# LETTERS TO THE EDITOR

## The Paired Tracheal Chain Preparation

SIR,—The guinea pig tracheal chain preparation described by Castillo and de Beer in 1947[1] possesses a quality which recommends this tissue for the study of spasmolytics, and of the inhibitory actions of sympathomimetic drugs. This quality is the high natural tone of the muscle, allowing relaxations to be obtained without prior addition of spasmogen.

A number of experimental difficulties arise when the tissue is prepared as the authors describe. These include the small size of the maximum possible relaxation, the wide variation in the sensitivity of individual animals, a very slow response to drugs and recovery therefrom, and an inability to assess the effect of the spontaneous relaxation of tone, which is often seen, on subsequent drug responses. The first of these difficulties has been overcome by Akcasu[2], in 1959, who opened the rings of trachea by cutting through the cartilage. This manoeuvre increased the magnitude of the recorded responses to drugs by a factor of three. By a very simple expedient, it has now proved possible to overcome the other difficulties.

Two guinea pigs (600 to 800 g.) are killed by stunning and bleeding. The tracheae are removed from larynx to carina, and each is cut into eight rings of

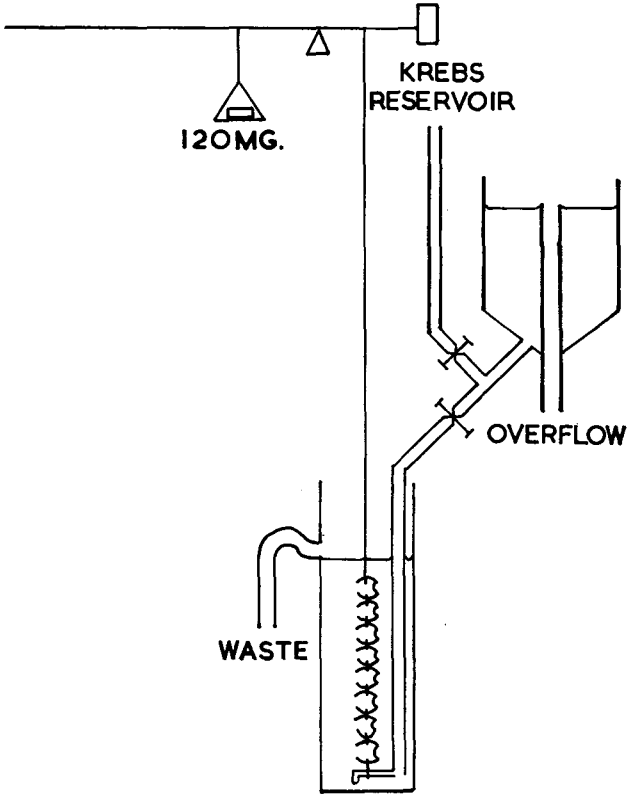


FIG. 1

equal width with scissors. Each ring is opened by cutting through the cartilage and, working from the laryngeal end, the odd numbered rings from one animal and the even numbered ones from the other are tied together to form a chain. The remaining pooled rings form a second preparation which, by this construction, is identical with the first. If, as often happens, only smaller guinea pigs are available, the same effect may be achieved by cutting each trachea into six rings, and using a third guinea pig to provide the other two rings in each preparation.

Each of the two preparations is set up in an apparatus like that shown in Figure 1. Though, for clarity, water jackets and gas lines to both baths have been omitted, each tissue is immersed in Krebs's solution at 38° aerated with oxygen and 5 per cent carbon dioxide. Washing is by displacing the bath fluid with fresh prewarmed and pre-aerated Krebs's solution. Responses to drugs are recorded by a lightly weighted, isotonic, balsa-wood side writing lever, so arranged that the tension applied to the preparation is about 240 mg.

