THE DESIGN, CONSTRUCTION AND APPLICATION OF APPARATUS FOR TELEMETERING BIOLOGICAL DATA FROM THE HUMAN ALIMENTARY TRACT

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A thesis presented for the degree of Ph.D. at the University of Edinburgh

October, 1962.

ACKNOWLEDGMENTS

The work reported here was carried out in the Department of Medical Physics on behalf of Professor John Bruce of the Department of Clinical Surgery. It was generously supported by a grant made to Professor Bruce by the Scottish Hospitals Endowment Research Trust.

I would like to express my sincere appreciation to the Director of the Department of Medical Physics, Dr. J. R. Greening, for allowing me to carry out this work in his laboratories and to the staff of his Department for the help that they have given me over this period. My particular thanks are due to Dr. David Simpson, not only for guiding me through the technical stages of this project, but for his advice and help throughout.

The clinical studies were carried out in the Gastro-intestinal Unit at the Western General Hospital, Edinburgh in conjunction with Mr. Adam N. Smith of the Department of Clinical Surgery and the Gastro-intestinal Unit. I would like to record my gratitude to Mr. Smith for his guidance and kind co-operation during these studies and I would also like to express my thanks to the other surgeons and physicians of the Unit, not only for permitting me to study some of their patients, but also for their continued interest in the work.

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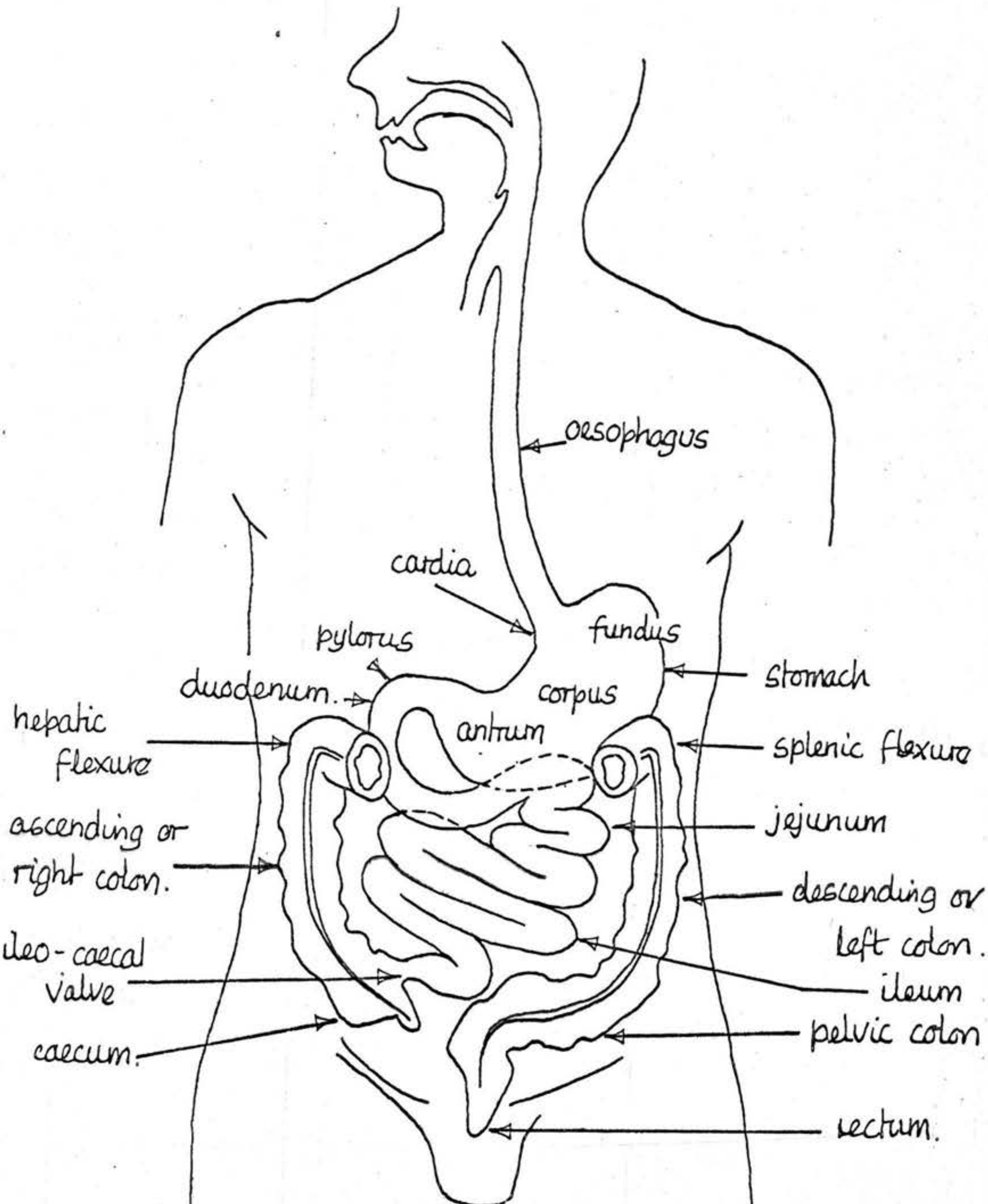

Figure 1

The human alimentary tract.

CHAPTER 1

Modern methods in the study of the alimentary tract

1.1 Introduction

For many years the investigation of gastro-intestinal disorders has been carried out using simple physical methods which are difficult to evaluate in clinical terms. At first this was because of an almost complete lack of instruments capable of providing accurate measurements of the variables associated with these conditions. More recently it has been the complexity and sometimes the high cost of the new methods that has hindered their widespread adoption.

The human digestive system consists of a series of complex and sensitive organs. They form a long, convoluted muscular tube, the mid-parts of which, being virtually inaccessible except at operation, are not easily studied by simple techniques. A series of valve-like structures, or sphincters, divides the tube into four major segments: the oesophagus, the stomach, the small intestine and the large intestine (Figure 1).

The digestive process starts in the stomach where the initial breakdown of protein takes place. After the food has been passed through the pyloric sphincter into the small intestine, the breakdown of the foodstuffs continues and all the protein, carbohydrate and fat is completely absorbed. The useful products of the chemical exchanges are thus passed into the blood-stream and the remaining material is removed through the ileo-caecal valve into the large intestine. The main function of the large intestine is the re-absorption of water and consequent passage of semi-solid matter to the rectum.

In health these functions appear to be precisely regulated processes, although the complicated mechanisms controlling the various stages of digestion and/

and many more of these vital processes are still only partially understood. Consequently, when these functions break down in disease, treatment cannot always be applied on a rational basis. Better techniques and more refined instruments will eventually enable investigators to extend their researches and perhaps to complement the limited procedures used for diagnosis. Modern methods, using for instance radioactive tracers to follow metabolic pathways in the body can offer completely new aspects to some of the clinical problems; whilst technological advances resulting in instruments such as the Fibrescope, used for viewing the inner surfaces of the upper part of the digestive system, and the biopsy-capsule for sampling the mucosal lining of the organs not only extend direct clinical methods into previously unpenetrated regions but help to make the investigations less trying for the patient.

1.2 Physiological validity

It is now widely accepted that emotional stress exerts a considerable effect on the functions of the digestive tract; so that as well as the ethical consideration for the patient's welfare, this is a very good reason for trying to keep the subject as comfortable and relaxed as possible during investigation. Generally patients dislike having tubes passed either by mouth or by rectum, and long lengths of tube are sometimes necessary if areas near the mid part of the bowel are being examined. The clinician, who unfortunately has rarely had alternative methods for making quantitative studies, has had to contend with inconsistency in his examinations from both psychosomatic and from reflex effects. It is difficult to estimate the errors created by psychosomatic effects because some people are less disturbed by these procedures than others and it is also difficult to assess the reflex effects, particularly that of the/

the physical stimulation resulting from mechanical intrusion into the organ. A valid comparison between different instruments cannot be carried out in humans without a long, carefully controlled trial because of the continual short-term variations in most biological phenomena and the mutually exclusive nature of each method. Diagnostic procedures, which can be based on empyrical data, do not require rigorous evaluation, and the results could tolerate small errors, provided that they are consistent. The 'instrumental error' in biological measurements may not become apparent until other approaches are made. For example: the secretory response to stimulation of cells in the gastro-duodenal area is routinely assayed by methods that require aspiration of the bowel content. Recently these responses have been studied 'in situ' using tiny swallowed transducers and found to be consistently lower than the values obtained by intubation. The difference has been attributed by several of the workers to 'the less disturbing' conditions prevailing during the transducer measurements (Rovelstad, 1952; Grieve, 1961).

There is also evidence to show that during the measurement of pressures developed in the bowel by the muscular activity of the walls, the presence of the instrument can interfere seriously with the physiological conditions by propping the lumen of the bowel open during the final phases of contraction. Brody and Quigley have reported that using air-filled tubes of 3 mm. tip diameter they frequently recorded peak pressures of 300 cms. of water from the distal antrum, whereas with similar tubes expanded to 5 mm. tip diameter they rarely recorded pressures in excess of 90 cms. of water from the same region (Brody and Quigley, 1951). They pointed out that a 'plateau' did not form during the measurements indicating that the series of lower values

could/

could not be attributed to there being insufficient material to 'drive' the manometer, even during times of maximum contraction.

Comparisons of this sort do not appear to have been carried out by other workers but this single report which is based on a great number of clinical experiments indicates a serious limitation to pressure recording within the bowel that is not generally appreciated.

1.3 Direct methods

Direct methods such as those used to examine the cellular lining of some of the digestive organs cannot usefully be applied to functional disorders. The muscular activity of the bowel can be seen during abdominal operations or through accidental and surgically constructed wounds, but the complex nature of the movements, complicated further by the effects of trauma and anaesthesia, prevents the collection of objective information.

Classically the approach to the problem of estimating the motility function of the bowel has followed the manometric methods used to investigate the cardio-vascular system. Unfortunately the propulsive mechanisms of the digestive system are more intimately bound up in the muscular walls of the conducting canal itself than they are in the vascular system which carries blood around the body and even empyrical methods remain difficult to evaluate. The concept of intra-luminal pressure breaks down of course when the bowel segment contracts and closes down completely on the measuring instrument.

1.4 Radiological techniques

Anatomical deformities can impair the functioning of the digestive system but these may be traced and identified using the skill of the radiologist and the X-ray techniques developed over many years. Radiology may also be used to show changes in the outline of the organs during digestive activity

and/

and the speed of progression of a radiopaque bolus, but because the barium shadow reflects the resultant of many forces, recording it can neither distinguish between them nor measure them. The heavy contrast materials, such as the barium paste commonly used to outline the walls of the digestive tract are not handled in the same way as normal foods, and in certain conditions it has been shown that they can stimulate activity (Childrey, 1930).

(i) Fluoroscopic observations.

The activity of different areas of the alimentary canal may be visualised simultaneously on a fluoroscopic screen, which is particularly useful when one or more instruments have to be located during the course of diagnostic investigations. The greatest single disadvantage with the method is that the period for which the patient can be exposed to irradiation from X-ray apparatus, even modern equipment which enables a much reduced X-ray intensity to be used, is very short in terms of the usual period required for diagnostic investigations of bowel motility.

(ii) Cine-radiography.

Permanent cine-records of radiological appearances, which can be studied at leisure, have contributed a great deal to our present understanding of the way in which bowel contents are mixed and propelled along the gut, particularly in the instances when simultaneous pressure measurements have been made (Van Trappen, 1958). The procedure is complicated and the apparatus expensive but the method forms a valuable tool for research.

(iii) Transit times.

The mean propulsive activity of particular lengths of bowel, which is sometimes a useful clinical parameter, may be estimated from periodic determinations/

determinations of the position of ingested marker materials. The value of these estimations is considerably enhanced if the marker is of approximately the same constituency and density as normal food materials, so as to avoid unnatural effects due to gravity and delay in the folds and irregularities of the inner surfaces of the tract.

