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A SIMPLE METHOD FOR RECORDING THE ELECTROCARDIOGRAM AND HEART RATE FROM CONSCIOUS ANIMALS

BY

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The small bioelectrical signals of the heart detected at the body surface of animals are usually relayed to the initial amplifier stage of the electrocardiograph by the use of plate, needle or clip electrodes (Clark, Szabuniewicz & McCrady, 1966). In a series of experiments in which rapid and repeated measurements of the electrocardiogram (e.c.g.) and resting heart rate from conscious, unrestrained guinea-pigs were required none of the standard methods proved suitable and a modification was therefore developed in which the animals stand on plate electrodes. This method has been used to obtain recordings from conscious mice, rats, cats and dogs, and some applications of the method are illustrated in the experiments described in this article.

METHODS

A diagram of the apparatus is shown in Fig. 1. It comprised four separate copper plate electrodes mounted in either cork or blockboard, each sealed with a waterproof mastic seal (Seelastik, Expandite Ltd.) to prevent leakage. The animal was placed on the apparatus so that each foot was in contact with a separate plate electrode. The front feet and left hind foot were used for recording standard leads while the right hind foot was grounded. Contact was facilitated by the use of gauze pads damped with isotonic saline. The dimensions of the apparatus were varied to suit the different animals. The electrical signals detected by the plate electrodes were amplified by a Devices ACI and sub-unit 3 preamplifier and displayed on a Devices pen recorder. Heart rate was measured by a Neilson instantaneous ratemeter (40–250 and 80–500 beats/min scales) triggered from the QRS complex of the e.c.g. Recordings were obtained in a quiet room maintained at 20°–21° C.

In the experiments described the following animals of either sex were used: mice of the I.C.I. strain (20–25 g); Wistar rats (200–300 g); cats (2–3 kg) and beagle dogs (10–17 kg).

Drugs

The following drugs were used: isoprenaline sulphate (Burroughs Wellcome), propranolol (Imperial Chemical Industries) and strophanthin-G (Ouabain; British Drug Houses). The drugs were dissolved in normal saline and administered by subcutaneous or intravenous injection. All doses are expressed in terms of the base.

RESULTS

Training and suitability of conscious laboratory animals for the method of recording

A preliminary training period which varied considerably in duration for different laboratory animals was required before e.c.gs of suitable quality and stable heart rate

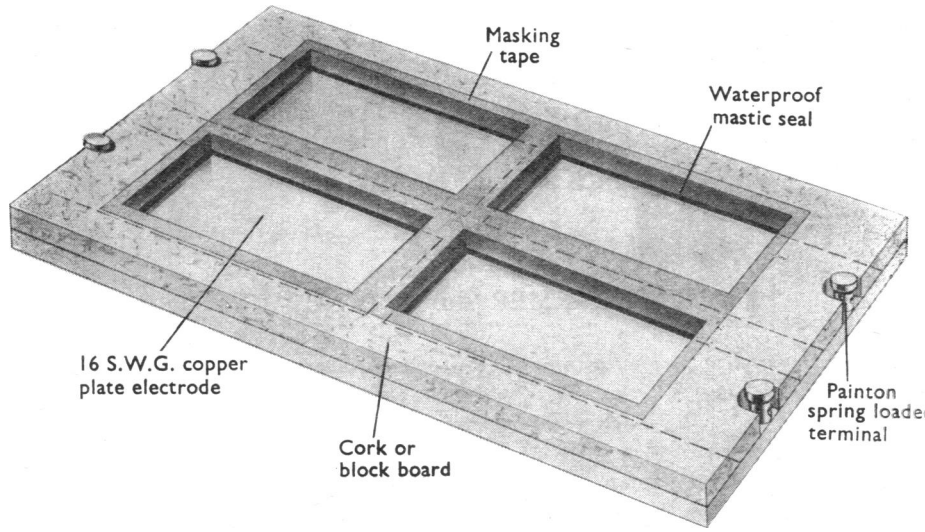

Fig. 1. Foot electrode apparatus for recording e.c.g. from conscious animals.

levels were obtained. Once stable heart rate levels had been reached, clear or reproducible e.c.gs could be obtained. Forcible restraint of nervous or untrained animals resulted in marked tachycardia.

