## Interaction of gases with monolayers

SIR,—Two apparently contradictory reports have been made, by Clements & Wilson (1962) and by Evans, Hamilton, Kuenzig & Peltier (1966), about the effects of gaseous anaesthetic agents on monomolecular films. Whereas Clements & Wilson (1962) showed that halothane had a significant effect on the surface pressure of a number of monomolecular films, Evans & others (1966) concluded that halothane did not alter significantly the surface pressure of dipalmitoyl lecithin films. Clements & Wilson, maintained their films at fixed areas and low surface pressures, whilst Evans & others varied their film areas and pressures over a wide range by use of a variable area trough. These latter films were subjected to repeated rapid compression-expansion cycles during which pressures of almost 70 dynes/cm, with average standard deviations of more than 2 dynes/cm, were observed. Based on our experience of the effects of gases on monolayers, the apparent differences in the results are probably directly traceable to basic differences in procedures and techniques.

Monomolecular films have been shown to be useful as biological models in the study of membrane interactions with a wide variety of materials in solution (Schulman & Rideal, 1937). It is reasonable to expect that such models could be applied to the study of membrane-gas interactions.

In recent work on the effect of gaseous air pollutants on monolayers we have established the need for rigid experimental standardization of the films to be used in gas-film studies. Without such standardization, meaningless and often misleading conclusions could be reached. A precise knowledge of the film properties in the absence as well as in the presence of the gases is required. For example, the rate of film compression, temperature, and history of the film markedly influence the surface pressure-surface area ($\pi$-A) isotherms of stearic acid monolayers (Rabinovitch, Robertson & Mason, 1960). Whereas the collapse pressure of stearic acid films has been reported to be as high as 62 dynes/cm using rapid compression methods (Dervichian, 1937), with very slow manual compression rates these films yield collapse pressures of about 15 dynes/cm. At pressures above 15 dynes/cm, the surface pressure values become significantly time dependent. More important, when the $\pi$-A isotherms were obtained for films subjected to repeated compressions and expansions, marked changes occurred in the shapes of the isotherms, especially in condensed regions. Similar effects would be expected for phospholipid films.

Furthermore, reproducibility of surface pressure values on successive highly condensed films, can produce serious errors. We have found that an error of 1% in the amount of spreading solution added to the subphase surface can easily produce errors of more than 10 dynes/cm at areas near the limiting area of the film molecules. Such large errors can easily obscure the small effects expected for low concentrations of gases with monolayers. Measurements of surface pressures on a single film, before and after exposure to the gas, would eliminate this source of error.

It has been shown that when interactions with the film are relatively weak, the interacting material may be squeezed out of the film at high pressures (Cockbain & Schulman, 1939). It would be expected that in most instances the gas-film interactions would be weak, involving only van der Waals' forces. Thus a gas which normally interacts with a film under expanded conditions might exhibit little or no interaction with a condensed film or with an expanded film having a history of compression beyond the "equilibrium" collapse pressure.

We therefore feel that more meaningful information would be obtained for the interactions of gases with film molecules when these are made on a single

film whose $\pi$-A characteristics have first been established in the absence of the gases. The rates of compression should be slow enough to allow the molecules in the monolayer to maintain "equilibrium" orientations at all areas at which measurements are made. Furthermore, the film should never be compressed beyond the collapse pressure when further expansion-compression cycling of the film is desired.

We have found that when these experimental conditions are adhered to, effects of gases on films that result in small surface pressure changes can be easily detected.

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### The effect of bradykinin and anti-inflammatory agents on isolated arteries

SIR,—Bradykinin constricts isolated perfused arteries from guinea-pig lung (Moog & Fischer, 1964) and from rabbit lung (Hauge, Lunde & Waaler, 1964). This vasoconstrictor effect is abolished by phenylbutazone (Klupp & Konzett, 1965), acetylsalicylic acid (Greeff & Moog, 1964), and flufenamic and mefenamic acids (Bauer, Gmeiner & Konzett, 1965) although the antagonism has been shown to be non-specific (Hauge, Lunde & Waaler, 1966). We have now examined the responses of other arteries to these drugs by the method of de la Lande & Rand (1965). Bradykinin and its antagonists were injected through the cannula into the perfusion fluid (McEwen's solution, 1956) which supplied the isolated artery preparation. Histamine, 5-hydroxytryptamine, acetylcholine, noradrenaline and kallidin were our standards of comparison. On occasions, the upper ends of the vessels were stimulated electrically (pulse width 1 msec, strength 10–20 V, frequency 1–20/sec) using bipolar platinum electrodes.

In our hands, also, bradykinin (1–10 $\mu$g) constricted the isolated pulmonary artery of the rabbit and the anti-inflammatory agents (sodium phenylbutazone, sodium mefenamate, sodium flufenamate, sodium meclofenamate and calcium acetylsalicylate) antagonised the response when administered by slow infusion (0·1–2·5 mg/min). The same concentrations of antagonists also antagonised the vasoconstrictor responses to histamine (0·1–0·5 $\mu$g), 5-hydroxytryptamine (5-HT) (0·1–0·5 $\mu$g), acetylcholine (0·2–10 $\mu$g) noradrenaline (0·1–0·5 $\mu$g) and kallidin (0·2–2 $\mu$g), and so it was proved that the antagonism was non-specific. The effects of electrical stimulation were also greatly reduced by the anti-inflammatory agents. In some experiments, tachyphylaxis to repeated doses of bradykinin was noted.