1.5 External manometric recording

Long before X-ray examinations made bowel functions visible in the intact human, investigators were trying to establish what happened to ingested food materials. The commonest method that they used to examine motility permitted observations and recordings to be made of these remote changes on apparatus outside the body. The first documented attempts at this type of quantitative recording appear to have been made during the latter part of the last century (Legros and Onimus, 1869; Pfunger and Ullman, 1887). Following these early experiments almost all subsequent investigators used swallowed balloons connected to water-kymographs outside the body until 1940, when Brody departed from the balloon methods and advocated strongly the use of open-ended tubes to conduct intra-luminal pressures to the external recording manometers. Much of the available data on bowel activity has, however, been obtained using closed conduction systems (Inglefinger and Abbott, 1940; Adler et al., 1941; Chapman and Palazzo, 1949). The most critical of Brody's arguments were really levelled at the crude nature of some of the probes passed into the bowel and the failure of almost all of the early workers to assess their apparatus critically when they presented their results. Often only a passing reference was made to the way in which the measurements had been carried out.

(i) ..../

(i) Balloon probes.

To prevent the balloon obstructing the bowel during contraction it must be made compressible. This can be done by filling the balloon and the conducting tube with a gas such as air which will compress, allowing the probe to reduce in volume during muscular activity. Unfortunately the commonest way of registering pressures when these experiments were first carried out was by the simple water manometer, which requires a considerable displacement of the conducting medium. The manometer was, therefore, simply connected to water filled balloons which had been passed into the bowel and inevitably the resulting records were complexes of the hydrostatic effects in the water column and volume changes resulting from deformation of the balloon by contractions of the bowel.

Many investigators have proved that intra-balloon pressures are altered in an unpredictable and inconsistent manner when the probe is compressed directly by the walls of the bowel; but to a certain extent this is true of any pressure measurement made with an instrument in a closed segment of bowel and clinical investigators, accepting the limitations of the simple balloon, continue to use air-filled probes for diagnostic studies in closed passages such as the oesophagus and the rectum. Experiments with balloons in the small intestines of dogs have shown that variations in size and the compressibility of the balloon can cause significant changes in the recordings of activity, resulting from direct physical stimulation of the bowel (Gruber and de Note, 1935). This reflex activity although undesirable during 'physiological' experiments has been used to provide a relatively steady basal level of activity when testing, in animals, the effects of drugs inhibiting bowel motility.

The most undesirable characteristic of balloon probes for the

usual/

usual type of clinical investigation is, like any other device in the bowel, the direct physical stimulation resulting from their bulk. This difficulty is clearly relative to the diameter of the bowel and small air-filled balloons can be used effectively in the larger organs especially where open-ended tubes are likely to be blocked by bowel contents.

(ii) Open-ended tubes.

Pressures may be conducted from the smaller diameter organs, with a smaller risk of causing direct stimulation by means of fine open-ended tubes. Liquid must be used as the conducting medium because the compression of a gas under pressure would allow the bowel contents to 'escape' into the tube, possibly resulting in artificial physiological conditions if the bowel cavity is small and also risking blockage of the conduction system with mucous or small food particles. Open-ended systems filled with air have been used, an expanded tip allowing a limited access of the bowel fluids during compression, but it is difficult to manoeuvre in the bowel and since the probe-tip must be of the same volume as an equivalent balloon probe it does not appear to have any advantage over the closed system. A simple calculation using Boyle's law shows that intra-luminal pressure increments up to about 200 cms. of water can be recorded without emptying a balloon probe completely or filling the probe-tip with bowel content, if the volume of the probe is not less than one-sixth of the total volume of air in the system.

If P represents the atmospheric pressure at the time of the recording, and p represents the greatest pressure increment to be recorded; and if V is the total volume of air in the system, a part v of which is the volume of the probe, then providing that the ambient temperature remains steady/

steady we have

$$PV = (P + p)(V - v)$$

or $$\frac{V - v}{V} = \frac{P}{P + p}$$

and rearranging $$\frac{v}{V} = \frac{p}{P + p}$$

so that to measure increments up to 200 cms. of water
($p = 0.2$ atmospheres)

$$\frac{v}{V} = \frac{0.2}{1.2} = \frac{1}{6}$$

that is, the volume of the probe should not be less than one-sixth of the total air volume in the system.

The ultimate reduction of the air filled system therefore depends on how fine the conducting tubes can be made without critically reducing the response of the system to rapid pressure changes.

Water filled tubes are usually kept patent by a slow continual flushing or 'bleeding'. The flow rate is kept at about 2 or 3 ccs. per hour by means of a part-open tap separating the 'flushing-pressure head', which is usually equivalent to at least 100 cms. of water, from the pressure-conduction tubes. If the flow is stopped by intra-luminal pressure forcing a solid particle against the open-end of the tube, the pressure in the conduction tube quickly rises until it is high enough to unblock the tip and re-establish flow.

If the level of the transducer is not maintained at the same level as the tip of the conduction tube when it is passed into the bowel a small hydrostatic pressure equivalent to the 'head' of water is recorded. This can be a serious limitation if accurate measurements of the basal pressure levels in the bowel are required because changes in the level of the tip/

tip in the body cannot be determined accurately or differentiated from small physiological pressure fluctuations. Basal pressure levels can be established accurately using an air-filled system.

1.6 Importance of manometer characteristics

Several investigators have reported on what they consider to be the minimum number of harmonics that must be recorded in order to preserve the significant characteristics of a periodic pressure wave (Wood, 1956). It depends completely of course on the complexity of the waveform, particularly on the nature of any discontinuities, and on the limits that are set on distortion. Relatively few harmonics are required to record the amplitude of the pressures accurately, whereas reproduction of the exact form of the wave requires a considerably greater number. Using a Fourier analysis McDonald has shown that a waveform representing almost 99% of a half-rectified sine wave can be synthesised using only the first five natural harmonics (McDonald, 1961). He used the sum of the variance of each term as a measure of the energy content of the wave to arrive at this figure, which is lower than the limits generally quoted for good fidelity in cardio-vascular recordings. It should be an adequate criterion for the relatively simple and slow changes that occur in the digestive system. Fairly fast transient fluctuations do occur in the oesophagus and the pyloric antrum, corresponding to a frequency of about 0.5 c/sec. although the most rapid periodic pressure changes are the 'segmenting' waves of the small intestine which are seldom faster than 15 or 16 c/min. A uniform pressure response therefore to 2 or 3 c/sec. should be adequate to record even the more rapid changes in the digestive system.

In the first instance a manometer may be regarded as a simple oscillatory system with a natural frequency of oscillation that is defined by Frank's equation (Frank, 1903).

$$f_o = \frac{1}{2\pi}\sqrt{\frac{E}{M}}$$

where E represents the volume coefficient of elasticity of the manometer, i.e. a recorded pressure change Δp produces a volume displacement $\Delta V = E.\Delta p$ at the recording tip, and M represents the effective oscillating mass of the system.

If the manometer is damped so that oscillation does not occur after each excursion, the amplitude response falls off as the frequency at which it is being driven approaches the natural frequency of the system. There is also a greater phase lag introduced between the pressure wave and the recorded wave at frequencies approaching the natural frequency. This latter effect is not serious when recording simple changes, but it can change the effects of the higher frequency harmonics in complex waves. To avoid serious distortion of this complex waves it is, therefore, desirable to keep the natural frequency of the overall system as high as possible; a safety factor of about 10 would enable the distortion effects and even the degree of damping to be neglected. For investigations of the human alimentary canal therefore a manometer with a natural frequency of at least 20 c/s is necessary.

The characteristics of the overall system naturally depends on the characteristics of each of its component parts. Pressure conduction systems using long narrow catheters not only damp the manometer system, they lower the overall natural frequency. If the natural frequency is below the critical value then it becomes important that damping should be light. In air-filled systems the effective mass of the column is very small but there is considerable movement of air in the tube which cannot therefore be made very narrow because viscous damping is proportional to the third power of the bore radius. Water-filled tubes are not heavily damped in this way because there is little

movement/

movement in the tube but the high effective mass of the column of water, which is proportional to the square of the radius, reduces the natural frequency. The need to reduce the fluid displacement has resulted in manometric recorders that do not require a large displacement to record even quite large pressures completely replacing the simpler water manometers.

Optical manometers, which were first developed to make measurements of blood pressure by direct connection to arteries, were introduced to intra-luminal pressure measurements by Brody in 1940. Basically they are simple instruments, easy to construct and stable in operation, but the principle of using the flexing of a pressure-sensitive membrane to deflect a light beam is like many other manometer systems in that low volume displacement and high sensitivity are opposing factors. Lengthening the optical lever enables the stiffness of the membrane to be increased without reducing the sensitivity but there is a practical limit to a simple extension of this kind and modern versions replace the photographic recording, which requires cumbersome light proof cabinets, with light-sensitive cells which produce voltage variations proportional to the deflection of the diaphragm. These voltages may then be amplified and used to operate a suitable pen recorder. Other forms of electronic manometers use the movements of pressure-sensing membranes to change either the resistance of a strain-gauge or other electrical parameters such as inductance or capacitance.

1.7 Direct measurement of intra-luminal pressure.

Although the physical characteristics of pressure-conducting systems with external recorders are adequate for making accurate measurements of the pressures in various parts of the bowel, 'tube' methods are far from ideal clinically. As a first step towards freeing the patient from the discomfort of/

of bulky tubes, small pressure-sensitive transducers were developed.

(i) Miniature transducers.

A transducer small enough to be swallowed could convert the pressure fluctuations into electrical changes dispensing completely with the limitations of hydraulic conduction in tubes. The electrical variations could be conducted by protected lengths of fine wire over indefinite distances without introducing any appreciable damping or restruction on the natural frequency of the transducer, which may be about 1,000 c/s or even higher. In 1943 Wetterer described a suitable miniature differential transformer unit and a device measuring 3 mms. x 12 mms., based on a modification of this device was built by Gauer (Gauer and Gienapp, 1950). A small centre-tapped coil with a soft-iron armature mounted on an elastic diaphragm at the tip of the instrument formed two remote arms of a balanced induction bridge. Voltages proportional to the pressures acting on the diaphragm could then be recorded outside the body. Despite the fact that this device was used successfully over five years to record pressures in the oesophagus, the small and the large intestine (Code, 1952), its use appeared to require a considerable degree of technical skill and such methods do not appear to have been used widely.

(ii) Telemetering capsules.

During the past few years a number of devices which permit the recording of gastro-intestinal motor activity without any connecting tubes or wires have been devised. The first apparatus of this kind to be reported consisted of a sensitive magnetometer, which, when placed near to the patient enabled movements of a tiny, swallowed magnet to be observed (Wenger et al., 1957).

Rather more complicated instruments using pressure-sensitive radio transmitters to pass information to external recorders were also developed, first in Sweden and the United States, and later in this country and in both East and West Germany. Intra-luminal pressures acting on the sensitive parts

of/

of these devices modulated the frequency of the encapsulated oscillator circuit. The radio-frequency transmission from the ingested capsule was detected by loop antennae held near to the body. These signals could be demodulated by a special radio-receiver and recorded as pressures. The great advantage of these capsules over other systems is that it frees the patient from the incumbrance and discomfort of connecting tubes, enabling investigations to be made for long periods from any part of the alimentary tract.

1.8 The ideal instrument.

The clinical requirements of the ideal instrument for recording pressures in the alimentary canal were expressed by Abbot and his co-workers in 1943 and have subsequently been restated by Farrar and Davidson in a comprehensive review of methods of measuring motility (Farrar and Davidson, 1958) as follows:-

(a) The pressure-sensitive elements must be small enough to be swallowed by the patient, without discomfort, and to be passed readily to any desired location.

(b) The instrument must be simple to calibrate in terms of absolute pressure, and capable of responding to small changes of the order of 0.5 cms. of water.

(c) It must provide simultaneous records of the pressure at several locations in the tract.

(d) The determinations, if not made continuously, must be sufficiently frequent to record all significant fluctuations.

(e) The pressure-sensitive elements must measure the average hydrostatic pressure in their vicinity and must/

must not be subject to error caused by contact with the gut wall or small pieces of the solid content.

(f) The device must not cause either obstruction or mechanical stimulation.

In certain aspects, the pressure-sensitive capsules reported approach this 'ideal' specification and investigations have been conducted at a number of centres to assess the clinical applicability of these new methods and to develop this tubeless technique. The following chapters in the first part of this thesis are devoted to the various technical and clinical considerations that have to be given to these new methods.

