Through motion M_1 of the assembly consisting of the illuminator and pinholes it was possible to adjust the N.A. of the telescope, and hence the separation of the pinholes, in a continuous manner to the desired value (in Airy units). Pinhole P_3 was included as a control and was located many Airy units from the tightly separated pinholes P_1 and P_2. The image of pinhole P_3 served, for example, to indicate whether or not $|\psi|$ equaled 2π, since the center of the diffraction image of an unresolvably small self-luminous particle becomes dark in the out-of-focus plane associated with $|\psi| = 2\pi$.

Qualitatively, the parfocal images of the double pinholes resembled the parfocal images of the zirconium arc in the microscope experiment. In one quantitative experiment, the separation of particles P_1 and P_2 was adjusted to 0.58 Airy unit, and resolved readily. In this experiment, the two pinholes had a diameter of 0.142 millimeter and a separation, from center to center, of 0.606 millimeter. Distance d_1 (Fig. 5) was 6032 millimeters, and the diameter of aperture A was 3.84 millimeters. Determined attempts to learn how nearly one can approach the limit 0.53 Airy unit of Fig. 3 were not made, since it was felt that a significant determination of an actual limit would require great care.

In an interesting set of preliminary experiments with the microscope arrangement, a marked amount of spherical aberration was added artificially to the 5× objective. It was found that this addition further increased the lateral resolving power, provided that the defocusing was performed on the "cooperative" side of focus.

When pinholes P_1 and P_2 of Fig. 5 were replaced by narrow slits, separations down to 0.73 Airy unit were resolved in the plane of sharpest focus. Defocusing improved lateral resolution of the two slits only slightly. The resolvable separation was decreased only from 0.73 to 0.71 Airy unit. It is noteworthy that the observed in-focus limit of 0.73 Airy unit practically coincides with the physical limit of resolution given by Osterberg (*2*) for two like slits in an opaque background for the case in which the numerical aperture of the substage condenser of a microscope is set equal to the numerical aperture of the objective.

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INSTRUMENTS AND TECHNIQUES

Radio Telemetering from within the Body

Inside information is revealed by tiny transmitters that can be swallowed or implanted in man or animal.

R. Stuart Mackay

It is rather inconvenient to swallow a physician. However, it is quite possible to swallow, or otherwise implant in various body cavities, measuring devices and miniature radio telemetering transmitters which will perform certain of his observation functions. This article attempts to summarize some of these developments and uses as examples some of the methods employed in one laboratory. In the first few sections, some of the physical aspects of these devices are mentioned, and in the last, some examples of application are given for such units. These units have been called endoradiosondes and are so termed here. They are important in studies of human beings because they leave the subject in a relatively normal physiological state, and they are at least as important in animal studies, where discussion and cooperation are lacking.

In the transmission of internal data there are essentially four possibilities: one can build a passive transmitter or an active transmitter, and one can employ 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. There seems no adequate reason to expect the optimum carrier frequency to be the same in any two of the methods. Skin depth gives a rough hint of frequency but can be misleading; more tests are needed if minimum energy units are desired. In general, these transmitters have been made to work in the frequency range of ½ to 10 megacycles. As in nuclear resonance experiments, passive magnetic transmitters (in which a resonant circuit alone is swallowed) can work either by absorption or by emission, and the best frequency is probably the same in either case. Physiological variables which can cause a change in reactance of a transducer lend themselves to passive as well as active transmission. Almost any system of modulation other than simple amplitude modulation is suitable in any of the methods. Transmitters whose power is induced in the capsule at one frequency or time and reradiated by an active transmitter at another do not involve any different concepts. Nonradio transmission methods, such as monitoring pressure by observing the size of an ingested balloon with ultrasound or x-rays, are not considered here.

Passive Transmission

In passive transmitters the capsule carries no power source but only a resonant circuit whose characteristic frequency is sensed from outside. This frequency is altered by some reactance whose magnitude changes in response to changes in pressure, temperature,

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voltage, and so on. This was probably the first method tried (*1*), and it still seems the most useful for extended experiments. For brief experiments, it is not certain that passive techniques are best, especially in view of the availability of small, low-power systems involving tunnel diodes or transistors, and of noise-reducing techniques for receivers.

These procedures can be implemented either by frequency-sensitive absorption or by re-emission. An example of the former is the use of a sweeping grid-dip meter to sense the resonant frequency of an ingested tuned circuit (*1*). Increased sensitivity seems to result if the functions of transmission and reception are, instead, separated by feeding a coil on one side of the subject with a cyclically varying frequency in the right range and displaying the output as a function of frequency on an oscillograph fed by a coil on the other side of the subject. Bridge techniques can be used to eliminate much of the steady signal arriving at the second coil.

In the emission method, one observes the ringing frequency of the ingested tuned circuit following application of a short pulse from outside. This input pulse must be a small radio-frequency pulse, so the tuned circuit will show a reasonable scattering cross section; that is, there is no value in having the energy spectrum extend to zero frequency, as it does with either a steady pulse or delta function. As in certain nuclear resonance experiments, in principle it is possible to orient the transmitter and receiver coils perpendicularly so that there is no direct coupling between them except by way of the tuned circuit. Some pressure observations with the emission method have been reported (*2*). It has been suggested that the activity of gastric juices might be studied through the closing of a contact by the digestion of a piece of meat and transmission of this two-valued variable by ringing or nonringing in a paralleled quartz crystal (*3*).

