TRANSMISSION OF CARDIOVASCULAR DATA FROM DOGS[1]

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Summary Prolonged acquisition of dynamic blood pressure data from animal subjects in various experimental conditions has become a special research area in numerous institutions. To properly conduct many of these experiments, the subject must be instrumented with blood pressure sensors and a means of conveying the indicated pressure level to a remote station. Quite often data must be obtained over several weeks in which recalibration can not be conducted. Telemetry techniques are quite adaptable to these problems and in many instances are the only solution available. To illustrate the special applications of telemetry, several experiments are described along with the hardware required to conduct these experiments.

Introduction The relationship of an organism's blood pressure to various internal and external conditions has become of prime importance to aid in isolating the causes of cardiovascular impairment and to more adequately describe the control function in an effort to prescribe corrective medication The effects of population density, social stress, diet and cultural stability on mouse blood pressure has been investigated by this and other groups. Sufficient data on larger animals has also been obtained to suspect that their blood pressure response is in some cases similarly effected by similar conditions. An intensive research project has been initiated to reliably establish the relationship of blood pressure to several parameters. The broad aspects of this program are to determine the dynamic blood pressure of various animals under a variety of environmental conditions, including weightlessness, emotional stress, exercise and diet. Much of the data will be obtained by telemetry in laboratory experiments conducted on dogs, chimpanzees, monkeys and various other animals. It is hoped that other data will be obtained from orbit experiments such as the NASA biosatellite and the Apollo application project. The data generally obtained will be blood pressure, blood flow and electrocardiogram.

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Hardware The design of hardware for such an experimental undertaking is largely influenced by the size of the animal and the experiment duration. Although there may be no intent to place the transmitting hardware subcutaneously, the size and power constraints are only slightly reduced because of weight limitation imposed by the animal's size. Therefore, if one elects to arbitrarily limit the size of the telemetry to 1/2 the size of a cigarette package, a feeling for the problem can be developed. A workable transmission distance is for a majority of experiments at least 50 feet. With inexpensive receiving antenna the power dissipation to establish this reception distance is from 0.6 mv to 6 mv. Power requirement for a single channel blood pressure signal conditioner is in a similar range. If the lower number is selected as feasible, the power requirements are 1.2 milliwatts, or a current drain of 200 μ from a 6 volt battery. To remain within the established dimensional envelope a non-rechargeable battery of 160 ma hours can be selected. With these conditions, a brief operating life of 30 days is available. An operating life of this duration is quite inadequate if the planned experiment is in months or years and implanting is anticipated. The alternative is that a 5% duty cycle is in many instances sufficient to obtain adequate data. This increases the useful operating life to approximately two years but complicates the system because of the necessity for a remote controlled switch if the unit is to be implanted. The switching requirements can be obtained by several techniques. We have elected to use a magnetically controlled switch as shown on the right in Figure 1. It requires little power and is quite small. The system is activated by positioning one pole of a large magnet near the switch. This closes the on contact and applies the the power. The "off" condition is induced by reversing the magnet and closing the off contact.

Every effort to reduce size and power in the system has been made. Since meaningful blood pressure must retain its DC characteristics, a DC couple data channel must be employed. However, the sensor which is typically a low impedance bridge, can require considerable power to operate properly with simple DC amplifiers. Drift can also result from various factors that can obsecure the baseline position. To reduce the drift and to eliminate insofar as possible all function not required, a chopper type high gain AC amplifier is used. The results of this design goal are illustrated in Figure 1. The circuit functions as a frequency variable oscillator with frequency proportional to the input between A and B. The summation of the amplitude modulated feedback from the AC chopper amplifier with the normal feedback through the parallel-T network produces a loop phase variation which is nullified by an appropriate frequency change in the system to maintain a total loop phase of 360°. Power requirements are typically 150 μ amp at 6 volts. Minimum size using discrete compartments is 0.146 cubic inches. Frequency of operation is currently limited to less than 30 Khz because of the capacitive spiking from the FET chopper. Maximum sensitivity is ±200 μv for ± 7/5% modulation. Other biological signals can be obtained by appropriate signal conditioner modules connected to the basic VCO at the chopper input.