CHAPTER 2

The design and construction of a capsule transmitter

2.1 General considerations.

The specification of an ideal clinical instrument has been outlined at the end of the previous chapter. The dimensions of the capsule are undoubtedly important, not only because it must be small enough to be swallowed and passed through narrow muscular passages but also because of the effect that the instrument is thought to have on the physiological conditions in the bowel. A foreign body in the tract may produce reflex stimulation affecting many of the local biological parameters or it may prop the lumen of the bowel open during the final phases of muscular contraction. There are, however, technological limitations to 'ultimate' miniaturisation; suitable transducing elements become difficult to construct and consequently they usually respond less accurately; the cases of small capsules are usually more fragile and consequently less safe to use in human applications; in telemetering devices the radiated field strength falls off rapidly with the dimensions of the radiating coil. A further consideration that must be balanced against the obvious desire to reduce the size of the capsule is that for uses where it is allowed to make its own way along the alimentary canal along with normal food materials, the specific gravity will increase as the ratio of circuit components to encapsulating plastic increases, resulting in an excessive and undesirable response to gravitational forces.

The capsule should present a smooth, seamless, preferably streamlined profile with an exterior surface of an insoluble and non-toxic material, which could be sterilized in chemical solutions. Several of the modern plastics fulfil these basic requirements but Perspex (the trade-name for an acrylic polymer)/

polymer) appeared to possess advantages over the other materials available at the time that experiments were started. It is a tough material, easily worked and cemented, and with a specific gravity not much greater than water. It may be sterilized with most hospital antiseptics except compounds containing phenols such as carbolic.

The problems of size and specific gravity are obviously eased if the number of heavy encapsulated components is kept to a minimum. It is, therefore, impracticable to design a transmitter that would radiate equally in all directions or to attempt to incorporate extra circuit devices to regulate spurious changes in the nominal frequency of the oscillator.

The information could be relayed from the transducer to the external recorders through the radio-frequency link by either simple frequency modulation or by some form of pulse-frequency modulation of the carrier. Pulsed operation would obviously lead to an economy in the current drained from the battery but it was decided that until the exact nature of the coupling through the body tissues could be evaluated 'in vivo', a steady radiated field would be the more desirable of the alternatives because random coupling changes resulting from mutual orientation effects and changes in the depth and nature of intervening body materials would lead to distortion of the data if amplitude modulation and possibly also if low frequency pulsed signals were used.

(i) Operating band.

The following five points were considered in making the choice of the operating frequency band:-

(a) Size: The encapsulated components, particularly the tuning coils must be physically small.

(b) Stray capacitance: The tuning capacitors must be large compared to possible stray capacitance effects within/

Waveband	Frequency kc/s		λ ms.	Transmitter
Long wave broadcast	150			
		200	1500	BBC Light (Droitwich)
	285			
	415			
Marine		500	600	Distress telegraphy
	525			
Medium wave broadcast		647	464	BBC Third
		692	434	BBC North
		809	371	BBC Scottish
		881	341	BBC Welsh
		908	330	BBC London
		1053	285	BBC West
		1088	276	BBC Midland
		1151	261	BBC N. Ireland
		1214	247	BBC Light
		1442	208	Luxembourg
		1456	206	BBC West
		1546	194	BBC Third
	1605			
Marine				
	1800			
Marine and amateurs	2000		150	

Figure 2

United Kingdom frequency allocations chart from 150-2000 kc/s; based on the Atlantic City Agreement, 1947.

within the body.

(c) Absorption: A minimum amount of the radiation from the capsule should be absorbed by the body tissues.

(d) Competitive generators: Channels in which powerful transmitters operate should be avoided as far as possible.

(e) Noise: The level of electrical noise generated in large hospitals is usually highest in the low radio-frequency ranges.

Considerable research appears to have been carried out at other centres investigating the cross-section and absorption coefficients of the human body both over a broad part of the radio-frequency spectrum and over a wide range of incident intensities. Not surprisingly there is an almost complete absence of evidence concerned with radio-frequency sources within the body. A theoretical consideration of all the different effects would be extremely difficult because the field strength outside the body is dependent not only on the dielectric and conducting properties of the different body layers but also an diffractive and capacitive effects resulting from the inhomogenity of the intervening tissue. Appreciable absorption is not thought to occur in body tissue at frequencies below about 1,600 kc/s (Schwann and Piersol, 1955) although experiments carried out with capsule-transmitters operating at 2 Mc/s seem to indicate a drop of approximately 30% in the field strength when the capsule is swallowed (Horowitz and Farrar, 1962). The international broadcast bands extend upwards from 200 kc/s but reference to the frequency allocations chart, (Fig. 2), shows that the range from 300 kc/s to 600 kc/s, between the long and the medium wave-bands, is relatively free from powerful transmitters, being reserved for various navigational and emergency services./

services. Most small radio-frequency transistors work well in this frequency band and the noise level was not found to be a serious factor in Edinburgh. Electrically screened rooms were available in the centres where the experiments were carried out but they were not found to be necessary.

(ii) Estimated radiated power.

The total amount of energy dissipated by the capsule during its transit through the body is stored in a hearing-aid battery, small enough to be encapsulated along with the transmitter circuitry. It is, therefore, highly unlikely that there is any radiation hazard associated with the use of these small transmitters in clinical investigations. The maximum permissible intensity level for the continuous exposure of body tissue to absorbable electromagnetic radiation quoted in the Post Office publication on "Safety precautions relating to intense radio-frequency radiation" (H.M.S.O. 1960) is 10 milliwatts/sq. cm. The maximum possible order of intensity from the capsule is a hundred times smaller than this figure and at a frequency thought to be below the threshold of absorption. Similarly the field strength at a distance of 10 metres will certainly be less than 0.5 millivolts/metre, which is the statutory limit for generating radio-frequency radiation that might interfere with domestic radio reception, quoted in the British Standards Code of Practice, C.P. 1002 (1947).

2.2 Transducing systems.

(i) Modulation.

Two types of transducer may be used to convert the parameter variations into changes in the frequency of a single transistor oscillator. The/

The transducer can be made part of the main oscillator tuning circuit so that frequency modulation occurs as its reactance varies with the parameter or else modulation can be achieved by introducing a variation in the base-bias current of the oscillator from an electrode type of transducer with an electrical output. For accurate results the modulation should be capable of changing the nominal frequency by at least 5%, so as to dominate spurious frequency drifts in the oscillator. This is particularly important if phenomena such as pH and temperature changes with long time constants of similar length to those of the spurious changes are to be studied.

(ii) Pressure transducers.

Because of the importance of keeping the natural frequency of the manometer high, a sensing system such as a diaphragm, which allows only a small volume displacement, is the most appropriate arrangement. For a given pressure, the force exerted on the diaphragm is dependent on its area and the mechanical response to this force varies with the geometry of the diaphragm and the stiffness of the material. A convenient method was to use the end of the capsule casing as the diaphragm, thus limiting the sensitive area to a circular section less than 1 cm. in diameter. The amount of rigidity that can be allowed for such a structure depends on how sensitive the movement detector in the modulation system can be made. Greater sensitivity could be obtained using a more compliant material, such as a rubber membrane, for the diaphragm, but it would have to be very firmly bonded to the plastic. A more rugged structure with the same sensitivity could be obtained by using a bellows or multidiaphragm, but unfortunately a sufficiently small system could not be bought and it proved to be too difficult to construct in the workshop.

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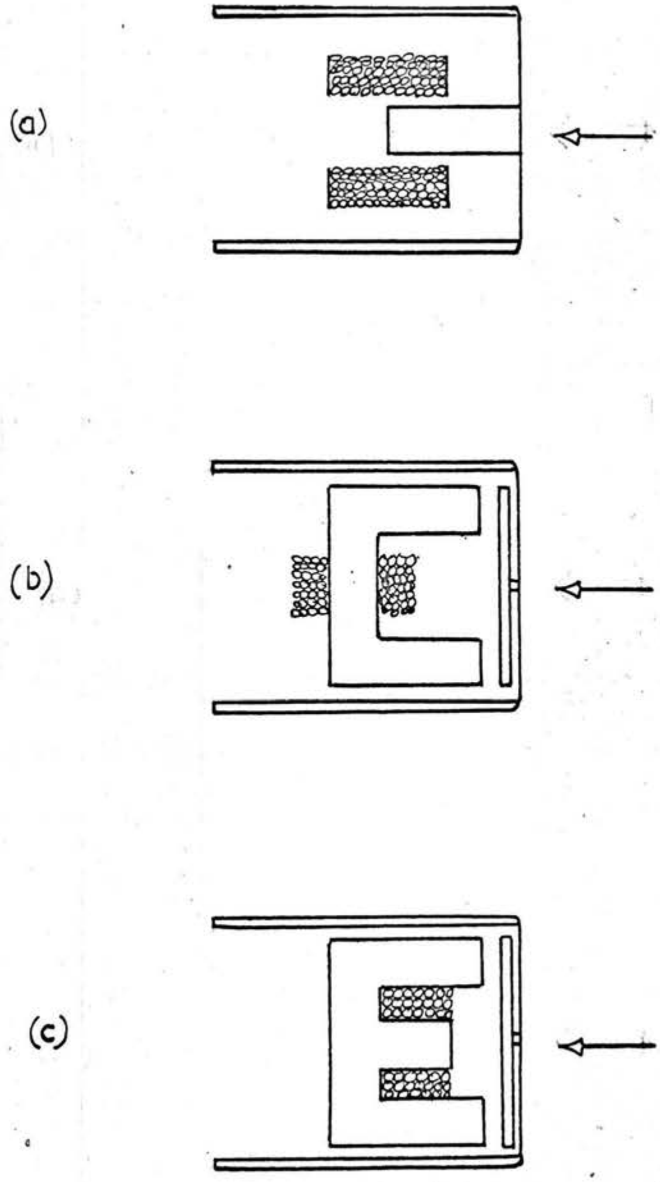

Figure 3

Three possible types of
inductive pressure transducer.

At these low frequencies greater sensitivity can be achieved by using a variable inductance modulator rather than a variable capacitance. Three possible arrangements are shown diagrammatically in Fig. 3. Ferrite materials were used where possible in preference to powdered iron cores because they have greater permeability and lower eddy current losses in the selected frequency band. The first system (a) in which a small slug of ferrite, attached to the centre of the diaphragm, moves in and out of the tuning coil as the diaphragm flexes, is most suitable for compliant diaphragm materials such as rubber which give relatively large displacement. The slug increases the inertia of the diaphragm and also decreases its sensitive area resulting in a low frequency response and poor sensitivity. In (b) the armature of a ferrite-cored coil is attached to the centre of the diaphragm, whereas in (c) high sensitivity is achieved by enclosing the coil completely inside a ferrite pot-core. The movement of the lid which is attached to the centre of the diaphragm varies the magnetic field passing through the body of the pot core, changing the inductance of the coil. Using this latter arrangement and a Perspex diaphragm, 1 cm. in diameter and 0.2 mm. thick, modulation of 7 - 10% was achieved for pressure changes of about 200 cms. of water.

(iii) Temperature transducers.

Each part of the intestine undergoes a characteristic rise in temperature of about 0.5^{o}C during digestive activity. Enteritis leads to a continuous elevation of the temperature level in the affected part of the intestine that is independent of the digestive processes. Non-functioning segments show no temperature response during digestion. The smallness of these temperature fluctuations requires a very steady transducer with a very high/

high temperature coefficient. I did not carry out any practical investigations into this form of transducer.

The earliest methods reported made use of the temperature sensitivity of the transistor in the oscillator circuit itself to give frequency modulation with temperature (Nöller, 1959). Changes of about 0.4% per ^{o}C can be achieved in this way, but when made up each unit will show a different temperature characteristic which is not generally linear and cannot, therefore be easily matched. Ceramic capacitors with high temperature coefficients appear to be a more practicable approach and frequency deviations up to 1% per ^{o}C have been reported (Jacobson, 1960). It was reported that greater sensitivity than this can be obtained by sealing a small chamber, partially filled with a low boiling-point mixture of pentane and hexane, over the diaphragm of a pressure transducer. If the chamber is sealed at a temperature close to that of the body even slight fluctuations cause considerable variations in the vapour pressure of the mixture which modulates the oscillator frequency by means of the pressure diaphragm (Rowlands and Wolff, 1960). Sensitivities of 2.5% per ^{o}C were obtained in this way but the mechanical properties of the diaphragm under continuous stress were such that slow deformations led to permanent or long-term frequency drifts. Another way of achieving a very high temperature sensitivity without this troublesome zero drift reported by Wolff is to employ a toroidally wound strip of a special nickel alloy, which has its Curie-point near to normal body temperature, as one of the tuning inductances in the tuning circuit of the oscillator (Wolff et al. 1962). The large changes in permeability resulting from even small temperature variations easily provide the sensitivity necessary for large frequency deviations.

