Table 1 The effect of UVC (254 nm) irradiation on exudate concentrations of PGE_2, $PGF_{2\alpha}$ and arachidonic acid as measured by radioimmunoassay and GC-MS

		Time after irradiation (h)				
	Control	*6*	*18*	*24*	*24 (+ oral indomethacin)*	*48*
Radioimmunoassay ng/ml						
$PGF_{2\alpha}$ equivalents	29.5 ± 7.1 (n=32)	53.7 ± 9.5 (n=7) P=0.1	50.4 ± 18.6 (n=5) P=0.2	55.1 ± 8.3 (n=13) P=0.05	6.6 ± 3.9 (n=4) P=0.01	32.3 ± 9.0 (n=3) P=0.9
GC-MS ng/ml						
(a) Arachidonic acid	284.6 ± 24.6 (n=46)	472.7 ± 35.5 (n=7) P=0.01	557.7 ± 64.5 (n=7) P=0.001	535.1 ± 73.02 (n=13) P=0.01	635.8 ± 124.0 (n=5) P=0.05	357.0 ± 26.9 (n=3) P=0.4
(b) PGE_2	21.9 ± 1.2 (n=46)	38.5 ± 2.6 (n=7) P=0.001	64.4 ± 12.0 (n=7) P=0.02	43.3 ± 6.4 (n=12) P=0.01	18.4 ± 1.7 (n=5) P=0.3	35.0 ± 4.9 (n=3) P=0.001
(c) $PGF_{2\alpha}$	18.2 ± 1.2 (n=46)	33.7 ± 4.4 (n=7) P=0.02	49.4 ± 10.2 (n=7) P=0.025	33.8 ± 4.2 (n=13) P=0.005	19.7 ± 3.2 (n=4) P=0.6	20.2 ± 0.7 (n=3) P=0.1

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The effect of anti-inflammatory drugs on the prostaglandin system in human subcutaneous adipose tissue

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Prostaglandins are released from rabbit fat tissue *in vivo* and *in vitro* during lipolysis stimulated by ACTH and from rat adipose tissue *in vitro* during adrenaline-induced lipolysis or electrical stimulation (Shaw & Ramwell, 1968). The experiments described show that human subcutaneous fat also releases prostaglandins during lipolysis.

Human subcutaneous fat was obtained (with informed consent) from patients (22–69 years) undergoing major abdominal surgery. The fat was washed several times in Krebs solution, divided into portions weighing 1 g, chopped into pieces approximately 2 mm^3 and rinsed again. Control and test samples of fat were incubated in Krebs solution for 4 hours. Lipolysis was investigated in fat incubated with either ACTH or adrenaline. Lipolysis was measured by glycerol release into the incubation medium; this and the levels of prostaglandins formed in the fat and incubation medium were measured as previously described (Chang, Lewis & Piper, 1977). Dexamethasone (2–4 μg/ml) and indomethacin (10 μg/ml) were used to inhibit prostaglandin release.

ACTH did not cause significant increase in glycerol levels but adrenaline induced lipolysis in a dose-

dependent manner. The minimum effective dose was not constant, probably due to differing ages of the donors but adrenaline (10 μg/ml) consistently stimulated lipolysis. Propranolol (10 μg/ml) inhibited glycerol release.

During incubation with adrenaline there was an increase in prostaglandin, assayed as prostaglandin E_2, released into the incubation medium (3.0 ± 1.2 ng/g) compared with control (1.0 ± 0.5). Prostaglandin content of control and adrenaline-treated fat were 1.9 ± 0.7 and 1.0 ± 0.2 respectively. Indomethacin completely blocked formation of prostaglandins in the fat and incubation medium. In the presence of dexamethasone (2 μg/ml), although the concentration of prostaglandins in the medium was slightly reduced (2.2 ± 0.5) the prostaglandin content of the fat was raised (7.2 ± 0.9) above that of fat stimulated with adrenaline alone.

Synthesis of prostaglandins was further investigated by incubating [^{14}C]-arachidonic acid with human fat microsomes for 30 min at 37°C. After extraction with diethyl ether, the extracts were subjected to thin-layer chromatography in benzene:dioxan:acetic acid 60:30:3 (Morrison, Nishikawa & Needleman, 1977).

After incubation, two peaks of radioactivity which co-chromatographed with prostaglandin $F_{2\alpha}$ and prostaglandin E_2 were produced. According to the amount of protein present, the conversion to prostaglandins was 0.4–2%. Adrenaline (50 μg/ml) markedly increased the synthesis of prostaglandins. In the solvent system used, 6-keto $F_{1\alpha}$ and prostaglandin $F_{2\alpha}$ have similar mobilities.

These results show that human fat stimulated with adrenaline synthesises prostaglandins during lipolysis. The sensitivity of human fat to adrenaline confirms that catecholamines have a role in regulation of fat mobilization in man. Indomethacin blocked synthesis of prostaglandins in human fat while dexamethasone prevented their release but not their synthesis. As prostaglandin $F_{2\alpha}$ and 6-keto-prostaglandin $F_{1\alpha}$ had the same chromatographic mobility, we are investigating whether this prostacyclin metabolite is also formed by human fat.

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Chemical mediators of vascular responses in inflammation: a two mediator hypothesis

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Since the work of Thomas Lewis (Lewis, 1927) on the skin reactions to histamine, putative mediators of inflammation have been evaluated according to their ability to mimic inflammatory reactions. Here, a different approach is suggested, namely that the chemical mediation of increased vascular permeability, and vasodilatation, be considered separately.

Plasma exudation and blood flow changes were measured in rabbit skin using [^{131}I]albumin and ^{133}Xe, as previously described (Williams, 1976a).

Intradermally-injected E-type prostaglandins were found to be potent at increasing blood flow with little vascular permeability-increasing activity (Williams, 1976b). However, bradykinin and histamine increased vascular permeability, but were not potent vasodilators (e.g. bradykinin 10,000 times less potent than prostaglandin E_1 on a molar basis, blood flow measured by ^{133}Xe clearance). In terms of inflammatory oedema, the importance of prostaglandins is that they are potent potentiators of histamine- and bradykinin-induced exudation (Williams & Morley, 1973; Moncada, Ferreira & Vane, 1973). From later observations (Williams, 1976b) it is concluded that prostaglandins do not affect histamine- or bradykinin-induced increased