Experiments previously conducted using this equipment have been in three classes: emotional stress induced by either obedience training or territorial defense, physical stress induced by treadmill work and modification of the blood pressure control system as produced by drug application. In all cases a blood pressure has been obtained by the placement of implantable sensors in the abdominal aorta of male mongrel dogs of German Shepherd descent. Typical experiments have not employed implanted transmitters as this technique has not been completely developed. However, external equipment placed in a jacket has been quite successful and has allowed the development of sensor implant and care techniques required for a large scale experimental undertaking. The following experiments illustrate the technique:

Exercise Studies The animals used in this study were generally male, mongrel dogs (50-75 lbs.) of German Shepherd breeding. Little was known concerning the previous history of the dogs other than that deduced after familiarization with the animal. The only requirements for selection were the large size for implantation of the aortic transducer and excellent health. These breeds are typically working animals, known for their ability to assimilate and retain training, their equable disposition, poise and intelligence. The animals were given distemper, hepatitis and rabies vaccines and placed under observation for approximately two weeks prior to surgery. They were housed in clean, air conditioned quarters in accordance with the latest regulations concerning animal care. The diet was composed mainly of commercially prepared Gaines Prime, with water given ad libitum. The animals were taken out of their cages for several hours daily and placed in runs for exercise.

The button type implantable transducer used in this study (Electro-Optical Systems Model 1017) was a small unalloyed titanium disc, 6.5 mm in diameter and 1.2 mm thick. The inner surface of the disc contained a pressure-sensitive diaphragm, 513 mm in diameter by 0.1 mm thick, forming a four arm Wheatstone bridge configuration. This diaphragm was in direct contact with the blood. When the bridge is excited by a DC voltage, a signal is produced directly proportional to the change in pressure in the vessel. The gauge was sealed with an internal pressure of 750 mmHg and therefore sensitive to daily barometric pressure changes. This did not post a problem in these investigations as variations in pressure are minimal in the surrounding area, e.g., the range of barometric pressure fluctuations for over a two month period was from 753 to 764 mmHg.

A major objective of the present study was to examine the feasibility of telemetry techniques for chronic blood pressure measurements in the unanesthetized free-roaming animal. To provide a basis for applicability, it was necessary to examine the method under various states of physical activity ranging from sleep to extreme exertion on a treadmill. A total of twenty-eight runs at various speeds and inclines on a treadmill were completed. The results from these graded treadmill studies suggest that heart rate mirrors metabolic demands and not necessarily emotional arousal. Heart rates of 300 beats/

minute were not uncommon at the higher gradients.(See Figure 2, solid curve). The increase in heart rate correlated well with increases in the work load, whereas blood pressure tended to remain unchanged or slightly increased. Blood pressure responses were found to change radically with training and the elimination of emotional factors associated with the treadmill task.

Considerable lability in blood pressure was observed during the spontaneously initiated natural activity of the animal over a twenty-four hour period. Situational stimuli produced increased lability but were notrepeated enough regularity to establish any concrete conclusions, but did point to the need for future investigation of the effects of emotional arousal on blood pressure.

This study illustrated that telemetry permits the necessary latitude for investigation of the cardiovascular response in behavioral studies. The only limitations of the method include the surgery for intravascular implantation, initial cost and availability of required technical apparatus.

Obedience Training Four male dogs (47 to 75 lbs.) were implanted with aortic blood pressure transducers which were later mated with FM/FM telemetry signal conditioning systems, portions of which were described earlier in this paper. The dogs were given a systematic basic obedience training regime which was designed to be the most important experimental manipulation of this study. The animals were their own controls; experimental values being compared with 'basal' (sleep) values or with values obtained earlier In the training period.

