mediators of the fever response to pyrogen. The action of pyrogens would be to increase synthesis and release of prostaglandins, and that of the antipyretics to inhibit the increased synthesis.

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Effect of prostaglandins A_1, A_2, B_1, E_2 and $F_{2\alpha}$ on the forearm arterial bed of man

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The effect of prostaglandins (PGs) on the forearm arterial bed of man was studied by measuring the changes in forearm blood flow produced by brachial artery infusions of PGs A_1, A_2, B_1, E_2 and $F_{2\alpha}$. Flow was measured plethysmographically by means of mercury-in-rubber strain gauges; the upper arm congesting cuff pressure was 40 mmHg and wrist cuff occluding pressure 200 mmHg. Saline, or PGs in saline, were infused through a 26 SWG unmounted needle introduced under local anaesthesia. Each dose of PG was infused for 5 min to obtain cumulative dose-response curves, and flows were measured for 10 s in every 15 s; the mean of the last five measurements at each dose rate was taken as the response. In most experiments PGs were infused at three dose levels.

All the PGs studied caused an increase in forearm blood flow, although in the case of $PGF_{2\alpha}$ subdilator doses produced a transient reduction in flow. Dose dependent increases in flow were seen in response to PGs A_1 and A_2 when infused over the dose range 0·1–10 μg/min (5 experiments), to PGB_1 in doses of 2 and 10 μg/min (3 experiments) and PGE_2 over the dose range 0·5–12·8 ng/min (3 experiments). Although the increases in flow were similar in studies with each PG, the pattern of the responses differed: within about 30 s of starting the infusion of PGs A_1 and A_2 there was an abrupt increase in flow which rose to a peak and then fell within 30–60 s to a level intermediate between the peak and the control. This pattern was repeated with each increase in dose. In contrast, the dilator response to PGs B_1 and E_2 developed slowly. The dilator response to $PGF_{2\alpha}$ was seen at infusion rates of 2–10 μg/min (5 experiments) and the constrictor response was seen at rates of 0·4–2 μg/min (7 experiments). The duration of

constriction varied, but in two experiments in which each dose of $PGF_{2\alpha}$ was infused for 10 min, flows returned to control levels before the infusion was completed.

The effect on forearm arterial blood flow of the PGs used in this study has not previously been reported in man. Bevegård & Orö (1969), however, examined the direct action of PGE_1 in man and found it to have a dilator effect at dose levels similar to those found by us to be effective with PGE_2. PGs A_1 and E_1 have been shown to have a dilator effect in the dog (Nakano, 1968; Greenberg & Sparks, 1969), but $PGF_{2\alpha}$ has a dominant constrictor effect in this species (Nakano, 1968; Greenberg & Sparks, 1969).

The relatively high potency of PGE_2 in the arteries of man as compared with other PGs is similar to that observed in the veins of man (Collier *et al.*, 1972). The finding that PGs B_1 and $F_{2\alpha}$ cause only constriction in veins but are capable of causing dilatation in arteries, while PGs A_1, A_2 and E_2 have the same effect in both beds suggests that the PG receptors for mediating constriction and dilatation are different. The response produced by PGs in any vessel would therefore be expected to depend, at least in part, on the relative numbers of each receptor present.

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Preliminary studies of serum levels and the excretion of a new cephalosporin derivative, the sodium salt of 7-cyanacetamido-cephalosporanic acid (CIBA 36,278A-Ba) in normal human subjects and rabbits

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CIBA 36, 278A-Ba is a new cephalosporin derivative which shows considerable activity against β-lactamase-producing strains of *S. aureus* (Knüsel, Konopka, Gelzer & Rosselet, 1971; Russell, 1972). In a study carried out in healthy adult human volunteers, five male subjects received CIBA 36,278A-Ba (500 mg dissolved in 10 ml sterile water) intravenously over 1–2 min. Antibacterial activity in blood and urine was assayed microbiologically using *B. subtilis* NCTC 8236 as test organism. Results are expressed in terms of CIBA 36,278A-Ba. The mean serum level of antibacterial activity 15 min after injection was 30·7 μg/ml (range 13·8–75·7 μg/ml). However, antibacterial activity disappeared rapidly from the serum and the mean half-life was 33·2 min (S.D. of mean $\pm$4·2). The phase of maximum urinary excretion of antibacterial activity occurred in the first 2 h of the drug being administered but small amounts of the active substance continued to be excreted