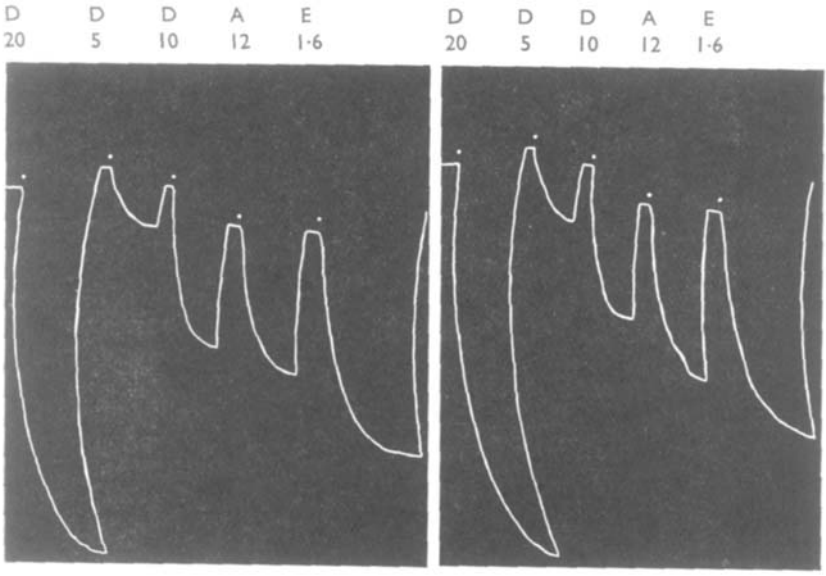


FIG. 2. The similarity of response obtained with the paired tracheal preparation. All doses are in $\mu$g. of base per ml. of final bath concentration.

D = Dopamine A = Aminophylline E = (–)-Ephedrine

The spontaneous elongation of the tissue, often seen when it permanently supports this load, may be minimised by removing all tension from it during the period of washing-out the drugs. The load is then reapplied five minutes before the next addition of drug. That such pairs of preparations do, as intended, behave very similarly is illustrated by Figure 2. The great similarity of behaviour of the two preparations to doses of dopamine, aminophylline, and (—)ephedrine is shown. Very important is the fact that the small spontaneous elongation of the tissue is similar in both.

This similarity of behaviour of a pair of preparations reduces the duration of an experiment, as one may be used as a control for drug procedures applied

to the other. The responses of the two preparations may be compared directly so overcoming the need for excessive repetition.

Prepared in the way described in this paper, the guinea pig tracheal chain has proved a consistent and useful tissue in the analysis of the inhibitory actions of sympathomimetics. It lends itself particularly well to the study of blocking and potentiating agents.

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2. Akcasu, *Arch. Int. Pharmacodyn.*, 1959, **122**, 201.

## Relation between Dispersibility and Adherence of Powdered Medicinal Substances in Liquid Medium

SIR,—In my recent communication[1] I have reported a method for measuring the dispersibility of powdered medicinal substances by the passage of part of a sample through hydrophilic gauze under the influence of liquid falling in drops. Zinc oxide, talc, bismuth subcarbonate, bismuth subgallate, bismuth subnitrate, bismuth subsalicylate, magnesium subcarbonate, kaolin, precipitated calcium carbonate, precipitated sulphur, mercury amidochloride, yellow mercury oxide, wheat starch, sulphacetamide, sulphadimidine, sulphaguanidine, sulphanilamide, and sulphathiazole, were investigated in this way. Three liquids, i.e. water, 1 per cent solution of Tween 80 in water, and ethanol (95 per cent w/w) were the dispersing media.

I have now determined the "tear off angle" ("Abreisswinkel") of the same substances in the same liquids by a method the principle of which had been suggested by von Buzágh[2]. Thus the adherence of powdered medicinal substances was studied and the relation between dispersibility and adherence was treated by regression analysis[3,4]. The rectification of the data and the due linear regression $\frac{\log u - \log u_k}{d} = 0{\cdot}4343b + 0{\cdot}4343cd$ ($d$ was plotted as abscissa and $\frac{\log u - \log u_k}{d}$ as ordinate) served as fundamentals for finding the values of parameters and the final form of regression equation which in the case of all three liquids proved to be of the following exponential type:

$$u = k.\exp(bd + cd^2) \quad .. \quad .. \quad .. \quad (1)$$

The meaning of symbols is as follows: $u$ = "tear off angle"; $u_k$ = selected reference value of "tear off angle" (in this instance the value for precipitated sulphur), $d$ = dispersibility; $k$, $b$, $c$ = parameters relative to the liquid used. The values of parameters for coded units of dispersibility are indicated in Table I (D = actual values of dispersibility); the coding was used in order to facilitate the computation.