A small coil outside the body gives a rather weak signal because the signal can decay with the sixth power of the distance. If larger coils are placed around the subject, generalization is more difficult and results are best predicted on the basis of transformer theory. If the tuned circuit is not fairly large and aligned for maximum coupling, then the signal can rapidly become unreliable. Brief attempts were made to cycle between several external antenna coils by using mercury contact relays, but the perfection of transistors made the investigation of active transmitters seem attractive (*1*). Several workers throughout the world independently began such investigations at approximately the same time (*1, 4, 5*).

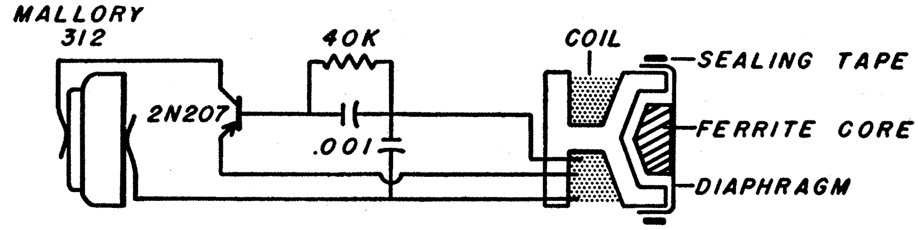

Fig. 1. Frequency-modulated radio telemetering transmitter which can be swallowed or otherwise inserted into body cavities to transmit pressure indications.

An Active Transmitter

The variable which has thus far been of most interest is the pressure whose fluctuations accompany peristaltic activity in the gastrointestinal tract. In our laboratory the unit shown in Fig. 1 is often used for its transmission. A 250-turn center-tapped coil is used in a Hartley circuit, the capacitors having a common point so that small three-wire double ceramic units can be used. A Burgess or Mallory mercury cell (*6*) will power the unit for about 3 days with a resistor of the size shown, placed as shown. With a similar circuit, a small nickel-cadmium cell has been recharged within the body by an external oscillator (*6*). A gastric-juice battery is a possibility, but it seems unreliable (*1*). With typical components, the pill is 9 millimeters in diameter and 25 millimeters long after it is enclosed in a disposable rubber finger cot. A smaller diameter was desired for endoradiosondes which were inserted into the human bladder for studying pressure changes during micturition, and handmade zinc-platinum cells of less stable voltage were employed (*6, 7*). The pills have either been mounted in

