most probably involved in the transformation of sulphadimidine and PA in random-bred albino rats of the Wistar stock. That adjuvant treatment did not affect PA acetylation compared with a increase of acetylated sulphadimidine in adjuvant-treated male rats (Zídek et al 1977) is indicative of different metabolic patterns of PA and sulphadimidine. Different doses of PA (1, 5, 10 mg kg^{-1}) failed to affect the percentage of NAPA in the urine. Only the higher dose (40 mg kg^{-1}) was accompanied by a decrease of NAPA % in the urine. This observation agrees with the findings of Olson et al (1978) who found this effect with sulphadimidine in man.

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Responses of guinea-pig lung parenchymal strips to prostaglandins and some selected autacoids

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Guinea-pig isolated tracheobronchial smooth muscle preparations have extensively been used in the immunopharmacological studies and for screening bronchodilators and anti-allergic drugs (Chand & Eyre 1978). In 1976, Lulich et al introduced the use of lung parenchymal strips for the pharmacological evaluation of the peripheral airways (bronchiolar-alveolar ducts and alveoli). The immunological release of histamine, prostaglandins, kinins and several other chemical mediators of anaphylaxis in the lung of man and animals has frequently been reported (Piper 1977). The study of the actions of the naturally occurring autacoids (histamine, prostaglandins etc . . .) on the airway smooth muscles is important for the better understanding of the pathophysiological mechanisms in the development of lung diseases. This report describes the effects of some selected pharmacological mediators of anaphylaxis on isolated lung parenchymal strips (peripheral airways) of guinea-pig.

Twenty-seven guinea-pigs of either sex, 450 to 700 g, were killed by cervical dislocation. Lungs were immediately removed and placed in cold oxygenated Krebs-Henseleit solution (Chand & DeRoth 1979). Lung strips of about 20 × 3 × 2 mm were prepared following the method of Lulich et al (1976). The lung strips were mounted in isolated tissue baths containing Krebs-Henseleit solution bubbled with 5% CO_2 in O_2, maintained at 37 °C. Tissues were allowed to equilibrate for at least 1 h under a resting load of 1·5 g. Cumulative dose-response curves to agonists were recorded at 60 min intervals using isotonic transducer and pen recorder. Appropriate controls for the solvent (ethanol for prostaglandins) were simultaneously carried out. Single dose-response curves to bradykinin were recorded. The relaxant responses to PGE_1 or PGE_2 were recorded on lung strips which were maximally contracted to $PGF_{2\alpha}$ (5×10^{-5}M). Drug concentrations are expressed as molar (M) bath concentrations.

The strips exhibited concentration-dependent contractions to bradykinin (BK), histamine, carbachol or $PGF_{2\alpha}$ (Figs 1, 3) with EC50 values of 4, 5, 7 and 10 μM for $PGF_{2\alpha}$, histamine, carbachol and bradykinin respectively. Therefore, the order of the relative potencies of these spasmogenic agents on GPLS was $PGF_{2\alpha}$ > histamine > carbachol > 5-HT. The latter produced only 20% of maximum response to histamine (Fig. 1).

Lung strips which were maximally contracted to $PGF_{2\alpha}$ (5×10^{-5}M) responded to PGE_1 and PGE_2 with relaxations in concentration dependent manner (Fig. 2). PGE_1 was about 2 to 5 times more effective than PGE_2 in relaxing the $PGF_{2\alpha}$-contracted lung strips (Fig. 2). Typical responses of the guinea-pig lung strip to histamine, carbachol and $PGF_{2\alpha}$ are shown in Fig. 3. Adrenaline (10^{-7} to 5×10^{-3}M) (Fig. 3) and noradrenaline (10^{-6} to 10^{-4}M) also relaxed lung strips which were pre-contracted to $PGF_{2\alpha}$, carbachol or histamine.

Guinea-pig lung parenchyma possesses large quantities of alveolar duct smooth muscle (Miller 1921) and may also contain contractile interstitial cells in the pulmonary alveolar septa (Kapanci et al 1974). The relaxation of the lung parenchymal strips to large doses of adrenaline and noradrenaline in guinea-pig (this study) and cat (Lulich et al 1976) is taken as a strong

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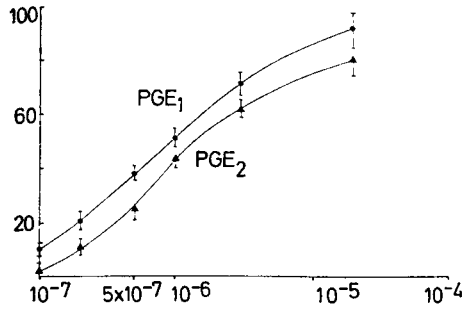

FIG. 1. Dose-response curves of bradykinin (■), $PGF_{2\alpha}$ (△), histamine (●), carbachol (○) and 5-HT (▲) on guinea-pig lung strips. Ordinate: maximum response (histamine). Abscissa: log concentration (M).

