other animals (Said 1974; Kadowitz et al 1975; Takano et al 1978).

Anaphylaxis in guinea-pig chiefly affects the bronchiola (Piper 1977). Therefore, this study suggests that among the chemical mediators released immunologically in the lung during anaphylaxis (Piper 1977), SRS-A, histamine, $PGF_{2\alpha}$ and bradykinin constrict peripheral airways, and thus could play a role in the pathogenesis of allergic respiratory diseases in man and animals. The in vitro demonstration of the peripheral airways constriction to SRS-A, $PGF_{2\alpha}$, bradykinin and histamine (Drazen & Schneider 1978; Drazen et al 1979; Chand & DeRoth 1979c) would assist in explaining the fall in airway dynamic compliance to these agents in guinea-pig in vivo (Colebatch et al 1966; Drazen & Austen 1974).

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Chlorhexidine kinetics in hard contact lenses

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We have previously shown that soft contact lenses are capable of absorbing relatively large amounts of chlorhexidine digluconate but the accumulation reaches a low-steady-state value during a normal lens wearing cycle with only small quantities being released from the lens (MacKeen & Green 1978). Although chlorhexidine is not normally used in the disinfection of hard contact lenses, its uptake by them has been examined for comparison with the soft lens findings since the lens materials are so different.

The procedures used were essentially those of MacKeen & Green (1978) with hard contact lenses (Polycon, (Silafacon A), Syntex Ophthalmics, Palo Alto, CA.) which were fitted to the eyes of albino rabbits, 1·8 to 2·4 kg (Cook's Rabbitry, Barnwell, S.C.). No lens had previously been exposed to any chlorhexidine.

'Maximal' uptake lens were prepared by continuous immersion in 166 ml volume of disinfecting solution per lens for 16 days, with replenishment of chlorhexidine which was lost to the Teflon coated stirrer. 'Minimal' uptake lenses were obtained by immersion in 1·5 ml of solution per lens for 16 h. Immersion for 1·6 h (as used previously for soft contact lenses) produced too small an uptake for accurate quantitation.

During preliminary experiments, a discrepancy was noted between the quantity of chlorhexidine contained in control lenses compared with that remaining in both the experimental lenses used and in either tear or saline washout solutions so experiments were made to determine the location of the unaccounted-for chlorhexidine.

The average values of chlorhexidine concentration in control and worn lenses at 2, 4, 8 or 16 days were: control, $3{\cdot}3 \pm 0{\cdot}3$, $3{\cdot}8 \pm 0{\cdot}4$, $3{\cdot}8 \pm 0{\cdot}5$ and $3{\cdot}9 \pm 0{\cdot}4$ ng mg^{-1} lens and the worn lens $0{\cdot}5 \pm 0{\cdot}2$, $5{\cdot}5 \pm 0{\cdot}3$, $3{\cdot}9 \pm 0{\cdot}6$ and $0{\cdot}5 \pm 0{\cdot}4$ ng mg^{-1} lens. These concentrations are calculated as the digluconate. The chlorhexidine concentration of the control lens rapidly reached a steady-state while the worn lenses showed an initial low level, a slightly higher value at 8 days and a return to values less than control at 16 days. The quantities are very small and the differences are unlikely to be clinically significant, although the control and worn lenses show statistically significant differences at 2, 4 and 16 days ($P < 0{\cdot}001$, $P < 0{\cdot}02$ and $P < 0{\cdot}001$, respectively).

Tables 1 and 2 list the data from the desorption experiments into unstirred saline and artificial tears, respectively. Irrespective of the lens uptake period for chlorhexidine, the fraction desorbed into the saline was the same, namely 43 and 39%, for minimal and maximal uptake respectively. Similarly, the desorption into the supernatant and precipitate fraction of artificial tears was similar for minimal and maximum uptake lenses. Relative to the saline desorption experiments more chlorhexidine was desorbed from the lenses; about 95%

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Table 1. Chlorhexidine* in hard (polycon) contact lenses and in saline immersion fluid†. Each lens was immersed in 8 ml of normal saline without stirring at 25 °C for 8 h. Each value in columns II and III is the product of measured concentration in each lens and immersion fluid, times the lens weight or 8 ml respectively. Minimum Group: each lens immersed in 1·5 ml of disinfecting solution for 16 h. Maximum Group: each lens immersed for 384 h in disinfecting solution at 167 ml per lens.