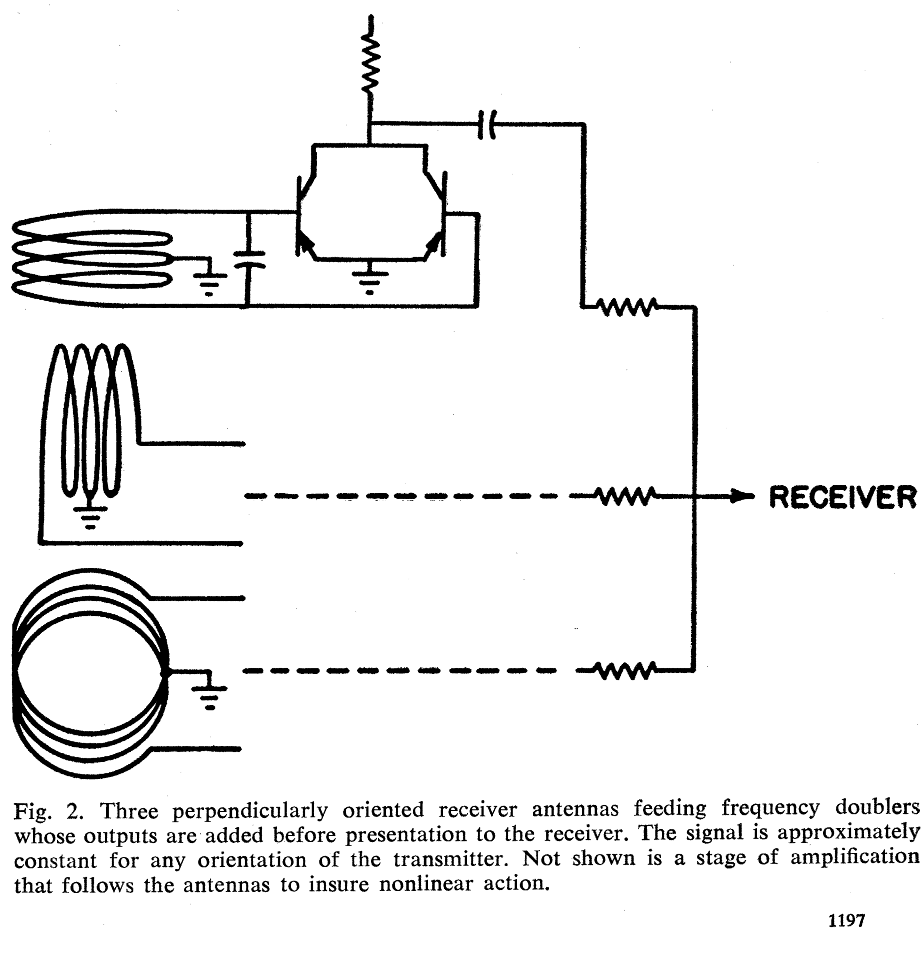

Fig. 2. Three perpendicularly oriented receiver antennas feeding frequency doublers whose outputs are added before presentation to the receiver. The signal is approximately constant for any orientation of the transmitter. Not shown is a stage of amplification that follows the antennas to insure nonlinear action.

a Lucite body or potted in silicone rubber.

The ferrite core (*7*) is glued to the thin rubber diaphragm; air leakage from behind the diaphragm is carefully avoided because this air cushion determines the restoring force. Frequency modulation is produced by motion of the core. Because the diaphragm supplies little of the restoring force, its changes with age and with passage through various body fluids do not cause major drift. There is still some residual drift, possibly due to gas diffusion, that interferes with long-term absolute measurements, but this does not interfere with the observation of peristaltic patterns. Sensitivity can be checked while the unit is within the body by varying the "atmospheric" pressure on the subject (*1, 8*), but this is usually unnecessary. Orientation sensitivity is minimized by the use of a light core, and barometric effects seldom occur rapidly enough to cause difficulty. A conducting rather than a magnetic core (*7*) is convenient in experiments in which one is attempting to restrain the pill or to introduce mechanical motions by external magnets. The pills that were inserted into the bladder were enclosed in a slightly inflated condom, so that pressure changes throughout a volume could be recorded, rather than forces applied at one end (*6*). This also reduces diaphragm leakage. Metallic and plastic diaphragms can also be used.

A change in temperature can shift the output frequency of the transmitter. In studies of human beings this can be convenient because a change in frequency after the subject has taken a sip of cold water is a clear signal that the endoradiosonde is still in the stomach and has not yet advanced into the intestine. Temperature sensitivity can be either enhanced or minimized. An increase in temperature affects the transistor in such a way as to drop the frequency; this effect is opposed by the effect on the gas pocket, on the tuning condenser (if it has a negative temperature coefficient), and on the ferrite core (*6*).

Various modifications (*8*), including use of a different turn ratio to prevent blocking, instead of a base resistor, and a split shield that simplifies calibration, have been demonstrated. A Clapp circuit minimizes the effect of the transistor (and thus the voltage) on frequency (*9, 10*). Capacitive as well as inductive transducers have been tested, and resistive ones consisting of conducting epoxy resin or of a liquid containing a hollow plastic sphere between electrodes gave fair performance. A small booster transmitter, with a frequency shift between input and output to prevent oscillation, can be used to relay the signal and give the subject freedom of movement (*6*).

Antenna Systems

Antenna coils are used in magnetic systems and body electrodes in the other systems. The active transmitter discussed above is often used in connection with a receiving loop, of 6-centimeter diameter, tuned to the operating frequency range of a few hundred kilocycles per second. Directional effects can be eliminated by using three orthogonal (or otherwise oriented) coils and switching between them, or by adding their outputs after frequency doubling and noting the variations in this doubled frequency at the receiver (*6*) (Fig. 2). Another way to achieve this result and yet avoid having rotating coils in the probe is to use a transformer-coupled radiogoniometer.

Omnidirectional schemes for passive transmitters are generally somewhat more complicated (*11*). For either absorption or emission, the most convenient method seems to be to use commutation and slip rings, or switching transistors, to switch between antennas, in each of which a complete analyzing function can take place. Recording is from the one, or ones, with the largest signal.

Because the wavelength is long as compared with the size and separation of the antennas, these experiments are carried out in the induction or near field. The coils can be considered as dipoles for many purposes. It seems possible, in principle, to have coupling for all orientations with only two perpendicular external coils, if the axis of one does not pass through the center of the other.

There are several receiving systems which can be used to determine these variations in frequency. In general, frequency-measurement systems can be divided into scanning systems and cycle-counter systems. Amusing arguments on the reality of side-band frequencies in modulated waves have arisen, since the former systems show them and the latter do not. Here, a parallel bank of simultaneously acting tuned filters is considered as a scanning system; its output can be scanned rapidly. Various forms of both systems are applicable to the present problem.

It is characteristic of digital systems that they are able to record a high fre-

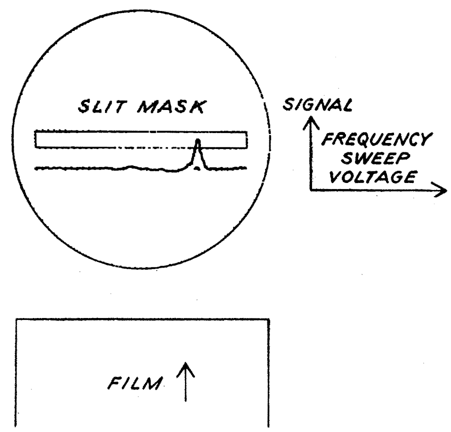

Fig. 4. Simplified arrangement for producing a time graph from a cyclically scanned narrow-band detector output.

