about 10 min after injection of PGE_1, PGE_2, 8-iso PGE_2, 15(S)15-MePGE_2Me ester and $PGF_2\alpha$.

The respiratory response was not influenced by bilateral cutting of the sinus nerves or bilateral vagotomy. Reduction of mean arterial blood pressure (up to 40 mmHg) by amyl nitrite did not influence the respiratory rate. Reponse to PGs was not affected when noradrenaline (20 μg ml^{-1}) was co-administered to maintain blood pressure

In conclusion, structural modifications among the prostaglandins dramatically influence their effect on respiration, and promotion of defaecation in the rabbit. Their action does not appear to involve directly the chemoreceptors or baroreceptors of the carotid body and sinus. Their effects are not simple reflex actions to blood pressure fluctuations.

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The effect of amantadine on the turnover of catecholamines in the rat brain

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The anti-Parkinsonian drug amantadine probably acts on dopaminergic mechanisms in the striatum. Direct stimulation of dopamine receptors, (Papeschi, 1974), blockade of neuronal uptake, (Fletcher & Redfern, 1970; Heimans, Rand & Fennessy, 1972; Baldessarini, Lipinski & Chace, 1972), catecholamine release, (Scatton, Cheramy & others, 1970; Von Voigtlander & Moore, 1971; Stromberg & Svensson, 1971; Farnebo, Fuxe & others, 1971) and increased synthesis, (Scatton & others, 1970), have all been suggested as being responsible for the clinical effectiveness of the drug. We have attempted to investigate this problem by examining the effect of amantadine on the turnover of catecholamines in the brain following α-methyl-*p*-tyrosine administration.

Groups of 10 male Sprague Dawley rats were injected i.p. with either saline or α-methyl-*p*-tyrosine methyl ester HCl, (α-MPT), 250 mg kg^{-1}. After 4 h the animals were killed and the brains rapidly dissected and homogenized in 0·4 N perchloric acid. Noradrenaline (NA) and dopamine (DA) were isolated on alumina and assayed fluorimetrically (Shellenberger & Gordon, 1971).

The rates of decline in NA and DA concentrations after MPT were taken as an indication of the rates of turnover of the amines. Blockade of dopamine receptors with either haloperidol, 1 mg kg^{-1}, or pimozide, 1 mg kg^{-1} injected i.p. 30 min before α MPT, significantly increased the rate of decline of DA, ($P<0{\cdot}001$) presumably by a process of negative feedback. On the other hand apomorphine 2 × 2 mg kg^{-1}, and ET 495 (1,-[2″ pyrimidyl-4-piperonyl-piperazine] 25 mg kg^{-1} both of which are believed to stimulate dopamine receptors (Corrodi, Farnebo & others, 1972), significantly decreased the rate of decline of DA ($P<0{\cdot}001$). The rate of change of NA concentrations was unaffected by haloperidol, pimozide or apomorphine but was reduced by ET 495 ($P<0{\cdot}02$).

Amantadine HCl 80 mg kg^{-1} i.p. did not significantly affect DA turnover, but produced a slight but significant increase in the rate of decline of NA concentrations. Rates of decline of both NA and DA concentrations in the brains of rats treated for 9 days with amantadine in the drinking water, (mean daily dose 63 mg kg^{-1}) were not significantly different from those in the brains of control animals.

The lack of effect of amantadine in this experimental situation, when compared to the effectiveness of other drugs, all of which are believed to stimulate or block dopamine receptors, suggests that amantadine does not owe its anti-Parkinsonian properties to a post-synaptic action at dopaminergic synapses in the c.n.s.

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The effect of surfactants on the radiation sensitivity of benzocaine in aqueous solution

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In a formulated cream the active drug may partition not only between the oil and aqueous phases but between the water and the surfacant micelles which are present in the aqueous phase. The observed rate of radiation-induced reaction may be represented by the expression.

$$K_{obs} = K_m F_m + K_w F_w$$

where K_{obs}, K_m and K_w are the observed, micellar and aqueous reaction rate constants respectively and F_m and F_w are the fractions of drug associated with the micelles and the aqueous phase, respectively, (Winterborn, Meakin & Davies, 1974). Therefore, depending on the relative values of K_m, K_w, K_m and K_w, the drug in a cream formulation may be protected to an extent which would make radiation-sterilization a feasible proposition. This communication is a report on the effect of cetrimide and Tween 80 on the sensitivity of benzocaine to ionizing radiation.

2 ml of $1{\cdot}25 \times 10^{-4}$ M aqueous solutions of benzocaine containing cetrimide (10^{-5}; 10^{-4}; 10^{-3}; and 10^{-2} M) or tween 80 (10^{-3}; 10^{-2}; 10^{-1}% w/v) were irradiated in a ^{60}Co source. The distilled water before use was saturated with oxygen by bubbling O_2 through it for 1 h. Following irradiation 1 ml samples were subjected to a modified Bratton-Marshall reaction and the absorbances of the resulting solutions were measured spectrophotometrically at 536 nm (Meakin, Tansey & Davies, 1971). Plots of percentage residual concentration of benzocaine against dose of radiation (Mrad) are shown in Fig. 1a and 1b.

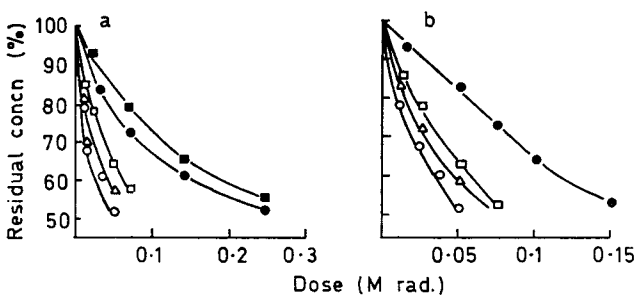

FIG. 1. Plots of % residual concentration of benzocaine against radiation. $1{\cdot}25 \times 10^{-4}$M benzocaine in (a) cetrimide (○—0; △—10^{-5}; □—10^{-4}; ●—10^{-3}; ■—10^{-2}M) and in (b) Tween 80 (○—0; △ 10^{-3}; □—10^{-2}; ●—10^{-1}%).

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