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FOREWORD

This report was prepared by the Psychophysiological Stress Section, Biophysics Branch, Biomedical Laboratory, 6570th Aerospace Medical Research Laboratories, under Project No. 7222, "Biophysics of Flight," Task No. 722201, "Psychophysiology of Flight." This survey was conducted from June 1962 to September 1962.

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ABSTRACT

Within the last 5 years endoradiosondes or "radio pills," have been developed employing tiny transducers and transmitters which can be swallowed or implanted in man and animals. The present state of the art of these instruments, including design, construction, uses, advantages, and limitations, is reviewed. The literature in this area to date consists largely of suggestions for design principles and considerations of circuitry. There is only the barest amount of useful data on equipment performance, reliability, response linearity, frequency response characteristics, and correlation with proven systems. The endoradiosonde promises to be a useful technique in physiological instrumentation, but much basic development remains to be done before this tool can be useful to any but the bioelectronic specialist.

PUBLICATION REVIEW

This technical documentary report has been reviewed and is approved.

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ENDORADIOSONDES: A STATE OF THE ART SURVEY

INTRODUCTION

Within the last 5 years, instrumentation techniques have been developed employing tiny transducers and transmitters which can be swallowed or implanted in man and animals. Such telemetry units have been termed endoradiosondes or radio pills (ref. 20). They are an important advance as they leave the subject in a relatively normal physiological state, unaltered by bulky or painful transducers and free to move unrestrained and to transmit data from inaccessible environments. The development of radio-telemetering capsules has been independently pioneered by at least four groups in Europe and the United States (refs. 2, 13, 20, 25). They were originally designed to record pressure fluctuations within the gastrointestinal tract.

In this paper we present a brief review of the present state of the art of these tools including design, construction, uses, advantages, and limitations. The approach will be, in general, descriptive. No attempt will be made at bibliographic completeness. The detailed mechanics and electronics of the pills will not be elaborated as the available literature covers these areas in detail.

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TYPES OF TRANSMITTERS AND TRANSDUCERS

Types of Transmitters

In the transmission of internal data there are essentially four possibilities: an active transmitter or a passive transmitter using a magnetic dipole or an electric dipole (in the latter using the conductivity of the body to carry out the signal). All except the passive electric dipole have been demonstrated. The optimum carrier frequency will vary with the method used. In general, these transmitters have been made to work in the frequency range of 1/2 to 10 megacycles. Physiological variables which can cause changes in the reactance of a transducer lend themselves to passive as well as active transmission. Almost any system of modulation other than amplitude modulation is suitable in any of these methods.

Passive Transmission

This was probably the first (reported) method used (ref. 20) and still seems the most useful for extended periods. In passive transmitters the capsule carries no power source but only a resonant circuit whose characteristic frequency is sensed from the outside. This frequency is altered by some reactance whose magnitude changes in response to changes in pressure, temperature, voltage, pH, etc. This can be done by frequency-sensitive absorption or by reemission. An example of the former used by MacKay and Jacobson (ref. 20) is a sweeping grid-dip meter to sense the resonant frequency of an ingested tuned circuit.

In the emission method, a ringing frequency of the ingested tuned circuit is produced by application of a short pulse from the outside. Some gastrointestinal pressure observations with the emission method have been reported (ref. 11). This capsule is smaller (2.5 cm in length and 0.7 cm in diameter), less dense, and simpler than a battery-powered capsule, and has a relatively unlimited life.

Active Transmission

The perfection of transistors and miniature batteries permitted the construction of small active radio transmitters and several groups throughout the world independently designed such units at about the same time (refs. 2, 13, 20, 25). The electronic theory, circuitry, and construction of these radio pills are described in detail in most of the early papers and will not be reviewed (refs. 2, 11, 13, 14, 16, 19, 20, 25, 29, 31).

