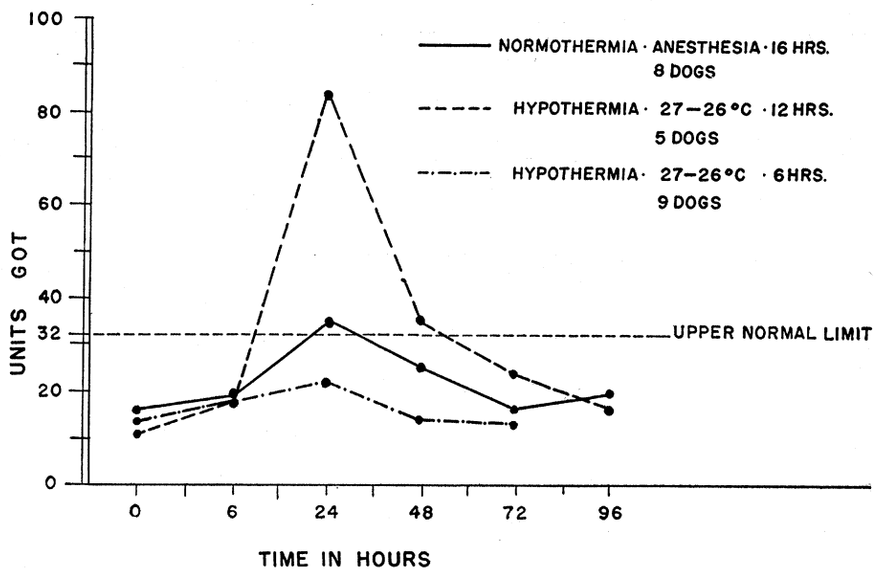

Fig. 1. Levels of glutamic oxalacetic transaminase (GOT) in prolonged hypothermia. Peak elevations occurred within 24 hours after arousal, with return to baseline levels within 72 hours. There was a tendency for serum glutamic oxalacetic transaminase to rise in the normothermia control animals.

its activity except for a lag in cellular oxidation (*8*).

Since a high level glutamic oxalacetic transaminase in the serum suggests tissue derangement, possibly due to necrosis, the present study was undertaken to determine serum levels of the enzyme in the pentobarbitalized dog cooled to 27°–26°C by the surface-immersion technique. Normothermic anesthesia controls were run for times approximately as long as those of the experiments involving prolonged hypothermia. Some of the animals breathed spontaneously, while others were given intermittent positive-pressure breathing with tank oxygen. Hypothermia was maintained for 6 and 12 hours in two separate groups, after which the dogs were rewarmed. Samples of arterial or venous blood, or both (the level of glutamic oxalacetic transaminase was the same in both), were drawn before the animals were cooled and 6, 24, 48, 72, and 96 hours after they were rewarmed. Sections of the following organs were taken after the last blood sample: ventricle, liver, kidney, adrenal gland, and skeletal muscle. The amount of the enzyme was determined by the method of Karmen (*9*). The upper limit of normal for this laboratory was established at 32 units.

All of the animals survived but were sacrificed for the tissue examinations. Spontaneously breathing and respiratory-supported animals demonstrated similar trends. Averages of the data are shown in Fig. 1. The control dogs showed tendency toward a rise in serum glutamic oxalacetic transaminase with the peak at 24 hours after the periods of anesthesia (8 and 16 hours) and return to normal in another 24 hours. In the treated animals there were no elevations until after 12 hours of cooling. Within 72 hours serum levels of the enzyme were normal, with one exception, which returned to normal in the next 24 hours. Histological examination revealed no necrosis in the tissue studied and no unusual morphological differences between the control and the treated groups.

The reason for the elevations in serum glutamic oxalacetic transaminase, both in the anesthetized and the hypothermic groups, is not clear, especially in the absence of cellular necrosis. Tissue oxygenation does not appear to be a factor, since no differences were found between the respiratory supported and the unsupported animals. The intracellular content of the enzyme is high, and a large gradient exists between the cell and the serum. It may be speculated that membrane permeability to the enzyme was altered sufficiently to permit escape of the enzyme into the serum, under the conditions of this study. Increased membrane permeability with increased flux of ions during hypothermia has been demonstrated (*10*). Cold may affect the rate of transamination.

The effect observed in this study, whatever its cause, is transient, and apparently the normal gradient is reestablished within 72 hours after recovery from hypothermia. Evaluation of physiological function during hypothermia has been limited to short-term observations, and, generally, function (certainly oxygenation) appears to be adequate. Effects from prolonged exposure to cold may prove serious. If elevation of serum glutamic oxalacetic transaminase may be used as a yardstick of functional integrity, then one might predict that prolonged hypothermia might result in physiological disturbances.

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Radiotelemetry of Physiological Responses in the Laboratory Animal

The measurement of physiological reactions in laboratory animals has long presented problems. Recording is usually accomplished under conditions varying from complete restraint to the partial restraint of extended wires. The animal may never grow entirely accustomed to the attachments, and this factor may constitute a source of stress. Restraint is reported in the literature as being extensively used as a stressor, the work of Selye on this topic being widely known. It is apparent, therefore, that measurement of physiological variables under conditions of even minimal restraint may yield a distorted picture of such responses. In addition, the cues inherently present in attachments of any kind, as well as the transfer of an animal to the study environment, are major—if not, at times, fatal—methodologic obstacles to classical conditioning. The development of the transistor offers new possibilities for classical conditioning.