Results of Obedience Study The telemetered aortic blood pressure or three out of four dogs being obedience trained is elevated initially, decreases as the time of training increases, and eventually level off (See Figure 3). The decreasing blood pressure with increasing time of training is statistically significant for a particular command and is attributed to the fact that as the animal learns the act and is consequently praised more and punished less, the emotional factor which initially elevated the parameter through novelty and rigorous correction is reduced. The heart rate of dogs being obedience trained decreases consistently with time of training only for the action command "beel." There is a trend for decreasing heart rates with time of training for the static commands but it is not consistent. Heart rate data obtained from arterial pressure waves is a more accurate index of systolic ejection than that obtained from the electrocardiogram. These data indicate that aortic blood pressure is a more sensitive visceral Index of emotion than is heart rate, whereas the heart rate is a better index for evaluating physical exertion than blood pressure.

This study emphasized the extreme importance in chronic physiological experiments of acknowledging and controlling the emotional environment of the experimental subjects.

It is of utmost importance to eliminate psychological influences over an autonomic parameter before reporting that an experimental condition has resulted in a certain quantitative functional value. The FM/FM telemetry systems and intracorporeal blood pressure transducers utilized allowed full appreciation for the labile nature of both parameters studied, especially heart rate, and telemetry is credited as the only method capable of yielding these data which were obtained from truly normal, unrestrained, unanesthetized dogs.

Drug Studies The purpose of this study was to investigate the role of circulating catecbolamines in the circulatory response to exercise. The drug selected for this study was pbenoxybenzamine because of its specificity in blocking the alpha adrenergic receptors.

Four phenoxybenzamine treadmill runs were completed on each test subject. Each animal received pbenoxybenzamine in a dose of 1 mg/kg of body weight prior to the run. The well diluted (1:50) drug was administered by intravenous injections over approximately a five minute period. No anesthetic agents were employed but attempts were made to keep the animal as quiet as possible during Injection. Time elapsing from completion of the pbenoxybenzamine injection to the commencement of the treadmill run varied between 30 minutes and 90 minutes.

Six control runs and four runs after pbenoxybenzamine injections were completed on all animals. The subjects were given several familiarization runs It on the treadmill before recordings were made. A “Hot Shot” shocking device was used to encourage participation in the tests. The handler stood in front of the treadmill holding the animal with a leash attached to a choke chain around the dog’s neck. This procedure coupled with the presence of an assistant using the shocking device at the rear of the treadmill enabled the handler to have control of the animal and prevented the subject from drifting toward the rear of the treadmill during the more strenuous phases of the exercise test.

No set format was established for the frequency of treadmill runs. However, no more than two runs a day were attempted during the control runs and no more than one run a day was attempted after phenoxybenzamine had been administered. All control runs were completed on each animal before the phenoxybenzamine runs were commenced.

Prior to each treadmill run the animal was placed in a “stand” position off the treadmill. After a suitable length of time for blood pressure and heart rate stabilization, be was “heeled” to the treadmill and again placed in a “stand” position on the treadmill, the animal was given a “beel” command and the treadmill turned on at a speed of 2.5 miles per hour. The animal was run at 2.5, 3.5, and 6.0 miles per bour (each speed for 3 minutes) at a 16 degree incline (Figure 2). The treadmill was turned back to a speed of 2.5 miles per hour for two minutes for a “cooling off” period prior to termination of the

run. The treadmill was then turned off and simultaneously the animal was given a “stand stay” command for post-exercise blood pressure and heart rate recordings.

Results of Drug Studies During the control runs blood pressures could not be correlated with increased work loads (Figure 2). The heart rates of all test subjects tended to increase in a linear fashion as the work load was increased (Figure 2). These findings support the conclusion made in the exercise studies, that during exercise increased work loads are reflected by increased heart rates while blood pressures tend to vary.

During the exercise phase of the phenoxybenzamine runs in all dogs, both systolic and diastolic pressures decreased significantly when compared with control run blood pressures (Figure 2). These blood pressure decreases were seen with higher heart rates attained during the pbenoxybenzamine runs.

Territorial Intrusion In this study territorial intrusion was employed as a situational stress to study the blood pressure response. Two male dogs were allowed on separate occasions to spend a period of time in an area in order to develop a territorial defense response. At the completion of the acclimatization period, an intruder animal was allowed to enter while the test animal’s response was observed. This was performed in both acute and sub-acute (24 hour) intrusion experiences.