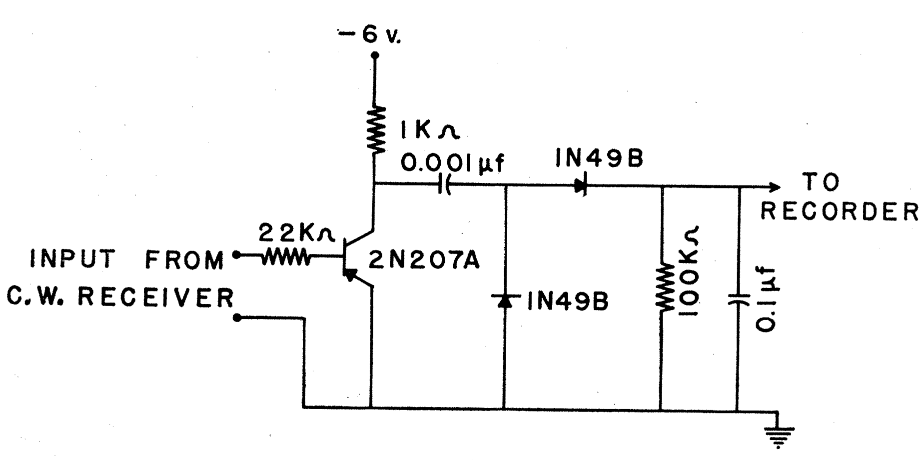

Fig. 3. Frequency-meter circuit which, when fed from the loud-speaker connection of a suitable receiver, will deliver a direct voltage proportional to frequency but relatively independent of amplitude.

quency and a large range of frequencies with an excellent degree of discrimination. Standard counting circuits can work at these frequencies, and crystal-gated ones have been used in such applications. In an alternative approach, use is made of a standard continuous-wave receiver in which the incoming frequency beats with a local frequency to give a lower frequency which varies rapidly with small percentage changes in the incoming radio-frequency signal. The normal loud speaker output cán then activate a resonant or gated-charge frequency sensor (*7*). In our laboratories it is customary to use this simple system with a well-stabilized local oscillator, and to feed the beat signal into a clipper circuit and "diode-pump" frequency meter and chart recorder, as shown in Fig. 3. This beat-frequency signal can be recorded directly on a magnetic tape for possible automatic analysis, and later it can be played into the demodulation circuit, if desired.

The permissible radio-frequency deviation is limited to the bandwidth of the receiver if loss of signal is never to

The permissible radio-frequency deviation signals by tracking them with a standard automatic frequency-control circuit, the frequency-discriminator signal then being the useful output (*8*). This is equivalent to continuously retuning the receiver with a servomotor or speaker-driven capacitor.

Another method is to scan a narrow-band filter cyclically through the possible range of frequencies until a response is found (*8*). This is usually done by sweeping the oscillator in a heterodyne system. The method is illustrated in extremely simple form in Fig. 4, which shows the arrangement actually tested in the early transmitters that employed passive transmission and a sweeping grid-dip meter circuit. At the frequency where there is a response, the oscilloscope trace becomes visible as a spot above the mask. This horizontally moving spot is recorded on the steadily moving film as a wavy line which is a graph of pressure as a function of time. Similarly, circuits can indicate where in the sweeping cycle the response occurs and generate a signal proportional to the time after the start of sweeping (*12*). This procedure overcomes noise in a predictable fashion at the expense of response time by processing the signal over successive small intervals (*11*).

Several variables, besides pressure, have simultaneously been transmitted from a single oscillator through multiplexing by blocking. The original circuit (*1*) was essentially the circuit of Fig. 1 without the resistor. It periodically turned its pressure-transmitting oscillations on and off at a rate dependent on temperature. A few cycles of oscillation bias off the transistor; after this there are a few cycles of ringing. Oscillations in successive bursts are not generally phase-coherent if there is no master oscillator, and the phase shifts introduce extraneous side bands. In the simplest method of analysis, tuned circuits are dispensed with and the signal passes through a wide-band amplifier into an oscilloscope for direct observation; the latter can be replaced by broad-band analyzing circuits. If both slow and

