A New Method of Administering Drugs by Mouth to Animals

SIR,—Since animals, even more than children, frequently refuse to take a drug by mouth, we have developed a method which can help overcome their reluctance. It is based on the fact that rats like chocolate (Teitelbaum and Epstein, 1962).

The drug is put up in a chocolate paste (Fry's chocolate spread 65 per cent, starch 35 per cent), stiff enough not to stick to the animal's paws or the cage, but not so stiff as to crumble. The paste is kept in an ointment tube; the dose can be gauged by measuring the length of the column extruded, or more precisely by weighing the tube before and after squeezing out the dose. A trained rat eats the paste off a spatula cleanly and completely in a few seconds, even when it is on a free diet of rat cubes.

Before a drug can be given by this method the animal must be offered control chocolate paste daily for two or three days after being without food for a few hours. It will then readily accept the paste. Training takes longer with more than one or two animals in a cage. The next step is to find a concentration of the drug in the paste which the animal will accept. The human sense of taste is a poor guide for this purpose. Thus hydrocortisone 12 mg./g. chocolate paste is accepted by rats, but tastes bitter to man; and stilboestrol 10 mg./g. paste is rejected by rats, but tastes like control chocolate paste to man.

We have successfully used the method to give hydrocortisone to rats for several weeks. The paste was put in a tube of nozzle diameter 5 mm.; the length of the column squeezed out was measured with a ruler. The mean weight of six

TABLE I

AMOUNTS OF QUININE DIHYDROCHLORIDE TAKEN IN CHOCOLATE PASTE AND IN SOLUTION. (MEANS FOR TWO RATS)

Concentration of drug	Amount of preparation consumed	Total dose of drug consumed
In chocolate paste*		
None	3·9 g. } in	
1 mg./g.	2·6 g. } 10	2·6 mg.
3 mg./g.	2·5 g. } min.	7·5 mg.
5 mg./g.	less than 0·4 g.	
In aqueous solution		
None	26·5 ml.	
0·1 mg./ml.	22 ml. } in	2·2 mg.
0·3 mg./ml.	16 ml. } 24	4·8 mg.
2·0 mg./ml.	3·5 ml. } hr.	7 mg.
2·0 mg./ml. together with sucrose 230 mg./ml.	13·5 ml.	28 mg.

* Presented in "doses" of 250–300 mg.

5 mm. lengths was 117 mg., with a standard deviation of ± 6 mg.; of six $4\frac{1}{2}$ mm. lengths, 105 ± 4 mg. These figures correspond respectively to doses of $1{\cdot}40 \pm 0{\cdot}07$ mg. and $1{\cdot}26 \pm 0{\cdot}05$ mg. hydrocortisone.

Can a rat be induced by this method to take more of a drug than it takes when the drug is put in its drinking water? Observations to answer this question were made on two singly housed male rats, fed rat-cubes *ad libitum*. On different days they were offered chocolate paste containing varied concentrations of quinine dihydrochloride, or control chocolate paste. For 10 min. each day they were allowed to eat as much paste as they wanted; the amount eaten was measured by weighing the tube. The rats drank either distilled water or a solution of quinine dihydrochloride. To minimize adaptation, successive presentations of quinine were separated by one or more days on which the paste or water was given without the drug. Chocolate paste containing 1 or

3 mg./g. of the quinine salt was eaten readily, though a little more slowly than the unmedicated paste. Higher concentrations were either consumed hesitantly and only in part (5 mg./g.), or rejected after sampling (10 mg./g.) (see Table I). The rejection behaviour was characterized by slow and intermittent chewing, followed by prolonged rubbing of the lower jaw along the floor or sides of the cage (cf. Teitelbaum and Epstein, 1962). When quinine was given in solution, a concentration of 0·1 mg. of the salt per ml. was accepted without any change in fluid intake; with 0·3 mg./ml. or more the fluid intake decreased, and with 2 mg./ml. it was only 10–20 per cent of the control value. When sucrose was added in high concentration (230 mg./ml.) in the presence of 2 mg./ml. quinine dihydrochloride, the fluid intake increased, but was still much below the control level. Table I shows that the rats took a similar total daily dose of quinine, in similar concentration, whether the drug was in chocolate paste or in solution. But all the paste was eaten at one time, whereas the solution was consumed gradually in the course of 24 hr. Normal rats will drink solutions and eat food containing higher concentrations of quinine, about 10 mg./g., but only when they have no choice (Teitelbaum and Epstein, 1962).

The advantages of our method are that it is relatively pleasant for the animal, and interferes minimally with its normal feeding and drinking behaviour. The method is convenient for the operator, and can be used on behalf of a licence holder, but in his absence, by a person unlicenced under the 1876 Act. Drugs keep well in a capped metal tube, and the dose can be accurately measured. However, the method becomes cumbersome with doses approaching 30 mg. and cannot be used for bulky medication.

In principle the method can be adapted to any species including man, with modifications to take account of differing food preferences.

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REFERENCE

Teitelbaum, P. and Epstein, A. N. (1962). *Psychol. Rev.*, **69**, 74–90.