The response of one of the animals was quite strong in the acute phase which was made evident by the aggressive nature of the test animal and the increases in both blood pressure and heart rate. The blood pressure response can be seen in Figure 4. The second animal was relatively unresponsive to the acute intrusion. In the sub-acute (24 hour) intrusion both test animals demonstrated a significant response by blood pressure and heart rate increases while awake and pressure increases while sleeping. There would appear to be discrimination among animals as to the degree of threat by an intruder animal in that one dog was unresponsive to one intruder and markedly responsive to another.

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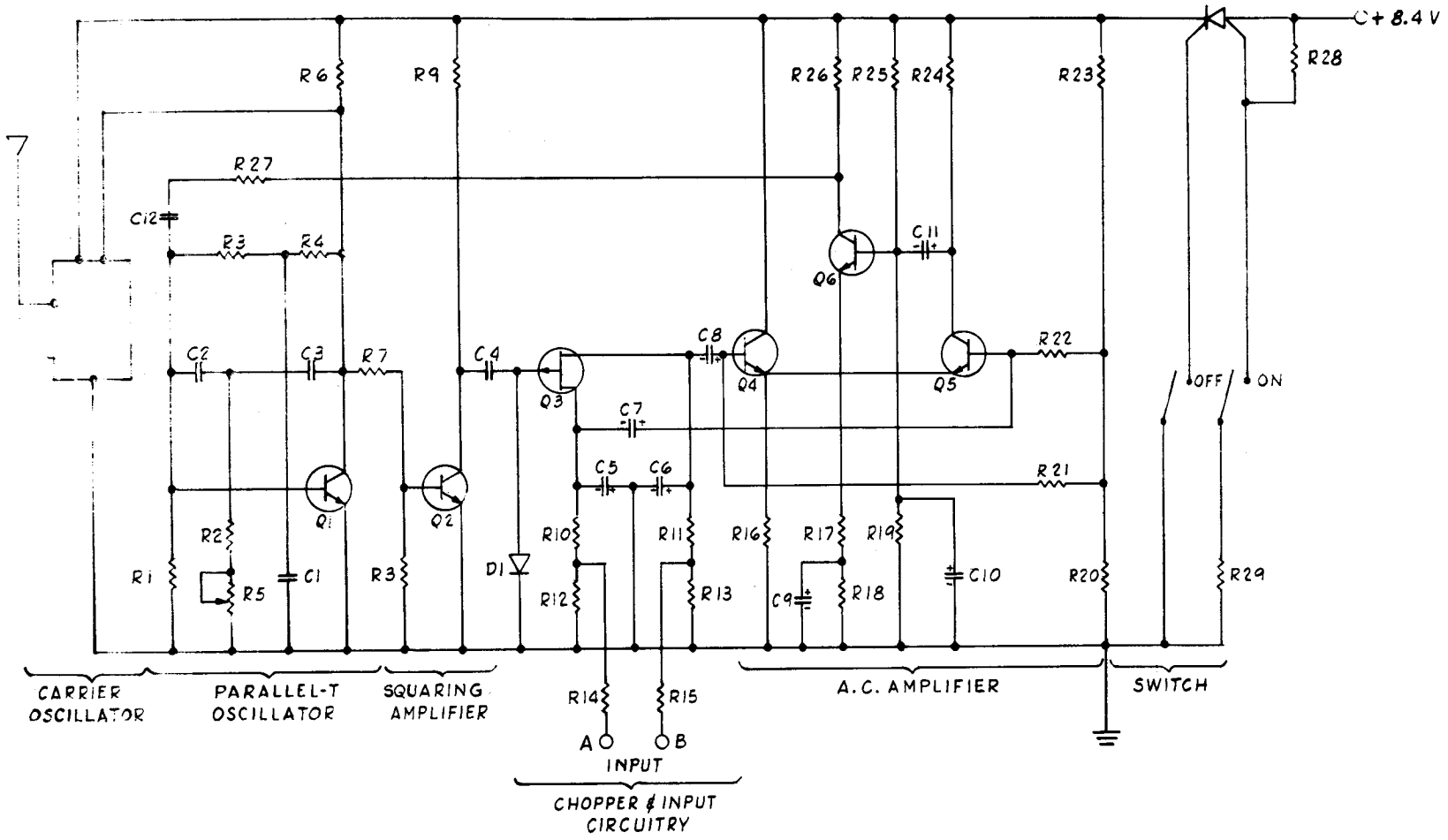