An active endoradiosonde must contain a transducer, a modulator, a transmitter, and a power supply. The radio pills are actually quite simple and easy to construct (if not to operate). A typical, pressure-sensitive radio pill consists of a coil, a disc of ferrite as the core (which, moved by changes in pressure on a rubber or plastic diaphragm, is the transducer), a transistor, condensors, a battery, a diaphragm, and a case (refs. 14, 29, 31). The signal is picked up on a suitable receiver with an antenna held close to the body. The output may be displayed on a cathode-ray tube or used to operate a pen-type recorder. The size of the plastic capsule decreases as new and smaller components become available. The unit originally described by MacKay and Jacobson (ref. 20) was 2.8 cm in length and 0.9 cm in diameter. It was capable of transmitting pressure and temperature signals simultaneously for about 2 weeks. The useful life of an active transmitter varies with the battery and the resistance involved and may be from 8 hours to 3 weeks. Mallory mercury cells have been the most useful batteries. A small nickel-cadmium cell has been used that could be recharged within the body by an external oscillator (refs. 10, 17). A gastric juice battery has been considered but seems unlikely (ref. 20). The pressure-sensitive radio pill designed by Dr. V.K. Zworykin and developed by Radio Corporation of America* engineers is essentially identical to the one described (refs. 13, 14).

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The radio pill is calibrated before the experiment by applying known pressures and observing the resulting signals as with any other transducer. Sensitivity can be checked during an experiment while the pill is within the body by varying the atmospheric pressure on the subject (refs. 20, 21), but this is usually unnecessary.

OTHER VARIABLES

Physiological variables other than pressure that have been transmitted with endoradiosondes are temperature, pH, oxygen tension, radiation intensity, chloride ion concentration, and pulse and respiratory rates.

Pressure

The greatest interest to date has centered on pressure transmission from the gastrointestinal tract (refs. 5, 12). However, gastrointestinal motility or the progression-producing activity of the intestines is not identical with pressure variation. There can be considerable muscular activity and rapid transport of intestinal contents with pressure variations of 1 to 2 cm of water, while large amplitude pressure waves may be recorded without any forward movement of contents. Simple methods are still needed to measure the tension of the muscular wall, the rate of flow of contents, and the electrical activity of the intestines. The simultaneous use of multiple endoradiosondes, cineradiography, and radio-tracking devices to plot the two-dimensional component of the motion of the capsule during its passage have been described (refs. 17, 18). The pressure-transmitting endoradiosonde has been used to transmit urinary bladder pressure (refs. 17, 19), steadiness in standing, teeth clenching (refs. 17, 19), uterine contractions, and fetal heart sounds (ref. 32).

Temperature

A change in temperature will change the output frequency of the transmitter as described by MacKay (refs. 18, 20). In human studies, this can be convenient because a change in frequency immediately after the subject has taken a sip of cold water indicates that the sonde is still in the stomach and has not progressed into the intestine. Inclusion of a temperature sensitive-reactance can maximize the temperature sensitivity (ref. 18). Small amounts of data regarding gastrointestinal temperature and temperature variation are available (ref. 24). However, no thorough or controlled studies of this subject are available. A passive transmitter consisting of a coil and a temperature-sensitive capacitor (ref. 19) has been implanted in laboratory animals as a permanent monitor of ovarian function (ref. 6), and used in the study of the incubation of penguin eggs in the Antarctic (ref. 7).

Hydrogen Ion Concentration

The transmission of information about hydrogen ion concentration is of interest to all physiologists as well as the gastroenterologist. The original pH endoradiosonde used a mechanochemical transducer of a copolymer of polyacrylic acid and polyvinyl alcohol that gave a reversible change of dimensions of 60 percent for a shift of pH from 3 to 8 (ref. 16). This system and others using antimony electrodes (refs. 1, 17) are unfortunately sensitive to ions other than hydrogen. Glass electrodes necessary for good pH measurement have a high impedance making them relatively incompatible with transistors. However, a pH-endoradiosonde circuit using glass electrodes has recently been reported (ref. 31). Circuitry problems entailed by the glass electrodes are discussed by MacKay (refs. 17-19). Clinical records of gastrointestinal pH in normal and disease states are described briefly by Nöller (ref. 24). If the transducer is in contact with stomach mucosa, large, rapid pH changes may be recorded and, if the sonde is surrounded by food, low, slow changes may be recorded.

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Oxygen Tension

Oxygen tension can be measured by the reversible mechanical expansion and contraction of certain chelates (ref. 22) against a pressure-sensing unit (ref. 20). The endoradiosonde applications of such materials have been discussed (refs. 17, 18), but data collected with such a radio pill has not been reported. Nöller has reported a polarimetric sonde for the study of oxygen tension (ref. 27). Such instruments might be used to identify and locate bleeding in the gastrointestinal tract (ref. 18).