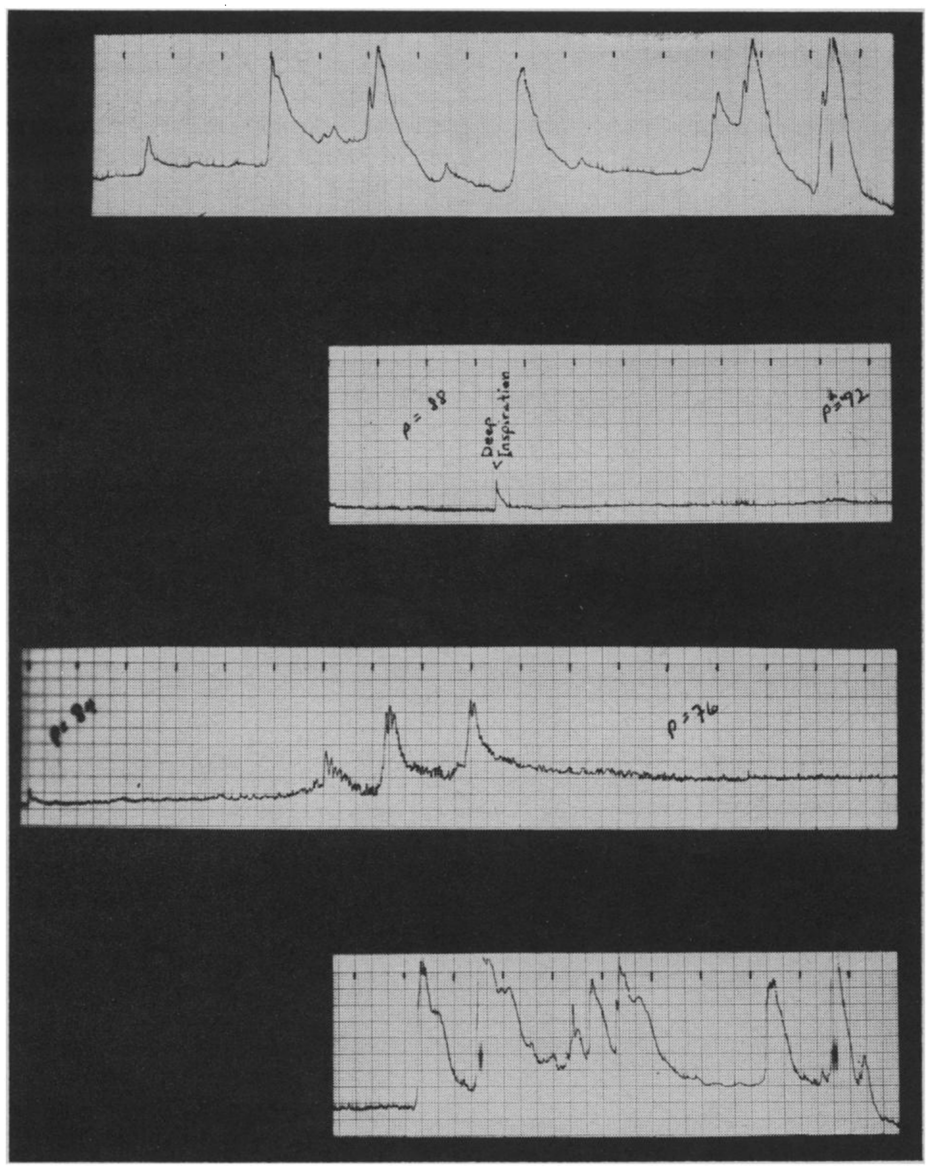

Fig. 5. Recordings from the sigmoid of a normal male. (Top) Seventy minutes of normal peristalsis was observed prior to administration of atropine sulfate. The contractions, of 3 to 7 minutes' duration (pressure increase, 110 to 190 mm-Hg), were interrupted by relaxation periods of 1½ to 4 minutes. (Second from top) Intravenous administration of atropine sulfate (0.4 mg) (pulse rate, 80) was followed by a 9-minute period of muscle relaxation (no change in pulse), then by three contractions of the type described. The subject fell asleep and slept for 22 minutes, during which time there was no recorded bowel activity. When he awoke, the original pattern reoccurred. Administration of a second dose of atropine sulfate (0.6 mg), 80 minutes after the first dose, was followed by 24 minutes of muscle relaxation (pulse, before injection, 80; 16 minutes after injection, 92). (Second from bottom) After the muscle relaxation there occurred a period of contraction of about 4 minutes' duration (increase in pressure, 90 mm-Hg), followed by 15 minutes of bowel relaxation (pulse, 76). (Bottom) A second period of contraction, recorded 42 minutes after the 0.6-mg dose of atropine sulfate, lasted 7 minutes, but pressure increased by only 26 mm-Hg. After a 20-minute period of inactivity, contraction frequency and intensity were as originally noted.

periodic rapid variables are of interest, then three simultaneous signals can similarly be sent and received from one oscillator by varying the average frequency (base line), the deviation frequency, and the frequency of an amplitude modulation.

Other Variables

Some variables other than pressure that have been transmitted by various workers are temperature, oxygen tension, acidity, and radiation intensity. In principle, any of these can be transmitted by either a passive or an active system in conjunction with a suitable transducer. Gastrointestinal motility (essentially the progression-producing activity of the gut) is of interest to clinicians and is not identical to pressure variation. More can be told of this by the simultaneous use of a number of transmitters (*6*), by x-ray movies accompanying the endoradiosonde observation, or by the use of a radio tracking device that plots out the two-dimensional component of the motion of the capsule during its passage (*13*).

A transmitter of the type used to transmit pressure in the gastrointestinal tract has also been used to transmit bladder pressure and steadiness in standing (*6*), uterine contractions and fetal heart sounds (*14*), and teeth clenching. When the transmitter is used in variable-acceleration situations, a projecting ring prevents direct pressure by the body on the diaphragm. A piezoelectric sensor is of no advantage here but, if vibrating, can measure viscosity by variable damping.