Fig. 1 - Blood Pressure Telemetry System

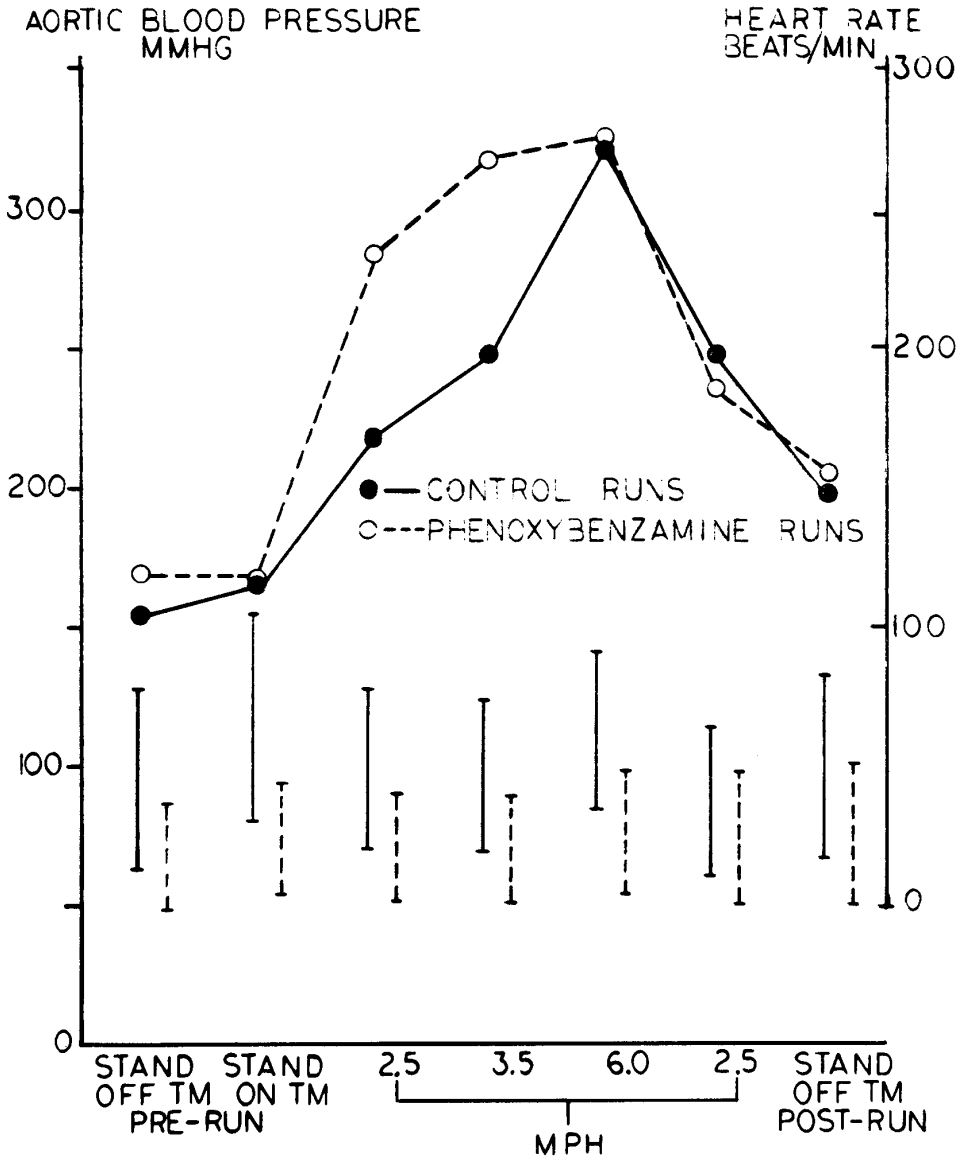

Fig. 2 - Effects of Graded Treadmill Exercise on Heart Rate and Blood Pressure

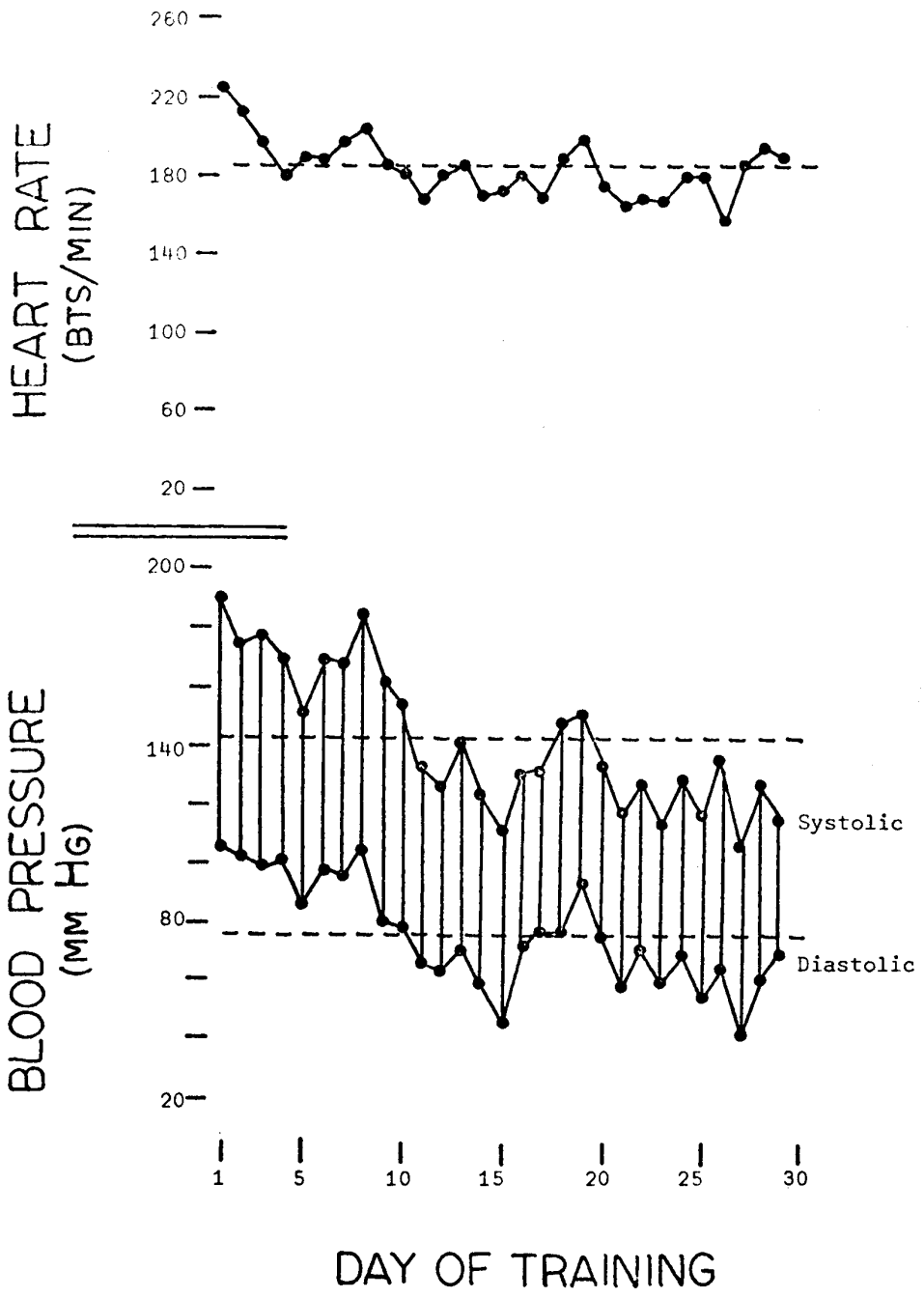

Fig. 3 - Telemetered aortic blood pressure and heart rate obtained from dog #215 on the "heel" obedience training command, a form of mild dynamic exercise. The systolic and diastolic pressures decrease with time of training as does the heart rate. Overall mean values for 29 days of obedience training are 142/75mm Hg and 184 beats per minute, and are indicated by the broken lines on this figure.