Radiation

Although the present endoradiosondes are relatively insensitive to radiation, an existing endoradiosonde could be modified into a low-voltage radiation detector (ref. 19), as has been suggested from the known batterylike action of a semiconductor junction exposed to radiation (ref. 34). Endless uses suggest themselves for a miniature, transmitting radiation counter, but such a device has not yet been constructed.

Chloride Ion Concentration

Using techniques similar to the pH-sensitive sonde, Nöller has been able to measure the chloride ion concentration of gastrointestinal fluids (refs. 24, 26).

Pulse and Respiratory Rate

Heart rate and respiratory rate can obviously be recorded by an appropriately placed pressure transducer. England and Pasamanick implanted a MacKay-type, pressure-sensitive endoradiosonde in the abdominal cavity of laboratory rats and recorded the heart beat and respiratory rate on a baseline of body temperature (ref. 9). Arterial pulse waves could easily be obtained by similar methods. Larger multiple-component telemetry systems have been implanted in monkeys to transmit respiration, ECG, and the phonocardiogram, but such systems are not radio pills in a strict sense (ref. 10).

ADVANTAGES OF ENDORADIOSONDES

Obvious Advantages

Endoradiosondes can be used to transmit data from inaccessible body cavities and from subjects or machines in inaccessible areas. The obvious advantage of the method is that no tubes or wires are needed between the signal transducer which may be inside the body and the recording equipment. In gastrointestinal physiology, for example, using traditional equipment with tubes and balloons, the distal small intestine and proximal colon are relatively inaccessible. In many fields, the parameters being observed are often reflexly altered by the instrumentation or the patient's discomfort. The limitations imposed by restraint and anesthesia in laboratory animal studies are a continuing problem to physiologists. The use of chronic, surgically implanted transducers permits the study of the intact nonanesthetized animals. The perfection of these techniques by workers such as Rushmer is perhaps the most significant advance in cardiovascular physiology of recent times. Implanted transducers have been discussed in recent reviews by Rushmer (refs. 3, 30).

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Closed Loop System Experiments

England and Pasamanick have suggested that the microminiaturization and telemetry techniques inherent in the radiosonde will permit coupling of classic conditioning experiments with an on-the-line digital computer to form a closed loop system approach to experimentation (ref. 9). This, in conjunction with automatic data processing and reduction, will lead to multivariant testing of old and new hypotheses under conditions of experimental control previously impossible.

Correlation with Classical Methods

Connell and Rowlands have made simultaneous gastrointestinal pressure recordings using a radio pill tied to the end of an open-end pressure tube inserted through the anus and ileostomy and colostomy openings of 13 patients (ref. 4). Of 100 pairs of waves selected at random, the amplitude of only 19 differed by more than 33 percent. There is no available data on the stability, linearity, or frequency-response characteristics of any endoradiosonde.

Use in Alien Environments

In the exploration of alien environments, particularly space, there is a real need for studies employing adequately instrumented, unrestrained animals (ref. 10). The endoradiosonde technique would seem to offer real advantages in this area. A serious disadvantage of existing endoradiosondes for space physiology is their rather marked G-sensitivity. Implanting sensors and transmitters in man is limited by psychological and philosophical objections, but the physiology of health and disease in normally active unrestrained humans in any environment is of intense interest to present-day researchers and clinicians.

PROBLEMS WITH THE ENDORADIOSONDE

Indications for Their Use

Endoradiosonde techniques should not be used when simpler and more reliable methods can be employed. When it is possible to connect a wire or a tube to the object under study without disadvantage, the endoradiosonde is inappropriate. The method occasionally used of keeping the sonde in a desired position in the alimentary tract by securing it with a silk thread to a tooth is often unwarranted. The errors and difficulties of endoradiosonde technique will be discussed.

Batteries

Frequency modulation is the most suitable principle for endoradiosonde transmission, and a common problem is unwanted modulation of the carrier. Good electrostatic shielding is necessary. The carrier frequency changes with the battery voltage, and carrier stability over the lifetime of the battery cannot be assured. The smallest available mercury battery (Mallory type RM 312) has a lifetime of 3 weeks in most pressure-sensitive sondes. The sondes should not be used the first day after a battery change when the initial voltage drop occurs.

