& Kassarich (1971) found that PGE_1 reduced the resistance and increased the compliance of cat lungs in which airway smooth muscle tone had been induced with neostigmine.

In our experiments open chested cats under pentobarbitone anaesthesia were used. Tracheal pressure and air flow were recorded on magnetic tape, and resistance and compliance were later computed using a modification of the method of Mead & Whittenberger (1953).

Prostaglandins were given by rapid intravenous injection
(i) to cats with no airway tone
(ii) in the presence of airway tone induced by continuous intravenous infusion of neostigmine
(iii) in the presence of airway tone induced by continuous intravenous infusion of methacholine.

In the absence of airway tone in each of thirteen tests, in three cats, PGA_1 and PGA_2 raised the resistance and lowered the compliance. The rise in resistance in response to PGA_1 was dose-dependent over the range from 1 to 25 μg/kg, giving increases in resistance from 10% to 80%. The fall in compliance ranged from 4 to 20%. In response to PGA_2 the rises in resistance were about double those to similar doses of PGA_1, and falls in compliance ranged from 10 to 40%.

In three cats neostigmine methyl sulphate infused at 100 μg/min raised airway resistance by 170 to 200%. Compliance fell by 40%. In each of four tests PGA_2 at 10 μg/kg lowered the resistance by 20 to 40%, and also lowered the compliance by 8 to 50%.

In two cats, methacholine chloride was infused at two rates, 10 μg/min and 400 μg/min, giving increases in resistance of 20% and 300% respectively with falls in compliance of 20% and 55 to 70%. In six tests PGA_2 at 25 μg/kg further raised the resistance and further lowered the compliance at both high and low infusion rates of methacholine.

We infer from these results that PGA_1 and PGA_2 have qualitatively similar actions. Their primary effect on the lungs is to increase airway resistance and to reduce compliance. This effects is still seen when methacholine is used to induce tone in the airway smooth muscle. Tone induced by neostigmine is inhibited by PGA, but a reduction of compliance is still seen. This bronchodilator action of PGA must be related to the mechanism by which neostigmine induces tone, insofar as that differs from the mechanism for methacholine. A direct or indirect action on release of acetylcholine could be involved. The use of neostigmine to induce airway tone may thus provide an unsatisfactory model for the study of potential bronchodilator drugs.

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Determination of the number of muscarinic receptors in chick amnion muscle

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Studies on the binding of the irreversible muscarinic blocking drug propylbenzilylcholine mustard (PrBCM) to the non-innervated smooth muscle of the chick amnion have been made and the results compared to those for ileum. Further, the amnion muscle is suitable for measuring drug responses, the results of which can be compared to those from binding studies (Cuthbert, 1962).

Experiments were made with groups of 6–8 amniotic membranes dissected from fertile hens' eggs incubated for 11 days. The membranes were incubated with ^{3}H-PrBCM (2·4 nM, 1·45 Ci/mmol) in Hank's solution at 30° C for various times. Binding to muscarinic receptors was taken as the difference in the amount of label bound in the

absence and presence of atropine, 10^{-7}M. A binding curve was constructed showing that the specific binding saturated between 15–30 minutes. Assuming that the rate of alkylation is faster than the rate at which the PrBCM-receptor complex dissociates (Gill & Rang, 1966) the rate constant for the formation of the reversible complex is approximately 6×10^5 M^{-1} s^{-1}. The maximal binding capacity of the tissue is 9 pmol/g dry weight. This value is low compared to 150 pmol/g wet weight for longitudinal ileum muscle of the guinea-pig (Young, Hiley & Burgen, unpublished). Since ileum muscle consists of 90% smooth muscle cells (Rang, 1967) compared to approximately 70% for amnions, the latter can have only 1–2% of the receptors in the ileum.

Further evidence that the specific binding of ^{3}H-PrBCM was to muscarinic receptors was obtained by incubating membranes with atropine at concentrations ranging from 10^{-10} to 10^{-7}M, after which ^{3}H-PrBCM (2·4 nM) was added. The uptake was measured at 12 min, that is before saturation was achieved. The concentration of atropine causing 50% inhibition of uptake under these conditions was about 10^{-9}M. This value is in good agreement with the pA_2 value for atropine of 8·8 for this tissue (Evans & Schild, 1959). The binding of ^{3}H-PrBCM was not affected by tubocurarine, 10^{-6}M.

Pharmacological studies, together with these results suggest the tissue has few spare receptors.

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The binding of labelled tetrodotoxin and cobra toxin by the rat diaphragm

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Denervation of skeletal muscle brings about two important changes: first a spread of acetylcholine (ACh) sensitivity away from the endplate (Miledi, 1960); and secondly, the development of tetrodotoxin (TTX)-resistant action potentials (Redfern & Thesleff, 1971). One way that these two phenomena might be linked would be that the normal TTX-sensitive sodium channels acquire, after denervation, a sensitivity to ACh and lose their sensitivity to TTX. We have examined this possibility by comparing, in rat diaphragm, the number of TTX binding sites in normal muscle with the number of cobra toxin binding sites (presumed ACh receptors (Lee, Tseng & Chiu, 1967; Lester, 1970)) that appear after denervation.

Hemidiaphragms from normal rats were incubated for 4 h at 21° C with ^{3}H-TTX (Colquhoun, Henderson & Ritchie, 1972) at concentrations from 0·6 nM to 590 nM, ^{14}C-inulin was included in the incubation medium so that the extracellular space could be estimated and used to calculate the amount of TTX bound to the muscle.

The curve (128 points) relating the amount of bound TTX to the TTX concentration was analysed with a least squares procedure into the sum of a linear component, and a saturable hyperbolic component, as in Colquhoun *et al.* (1972). The saturable component has an equilibrium dissociation constant of 12·7 nM (95% likelihood interval 7·1 to 22·2 nM), a value roughly consistent with electrophysiological results.

The TTX-binding capacity of the saturable component is 3·9 fmole/mg wet (95% likelihood interval, 2·50 to 6·31 fmole/mg wet). If the fibre diameter is assumed to be 40 μm and the transverse tubular system is ignored, the membrane area would be

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