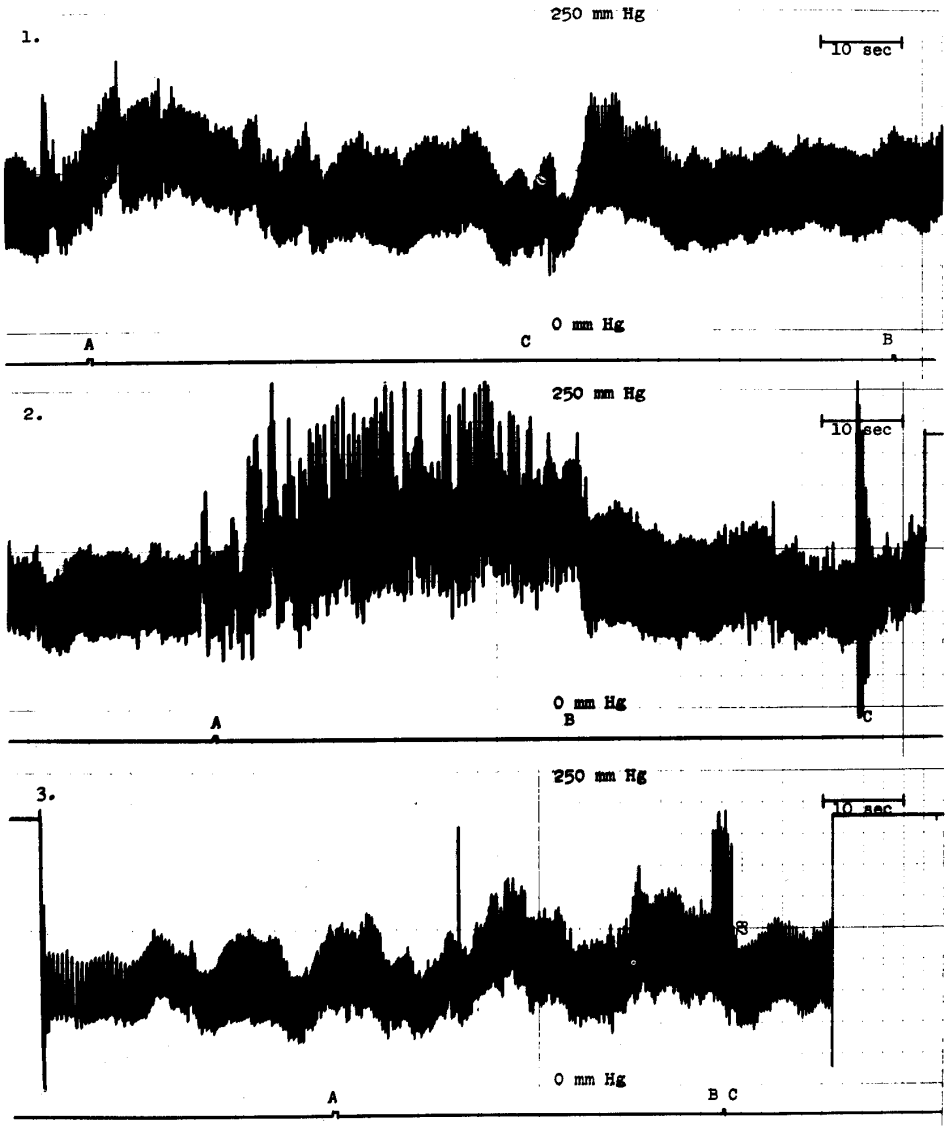

Fig. 4 - Acute intrusion recordings of Dog #215. 1. Day 1 control encounter; no territorial identification, 2. Typical Intrusion, 3. Typical neutral encounter. (A-intruder enters, B-intruder exits, C-test animal shaking.)