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Drift

Another common error is drift with temperature. Transistors must be carefully selected to minimize this artifact if it is unwanted. Recordings of absolute pressures for long periods are extremely difficult to make with endoradiosondes because of drift. In the pressure-sensitive sonde drift may be due to leakage of air through the diaphragm membrane or changes in the membrane elasticity. The leakage may be prevented by using silicone jelly on the diaphragm (ref. 31). Such drift, however, does not interfere with the study of relative pressure events such as peristaltic pressure waves. Frequent calibrations may be needed while the sonde is in the subject and, if necessary, allowance must be made for atmospheric pressure changes.

Antennae

The original endoradiosondes used standard FM receivers and directional loop antennae (refs. 2, 13, 20, 25). The strength of the signal induced in a receiving loop antenna changes with the orientation of the pill. Connell and Rowlands observed radio pills in the gastrointestinal tract fluoroscopically during periods when radio contact was repeatedly lost and noted that this loss correlated with motion of the radio pill particularly spinning on its long axis (ref. 4). All workers in the field have admitted that the antenna problem or reception is the largest single impediment to the routine and standardized use of the technique. At the present time it is safe to say that a full-time operator well versed in radio-receiving equipment is needed to keep a sonde maximally tuned. Several special endoradiosonde receiver systems with multiple and omnidirectional antenna configurations have been presented (refs. 15, 18, 23).

Signal Strength

The signal strength must also vary with the strength of the battery and the distance of the subject from the receiver. In all reported endoradiosonde systems the receiver (antenna) is closely applied to the subject. If the signal is to be transmitted some distance, a larger power source can be used with a necessary increase in size of the pill. Or the signal can be retransmitted with a booster transmitter carried externally to the subject. Retransmission systems are not available. Using large batteries rumen pressures have been transmitted from cattle grazing freely in a 150-square-yard pen (ref. 28). The pill was 2.5 cm in diameter and 15 cm in length. Due to marked signal attenuation by water, it seems unlikely that signals could be transmitted from immersed subjects such as skin divers without major modifications of existing systems.

Gastrointestinal Transit Time

Whether radio pills will give any useful information about the normal gastrointestinal transit time is doubtful because the pills are fixed in mass and shape. Although the pills have been described as "more physiologic" than balloons and tubes, this is obviously only a relative matter. The statement that the endoradiosonde "does not alter normal physiological processes" of the gastrointestinal tract has not been verified (ref. 13).

Localization of the Pill in the Gastrointestinal Tract

For accurate use it is necessary to know the precise position of the radio pill in the gastrointestinal tract. Suspending the pill on a thread of known length is obviously accurate, but indirect methods such as using fluoroscopy and omnidirectional receiving antenna only give relative position and cannot always distinguish between the large and small bowels. Characteristic pressure patterns at different levels in the gastrointestinal tract also aid in localization.

Expense and Recovery of Radio Pills

The expense of the individual radio pill and the necessity of recovering it from the subject's feces have been mentioned as disadvantages to the technique. Such considerations do not seem to be real obstacles to using endoradiosondes where they are needed.

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RELATED TECHNIQUES

The Magnetometer

The magnetometric technique for recording gastric motility was first introduced by Wenger et al. (ref. 35). The subject swallows a permanent magnet about the size of a vitamin pill and a magnetometer senses the field variations produced by motion of the magnet. The device must be calibrated with consideration to the ambient magnetic field. The field variations are obviously a function of change in the orientation of the magnet with regard to the detector as well as the amplitude of magnet motion. Such a device is limited in that it can sense only motion and perhaps acceleration but not pressure or chemical change. Engel and McFall (ref. 8) and Sternbach (ref. 33) have chronically implanted magnets in the stomach walls of laboratory animals and obtained records of gastric motility. Simultaneous records show excellent correlation between this and classical balloon records (ref. 33). The magnet is cheaper, more easily implanted, and has a nearly unlimited lifetime. However, the sensing device must be closely applied to the subject, restraining activity.

CONCLUSIONS

The endoradiosonde promises to be a valuable technique in physiological instrumentation. However, it should be used only when more conventional methods will not suffice. The literature in this area to date is, in large part, a collection of suggestions for design principles and considerations of circuitry. There is only the barest amount of useful data on equipment performance, reliability, response linearity, frequency response characteristics, and correlation with proven systems. Endoradiosondes are in their infancy and much thorough basic work remains to be done before this tool can be useful to any but the bioelectronic specialist.

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