THE EFFECT OF PROSTACYCLIN ON PITUITARY HORMONE RELEASE

A role has been proposed for prostaglandins in the regulation of anterior pituitary hormone release (Harms, Ojeda, McCann, 1973; Deis & Vermouth, 1975). Pretreatment with indomethacin blunts the preovulatory surge of plasma luteinizing hormone (LH) in deer mice (Meeuwsen & Seeley, 1979) and rats (Tsafriri, Koch & Lindner, 1973), and infusion of PGE_2 and $PGF_{2\alpha}$ into the lateral ventricle of male rats elevates both plasma LH and prolactin (Warberg, Eskay & Porter, 1976).

We have studied the effect of prostacyclin (PGI_2) on anterior pituitary hormone release in man.

Five normotensive male volunteers were infused intravenously with PGI_2 (8 ng kg^{-1} min^{-1}) or vehicle alone (glycine buffer), continuously for 4 h. All subjects were fasting and had abstained from medication for at least 2 weeks prior to the study. The infusion sequence was randomized and the administration double-blind. A minimum of 6 days separated the two infusions. Blood samples for prolactin, LH, FSH and cortisol were taken before the start of the infusions and at frequent subsequent intervals. All hormones were measured by radioimmunoassay.

Haemodynamic effects were maximal following 20 min of PGI_2 infusion when blood pressure had altered by + 12.0 ± 1.6/–11.0 ± 0.7 mmHg and heart rate by +20.6 ± 1.4 beats/min from control values ($P < 0.001$). The infusions were well tolerated in three subjects, however, the two others complained of nausea and abdominal discomfort 1 to 2 h after commencing PGI_2. Both plasma cortisol and prolactin increased with the onset of symptoms in these subjects while not changing from control values in the problem-free volunteers (Figure 1). Plasma FSH and LH did not alter during PGI_2 (Table 1).

Recently Kimball, Porteus, Kirton, Frielink, Creasey & Dayan (1979) have demonstrated that intravenous PGI_2 markedly increased both prolactin and LH in oestradiol treated, ovariectomized rats. Subcutaneous PGI_2 for 7 days resulted in a significant depression of LH but had no effect on prolactin in intact male and female rats. However, stress is a potent stimulus to prolactin release. Although prostaglandins may act independently they do not increase prolactin release from pituitaries *in vitro* (Sundberg, Fawcett, Illner & McCann, 1975). Similarly PGI_2 does not appear to have a primary effect on adrenal steroidgenesis (Laychock, 1979). Our results suggest that intravenous PGI_2 does not stimulate prolactin or pituitary gonadotropin release in healthy male volunteers. However stressful side effects during PGI_2 infusion may secondarily elevate circulating levels of both cortisol and prolactin.

