An apparatus for automatically recording diuresis in laboratory animals

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An apparatus has been developed for the continuous recording on photographic film of diuresis in laboratory animals. Ten mice are housed in each of 16 metabolic cages, arranged in a circle mounted on a table. Urine from each cage is collected in a measuring cylinder. A 35 mm camera (Shackman Auto Camera, Mark 3) and an electronic flash unit (National PE-243) are mounted on a motorized turntable revolving once per hour. The volume of urine contained in each cylinder is photographed at predetermined intervals of time. The measuring cylinders containing the urine samples are automatically removed at the end of the experiment enabling subsequent estimation of electrolytes. After development of the film, the urine volumes are read from the negatives, using a projector.

The apparatus has the advantages of providing a permanent record of the data on film and does not require constant supervision. In addition, experiments can be performed during periods of the day or night when stressful stimuli are at a minimum. The apparatus can be readily adapted for use with different laboratory animals, and the effects of diurnal variation in urine excretion on the actions of drugs can be studied.

A simple and inexpensive device for the *in vivo* detection and counting of ventricular extrasystoles

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A tedious aspect of experiments aimed either at producing cardiac arrhythmias or assessing potential antiarrhythmic drugs is the detection and counting of the arrhythmias under examination. Ventricular ectopic beats or extrasystoles are recognized typically by large negative deflections of the lead II or chest leads of the electrocardiogram. We have utilized this effect and report here the development of an inexpensive and simple device to detect and automatically count ventricular extrasystoles. A block diagram of the major interactive components is shown in Figure 1.

After amplification the ECG is switched through one of two clipper diodes admitting either positive only or negative only signals via a Schmitt trigger and

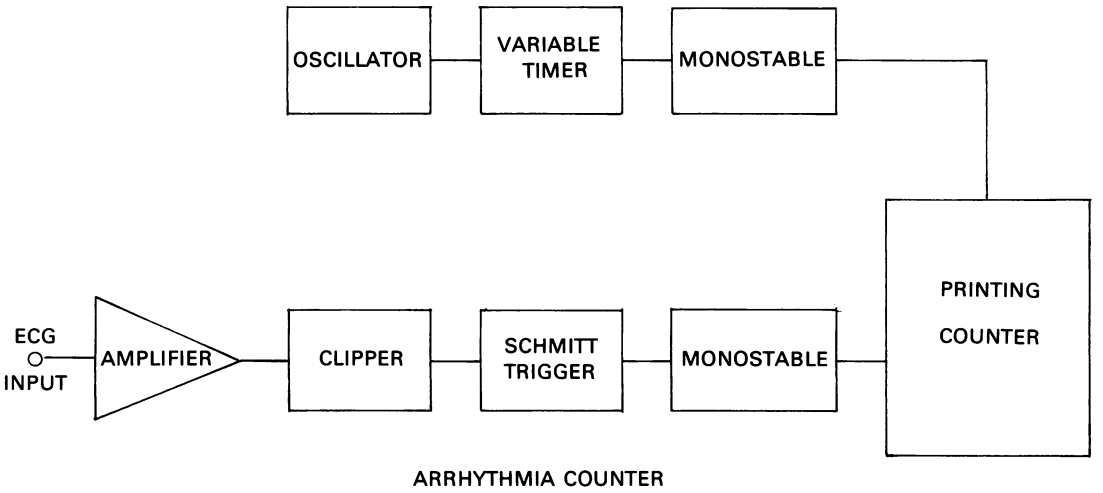

Figure 1

monostable to a printing counter. The printer is controlled by a variable timer allowing the printing of numbers of arrhythmias in any desired time interval of between 6 s and 100 minutes.

With the Harris (1950) two-stage coronary artery ligation model of ventricular arrhythmias in the dog, we normally use ECG lead II or CR and allow the counter to be triggered in the negative mode. If, for any reason, the ECG is itself negative, then a switch permits the user to choose positive triggering of the counter. On occasions, the baseline of the ECG may wander because of respiratory or other skeletal muscle movements by the animal and to prevent negative excursions of the baseline giving rise to artefactual counts a d.c. level clamp may be included prior to the amplifier.

Reference

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Substituted benzamides as dopamine antagonists

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A number of substituted benzamides have recently been developed for their anti-emetic and anti-psychotic properties. Previous studies with one such compound, metoclopramide (*N*-[diethylaminoethyl]-2-methoxy-4-amino-5-chlorobenzamide) have indicated that it has biochemical and behavioural properties associated with the blockade of cerebral dopamine receptors (Dolphin, Jenner, Marsden, Pycock & Tarsy, 1975; Peringer, Jenner & Marsden, 1975; Donaldson, Jenner, Marsden, Peringer & Miller, 1976). These studies have now been extended to include sulpiride (*N*-[1'ethyl-2'-pyrrolidinyl methyl]-2-methoxy-sulphamoyl benzamide), tigan (*N*-[(2'dimethylaminoethoxy) benzyl]-3,4,5-trimethoxyl benzamide) and clebopride (*N*-[*N'*-benzylpiperidin-4'-yl]-4-amino-5-chloro-2-methoxy-benzamide) and its debenzylated metabolite.

All of these compounds were found to: inhibit the apomorphine (2 mg/kg i.p.) reversal of reserpine (10 mg/kg i.p. 18 h before apomorphine) induced akinesia in mice, inhibit the apomorphine (0.5 mg/kg s.c.) induced circling in mice with unilateral 6-hydroxydopamine induced striatal lesions, induce some degree of catalepsy, induce ipsilateral circling in apomorphine (0.5 mg/kg s.c.) treated rats following their administration via intrastriatal cannulae (25 or 100 μg in 3 μl 0.9% saline).

Thus these compounds all exhibit behavioural properties thought to be associated with blockade of central dopamine receptors. Biochemical studies have shown that these compounds induce a rise in the brain concentration of the dopamine metabolite homovanillic acid and, to a lesser extent, the intraneuronal metabolite dihydroxyphenyl acetic acid. These findings are also consistent with a central blocking action of the compounds on dopamine receptors (Donaldson *et al.*, 1976).

In the *in vitro* rat striatal dopamine (10^{-4} M) stimulated adenylate cyclase system, however, metoclopramide, sulpiride, tigan and the clebopride metabolite had no inhibitory action at 10^{-7}–10^{-4} M. Clebopride caused a small reduction in cyclic AMP production at 10^{-4} M.

Thus, although these substituted benzamides exert pharmacological and biochemical effects consistent with their being dopamine antagonists, they have little effect in the adenylate cyclase model of the dopamine receptor. Their mode of action therefore remains an open question.

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