Orig. concn $\mu g\ mg^{-1}$ (I)	Total amount in lens after desorption (μg) (II)	Amount desorbed into 8 ml of saline (III) Total μg	(IV) % Original lens total
	Minimum uptake group**		
0·004	0·032	0·024	42·8
	Maximum uptake group**		
0·006	0·047	0·03	38·7

* Calculated as the digluconate salt.
** The value for each group is the average from 12 lenses.

Table 2. Chlorhexidine* in hard (polycon) contact lenses and in artificial tear immersion fluid. Each lens was immersed in 8 ml of normal saline without stirring at 25 °C for 8 h. Each value in columns II and III is the product of measured concentration in each lens and immersion fluid, times the lens weight or 8 ml respectively. Minimum group: Each lens immersed in 1·5 ml of disinfecting solution for 16 h; Maximum group: Each lens immersed for 384 h in disinfecting solution at 167 ml per lens.

Columns II, III and V represent measured values times lens weight, 8 ml or total precipitate weight respectively.

Lens		Artificial tears solution		Precipitate	(VI)
Original (I) $\mu g\ mg^{-1}$	Remaining (II) μg	(III) Total μg	(IV) % Lens total	(V) Total μg	% Eluted materials in ppt
	Minimal uptake group**				
0·0050	0·0160	0·0389	70·9	0·0124	24·2
	Maximum uptake group**				
0·0059	0·0214	0·0401	65·2	0·0168	29·5

* Calculated as digluconate salt.
† NaCl 0·8%, bovine submaxillary mucin, 0·22%; bovine serum albumin, 0·2%; gamma globulin 0·1% and egg lysozyme 0·08%.
** The value for each group is the average of 12 lenses.

of all lens chlorhexidine was desorbed in artificial tears compared with about 40% in saline.

Table 3 shows that the chlorhexidine concentration in free solution rapidly decreases in glass containers. After 5 h the concentration is only about 25% of the original value. When a chlorhexidine solution containing 50 $\mu g\ ml^{-1}$ (0·005%) is placed in a glass vial approximately 2·5% is immediately lost to the glass, and the value remains constant over 3 h. The low concentration solution gives a value of 32 ng cm^{-2} of glass and the high concentration solution gives 950 ng cm^{-2} of glass, thus giving 'upper' and 'lower' limits of adsorption capacity of the glass for chlorhexidine.

As hard contact lenses contain no water, the 4 ng mg^{-1} lens weight chlorhexidine salt found must be absorbed to the lens surface. This is in contrast to soft lenses which achieve concentrations 2000 fold greater than the ambient solution (MacKeen & Green 1978).

The daily uptake and loss of chlorhexidine by hard contact lenses is minimal because of their lack of absorbtivity. Small amounts of surface-absorbed chlorhexidine are released into the tears from the worn lenses since the concentration is less than the controls. The calculated release-rate is approximately 0·5 ng mg^{-1} lens h^{-1}. Thus more chlorhexidine would seem to be desorbed from lenses immersed in artificial tears than from those in saline solution since lenses in saline retain twice as much chlorhexidine as those immersed in artificial tears. This is presumably a reflection of the number of binding sites available in the artificial tear (i.e. proteins and mucin) which may compete for chlorhexidine occupation. When more chlorhexidine was available, as in desorption from soft contact lenses, the proportion of chlorhexidine found in the precipitated protein was 3 to 4 times greater than that found in the supernatant (MacKeen & Green 1978), while in the present experiments there was 2 to 3 times more in the supernatant. Possibly more is bound to unprecipitated mucin, together with a low rate of protein site-occupation due to the low concentration of chlorhexidine. When chlorhexidine is present in high concentrations,

Table 3. Glass surface uptake of chlorhexidine from a dilute aqueous solution. * The concentration of chlorhexidine placed into the 20 ml glass vials was 50 ng ml^{-1} to a total volume of 8 ml. The uptake value was 32 ng cm^{-2}. The maximum uptake from a solution of 50 $\mu g\ ml^{-1}$ was 950 ng ml^{-1}. Values are the mean of 3 determinations at most times.

Time	Decrease in chlorhexidine* concn (%)
10 min	16·8
20 min	26·7
30 min	42·2
40 min	55·6
50 min	63·5
1 h	57·2
2 h	70·4
3 h	74·3
4 h	80·5
5 h	84·3

* Calculated as the digluconate salt.

such as during soft-lens desorption the greater quantities of disinfectant may occupy more sites since more molecules are available.