(iv) pH transducers.

Jacobson,/

Jacobson, who has carried out a considerable amount of work on small pH transducers measured pH at first by means of a mechano-chemical element 0.5 cms. long, fixed over the sensitive end of an inductive pressure transducer (Jacobson and Mackay, 1957). The element consisted of a vulcanised co-polymer of 20% polyacrylic acid and 80% polyvinyl alcohol. It gave a reversible change in dimension of about 60%, for a pH shift from 3 to 8, but suffered from a slowness of response. To reduce this lag, however, the film had to be made so thin that considerable error arose from variations in the concentration of the body electrolytes.

Other workers have used methods based most commonly on forming a pH-sensitive cell between a reference electrode within the capsule and a metal electrode in contact with the body fluids (Nöller, 1959; von Ardenne, 1959) but they do not appear to be satisfactory. Polarisation rapidly takes place at the electrode if current flows through the system, resulting in desensitisation of the electrode and false changes in the indicated electro-chemical potential. A true potentiometric arrangement cannot conveniently be used to modulate the oscillator so the method cannot be considered accurate or reliable after long periods. Antimony electrodes are also sensitive to other agents commonly found in digestive fluids and according to Mackay they should be termed 'antimony numbers' rather than pH (Mackay, 1960).

The true hydrogen membrane potential can only be achieved using a glass electrode/reference electrode system which does not allow polarisation to occur. Units small enough to be swallowed are best constructed by expert technicians and they are not yet available in capsule form so I did not carry out any practical investigations on this form of transducer. Wolff appears to have solved the problem of modulating a transistor oscillator satisfactorily using/

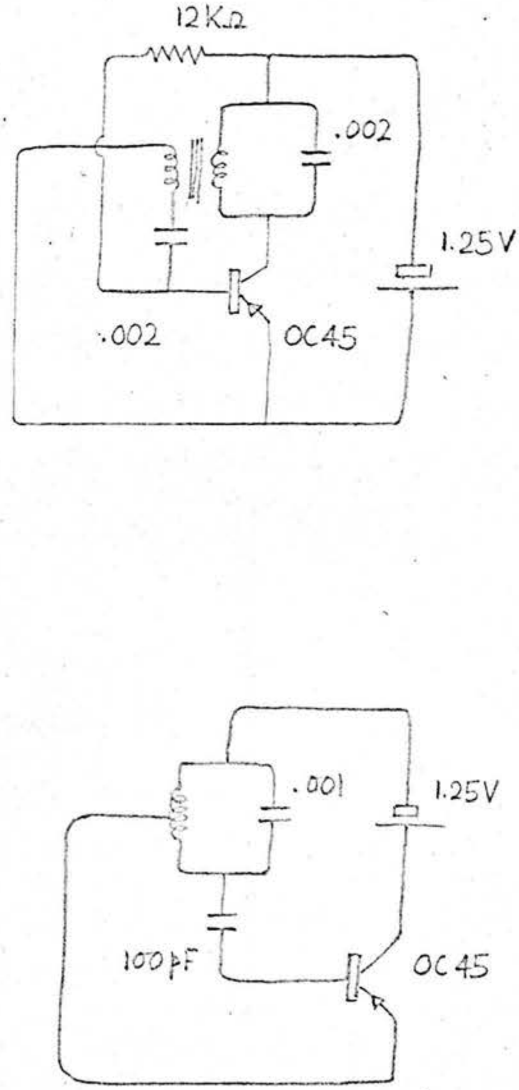

Figure 4

Above - Reaction coil oscillator
Below - Hartley oscillator

using the small voltage output from these cells (Wolff et al, 1962) and the modification to the transmitter circuit will be discussed in the next section.

2.3 Oscillator circuits

The oscillator forming the capsule's transmitter must be a simple circuit in order to keep the number of encapsulated components to the absolute minimum consistent with reasonable stability. A single transistor oscillator is required giving continuous oscillations at about 450 kc/s and powered by a low voltage cell. Three types of circuit were investigated during October and November, 1959.

(i) Reaction-coil oscillator.

This type of circuit, which was used in one of the earliest capsule designs (Farrar et al, 1957) employs feedback from the collector to the base circuit by means of a double wound inductance. Forward bias must be applied to the emitter base diode if the circuit is to be self-starting. This can be arranged either by an autobias resistor in the emitter circuit or by a fixed potential divider across the battery. The operating frequency is determined by a tuned circuit in the collector line and the tuning capacitance therefore includes shunt capacitances and also the temperature sensitive output capacitance of the transistor.

I made up a practical form of this circuit (Fig. 4) using components which were all full scale, except for the tuning coil which was wound into a small home-made pot core. Ferrite pot cores less than 1 cm. in diameter were not available and special units made up of powdered high-frequency core material and adhesive were used. Sufficient loop gain could be achieved to start oscillation using 100 turns of 40 s.w.g. enamelled wire in the collector line to 30 turns in the base line. The current drain was set at a mean level/

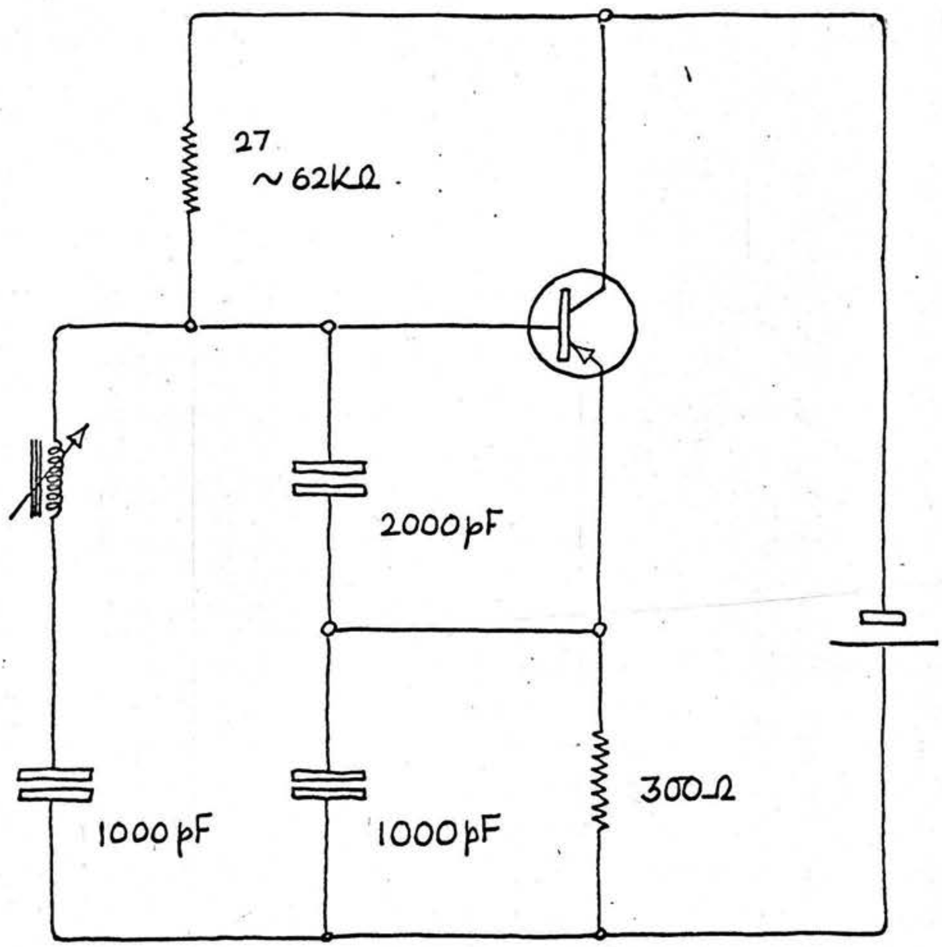

Figure 5

The Gouriet oscillator.

level of 0.65 mA's by means of the 12 KΩ resistor but the circuit appeared to be extremely temperature sensitive even at this low value. It did not appear promising and I did not carry out a complete miniaturisation of the circuit.

(ii) Hartley oscillator.

The other type of circuit prominent in the early reports uses a transistor analogue of the Hartley circuit in which feedback is provided by a tapped inductance. The practical form of this circuit that I made up (Fig. 4) could be made to oscillate at 450 kc/s quite easily. The windings were made on a thin paper former and 10% frequency modulation could be achieved by moving a small ferrite slug near the collector end of the coil. The collector to base turns ratio was 60 to 25. I again found that the frequency stability of the circuit with temperature was poor and changes of 30 kc/s or more could be induced by blowing gently at the components or by introducing the stray capacitance to a hand. A similar change could be obtained by reducing the supply voltage from 1.3 to 1.1 volts. Adjustment of the component values was carried out somewhat empyrically because of the interactions between the various components when physically smaller units were substituted to achieve a reasonably compact oscillator unit.

(iii) Clapp oscillator.

Neither of the first two circuits that I had tried showed either promise in performance or any practical advantages and I decided to use the slightly more complex, but stable, Gouriet circuit which is the transistor version of the Clapp circuit (Fig. 5). This circuit operates at a frequency slightly above the series resonant frequency of the tuning elements L and C, so that the series combination acts as a pure inductance and phase shift of 180° takes place/

place between the emitter and the base of the transistor. It is superior to the Colpitts type of circuit, which it resembles at this off-tune resonance, in that spurious changes in the values of the capacitors result in much smaller frequency shifts. Better frequency stability is achieved if the L/C ratio is high and C_1, C_2 are made as large as possible. Bias current is provided by a series resistor in the collector-base circuit and kept to a minimum its value varied from 27 KΩ to 62 KΩ with different transistors.

Comparative tests carried out by Scroggie on this and other types of transistor oscillator showed that the stability of this curcuit is exceptional (Scroggie, 1957). For a controlled ambient temperature rise of $1^{o}C$ the frequency decreased by about 0.05% or 250 c/s at 500 kc/s, and a 10% decrease in battery voltage caused the oscillator frequency to decrease by about 0.01% or 50 c/s at 500 kc/s. If full scale indication is obtained with 45 kc/s, that is if the transducer is capable of 10% modulation, these theoretical figures for the drift amount to less than 1%, but at the other extreme if the transducer only modulates the carrier 1% at the most, then the drift may cause about 6% error in the indicated level.

The Gouriet circuit has other practical advantages as well as its exceptional frequency stability in that it avoids the use of multiple windings and tapped coils. This is a particularly valuable feature because the coil and pot-core assembly is the most difficult of the circuit elements to miniaturise successfully.

2.4 Capsule construction

(i) Miniature components.

After these preliminary investigations using normal scale components

attempts/

attempts were made to produce a miniaturised version of the Gouriet circuit. The most serious of the immediate problems was the difficulty experienced in obtaining suitable small components. Small carbon resistors could be obtained fairly easily from hearing-aid manufacturers but the pot cores, transistors and capacitors proved to be something of a problem. Fairly satisfactory pot cores and capacitors were eventually made up from parts of larger components and standard Mullard OC45 and Ediswan XA104 transistors were removed from their protective casing and re-potted in opaque epoxy resins, without apparently impairing their performance. Three small oscillator units were eventually constructed using the home-made components potted in epoxy resins. Two of the units failed during the final stages of assembly due to untraceable faults but the third, although it did not modulate particularly well and started to 'ring' if it was held too long in the hand, was used in experiments with the casings.

(ii) The diaphragm.