Mice and rats required a training period of 1 or 2 days before stable readings of heart rate could be obtained; gentle restraint was used. In addition three or four preliminary readings at 10 min intervals on any subsequent day were often required to reach such levels. Neither animal was suitable for continuous recording of e.c.g. or heart rate over long periods; however, repeated readings at short intervals could be obtained. Forcible restraint of rats resulted in particularly rapid and large increases in heart rate, of the order of 100 beats/min in a few seconds, and special care was required in obtaining consistent readings from this animal.

Guinea-pigs required little training before giving continuous stable readings while sitting unrestrained on the apparatus, but as with mice and rats it was advisable to obtain three or four preliminary readings to ensure that stable levels had been reached.

Although rabbits were trained in a short time to sit unrestrained on the apparatus the e.c.g. records were of poor quality and unsuitable for triggering the ratemeter.

Cats have not been extensively investigated with respect to this type of apparatus. It was found that on the first day many attempts had to be made to keep animals on the apparatus but after 2–3 hr, continuous and stable heart rate readings could be obtained from the unrestrained animal sitting on the apparatus. On subsequent days continuous recordings were obtained in a much shorter time.

Dogs gave continuous and stable readings after 5 min either standing or sitting unrestrained on the apparatus. It should be noted that these dogs were adult animals used to frequent handling.

Occasionally individual animals of all species were rejected because of unsuitable temperament or large fluctuations in heart rate.

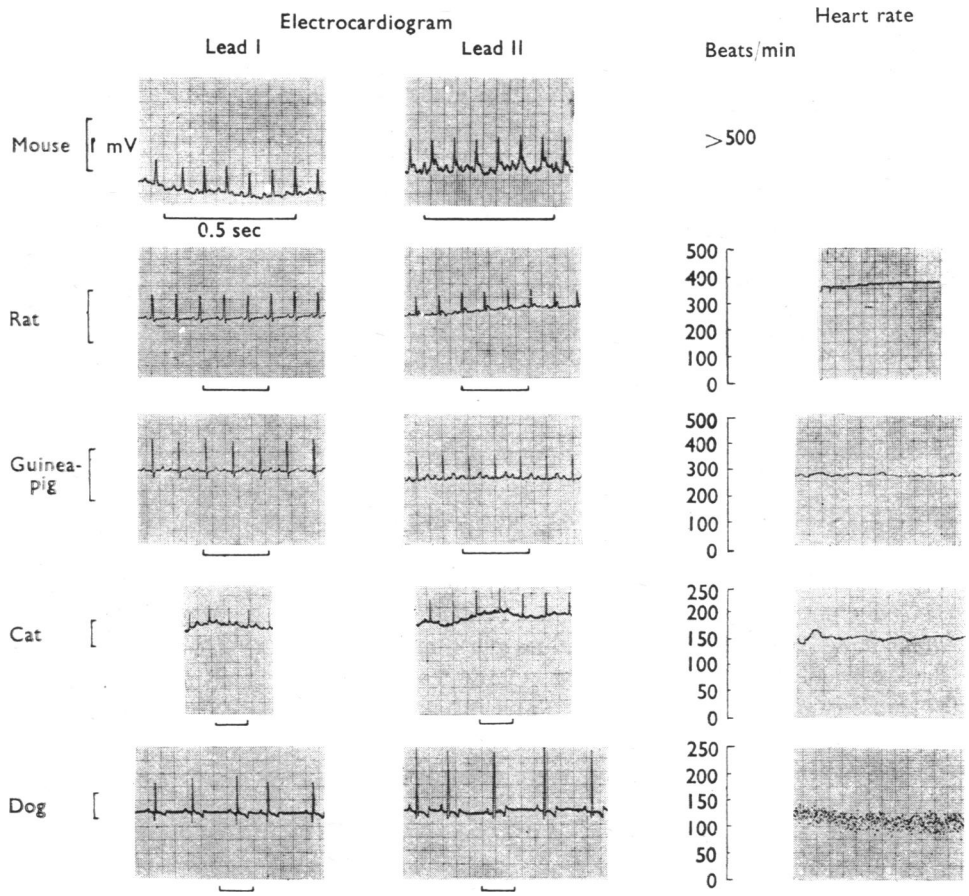

Fig. 2. Electrocardiogram and heart rate recordings obtained from conscious animals using foot electrode recording system.