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α- and β- Adrenoceptors and PGE_2 in the modulation of catecholamine secretion from bovine adrenal medulla in vitro

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We have previously reported that release of catecholamines (CA) from rat adrenal medulla incubated in vitro can be inhibited by α-adrenoceptor agonists and by PGE_1 and PGE_2 (Gutman & Boonyaviroj 1975) and enhanced by β-adrenoceptor agonists (Boonyaviroj & Gutman 1977a,b). This is similar to the effect of the same modulators in adrenergic nerve endings (Langer 1974; Starke et al 1977).

However, since rat adrenals incubated in vitro included cortex as well as medulla, a possible mediation or modulation of the observed effects by corticosteroids could not be ruled out, e.g. the α- and β-agonists or PGE_2 could affect primarily the adrenal cortex, and a compound (s) released from the adrenal cortex could then act on the chromaffin cells of the medulla. To clarify this point we have used bovine adrenals, where cortex and medulla can be easily separated.

Bovine adrenals were obtained at the slaughterhouse, immediately placed in ice and the adrenal medulla dissected free of cortical tissue and sliced (10–20 mg per slice). Each slice was placed in a 50 ml Erlenmeyer flask containing 10 ml of Locke solution (mM: NaCl–145, KCl–5·6, $MgCl_2$–5·5, $CaCl_2$–0·5, glucose–5) and incubated at 37 °C for 10 min, with constant shaking. At the end of the incubation, slices were separated from incubation medium and slices and medium were acidified with $HClO_4$. The extracted CA were adsorbed on alumina columns, followed by columns of Biorex 70, as previously described and were assayed (adrenaline and noradrenaline) by the trihydroxyindole method (Feuerstein et al 1977). Catecholamine release is given as a percentage of the total CA present in the slice at the beginning of incubation.

Materials: Acetylcholine chloride and phenylephrine were purchased from Sigma, St. Louis, Mo. Salbutamol was generously supplied by Allen & Hanbury Ltd. Ware, England. Naphazoline was kindly supplied by Assia Ltd. Ramat-Gan, Israel, Phenoxybenzamine was a gift from Smith, Kline & French, Philadelphia, Pa. PGE_2 was kindly sent by Dr J. Pike from Upjohn Co., Inc., Kalamazoo, Mi. H 35/25 ((±)-erythro-4′-methyl-α-(1-isopropylaminoethyl)-benzyl alcohol hydrochloride) was purchased from Kistner Labs. Goteborg, Sweden. Phentolamine was a gift of Ciba, Ltd., Basel.

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The release of CA into the medium (Locke solution) was 0·25 ± 0·01 μg mg^{-1} of medulla during the incubation. This release constituted 25·1 ± 0·3% of the total CA present in the slice. Fig. 1 shows that acetylcholine (ACh) induced a substantial increase of CA secretion. When α-adrenoceptor agonists, phenylephrine (10^{-5}M) or naphazoline (10^{-5}M), were added, in the presence of ACh (10^{-4}M), the increase of CA secretion induced by ACh was abolished. The addition of the α-adrenoceptor antagonists (phentolamine and phenoxybenzamine) into the medium (without ACh) increased the secretion of CA significantly, compared with the control. Addition of a β_2-adrenoceptor agonist, salbutamol (10^{-6}M) to the medium also enhanced release of CA significantly.

PGE_2 caused a significant inhibition of the release of CA induced by ACh (Fig. 1).

Incubation of medulla in calcium-free Locke solution, supplemented with 2 mM EGTA, caused reduction of

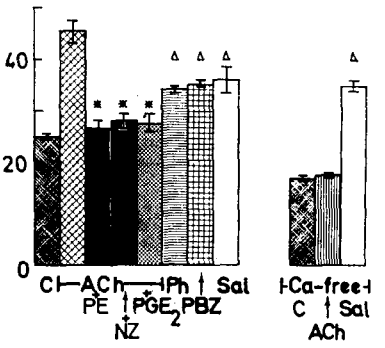

FIG. 1. Effect of various agents on catecholamine secretion (Ordinate: % release) from bovine adrenal medulla slices. C, release of CA during control incubation. ACh, 10^{-4}M acetylcholine present in incubation medium. PE, phenylephrine (10^{-6}M) added to medium. NZ, naphazoline (10^{-5}M) added to medium. PGE_2, PGE_2 (10^{-7}M) added to medium. Ph, phentolamine (10^{-5}M) added to medium. PBZ, phenoxybenzamine (10^{-5}M) added to medium. Sal., salbutamol (10^{-6}M) added to medium. Ca-free, incubation medium without calcium and 2mM EGTA added. Vertical bars, s.e. Each column is the mean of 10 experiments.
*$P < 0.01$ compared with release induced by acetylcholine alone (cross hatched column).
Δ $P < 0.01$—compared with release in control (C).