I made many attempts to produce a pressure-sensing diaphragm integral with the outer Perspex casing that would flex sufficiently to modulate the oscillator unit that had been built, but it became clear that the stiffness of the plastic would require a thinner wall than could be machined consistently by even the most refined workshop techniques. In very thin sections Perspex becomes particularly vulnerable to fractures in the form of small cracks radiating from the points of maximum stress. It did not prove practicable to cement thin Perspex sheet to the outer casing because of the difficulties in obtaining a firm seal and keeping the solvent away from the thin section where it might etch the surface, thus making it liable to rupture under stress. The most satisfactory technique for producing consistent results would/

would be by some form of injection moulding, but I did not consider this further after being advised that it would require a complex and expensive former.

A search was made for a suitable form of bellows but without success. The larger manufacturers considered the small size impracticable and because the problem of protecting such a metal system from the action of digestive juices did not appear to have an easy solution either, the search was not carried any further.

(iii) Power source.

The power for the transmitter must be supplied from a source within the capsule. This could be either a primary cell or a storage type of cell. For straight forward experiments lasting up to about 50 hours, the simplest arrangement is to activate the transmitter just before it is to be used and to draw a current that will not exhaust the battery before the end of the experiment. A low current drain also reduces the temperature sensitivity of the transistor and steadies the voltage fall as the battery is drained. The Mallory RM312 cell appears to be particularly well suited to this type of application. It is a primary cell with a mercuric oxide depolarising cathode in an electrolyte of 35% potash. It is of robust construction with a crimped and hermetically sealed case of plated steel. There is no danger of leakage of the cell contents and it does not gas during discharge. Jacobson reported that one of these cells left unprotected in 0.1N hydrochloric acid for 12 hours formed no detectable mercury salts (Jacobson, 1960). It is readily available, has a long shelf life of 8 to 12 months and it is small with an excellent stored energy to volume ratio. It shows a favourable/

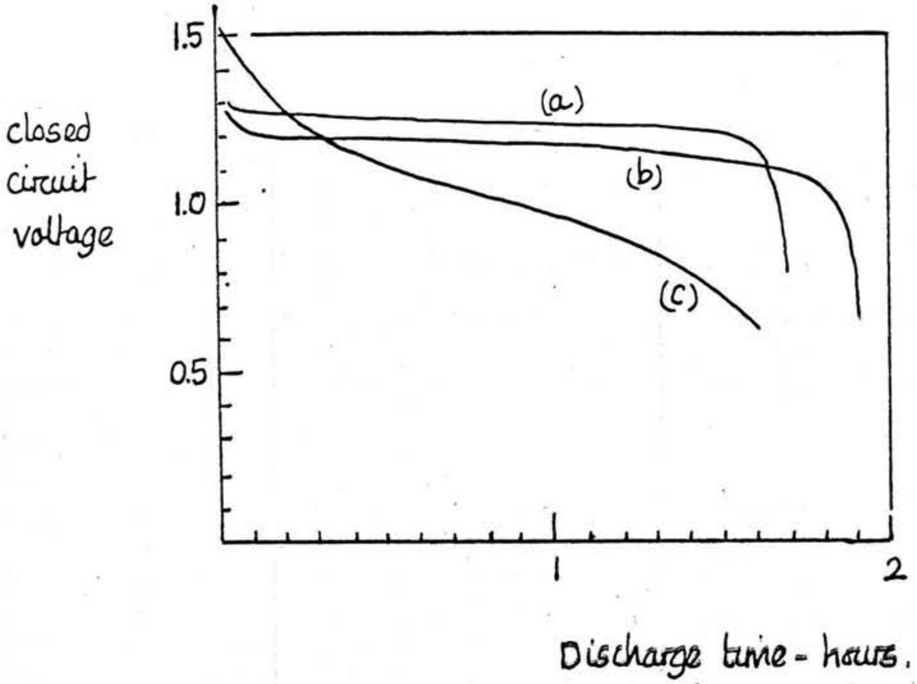

Figure 6

Discharge curves for three batteries of approximately the same size

(a) Zinc-mercuric oxide dry cell - RM.312
(b) Nickel-cadmium storage cell
(c) Zinc-manganese dioxide dry cell.

(from Jacobson 1960)

favourable drainage characteristic (Fig. 6) with an almost constant voltage on load.

Later it may prove possible to use circuits that enable the transmitter to be switched by apparatus outside the body from a steady state to normal oscillation. Intermittent use would effectively extend the active life of the capsule or enable transmissions to be made for similar periods over greater distances. Alternatively, at the price of additional bulk and complexity, circuits could be added so that the cell could be telecharged 'in situ' at some frequency different from that of the transmitter.

In March 1960, after I had carried out these preliminary experiments on both the transducer and the miniature oscillator problem I found that another group of investigators in this country lead by H. S. Wolff of the Bio-engineering Laboratory at the National Institute for Medical Research in London, had also been working on the production of a telemetering system for use in the alimentary tract. They had adopted similar mechanical and electronic designs to those I had envisaged. Exchanges of ideas and a pooling of the small components collected by them soon resulted in more rapid progress. Very small transistors and capacitors became available through their contacts and 6 mm. ferrite pot-cores were imported from Germany. An important decision had to be made as to whether the capsule was to a rugged and very accurately finished instrument which would be recovered and used many times over, or whether it was to be made very economically so that it might be expended after a single experiment or investigation. Clinically the latter alternative would be preferable if it could be made economically feasible and if the battery life could be made sufficiently long to allow adequate testing of the instrument without losing a large proportion of its useful life.

In/

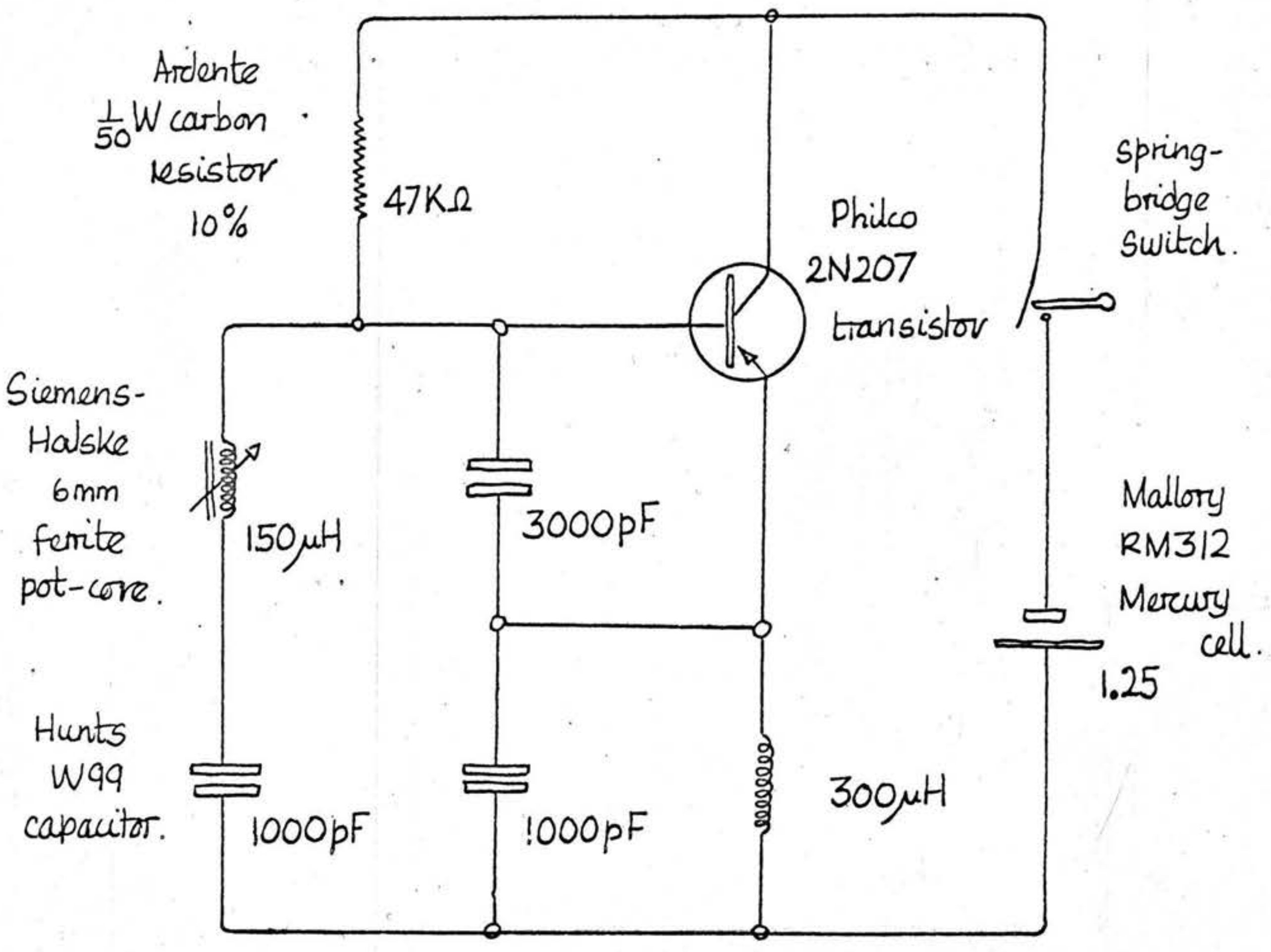

Figure 7

Wolff's prototype design for the capsule circuit

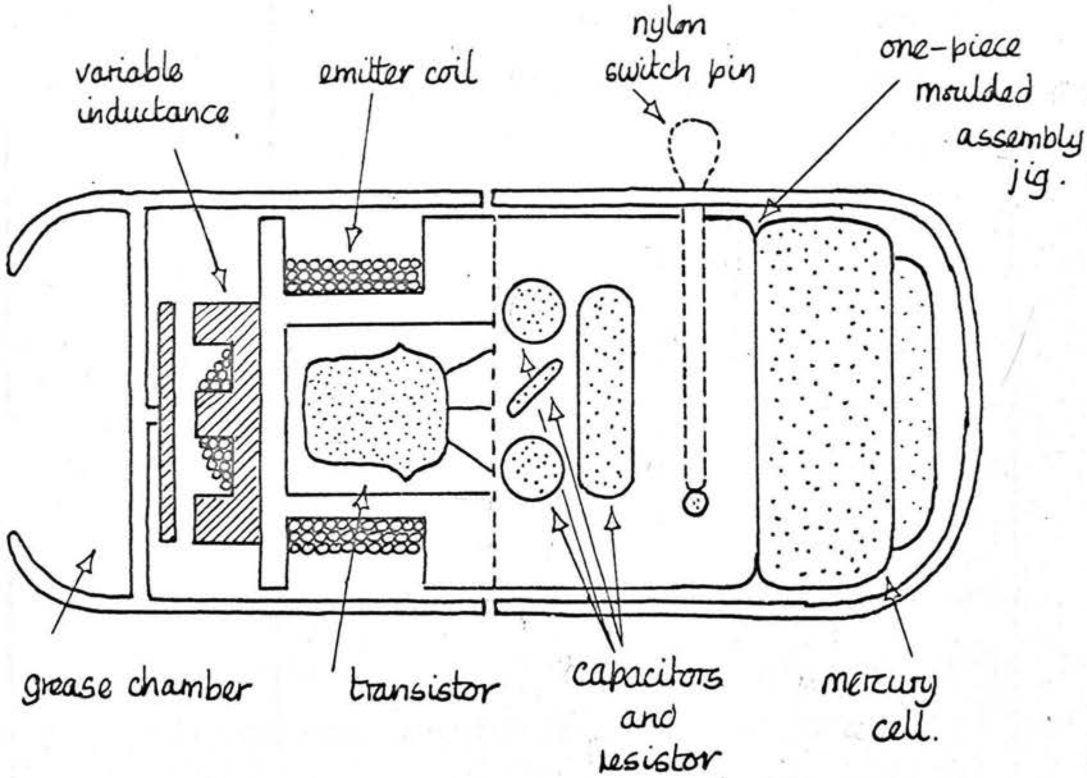

Figure 8

The mechanical design of the Solartron pressure capsule.

In consultation with the other interested groups in this country it was decided that the clinical value of this new technique could best be assessed if the capsule became available in large numbers and of a reasonably constant quality and performance. Subsequently Wolff's group, which had the most advanced system in the country at that time, approached the Solartron Electronic Group, which specialises in the production of very small transducers, with their capsule design which is based on the Gouriet circuit (Fig. 7). This could be made up using readily available components and it was hoped and expected that it could be produced cheaply and in large quantities. There are obvious advantages in using a cheap, commercially produced, capsule once the technical problems of mass-production had been overcome so no further investigations were made into the problems that had been encountered even though a considerable period of this first year's research had been spent in developing the special techniques of miniature electronic circuits, and the associated mechanical methods.