With this in mind we set out to develop a system of radio telemetry for use as an adjunct to studies in classical conditioning. This methodological ad-

vance will permit the monitoring and recording of selected physiological reactions in intact, unanesthetized laboratory animals during their normal daily routines in a simulated normal environment uncontaminated by the intervention of the experimenter and experimental procedures, except for planned changes in the controlled environmental chambers. Transistorized, miniaturized, battery-powered packages are being developed in our laboratories and permanently implanted in laboratory animals. The modulation of the radio-frequency carrier with biological information permits short-distance propagation of selected physiological activities, with the possibility also of providing remote control of selected stimuli (*1*). Continuous measurement of physical conditions within the environmental chambers—ambient temperature, humidity, air ionization, barometric pressure, air velocity, light intensity, chemical composition of the air within the chambers, and such other physical parameters as may be shown to be significant—may be recorded along with the physiological activity specific to the animals. The behavior of the animals may be observed by a remote visual system. Classical conditioning experiments with animals may be conducted over periods of weeks and months, with observation periods before, during, and after experimental manipulation. We feel this innovation, growing out of the technique of telemetering, to be important and an improvement over techniques more familiar to those engaged in classical conditioning investigation.

Figure 1 (top) shows a signal output of respiration from a laboratory rat, obtained by means of the accelerometer principle incorporated into a small capsule (Fig. 1, bottom left) very much like that reported by Mackay (*2*). A brass pellet mounted on a rubber diaphragm near the oscillator coil modulates the radio-frequency carrier. We have found that we can obtain a radio-frequency signal of 6.8 Mcy/sec and of about 250 μv at the antenna terminals of the receiver, with the circuit shown in Fig. 1 and battery current of 200 μa. This by no means represents a lower limit to power requirements, but rather an arbitrary stopping point for the moment. The characteristics of the transistor are such that an increase or decrease in power is effected by changing the collector voltage and adjusting the emitter bias

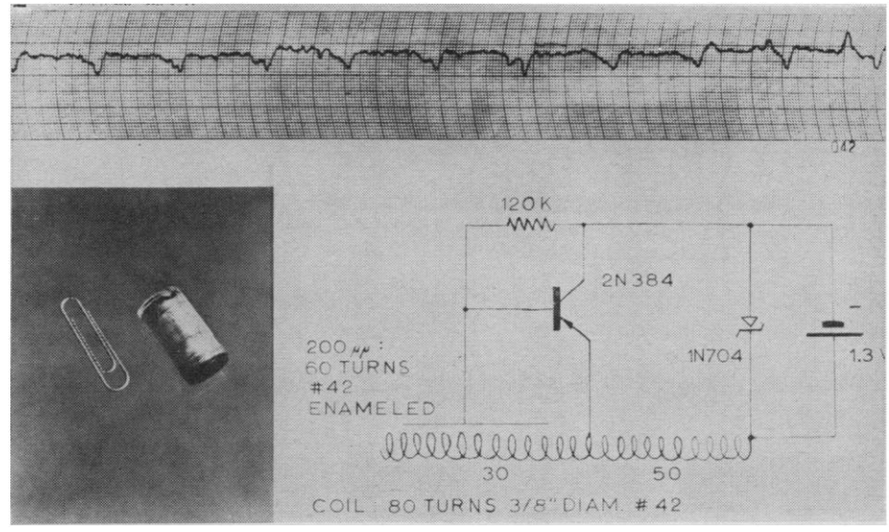

Fig. 1. (Top) Pen recording showing respiration and heartbeat on a base line of body temperature. (Bottom, left) Photograph of the active telemetering capsule. (Bottom, (right) circuit diagram of the transistor transmitter.

to increase or decrease the collector current. There is no reason that the current cannot be of the order of 50 μa, if this is permitted by the radio-frequency noise level within the environmental chamber. A transistorized, miniature, radio-frequency amplifier can be constructed within the antenna probe and supplied with low-voltage d-c power through the coaxial cable. We have found that, by exciting the capsule from an external source of radio-frequency power of about 3.9 Mcy/sec from a 100-watt exciter, about 2 ma of reverse current can be realized in the battery circuit within the capsule, in which we have included the Zener diode rectifier shown in the circuit diagram (Fig. 1). A rechargeable dry cell is being tested for the planned indefinite implantation of the capsule.

After the transmitter has been assembled and dipped in toughened paraffin, it is inserted by surgical procedures into the abdominal cavity of the rat, where ballistic movements are sensed by the accelerometer. The signal is picked up by a "ferri-loop-stick" antenna mounted within the environmental chamber and conducted through a coaxial cable to a communications receiver. The incoming frequency-modulated signal is mixed with a beat-frequency oscillator within the receiver, or with another radio-frequency signal from a frequency meter. The audio output of the receiving system is recorded on magnetic tape for subsequent playback and data analysis.

While the base line of the trace (Fig. 1, top) is an accurate (0.2° per 1000 cy/sec of audio output) and reproducible (±0.5 percent) measure of the core temperature of the animal, a transistor alone will not detect rapid changes of temperature. The response time constant of the radiosonde used at this writing is of the order of 100 seconds. It is therefore necessary to introduce a thermistor transducer into the circuit to effect this measurement.

The improvement in techniques inherent in microminiaturization and telemetry permit the coupling of classical conditioning experiments into an on-line digital computer to form a closed-loop systems approach to experimentation. This, in conjunction with automatic data processing and reduction, would seem to lead to qualitatively different testing of old and new hypotheses with multiple independent and dependent variables, under conditions of experimental control previously impossible.

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