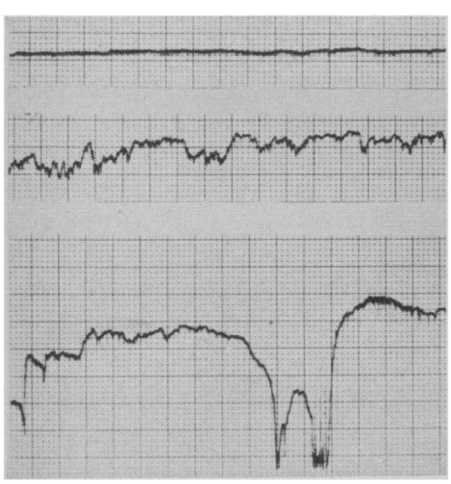

Fig. 6. Spontaneous restoration of peristalsis in the large intestine (cecum) after cessation following the trauma of gallbladder removal. The small regular fluctuations are pressure changes due to breathing. Major time divisions are 20-second intervals. (Top) No activity after 1 hour. (Middle) Ten minutes later, activity starts. (Bottom) Three hours after the previous record. In the top and middle records the deflection times 1.6 gives the pressure in millimeters of mercury; in the bottom record the factor is 3.2.

The sensitivity of the capsule to temperature has been mentioned. Inclusion of a temperature-sensitive reactance can maximize this. A passive transmitter consisting of a coil and temperature-sensitive capacitor (*7*) has recently been tested as a permanently implanted monitor of ovarian function (*15*). The original blocking oscillator (*1*) was quite sensitive in monitoring temperature, and this is essentially the circuit used to study the incubation of penguin eggs in the Antarctic (*16*).

The significance of acidity measurements along the gastrointestinal tract is not always clear, but there are experiments one might wish to perform. For example, one might determine whether administration of vitamin D to a child with rickets changes the *p*H in the intestine as a result of the effect on calcium, or one might investigate whether the difference in intoxicating effect of different alcoholic beverages is due to a buffering action by some and not by others. The use of an antimony electrode to measure *p*H has been mentioned (*6, 17*). These electrodes, though having a low impedance convenient for transistor circuits, are sensitive to various other chemical systems in the body. Thus, the data they transmit, which may prove clinically useful, possibly should be termed "antimony numbers" rather than *p*H. A tungsten electrode seems no better. If the second electrode is made of silver chloride, rather than of standard materials in a wick configuration, then additional sensitivity to chloride ion is found. The original *p*H endoradiosonde (*4*), based on the reversible mechanical expansion and contraction of certain copolymers that accompany changes in acidity, suffers from some of these same difficulties.

The acceptable method of measuring *p*H is to use a glass electrode with a transistor circuit having over 100 megohms of input resistance. Feedback circuits with silicon transistors have been built with this degree of input resistance, and with recent techniques they probably could be sufficiently miniaturized. A better approach seems to be to apply the voltage to a nonlinear condenser whose change in capacity produces frequency modulation in the oscillator. Improvements over the biased-diode variable condensers mentioned earlier (*7*) have been achieved through the use of newer dielectric-amplifier components, and suitable resistance is found both in polarized titanates and in back-biased silicon diodes (*10, 11*). The field-effect transistor appears promising for situations where added gain is needed.

Various bioelectric potentials can be transmitted similarly; a lower input impedance is adequate, and so the direct effect of an injected voltage on the oscillator often suffices. With the high input resistance modulator, one can use the large pyroelectric signals from barium titanate to detect changes in temperature, such as those that may occur at the edge of some inflammations.

A problem that has received some investigation is that of localizing the site of internal bleeding along the gastrointestinal tract, or even of distinguishing stomach bleeding from duodenal bleeding. In an appreciable number of clinical cases this site is difficult to determine by present methods. Several approaches have been tried that would sensitize an endoradiosonde to the presence of blood. Chemical methods seem ambiguous when applied to the normal contents of the tract, but possibly some colorimetric method could be made to work. Oxygen tension can be measured by the reversible mechanical expansion and contraction of certain chelates (*18*), which can be encased in a thin film of Teflon for protection (*1, 6*). These can be used with a pressure endoradiosonde to detect the presence of a pool of blood, though swallowed air can interfere with such an observation. Powering the oscillator with an oxygen depolarized battery (reduced version of Eveready 1002 E), or with a fuel cell with hydrogen reservoir, gives similar results. A polarimetric method has been reported for this same purpose (*19*). Promising approaches search for the presence of the red corpuscles themselves. Erythrocites, because of their thin capsule, have insulating properties and a very high effective dielectric constant. However, direct electrical measurement is complicated by the active sloughing off of cells by the lining of the gut (*11*).