Some time had been spent in developing a reliable switching arrangement which would enable the capsule to be sealed completely after construction. It is difficult to get an effective mechanical action at this magnitude and experiments were made with magnetic and mechanical fly-over arrangements but no useful result materialised until a simple shorting arrangement was constructed which gave good results and appeared to be mechanically reliable. A rotating Perspex plate with a shorting segment of platinum foil cemented to it was held firmly against two platinum contacts exposed at the back of the capsule casing by a small Perspex clip cemented round the periphery of the capsule. The capsule could be switched simply by rotating this plate with a pair of forceps. The first capsules were produced by Solartron/

Figure 9

The Solartron pressure capsule:

left - switched 'off' with nylon pin in position.
right - switched 'on'. The pin has been removed and the case sealed with polyester tape.
Below are shown the components used in the circuit.

Solartron late in 1960 at a sale price of £5.10s. each.

2.5 The Solartron capsule.

(i) General description.

The capsule is a rigid cylindrical shape 2.5 cms. long, 0.88 cms. in diameter. It weighs 2.2 gms. and has a specific gravity of 1.45. One end of the Perspex case forms the pressure-sensing diaphragm. A small stalk at the centre of this diaphragm carries a light ferrite disc which moves towards the tuning coil, wound inside an adjacent ferrite pot-core, when external pressure changes cause the diaphragm to flex. This changes the inductance of the coil and hence modulates the frequency of the transmitter. The stiffness of the diaphragm thus determines the frequency shift for a given pressure change. A typical capsule with a diaphragm 0.2 mms. thick, would be set with an air gap between 0.2 and 0.3 mms. and a pressure of 100 cms. of water will shift the frequency about 6% or 25 kc/s. Even using production line methods there is still a widespread in the sensitivities of the capsules and maximum frequency shifts may vary between 10 kc/s and 40 kc/s. The response of the receivers to this frequency shift can be adjusted to accommodate these divergencies but the effects of spurious drifts are changed in the same proportion. Temperature effects are generally more serious when an insensitive capsule is used.

The reference pressure, which is that pressure at which no force acts on the diaphragm, is equivalent to the pressure of the air trapped inside the capsule at the time when it is sealed. To allow for possible changes in atmospheric pressure after manufacture, a small hole is left in the outer casing. This may be blocked and sealed with a strip of polyester tape which is not affected/

Figure 10

The calibration system -

a closed vessel, a sphygmomanometer bulb and a simple water manometer.

affected by the digestive juices (Fig. 9). Use is made of this hole during the shelf-life of the capsule to accommodate a removable nylon 'pin', which holds open a spring contact in the battery supply circuit enabling the battery contacts to be firmly welded during manufacture.

(ii) Characteristics.

In the earliest capsules the transmitter 'life' was extremely variable, sometimes being as short as 20 hours, which made it difficult to carry out adequate tests on their performance. Progressively improvements in reliability have been made by the manufacturers and the latest versions generally last between four and five days.

Before each experiment the capsules are slowly warmed to body temperature and allowed to stabilise for about an hour in a temperature controlled water bath, until they reach complete thermal equilibrium. This precaution also ensures that the battery voltage is run down to the beginning of its 'plateau' value (Fig. 6) before calibration. The capsule is calibrated either in a closed vessel (Fig. 10) against a simple water manometer or by progressive immersion to a depth of 70 cms. in a long water-filled glass tube. Over the range 0-70 cms. of water the linearity of the response curve is usually acceptable, rarely deviating by more than 5% of the true linear value. In most clinical investigations a constant error of this magnitude in the measured height of the peaks may be neglected and an individual calibration curve for each capsule always allows more accurate measurement.

(iii) Frequency stability.

Initially Wolff found that capsules which were perfectly stable in air, developed a serious long-term frequency drift as soon as they were immersed in water. This was eventually traced to the action of water on the surface/

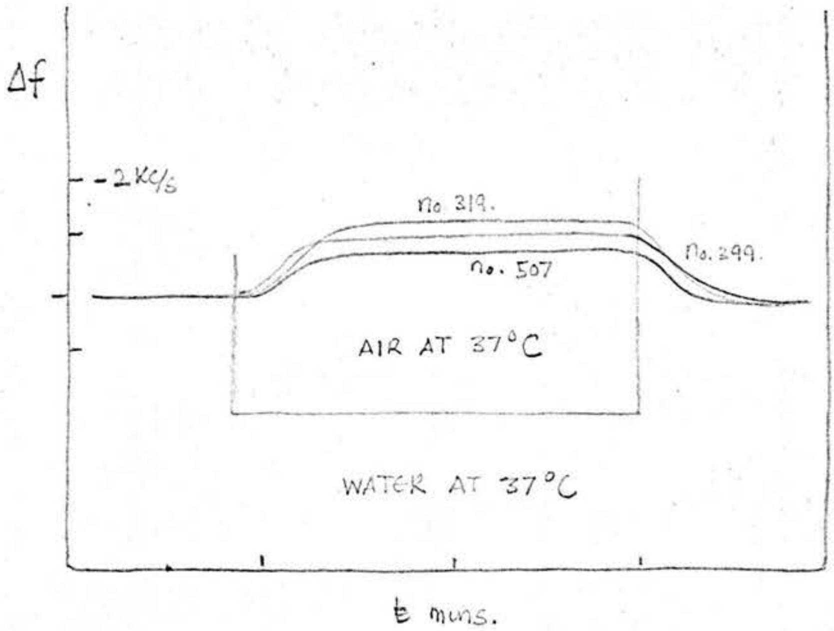

Figure 11

The short-term effect on the basal pressure level when the surrounding medium is changed from water to air at the same temperature.

surface of the Perspex causing a small dimensional change and consequent buckling of the diaphragm. The diaphragm is protected during routine use by a layer of silicone grease held in a chamber at the sensitive end of the capsule (Rowlands and Wolff, 1960).

Besides this absorption effect, unwanted frequency changes can arise in three ways; (a) from a change in the dielectric nature of the surrounding medium, such as might occur when the capsule passes into a large bubble of gas trapped in the intestine; (b) from a change of voltage due to an intermittent circuit fault or as the cell voltage falls during operation; (c) from a change of ambient temperature due either to normal body temperature fluctuations, a pathological condition of the bowel such as enteritis, or possibly from the ingestion of hot or cold food materials.

(a) Wolff's prototype capsules on which the Solartron capsule is based, had the oscillator components completely enclosed in a second coil of about 300 μH which was part of the emitter circuit. This performed a double function, acting both as an unscreened radiating coil and as an electrostatic screen. With this arrangement it was reported that changing the surrounding medium from air to water only changed the frequency by 10 c/s at 500 kc/s. (Rowlands and Wolff, 1960). The Solartron capsules are not shielded in this way and small frequency increases occur when the capsules are immersed in water (Fig. 11).

(b) The variation of frequency with battery voltage should be of about the same magnitude as that reported by Scroggie for the Gouriet circuit, that is about 50 c/s for a 10% voltage drop perhaps varying slightly with the production spread in the quality/

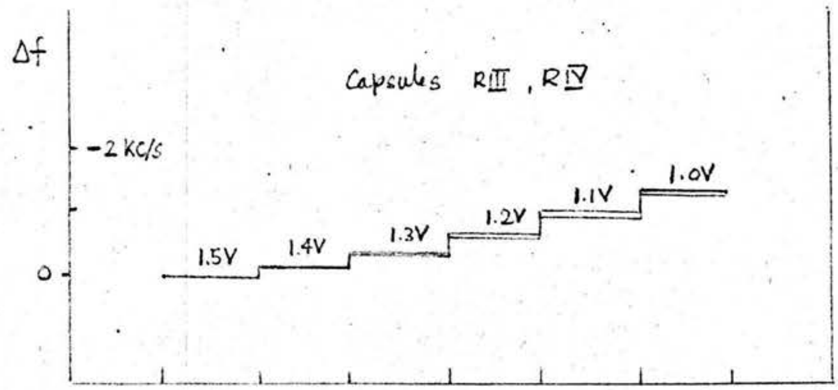

Figure 12

Variation of frequency with battery voltage in two capsules.

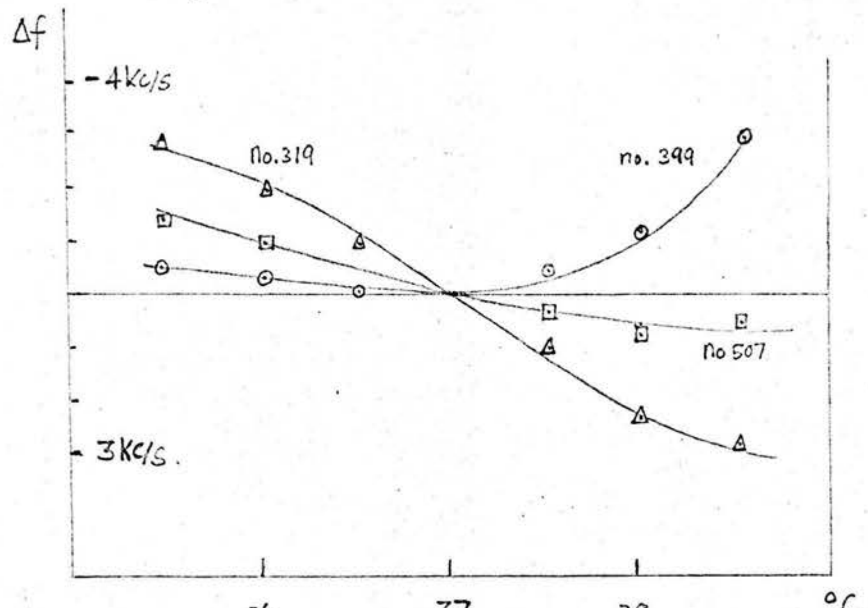

Figure 13

Temperature characteristics of three typical capsules.

quality of the transistors. Typically the frequency of the transmitter decreases with a falling supply voltage which makes the indicated basal pressure level appear to rise. The changes are usually greater in magnitude than the amount which might be expected from Scroggie's figures (Fig. 12). This is perhaps due to a change in the impedance of the battery during discharge. The 'supply line' voltage from the Mallory cell drops from 1.3v to about 1.25v over the first thirty minutes and then remains virtually steady until very near the end of its 'life' when it falls rather quickly from about 1.2v (Fig. 6).

(c) A change in the ambient temperature of the capsule may affect the frequency of the oscillator in three ways - by changing the pressure of the small volume of air trapped inside the capsule, so that the basal level falls with a temperature increase, - by changing the characteristics of the transistor; the basal level rises with a temperature increase - by changing the values of the other circuit components. The latter effect is unpredictable depending on the individual capsule constructions; all the components in the Solartron capsule are mounted either on Perspex formers or in a Perspex jig and differential stresses may well occur because the linear coefficient of expansion of Perspex is nine times that of steel.

The first two effects are of opposite sign so it should be possible to balance the effects over a small temperature range if the effect of the air expansion/

expansion is greater than that due to the transistor. This could be done by injecting a small amount of a light but non-volatile liquid to displace a little of the enclosed air. The temperature characteristics of three randomly selected capsules are shown in Fig. 13.

From a total of 40 capsules swallowed, 14 were recovered within their 'active lifetime' and were tested before the battery ran down completely. This low proportion is due to the rather short 'active lifetime' of the earlier capsules and the length of some of the later clinical experiments. Of the 14 recovered, 1 had leaked through a faulty casing, 4 had drifted more than 10% of the original nominal frequency and 9 had remained apparently steady. It was re-assuring to find that in all, except two of the recovered capsules, the dynamic characteristics had changed little by the end of the experiment, showing that even though the absolute basal pressure level may not have been reliable, the short phasic pressure changes had been recorded accurately.

A number of capsules were dismantled and re-batteried, some several times, because there were periods when the commercial capsules were in short supply. A limited number of these 'salvaged' units were used for experiments where the capsule was placed directly into the small bowel at operation. They generally performed satisfactorily for a number of experiments before they either failed completely through untraced faults, or until they drifted out of the frequency range of the receiver.