Electrocardiogram and heart rate records obtained from conscious laboratory animals

Typical e.c.g. (leads I and II) and heart rate records obtained from the mouse, rat, guinea-pig, cat and dog, are shown in Fig. 2. Amplification and paper speed were varied to obtain clear records in each case. Electrocardiographic data obtained from the different animals are summarized in Table 1. Although e.c.gs among individuals of a species varied slightly they remained constant for a given animal over long periods of time.

The heart rate of the mouse was greater than 500 beats/min and readings could not be obtained from the ratemeter; heart rate was therefore derived from the e.c.g. record. In lead I upright P waves, QRS complexes and usually T waves were present. There was no S-T segment; the T wave, when present, followed immediately after the QRS complex. In lead II the upright P waves were larger than in lead I. The QRS complex in lead II was notched; this is a recording artifact caused by the limited frequency response

TABLE 1

ELECTROCARDIOGRAPHIC DATA OBTAINED FROM CONSCIOUS ANIMALS

Figures represent mean values from stated number of animals. For each animal data were obtained from six cardiac cycles

Species	No. of animals	Resting heart rate (beats/min)	Duration of cardiac cycle (sec)	Duration of P–R interval (sec)	QRS Complex			Duration of Q–T interval (sec)
					Duration (sec)	Amplitude Lead I (mV)	Amplitude Lead II (mV)	
Mouse	6	>500	0·06	0·04	0·015	0·5	0·65	0·03
Rat	8	260–380	0·11	0·05	0·02	0·5	0·35	0·06
Guinea-pig	10	240–310	0·18	0·07	0·02	0·6	0·4	0·11
Cat	4	110–175	0·26	0·09	0·03	0·6	0·8	0·16
Dog	9	70–120	0·32	0·11	0·04	1·2	2·4	0·21

of the pen amplifier (Rappaport & Rappaport, 1943). The heart rate of the rat ranged from 260 to 380 beats/min. The rate was higher in the morning than in the afternoon. This gradual decline in heart rate throughout the day paralleled the decline in spontaneous activity of the animals. In lead I upright P waves and QRS complexes were evident but T waves were absent. S waves could be seen but Q waves were rare. In lead II P waves, QRS complexes and T waves could be distinguished ; again there was virtually no S-T segment. The heart rate of the guinea-pig ranged from 240 to 310 beats/min. P, R and T waves were upright in both leads. Q and S waves were evident in lead I and either small or absent in lead II. In the cat, heart rate ranged from 110 to 175 beats/min. A slight sinus arrhythmia associated with respiration was observed in some animals. Electrocardiogram records of the cat were difficult to analyse because of fluctuations in base-line. In those sections suitable for analysis, upright P, R and T waves could be distinguished in both lead I and II. All amplitudes were smaller in lead I. Q and S waves were not prominent in either lead. Heart rate in the dog ranged from 70 to 120 beats/min with a phasic sinus arrhythmia associated with respiration present in all dogs. P waves and R waves were upright in both leads and larger in lead II than lead I. Q waves were present in both leads but S waves were often absent in lead I. An S-T segment was present in both leads. T waves were variable, being either upright or inverted in either lead I or II.

Effect of ouabain on e.c.g. and heart rate of conscious guinea-pigs

Ouabain 100–200 μg/kg given subcutaneously or intraperitoneally to conscious guinea-pigs caused a tachycardia of 20–40 beats/min in approximately half the animals treated ; the remainder were unaffected. Subsequent recordings revealed most of the common manifestations of cardiac glycoside toxicity such as prolongation of P-R interval, loss of T wave, S.A. block, A.V. block, interference dissociation and auricular and ventricular dissociation. Many animals exhibited violent muscle tremors and convulsions. In this dose range ouabain proved fatal to most animals within 3 hr. Recordings obtained from one animal are illustrated in Fig. 3. There was a progressive reduction in cardiac muscle excitability with development of an A.V. block and establishment of an idioventricular rhythm. The ventricular ectopic focus caused three successive abnormal ventricular beats after which normal rhythm was re-established.