Red corpuscles can be labeled with any of several beta-active radioactive elements (*20, 21*) and then reinjected into the donor. Relatively simple animal experiments employing a Geiger counter with a little shielding show that one can detect a lesion if some of the red corpuscles have been labeled (*21*) with phosphorus-32. Decomposition products in the bile do not seriously interfere. Such a label lasts only about 2 hours, and thus several endoradiosondes, simultaneously operating on different frequencies, would have to be placed at intervals along the gastrointestinal tract. A preliminary discussion of low-voltage radiation detectors for this purpose has been given elsewhere (*7*).

A transistor with a floating base connection is quite sensitive to light. Thus, if the cover of the transistor in Fig. 1 is removed, small changes in light intensity will produce frequency modulation of the output signal. An even more sensitive circuit is obtained by replacing the resistor in Fig. 1 with a cadmium sulfide cell; in this circuit the radiofrequency oscillations are periodically interrupted at a frequency that depends on the light intensity. In this last application a silicon transistor (for example, the Pacific Semiconductor, type PMT-012) gives a better blocking action at the elevated temperatures of the body. With a radioactive or other light source, these circuits could perhaps be used for colorimetric measurement. In conjunction with a scintillation plastic or crystal, they also make a low-voltage radiation-sensitive unit that has applications in radiology. Because of the inefficient use of the light, such a radiation detector is at present too insensitive, by several orders of magnitude, to detect the presence of beta-particle-emitting red corpuscles. The junction region of a transistor shows direct sensitivity to beta particles, but because of thinness, little of the particles' energy is made available, and insensitivity results. The sensitivity of a Geiger counter is needed, and tiny ones are readily fabricated. A small several-hundred-volt blocking-oscillator power supply was constructed in which an elevated counting rate, due to increased loading, caused a shift in frequency (to combine transmission and modulation with voltage generation). Radiation of the signal must be from a separate coil of a few turns around the capsule when a ferrite core transformer is used to step up the voltage. Small mechanical motions can be introduced into these capsules by the subject himself, by external pressure changes, or by the use of external magnets, and thus one might alternatively consider using either an electrophorus or an electret as an electrostatic voltage source for these small currents. Radioactive batteries and small voltaic piles are other possibilities. A resistance-strip magnetic multiplier (*22*) could probably be miniaturized, but it would present the same voltage-source problems.

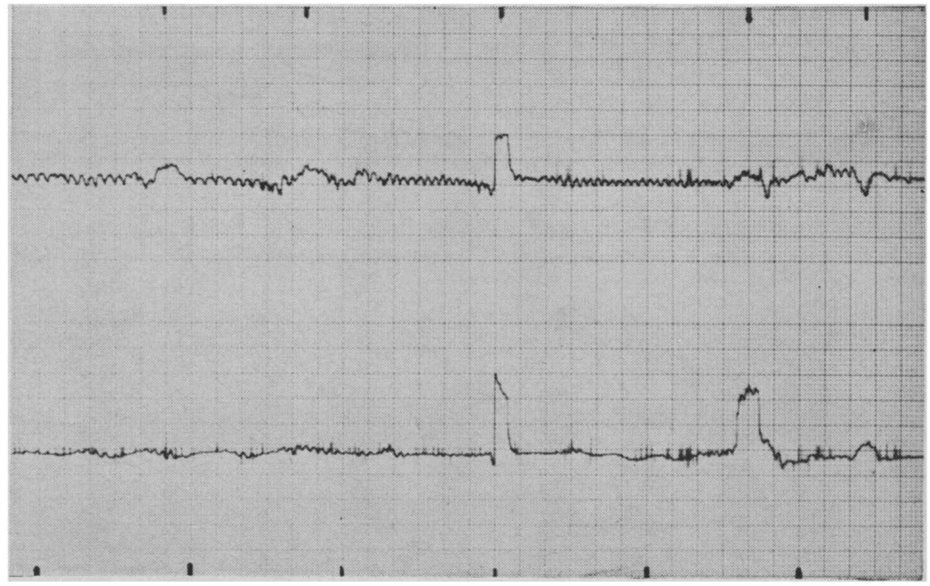

Fig. 7. Simultaneous signals from two transmitters, the upper from the esophagus and the lower from the stomach, of a representative healthy subject as various maneuvers were performed (marks at top, from left: swallow, swallow, Valsalva, Müller, deep inspiration). Increase in pressure is upward, with sensitivity in the top channel approximately half that in the lower channel. The small regular fluctuations are due to breathing. Marks at bottom, 1-minute intervals.

Alpha particles, because of their high density of ionization, are able to directly activate a transistor more vigorously (again through use of a floating base connection). The best solution thus may be to label the corpuscles with an alpha emitter. One beta-labeling procedure (*20*) also produces alpha-active daughter products that tend to remain in the corpuscles, and some such method may prove satisfactory. Only those corpuscles directly in contact with the detector would be detected. Taking the relative biological effectiveness of alpha particles as being between three and ten times that of beta particles, one can calculate the permissible dose for a human being, and the result indicates the practicality