2.6 Electrical output transducers.

In order to incorporate transducers with electrical outputs such as pH-indicating glass electrode systems, into capsule-transmitters, several other workers developed a new form of the oscillator circuit which would result in frequency modulation at 450 kc/s.

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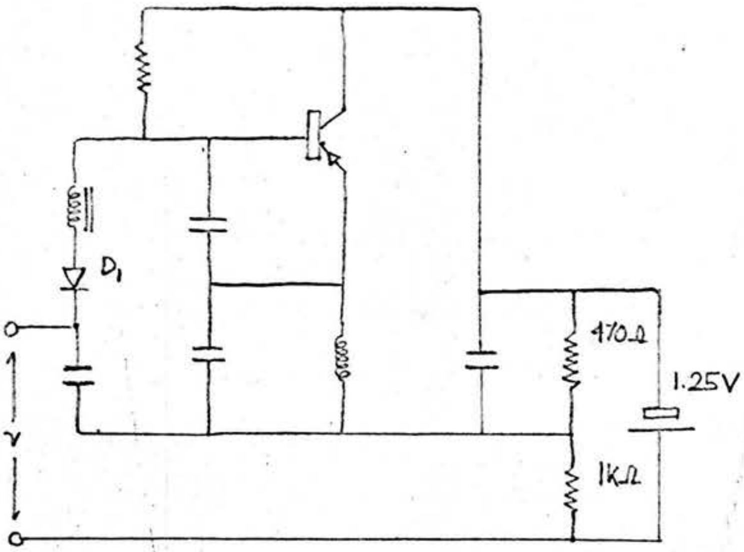


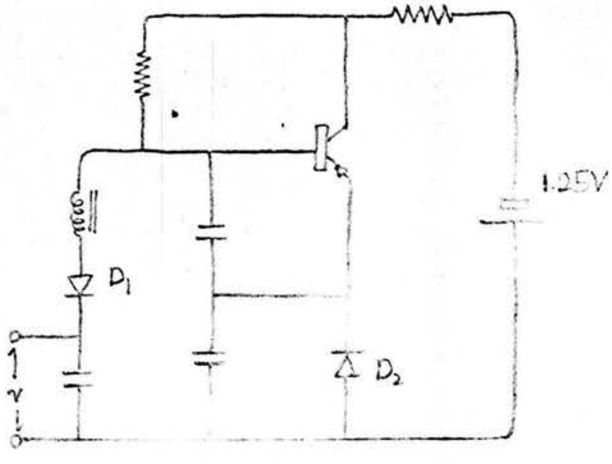


Figure 14

Two versions of Wolff's oscillator circuit which is frequency modulated by a small voltage.

The glass electrode-reference electrode system can be regarded as forming a cell which produces an electromotive force of between 0.05v and 0.5v, depending on the pH of the fluid in the system. The cell has an internal resistance of between 10 and 30 MΩ, which is very temperature dependent, so for accurate measurements the input resistance of the detecting circuit should be large in comparison. Wolff has described a very effective method of producing accurate modulation from these transducers using voltage-sensitive capacitors (Wolff et al. 1962). A silicon junction diode is biased in the non-conducting direction by a potential divider so that the transducer voltage appears in series with the bias (Fig. 14). The voltage-sensitive diode (D_1) is biased in the non-conducting direction by the voltage drop across a second diode in the emitter circuit. The sum of the voltage drop across this diode and the base-emitter voltage of the transistor is about 0.75v. The diode is of the Zener type, so that neither of these voltages is very dependent on the current flowing through the circuit, and the bias, which regulates the nominal frequency, is relatively independent of the battery voltage. The radio-frequency voltage across the diode should not drive it into conduction so the oscillator must not be allowed to develop large voltage swings in the resonant circuit. This can be limited by running the transmitter from a low voltage obtained by putting a limiting resistor in series with the power supply (Wolff et al. 1962) although this obviously limits the radio-frequency output from the transmitter.

The only current drawn from the electrode system is the reverse leakage current of the diode. This is about 3×10^{-7} milliamps which is sufficiently low to make the variation of electrode resistance unimportant.

CHAPTER 3

External detecting equipment

3.1 Principles of the transmitter-receiver coupling.

(i) Nature of the electromagnetic field.

There is a continuous distribution of electromagnetic energy in the space surrounding a resonant oscillating circuit. A part of this energy, constituting what is known as the inductive field changes direction and returns to the circuit during every cycle of the oscillation. The strength of this field falls off inversely as the square of the distance from the coil of the circuit. The remainder of the distributed energy constituting the electromagnetic radiation from the circuit becomes completely detached from the source. The strength of the latter field falls off inversely as the distance from the circuit, and it can be shown that the two components are of equal magnitude at a distance equal to the wavelength of the oscillations divided by 2π. The wavelength of oscillations at 450 kc/s is approximately 666 metres, so this distance is about 100 metres and using a transmitter - receiver link of less than a metre it is therefore the inductive field which must be considered. Under these conditions a simple antenna loop acts in the same way as the secondary winding of a loose-coupled radio-frequency transformer. The voltage induced in the coil by the flux of the 'primary coil' in the capsule depends on three factors:

(a) the ratio of the 'secondary' to the 'primary' turns.

(b) the Q-factor of the antenna or 'secondary'loop.

(c) the coefficient of coupling between the two loops.

The flux generated by the capsule transmitter varies directly with

the/

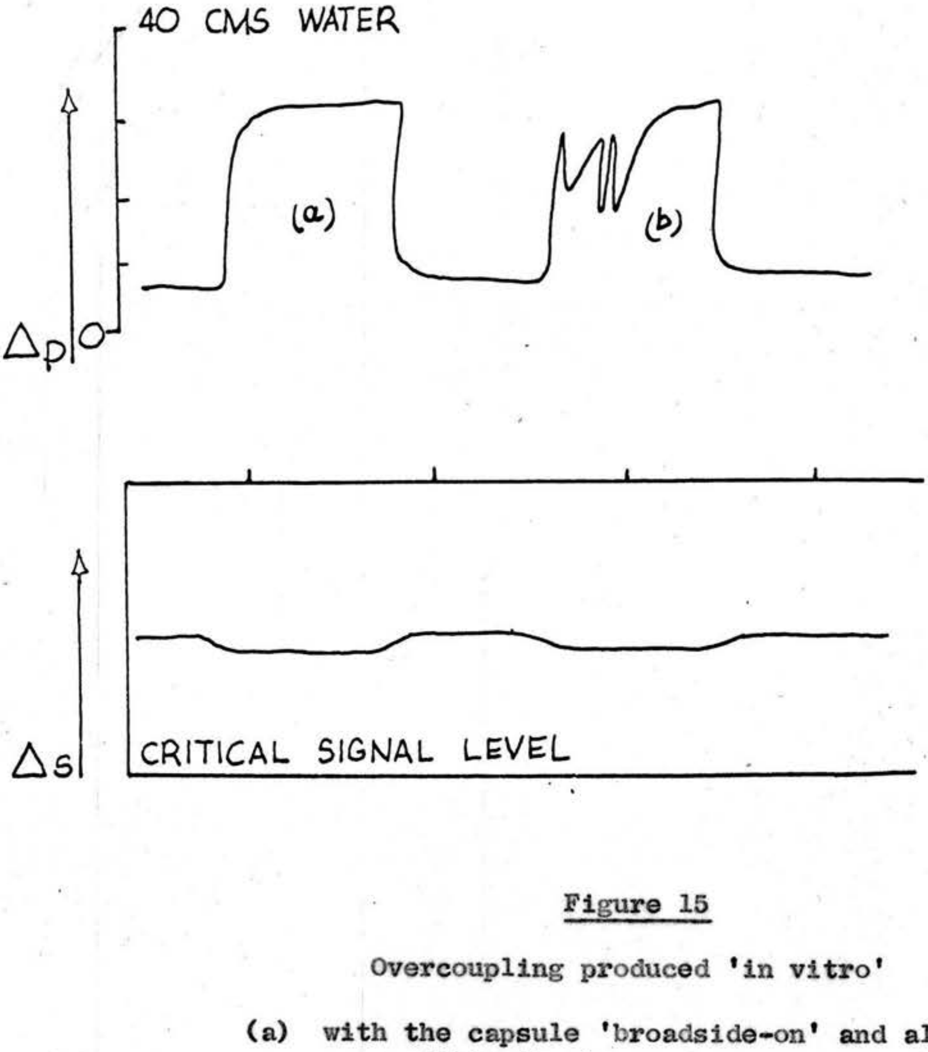


Figure 15

Overcoupling produced 'in vitro'

(a) with the capsule 'broadside-on' and almost within the loop.

(b) with the capsule 'end-on' and about 9 cms. from the loop.

the voltage of the oscillator supply and the Q-factor of the resonating circuit components. The antenna loop will be tuned by self capacitance in the loop and the input capacitance of the receiver; so some extra variable capacitance must be added to tune it to the nominal frequency of the capsule transmitter, which may vary between 400 kc/s and 500 kc/s. To provide a bandpass of about 50 kc/s the Q-factor of the input circuit is reduced by winding the antenna loop from resistance wire.

The coefficient of coupling which is proportional to the ratio of flux linking the coil in the transmitter circuit and the antenna loop, to the total flux generated, is dependent on the geometry and the relative positions of the two coils. It is generally stated that the sensitivity of a loop antenna is directly proportional to its area, but this is not true when the loop is so close to the dipole source that voltages of comparable magnitude and opposite phase are induced from the opposite 'poles'. The best value for the ratio of the two diameters, determined empyrically, appears to be between five and ten to one.

(ii) Overcoupling.

If the coupling coefficient becomes greater than about 0.5, the transmitting and receiving loops become closely linked and there is a sharp rise in the basal level, corresponding to an apparent drop in the nominal frequency of the capsule transmitter (Fig. 15). The change is always a frequency decrease and appears to be always of the same magnitude for each capsule, generally between 20 and 35 kc/s. The modified signal is still modulated by the pressure transducer in the capsule and phasic pressures can still be recorded. Experiments with no intervening materials show that this effect is only seen when the capsule is within a cone-shaped volume of altitude about 10 cms., based on the aerial coil; and it is probably the result of a very large signal from the input stages of the receiver pulling

the/

the frequency of the main oscillator. In practice it is not a troublesome feature because it can usually be seen to be a function of the loop position and it is useful when it occurs because it provides one method of locating the capsule fairly precisely within the body volume. It is most commonly seen when the capsule happens to be lying 'end-on' to the surface of the body in a patient with a thin abdominal wall.

(iii) Coupling geometry.

As the capsule makes its way through the alimentary canal its attitude to the axis of the antenna loop is continually varied. Changes in position and orientation occur however, not only as the capsule is moved onward along the tract, but also as a result of the capsule lying against the lower surface of the organ where it may be 'rocked' by shallow muscular contractions that do not completely close the bowel, or by movements transmitted through the bowel wall from other active organs within the abdomen. Expressions for the spacial relationships would be complex because the dipole axis and the antenna axis do not necessarily intersect in space, and the angular parameters would be further complicated by the inhomogenous nature of the dipole field; a theoretical analysis of the situation has not been attempted. In simple terms, for each particular position in space, the coupling is greatest when the number of flux lines threading the antenna loop is a maximum. The magnitude of the changes in signal strength resulting from changes in the coupling, cannot be used to deduce the amount of capsular movement, but under certain conditions the regularity of these changes and relative amplitude values can be clinically significant. The particular applications of these statements will be described later in Chapter 5.