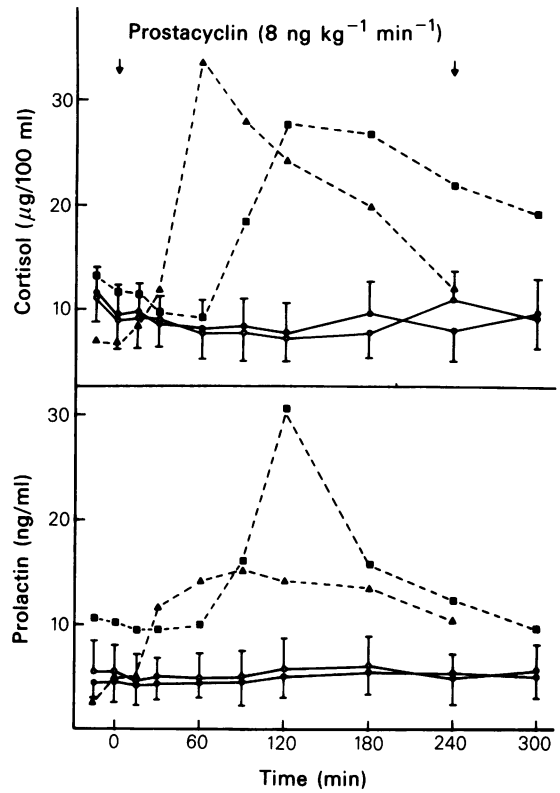

Figure 1 Changes in plasma cortisol and serum prolactin during a 4 h intravenous infusion of PGI_2 (8 ng kg^{-1} min^{-1}). Individual results in two subjects (▲- - - -▲; ■- - - - -■) with stressful side-effects are shown, with mean changes (± s.d.) in three asymptomatic subjects (●—●) during PGI_2 and in the entire group during the control infusion (○——○).

Table 1 Concentrations of luteinizing hormone (LH) and folicle stimulating hormone (FSH) during a 240 min infusion of prostacyclin (PGI_2) at 8 ng kg^{-1} min^{-1} or glycine buffer

	LH (mIU/ml)		*FSH (mIU/ml)*	
Time (min)	*PGI_2*	*Buffer*	*PGI_2*	*Buffer*
–10	6.5 ± 1.5	6.1 ± 0.5	3.3 ± 1.0	3.4 ± 0.9
0	6.1 ± 0.8	6.0 ± 0.5	3.0 ± 0.7	3.5 ± 1.1
15	6.1 ± 0.5	6.0 ± 0.5	3.2 ± 1.1	3.4 ± 0.9
30	6.3 ± 1.1	6.0 ± 0.5	3.4 ± 1.2	3.4 ± 0.9
60	5.8 ± 1.0	6.2 ± 1.0	3.2 ± 0.6	3.2 ± 0.6
90	6.7 ± 0.4	6.4 ± 1.1	3.4 ± 0.9	3.4 ± 0.9
180	6.2 ± 1.4	6.0 ± 0.5	3.5 ± 1.1	3.4 ± 0.9
300	6.1 ± 1.5	6.0 ± 0.5	3.2 ± 1.1	3.1 ± 0.7

All results are expressed as mean ± s.d.

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SOME EFFECTS OF ATROPINE ON SHORT-TERM MEMORY

Several reports provide evidence that scopolamine impairs memory function by an effect on information storage processes (Safer & Allen, 1971; Drachman & Leavitt, 1974; Ghoneim & Mewaldt, 1975, 1977; Petersen, 1977; Sitaram, Weingartner & Gillin, 1978). The present study was to determine whether atropine, which has some similar and some dissimilar central actions to scopolamine, also impairs memory function. Two experiments are reported.

In Experiment 1, ten subjects (aged from 19 to 29 years; median 22 years) performed a digit-recall task before, and at 60 and 120 min after an intramuscular injection of 2 mg atropine sulphate (in 2 ml water), or 2 ml isotonic saline (placebo), administered according to a double-blind, crossover design with 1 week between treatments. Subjects had to listen to, and repeat, sequences of random digits which were lenghtened by one-digit steps until errors were made in two consecutive sequences. This procedure was then repeated, requiring subjects to recall the digits in reverse order. The scores were the numbers of digits in the longest, correctly-recalled sequences.

At 60 min after dosing, atropine-treated subjects recalled fewer digits than they did before treatment or when treated with placebo.

In Experiment 2, six subjects (aged 19 to 26 years; median 20 years) performed the digit-recall task 75 min after an oral dose of 2 mg atropine sulphate or a

Table 1 Experiment 1: Mean digit-recall scores

	'Same-order' recall		*'Reverse-order' recall*	
Time	*Atropine*	*Placebo*	*Atropine*	*Placebo*
Dose − 30 min	7.3	7.4	5.4	5.7
Dose + 60 min	6.6 *	7.6	4.8	5.2
Dose + 120 min	7.0	7.6	5.8	5.7

* Significance at $P = 0.056$ (Walsh test; Siegel, 1956).