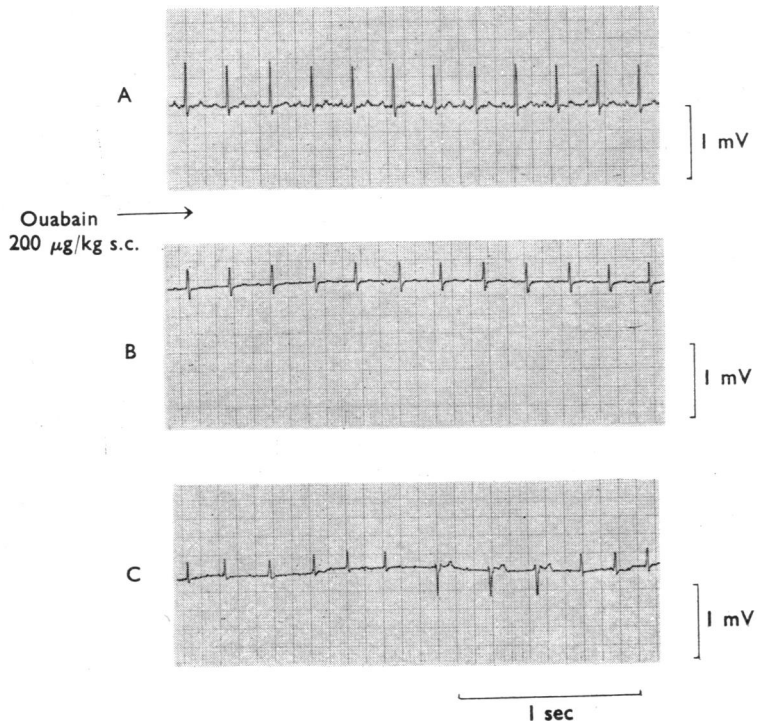

Fig. 3. Electrocardiogram of guinea-pig (350 g). Panel A, control reading; panels B and C, 30 and 60 min after the subcutaneous injection of ouabain 200 μg/kg.

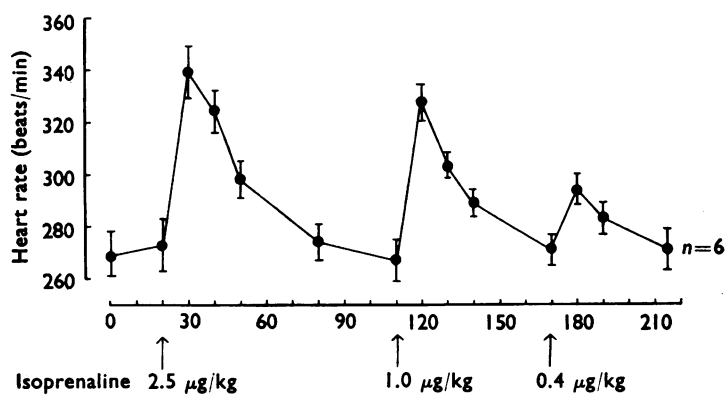

Fig. 4. Effect of graded doses of isoprenaline, given subcutaneously on the heart rate of the conscious guinea-pig.

Effect of isoprenaline and propranolol on heart rate of the guinea-pig, rat and dog

The effect of graded doses of isoprenaline on heart rate of a group of six guinea-pigs is shown in Fig. 4. The net increase in heart rate produced by isoprenaline 0.4, 1.0 and 2.5 μg/kg was 24, 60 and 70 beats/min, respectively. The response to repeated subcutaneous administration of isoprenaline 1.0 μg/kg, when given at 1 hr intervals was constant. Propranolol 10 mg/kg given subcutaneously to a group of six guinea-pigs

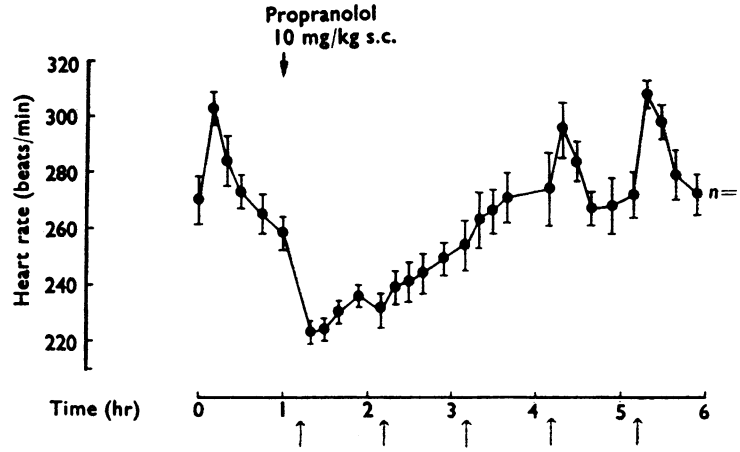

Fig. 5. Effect of propranolol 10 mg/kg given subcutaneously (↓) on the resting heart rate and on isoprenaline induced tachycardia in the conscious guinea-pig. At ↑ isoprenaline 1 μg/kg was given subcutaneously.