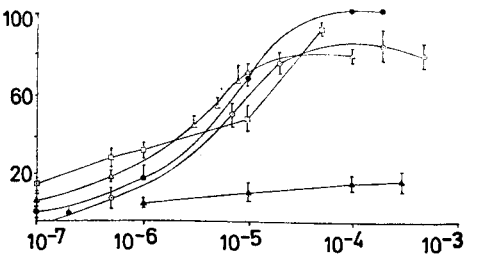

FIG. 2. Dose-response curves of PGE_1 (●) and PGE_2 (▲) on lung strips which were maximally contracted to $PGF_{2\alpha}$. Each point represents the mean of observations on lung strips from 7 to 9 guinea-pigs. Vertical bar show the s.e.m. Ordinate: maximum relaxation (%). Abscissa: log concentration (M).

pharmacological criterion for the non-involvement of the pulmonary micro-vasculature in the mediation of responses to the spasmogenic agents (Lulich et al 1976).

Guinea-pig lung strips were found to contract to $PGF_{2\alpha}$ > histamine > carbachol > bradykinin > 5-HT. Similar responses to these agents on the lung strips of cat (Lulich et al 1976), horse (Chand & DeRoth 1979a), dog (Chand et al 1979), rabbit and neonatal piglets (Chand & DeRoth 1978, 1979b) have recently been reported. However, contrary to the responses of lung strips of the cat (Lulich et al 1976) and guinea-pig (this study), the lung strips of horse, rabbit and neonatal piglet exhibit contractions to adrenaline, noradrenaline and phenylephrine (Chand & DeRoth 1978, 1979a, b). These contractions in part may be mediated by their actions on the pulmonary micro-blood vessels and contractile interstitial cells in the pulmonary alveolar septa (Kapanci et al 1974).

In general, carbachol is up to 100 times more potent than histamine on the tracheobronchial smooth muscle of man and other animals. However, on the lung strips of all the species investigated, the potency of histamine is at least equal to that of carbachol. Therefore there are remarkable qualitative and quantitative differences in the reactivity of the central and peripheral airways to autonomic and autacoid agents (Lulich et al 1976; Chand & DeRoth 1978, 1979a, b; Chand et al 1979; Drazen & Schneider 1978; Drazen et al 1979; this study).

The strong and opposite effects of $PGF_{2\alpha}$, PGE_1 and PGE_2 on the guinea-pig lung strips are consistent with those on the tracheobronical smooth muscle in man and

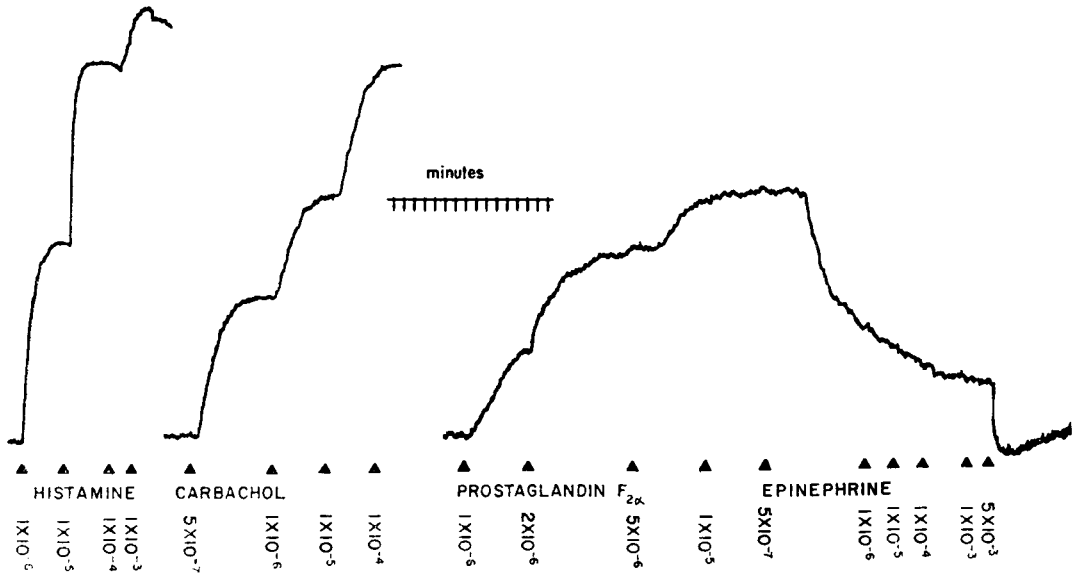

FIG. 3. Isolated guinea-pig lung strip in Krebs-Henseleit solution bubbled with 5% CO_2 in O_2, at 37 °C. Resting tension: 1·5 g. Contractile responses to histamine, carbachol and $PGF_{2\alpha}$. Relaxation to adrenaline on the $PGF_{2\alpha}$-contracted lung strip. Time marker indicate intervals in minutes. The doses of agonists are expressed as final bath concentration (M).

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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