incubated in Krebs medium alone a small amount of PGE_2 (measured as ng/5g fat tissue) appeared in the fat sediment (5.4 ± 0.4) and in the supernatant (4.9 ± 0.5).

After stimulation with ACTH there was a statistically significant increase in the PG content of the fat (13.4 ± 0.7) and of the supernatant (17.0 ± 1.3). When incubated in the presence of indomethacin (1 μg/ml), ACTH failed to cause an increase either in the fat (1.5 ± 0.3) or supernatant (2.3 ± 0.5), the PG levels remaining below control values. On the other hand, in the presence of the corticosteroid, betamethasone (10 μg/ml) the content of PGE_2 in the supernatant was lower (5.8 ± 0.8) whilst that in the fat was higher (24.4 ± 1.5) than with ACTH alone. Hydrocortisone (10 μg/ml) produced the same effect.

Thus whereas a non-steroid anti-inflammatory agent, indomethacin, reduced the total amount of PG formed during lipolysis, anti-inflammatory steroids did not reduce the total but increased the tissue/supernatant ratio. These results support the hypothesis that in rabbit adipose tissue corticosteroids inhibit the release of prostaglandins but not their synthesis.

J.C. is an M.R.C. research student.

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Effects of steroid hormones on tissue levels of prostaglandin 15-hydroxydehydrogenase in the rat

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Blackwell, Flower & Vane (1975) showed that prostaglandin 15-hydroxydehydrogenase (PGDH) —the enzyme catalysing the initial step in prostaglandin metabolism—has a short life within the cell, and suggested that the enzyme might be under hormonal control many metabolic processes and there is already some evidence that steroids, after PGDH levels in the pregnant rabbit (Bedwani & Marley, 1975; Sun & Armour, 1974). We have now studied the tissue activity of PGDH in rats in which steroid hormone levels were altered by adrenalectomy, ovariectomy or pregnancy.

PGDH activity was estimated in the high speed supernatants of kidneys (and sometimes in lungs) by measuring the conversion of [^{3}H]-PGE_2 to its 15-keto derivative as previously described (Blackwell, Flower, Parsons & Vane 1975). Metabolism in the particle-free fractions of kidneys from adrenalectomized rats was greatly (140%) increased above control levels (see Table 1); however, after hydrocortisone hemisuccinate (two doses of 5 mg i.p., 8 h apart) PGDH activity was returned to control levels or below. A synthetic glucocorticoid, dexamethasone (two doses of 1 mg i.p., 8 h apart) also reduced the tissue levels of PGDH in control rats by about 40%.

Metabolism in high speed fractions of ovariectomized rat kidneys was again higher (116%) than in the control group. Administration of oestradiol-17β (1 mg each day for 3 days) reduced metabolism to 17% of control levels whilst progesterone (same dose) had only a very slight inhibitory effect ($< 5\%$).

None of the exogenous steroids had any direct effect on enzyme activity *in vitro*.

Metabolism of PGE_2 in the lungs and kidneys of pregnant rats varied; for example in well advanced pregnancy (day 18) metabolism by lung was higher than in the ovariectomized controls (185%). However, in rats during parturition the enzyme levels were extremely low, less than 3% of control levels. Similar effects were seen on kidney PGDH levels.

These results suggest that exogenous or endogenous steroid hormones can greatly modify PGDH levels. In particular the profound

Table 1 Effect of steroid hormones on tissue levels of PGDH in the rat

Tissue source	*Treatment*	*PGE_2 oxidized*	
		fmol mg^{-1} min^{-1} (mean ± s.e. mean)	
Kidney	Control (♂)	594.4 ± 9.5	(*n* = 5)
	Adrenalectomized	835.5 ± 5.5	(*n* = 3)
	Control + hydrocortisone	525.0 ± 3.1	(*n* = 3)
	Adrenalectomized + hydrocortisone	486.7 ± 4.1	(*n* = 3)
	Control + dexamethasone	348.1 ± 6.6	(*n* = 5)
	Control (♀)	609.6 ± 82.2	(*n* = 3)
	Ovariectomized	704.4 ± 25.6	(*n* = 5)
	Ovariectomized + progesterone	583.4 ± 19.0	(*n* = 5)
	Ovariectomized + oestradiol 17β	103.2 ± 5.4	(*n* = 5)
Lung	Control (♀-ovariectomized)	914.4 ± 121.57	(*n* = 3)
	Pregnant (18 day)	1699.6 ± 58.8	(*n* = 3)
	Pregnant (Parturition)	24.8 ± 6.6	(*n* = 3)

depression of PGDH levels occurring during parturition—which could perhaps be due to the oestrogen surge occurring about this time—could be a controlling factor in determining the rise in prostaglandin activity during parturition.

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Formation of prostaglandin endoperoxides and rabbit aorta contracting substance (RCS) by coupling two enzyme systems

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Piper & Vane (1969) detected the release of an additional and labile substance during anaphylaxis in isolated lungs from sensitized guinea-pigs. Because of its activity, they called it 'rabbit aorta contracting substance' or RCS. The half life of RCS was less than 2 minutes. Thromboxane A_2 (TxA2) has a half life of 30 s, induces platelet aggregation and contracts rabbit aorta; it is thought to be RCS (Samuelsson, 1975). TxA_2 is generated from prostaglandin (PG) G_2 or PGH_2 by tissues such as lungs or platelets (Samuelsson, 1975).

We have used washed platelets obtained from fresh citrated horse blood to show that conversion