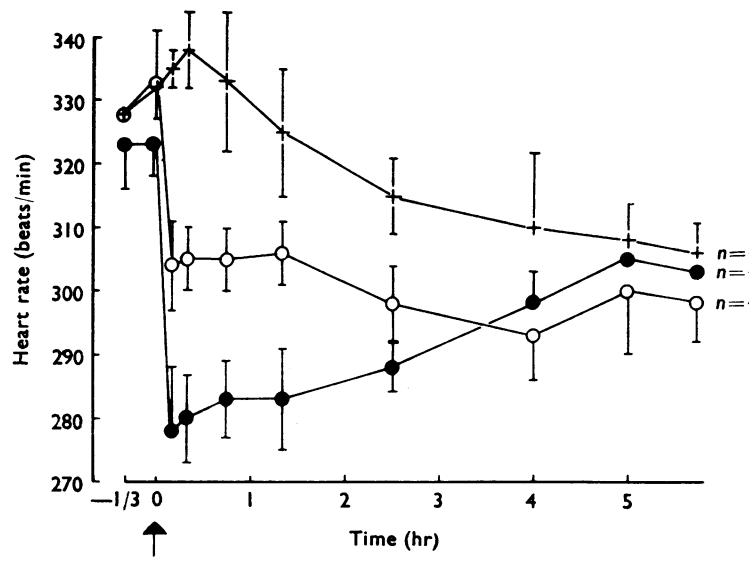

Fig. 6. Effect of propranolol given subcutaneously (↑) on resting heat rate in groups of conscious rats (four rats/group). Saline control (+); propranolol 2 mg/kg (○); propranolol 10 mg/kg (●).

produced a mean decrease in heart rate of 35 beats/min which was maximal at 15 min and blocked the response to isoprenaline (Fig. 5). The heart rate returned to control levels in 3 hr but the response to isoprenaline did not recover until 4 hr.

In the rat, propranolol also produced a decrease in heart rate (Fig. 6). The net decreases in heart rate produced by propranolol 2 and 10 mg/kg given subcutaneously to groups of four rats was 26 and 45 beats/min, respectively. The duration of action of propranolol was about 4–5 hr. Untreated rats also showed a decline in heart rate over this period as described earlier.

In the conscious dog a submaximal tachycardia was produced by isoprenaline 0.3 μg/kg given intravenously. Propranolol 0.2 mg/kg also given intravenously blocked the response to isoprenaline by 80%. The degree of blockade declined over a period of 2 hr. Propranolol had no effect on resting heart rate. These results are essentially the same as those obtained by Black, Duncan & Shanks (1965) who used fine needle electrodes implanted subcutaneously.

DISCUSSION

The method described has many advantages over existing methods for recording e.c.g. or heart rate in conscious laboratory animals. Only a little time need be spent on training animals for this recording procedure because the animal remains in a natural standing or sitting position and there are no attachments or implantations of electrodes to be made. These are important factors when resting heart rate is required. Many animals have been reported to object to the manual or mechanical restraint required by conventional electrodes (Lalich, Cohen & Walker, 1941; Clark, Szabuniewicz & McCrady, 1966). Essler (1961) has also pointed out that measuring techniques themselves may disturb measurements and showed that subdermal telemetry is probably the best method of obtaining physiological heart rates. Using subdermal telemetry Essler noted a 24 hr heart rate periodicity in the dog, cat and rabbit in which periods of fast heart rate coincided with normal periods of activity and periods of low heart rate with normal resting periods. While the method described here did not enable physical isolation of the animal as does radio telemetry, the fact that an analogous heart rate rhythm was detected in the rat, in which a decline in heart rate was correlated with a decline in activity, illustrates that recordings were obtained from animals with a minimum of disturbance. In contrast to subdermal telemetry this method does not allow basal recordings from sleeping animals or recordings from animals in their natural environment to be obtained. When repeated recordings with minimum disturbances are required from laboratory animals, however, this method provides a simple and inexpensive alternative to radio telemetry.

