curve of which is not flat. Cross-sections of this retina show that some receptors (probably the class C double rods) contain yellow fluorescent ellipsoids. If the outer segments of these cells produced blue fluorescence, the combination seen end-on would make green. This corresponds to one of the fluorescent colours seen in end-on view. The large ellipsoid of the class B double fluoresces bright blue, consistent with the presence of NADH. We have not yet identified the other fluorescent types with histological types. Only two visual pigments have been found in *Gecko gecko* so far (ref. 6 and my unpublished results).

Finally, when edge-folded frog retinas are examined by 366 nm illumination, a dim orange glow which fades in about 10 s is seen in the rod outer segments. If the ultraviolet exciting light is plane polarized, the orange fluorescence is observed only when the polarization plane is normal to the long axes of the layer of rod outer segments. Similarly, outer segments of rods in porphyropsin containing retinas fluoresce a dim red only to exciting light polarized across their long axes. Because the colour appears brightest immediately on turning the exciting light on, and grows dimmer with time, we believe we are observing directly the fluorescence of visual pigment reported recently by Guzzo *et al.*[7].

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Cardiovascular Effects of AH.3365 (Salbutamol)

THE β-adrenergic stimulant α-[(*t*-butylamino)methyl]-4-hydroxy-*m*-xylene-α^1,α^3-diol (salbutamol) acts selectively on bronchial muscle[1]. Studies with guinea-pig tissue have shown that although it is as active as isoprenaline on bronchial muscle, it is 2,000 times less active on the isolated atria. Clinical studies have shown it to be an effective bronchodilator[2], and we now present evidence that its cardiovascular effects in man are negligible compared with those of isoprenaline.

The investigation was made with ten asthmatic outpatients. The purpose of the experiment had been explained to them and all had given their permission. Each was given either salbutamol (200 μg) or an equivalent dose of isoprenaline (800 μg) by aerosol-inhalation; the other drug was given after an interval of 15 min. Neither the patient nor the administrator knew which drug was being given and the order was randomized from patient to patient.

Two and 5 min after the drugs were administered, we measured the heart rate, the fastest circulation time and mean circulation time (SVC to ear). The last two were determined by injecting 3·5 mg of indocyanine green into the superior vena cava (SVC) through a central venous catheter, and measuring its concentration, as a function of time, at the ear using a photo-electric earpiece densitometer. The mean circulation time ($\bar{t}$) was calculated from the formula $\bar{t} = \int_0^\infty t\, c(t)\mathrm{d}t / \int_0^\infty c(t)\, \mathrm{d}t$, where $c(t)$ is the concentration of dye in the blood passing the earpiece at time t. The effects of recirculation were eliminated in the usual way[3]. Provided there is no change in the volume of blood between the site of injection and the earpiece, mean circulation time is inversely related to cardiac output[4]. Similarly, it can be shown mathematically that in these conditions there is an inverse relationship between cardiac output and fastest circulation time. Actual measurement of cardiac output by dye dilution with the earpiece is sometimes unreliable because the relationship between $c(t)$ and the response of the photoelectric earpiece is sensitive to changes of the blood content of the ear. This criticism does not apply to measurements of fastest and mean circulation times because these do not depend in the same way on the relationship between $c(t)$ and the earpiece response.

The results (Table 1) are expressed as a percentage of the control values (100 per cent) determined in the resting subject before the administration of either drug. Salbutamol has no significant effect on heart rate, fastest circulation and mean circulation time, whereas isoprenaline has a significant effect on all three parameters. These changes are all consistent with an increase of cardiac output. Although we would not suggest that the activity of the first drug had ceased completely at the end of 15 min, the changes were similar in magnitude irrespective of the order of drug administration.

Table 1. HEART RATE, FASTEST CIRCULATION AND MEAN CIRCULATION TIME (SVC TO EAR) AFTER ADMINISTRATION OF SALBUTAMOL AND ISOPRENALINE

	Salbutamol		Isoprenaline	
	2 min	5 min	2 min	5 min
Heart rate	100·1 ± 0·68	100·5 ± 0·96	104·8* ± 2·56	104·7 ± 2·98
Fastest circulation time	101·9 ± 1·61	101·4 ± 1·19	94·7† ± 1·44	95·1 ± 2·72
Mean circulation time	102·3 ± 1·79	102·3 ± 1·47	95·7† ± 1·47	94·4 ± 2·54

* $0{\cdot}05 < P < 0{\cdot}1$
† $P < 0{\cdot}05$.

Results (mean ± *S.E.M.*) are expressed as percentage of control value.

As a result of this experiment we suggest that in the human subject, as in the experimental animal, administration of salbutamol by aerosol-inhalation has minimal effects on the cardiovascular system when compared with isoprenaline.

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Biological Activity of Synthetic Prostaglandins

THE total synthesis of prostaglandin E_1 and prostaglandin $F_{1\alpha}$ has recently been achieved by methods which also make available various derivatives and steroisomers of the prostaglandin series[1,2]. Biological studies on the synthetic prostaglandins, and certain unnatural synthetic stereoisomers, have been undertaken first to provide biological confirmation of the chemical synthesis and, second, to explore the metabolism and pharmacological activity of