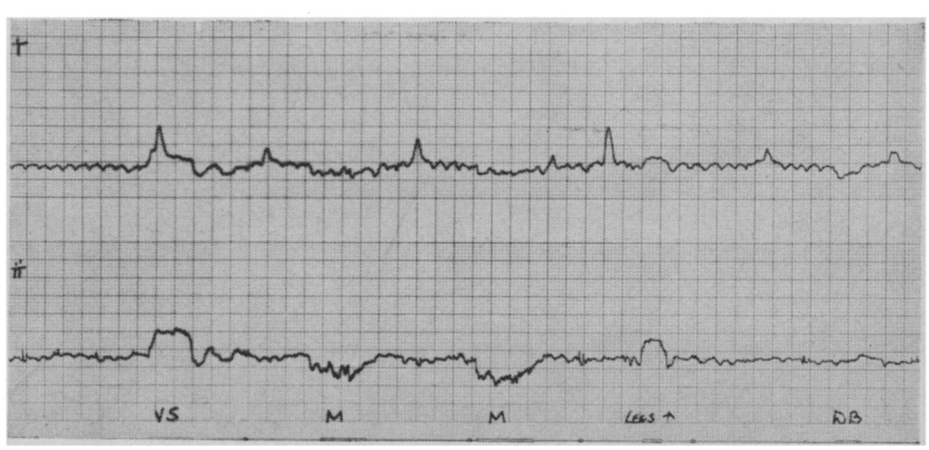

Fig. 8. Recordings from a subject with hiatus hernia; the upper tracing is from the esophagus, the lower from the pouch above the diaphragm. Normal periodic contractions are seen in the top tracing. The deflection in millimeters (small divisions) divided by 1.5 for the top tracing and 0.4 for the bottom tracing gives the pressure in millimeters of mercury. *VS*, expiration against resistance; *M*, inspiration against resistance; *DB*, deep breath (sometimes producing a drop in both channels); *Legs*, raising legs from bed.

of obtaining a distinct pulse every few seconds in the circuit, with practically no confusing radiation background. A bit more gain than is shown in Fig. 1 would be required between the detector and the oscillator; nevertheless, this may prove to be one of the more practical methods.

Clinical Observations

Various groups of workers (*23*) have made recordings from all parts of the gastrointestinal tract, as have John Carbone and I. I will cite a few examples of clinical observations from our studies in connection with the pressure-transmitting unit. These units have proved useful in studying normal patterns of activity. They are important because the subject has no sensation and thus is in a relatively normal, nonapprehensive state. The observations can be more reliable than the sometimes exaggerated readings obtained with the inflated-bag technique, in which both the size of the bag and its trailing attachment are disadvantages. Since the signal does not travel along a pneumatic tube, the frequency response is good. The spot in the body occupied by the endoradiosonde can be determined approximately by using the receiving antenna in a direction-finder fashion, and more accurately by radiography. Passage from the stomach is often judged by the temperature response to a sip of cold water.

The pressure-sensitive capsule can transmit the small pressure fluctuations due to breathing, and even smaller ones due to arterial pulsations are often observed; on the other hand, the same type of transmitter in the sigmoid has recorded momentary pressures greater than the blood pressure of the subject. Not only are normal patterns recorded but it is possible to test the effects of various drugs—for example, spasmolytics. Figure 5 shows a series of recordings in the sigmoid from a freely moving transmitter before, during, and after the administration of atropine.

In the field of surgery, one can study the restoration of normal activity after the trauma of a surgical procedure. The capsule can either be ingested in advance or it can be inserted through the wound, where it will stay until the return of normal activity forces it onward. Figure 6 is a tracing from such a study. The effect of such drugs as Hopan or Cozyme in hastening intestinal activity in the postoperative period is being investigated in this way.

To take an example from the other end of the gastrointestinal tract, and an application in the study of pathological conditions, we might note the simultaneous use of two transmitters. The same type of transmitter is used here as in the experiments described, but the pressure range is considerably less. One transmitter was placed in the stomach and the second in the esophagus of a normal subject, and their simultaneous signals were recorded on a double-channel recorder, as in Fig. 7. The two transmitters were kept from moving onward, without discomfort to the subject, by threads extending up into his mouth and tied around a tooth. The results of various maneuvers may be seen. Similar observations on subjects with hiatus hernia are being compared with the results of these various maneuvers in normal subjects. In hiatus hernia the stomach does not lie entirely below the diaphragm, which is normally penetrated by the esophagus, and a fold of the stomach itself extends up through the diaphragm. Figure 8 is a record made with one transmitter in the esophagus and the other in the pouch above the diaphragm. We hope that by recording the relative pressures in the areas above and below the diaphragm and in the esophagus we can learn why some patients suffer distress from this condition while others never know they have it. Possibly there is a physical explanation involving the shifting back and forth of the stomach contents with normal activity. The pressure difference across the pyloric sphincter has significance in other diseases as well. Recordings have been made from all parts of the alimentary tract and from various other body cavities, but the examples given here were selected as being somewhat varied. (For other relevant references, see *24*.)

As new techniques develop, the endoradiosondes can be made much smaller. For the alimentary tract, the presently available commercial components seem quite satisfactory, but extreme miniaturization and passive transmission are needed, for example, for placing a pressure transmitter in the anterior chamber of the eye of an experimental animal in order to study glaucoma (*25*).

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