The e.c.gs obtained from rats, guinea-pigs and dogs were of good quality and free from muscle artifacts. Recordings can be obtained from the standard bipolar limb leads I, II and III and also from the augmented unipolar limb leads aVR, aVL and aVF. A small amount of baseline fluctuation was usually observed but this is probably inherent in any method of recording e.c.g. from conscious animals. In the cat, slight changes in posture are probably responsible for poor contact with the electrodes, and in consequence e.c.gs of poor quality with large baseline fluctuations were observed. Similar difficulty was encountered with rabbits where the e.c.g. was unsuitable to trigger the ratemeter. The ventricular depolarization time (QRS interval) was relatively constant in all species examined. In contrast, however, the ventricular repolarization time (S-T interval) showed a large increase from mouse to dog caused mainly by the increase in the duration of the depolarized state of ventricular muscle (S-T segment). Thus the S-T segment was virtually zero in the mouse but was 0.08 sec in the dog. Electrocardiogram recordings obtained by this method compared in all respects with those obtained using conventional methods (Lombard, 1952; Hill, Howard & Gresham, 1960; Pratt, 1938; Blok & Boeles, 1957; Peterson, Ricketts, Brewer, Lints, Test & Tupikova, 1951).

The usefulness of the method in assessing the effect of drugs on the e.c.g. and heart rate is illustrated by the studies with ouabain and with adrenergic stimulant or blocking drugs. The classical manifestations of cardiac glycoside toxicity after injection of ouabain were readily observed by this method. Propranolol, in addition to blocking isoprenaline tachycardia, was shown markedly to reduce the heart rate of rats and guinea-pigs in a dose-dependent fashion. The guinea-pig was a more suitable animal than the rat for these studies because the heart rate of the guinea-pig was stable over the experimental period (6 hr). In the dog propranolol, at the dose level used, blocked the isoprenaline tachycardia without affecting heart rate. We have observed, however, that larger doses of propranol given orally (1 mg/kg and more) caused a fall in heart rate.

SUMMARY

1. An apparatus suitable for recording e.c.g. from conscious mice, rats, guinea-pigs, cats and dogs using foot electrodes is described.

2. Training procedures and measuring techniques for obtaining stable heart rates and reproducible e.c.gs from the different species are detailed.

3. Electrocardiogram and heart rate recordings obtained from the different species are described and compared.

4. The effect of ouabain on the e.c.g. of the guinea-pig and of isoprenaline and propranolol on heart rate in the rat, guinea-pig and dog are described to illustrate some possible applications of the method.

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REFERENCES

BLACK, J. W., DUNCAN, W. A. M. & SHANKS, R. G. (1965). Comparison of some properties of pronethalol and propranolol. *Br. J. Pharmac. Chemother.*, **25**, 577–591.

BLOK, J. & BOELES, J. TH. F. (1957). The electrocardiogram of the normal cat. *Acta physiol. pharmac. néerl.*, **6**, 95–102.

CLARK, D. R., SZABUNIEWICZ, M. & MCCRADY, J. D. (1966). Clinical use of the electrocardiogram in animals. Part I: Fundamentals of E.C.G. examination. *Vet. Med.*, **61**, 751–760.

ESSLER, W. O. (1961). Radio telemetry of electrocardiogram and body temperatures from surgically implanted transmitters. *St. Univ. Stud. nat. Hist. Iowa*, **20**, 1–35.

HILL, R., HOWARD, A. N. & GRESHAM, G. A. (1960). The electrocardiographic appearances of myocardial infarction in the rat. *Br. J. exp. Path.*, **41**, 633–637.

LALICH, J., COHEN, A. M. & WALKER, G. (1941). The frequency of electrocardiographic variations in normal unanaesthetized dogs. *Am. Heart J.*, **22**, 105–111.

LOMBARD, E. A. (1952). Electrocardiograms of small mammals. *Am. J. Physiol.*, **171**, 189–193.

PETERSON, E. S., RICKETTS, H. T., BREWER, N. R., LINTS, H. A., TEST, C. E. & TUPIKOVA, N. A. (1951). Electrocardiogram of the beagle dog. *Proc. Soc. exp. Biol. Med.*, **77**, 330–332.

PRATT, C. L. G. (1938). The electrocardiogram of the guinea-pig. *J. Physiol., Lond.*, **92**, 268–272.

RAPPAPORT, M. B. & RAPPAPORT, I. (1943). Electrocardiographic considerations in small animal investigations. *Am. Heart J.*, **26**, 662–680.