or any PGE metabolite. However, $PGF_{2\beta}$ was metabolized at the same rate as $PGF_{2\alpha}$ by the conventional two step pathway to a compound provisionally identified as 13,14-dihydro-15-keto $PGF_{2\beta}$.

These results show that the rabbit renal cortex contains an enzyme capable of converting $PGF_{2\alpha}$ directly to PGE_2. Pace-Asciak (1975) has described a similar enzyme in rat kidney and called it prostaglandin 9-hydroxydehydrogenase, but in this species it converts a $PGF_{2\alpha}$ metabolite to its PGE_2 equivalent. By contrast, the rabbit enzyme may be an important modulator of renal function, since $PGF_{2\alpha}$ has less potent or different actions than PGE_2 on renal functions (McGiff & Nasjletti, 1973).

References

ANDERSEN, N.H. (1969). Preparative thin layer and column chromatography of prostaglandins. *J. Lipid Res.*, **10**, 316–319.

HOULT, J.R.S. & MOORE, P.K. (1977). Pathways of prostaglandin $F_{2\alpha}$ metabolism in mammalian kidneys. *Br. J. Pharmac.*, **61**, 615–626.

McGIFF, J.C. & NASJLETTI, A. (1973). Renal prostaglandins and the regulation of blood pressure. In *Prostaglandins and Cyclic AMP*, ed. Kahn, R.H. & Lands, W.E.M., pp. 119–151. New York: Academic Press.

PACE-ASCIAK, C. (1975). Prostaglandin 9-hydroxydehydrogenase activity in the adult rat kidney. Identification, assay, pathway and some enzyme properties. *J. biol. Chem.*, **250**, 2789–2794.

Thyroxine-induced hyperthyroid state in rats suppresses renal prostaglandin metabolism

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15-Hydroxyprostaglandin dehydrogenase (15-PGDH) and prostaglandin Δ-13 reductase (Δ-13 R) in high-speed supernatants from rat kidney metabolise prostaglandin (PG) $F_{2\alpha}$ rapidly to 15-keto $PGF_{2\alpha}$ and then to 13,14-dihydro-15-keto $PGF_{2\alpha}$ (Hoult & Moore, 1977). A prostaglandin 9-hydroxydehydrogenase (9-HDH) further converts PGF metabolites to their PGE derivatives. Since 15-PGDH appears to have a rapid turnover (Blackwell, Flower & Vane, 1975) and its levels are influenced by steroid hormones (Blackwell & Flower, 1976) as well as in pregnancy (Bedwani & Marley, 1975), we examined the effect of altered thyroid status on rat renal PG metabolism.

Groups of 45 g and 275 g male Sprague-Dawley rats were made hyperthyroid or hypothyroid by 18 daily s.c. injections of (−)-thyroxine (200 μg) and methimazole (2 mg) respectively. Hyperthyroid rats showed reduced rates of growth, cardiac hypertrophy, elevated serum thyroxine levels and thyroid atrophy; hypothyroid animals appeared normal apart from thyroid enlargement. 100,000 *g* cytoplasmic supernatants were prepared in pH 7.4 phosphate buffer, incubated with NAD^+ (5 mM) and $PGF_{2\alpha}$ (10 μg/ml) labelled with 0.11 μCi [^{3}H-9β]-$PGF_{2\alpha}$ and extracted for assay of 15-PGDH, Δ-13 R and 9-HDH activity as described previously (Hoult & Moore, 1977).

$PGF_{2\alpha}$ metabolism by both conventional 15-PGDH and Δ-13 R pathways and by conversion to PGE metabolites by 9-HDH was inhibited 40% in hyperthyroid animals. In 10 min incubations of renal supernatants from 45 g rats overall PG metabolism was 68.3 ± 2.3% in saline-injected control rats, but reduced to 40.3 ± 2.9% in hyperthyroid rats ($n = 9$, $P<0.001$). In 275 g rats, metabolism in 75 min incubations was reduced from 83.4 ± 2.6% to 50.1 ± 3.2% ($n = 10$, $P<0.001$). There was no difference between any of the renal supernatants in soluble protein content, rates of utilization of NAD^+ by endogenous enzymes and substrates, or of NAD^+ dependence of 15-PGDH. Thyroxine did not inhibit PG metabolism up to 200 μg/ml.

We conclude that thyroxine treatment reduces endogenous levels of 15-PGDH and other PG metabolising enzymes, probably by a direct effect on protein metabolism, consistent with the known biochemical actions of this hormone (Wolff & Wolff, 1964). The results also show that levels of these enzymes are lower in older rats.

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References

BEDWANI, J.R. & MARLEY, P.B. (1975). Enhanced inactivation of prostaglandin E_2 by the rabbit lung during pregnancy or progesterone treatment. *Br. J. Pharmac.*, **53**, 547–554.

BLACKWELL, G.J. & FLOWER, R.J. (1976). Effect of steroid hormones on tissue levels of prostaglandin 15-hydroxydehydrogenase in the rat. *Br. J. Pharmac.*, **56**, 343P.

BLACKWELL, G.J., FLOWER, R.J. & VANE, J.R. (1975). Rapid reduction of prostaglandin 15-hydroxydehydrogenase activity in rat tissues after treatment with protein synthesis inhibitors. *Br. J. Pharmac.*, **55**, 233–238.

HOULT, J.R.S. & MOORE, P.K. (1977). Pathways of prostaglandin $F_{2\alpha}$ metabolism in mammalian kidneys. *Br. J. Pharmac.*, **61**, 615–626.

WOLFF, E.C. & WOLFF, J. (1964). The mechanism of action of the thyroid hormones. In: *The Thyroid Gland*, ed. Pitt-Rivers, R. & Trotter, W.R. London: Butterworth & Co Ltd.