It is not desirable to have to continually re-adjust the position of the antenna loop when the capsule assumes an orientation where insufficient signal/

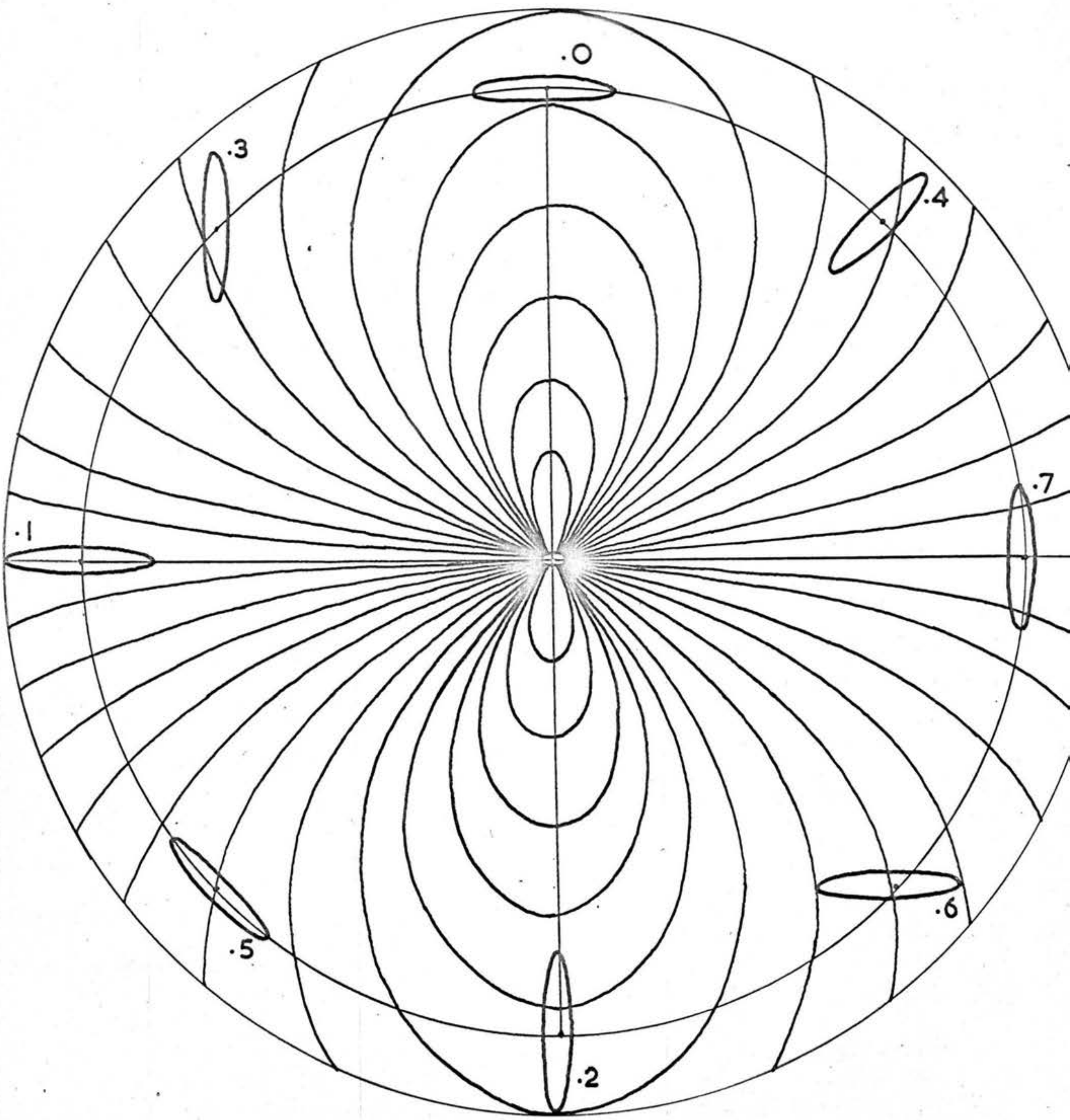


Figure 16

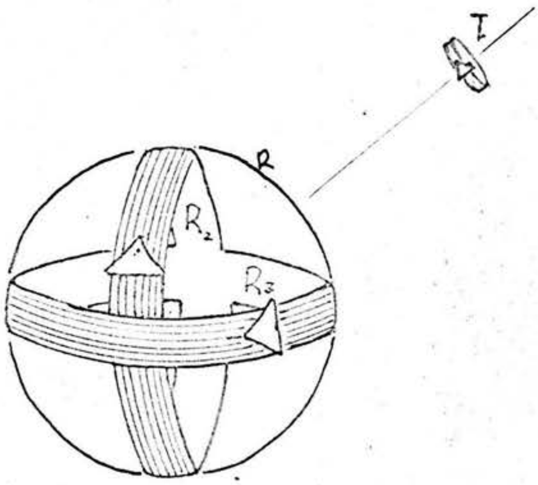
The distribution of flux around a magnetic dipole. Approximate values for the relative signal strengths are shown at different positions and orientations.

signal is intercepted. The receiving equipment requires a certain minimum amount of signal in order to produce an undistorted output and an antenna system without the directional sensitivity of a simple loop would be convenient for completely automatic recording.

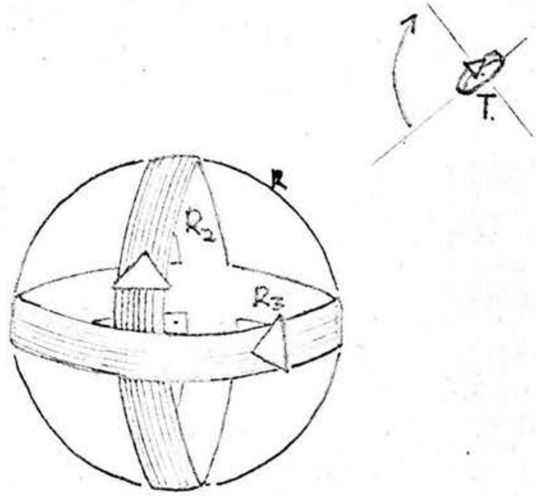
3.2 Non-directional antenna systems.

It is possible to construct antenna systems using three mutually perpendicular co-centred loops with characteristics such that changes in signal strength resulting from orientations of the capsule are minimised. Mackay has suggested that the inhomogenity of the flux distribution (Fig. 16) is such that two loops would be adequate, provided that their axes do not intersect (Mackay, 1960), but this seems to be difficult to justify on theoretical arguments alone and no one has reported using a two-loop antenna with non-directional characteristics.

An obvious and simple approach is to orientate several loops around the abdomen and to switch either manually or electronically to that loop which is receiving the most steady level of signal. The switching interval during which the signal is lost can be made very short and I have relied on simple manual switching between four loops. Although this switched loop system appears to be the most satisfactory from the theoretical arguments, we have persisted in using a simple manual switch for the clinical experiments, because of the technical complexity of adding a reliable electronic or mechanical switch to the receiver and the constant pressure of the clinical experiments which require a reliable instrument. Three mutually perpendicular, co-centred loops connected in series to the input of the receiver, do not unfortunately form a system which shows omni-directional sensitivity. Consider for instance the special case where the capsule turns in the plane of one of the loops (say loop/



Loops R_2 R_3 in the same sense as the transmitting coil T



If T is rotated through 90° the loop R_2 is still in same sense as T, but loop R_3 is now in the opposite sense to T.

<u>**Figure 17**</u>

The directional property of two antenna loops in series.

loop R, Fig. 17), so that we need only consider the effect on the two loops R_2 and R_3. If the two loops are connected so that at the first position where the induced voltages are of approximately equal magnitude, they are in the same phase and the resulting compound voltage is simply the sum of the two values - then at a second position, after the capsule has been rotated through 90° where the induced voltages are again of approximately equal magnitude, they will be out of phase because the sense of one of the receiving loops (R_3) has changed with respect to the sense of the transmitting coil (T). If the capsule transmitting coil were rotated in this plane through a complete turn of 360°, the resulting compound voltage from the antenna system would go through two maximum values and two very small values. A similar directional effect results from a system of three co-centred loops.

(i) Frequency doubling.

To obtain a compound antenna which does not show the 'null' positions seen with series connected loops a circuit arrangement must be used which will produce the same output even after a phase reversal on one of the loops due to the directional effect. If the alternating voltage induced on each loop is fed through a frequency doubling circuit so that the negative and positive peaks lose their identity, the compound voltage resulting from summing these voltages in a resistive adding circuit never falls to zero. This operation is virtually the same as squaring and adding the three mutually perpendicular components of the field at any point in space since

$$\cos 2wt = 2 \cos^2 wt - 1$$

Unfortunately the proper action of non-linear elements such as might be used in the frequency doubling circuits would require considerable amplification of the signal on each loop.

(ii) .../

(ii) Multi-channel antennae.

If seperate amplifiers must be introduced into each of the three channels to overcome the phase effects, it would be just as simple to use the direct outputs from discriminators in each channel. The output would never fall to zero during turning movements of the capsule, but the output from each channel would require some form of output clamp so that a 'peak-riding' rather than an averaging system was the result.

(iii) Switched antennae.

A third way to use the three loop antenna would be to connect each of the loops to the receiver input for a short period of time. It is practicable to do this electronically when the modulation frequencies are low, as they are in most gastro-intestinal applications, but the possibility that a working level of signal may be detected on only one or two of the loops restricts the overall response to the higher frequencies. A transient pressure change which rises and falls during the period that two loops without any incident signal are connected to the receiver, represents the theoretical frequency limit of the antenna system. Pressure changes occurring at a frequency lower than this limit may be distorted by the switching, but changes occurring at a frequency above the limit may be completely undetected. The limit frequency (f_{limit}) is related to the rate at which each antenna is switched on (f_{switch}) in the following way.

If one loop is blank $f_{limit} = 3\, f_{switch}$

and if two loops are blank $f_{limit} = \frac{3}{2}\, f_{switch}$

This follows because if each one of the three loops is connected to the receiver for t seconds, that is if the scanning frequency is $\frac{1}{3t}$ c/s, and two of the loops are without incident signal, then the longest transient change which can be fitted into this period of 2t seconds has a frequency of/

of $\frac{1}{2t}$ c/s. Therefore

$$f_{limit} = \frac{3}{2} f_{switch}$$

Clearly if only one loop is 'blank' the transient must rise and fall twice as quickly in order to be completely undetected, and limits for harmonics of symmetrical bi-phasic changes will be half these values for unsymmetrical transient changes.

3.3 Receiving systems.

Although the characteristics and technical requirements of different receiving systems vary depending on features such as the way the antenna picks up signal, there are certain general observations which can be made about its design.

(a) The receiver should show good sensitivity so that small radiated powers may be detected from the capsule transmitters.

(b) It should be relatively insensitive to large changes in the level of signal at the input because the distribution of energy around the transmitter is not homogeneous, even as seen by a non-directional antenna.

(c) It should be equally responsive over a wide frequency band, sufficient at least to accommodate frequency deviations up to 10%.

(d) It should remain sufficiently selective to provide reasonable signal to noise ratio in the chosen frequency band.

(e) The complete system should respond to modulation frequencies at least up to 20 c/s.

(f) If changes with very long time constant are to be studied, the receiver must have exceptional frequency stability.

Considered/

Considered together, these requirements are quite different from those for conventional radio-receivers, especially in that a broad working bandwidth and good sensitivity are generally incompatible design features. Four basic types of receiving system are reported to have been used with capsule-transmitters.

(i) Cycle-counting systems.

These circuits are both simple and sensitive and they respond to changes well above the frequency of those encountered in most physiological applications. They can be made to operate at either audio or low radio-frequencies so they are commonly used with a tuned radio-frequency amplifier and oscillator in a simple heterodyne system or in a supersonic heterodyne (super-het) arrangement. Although a super-het can produce a good signal to noise characteristic, the narrow bandwidth of a tuned intermediate frequency strip restricts the maximum frequency deviation to 1 or 2% unless some form of automatic tuning is also employed. Broad-band amplifiers show a poor signal to noise characteristic and both of these conventional systems are limited by a poor long-term stability associated with the local oscillator circuit, unless additional drift-control circuits are used.

(ii) Frequency-correction systems.

A super-het receiver can be modified so that a servo loop with a fast response continually tunes the input stage to the signal frequency by a feedback voltage controlling the local oscillator. This 'correction voltage' which varies with the frequency excursion of the transmitter forms the useful output of the system. Provision must also be made for the oscillator to undergo an automatic frequency sweep if the signal is momentarily lost. The additional circuitry of the feedback and the automatic sweep arrangement means that the system becomes very complex and it still shows the long term drift associated with/

with the basic unit which is a standard radio receiver. Good selectivity is obtained together with a wide band characteristic and modulation frequencies up to about 1,000 c/s can be easily followed.

(iii) Scanning systems.

The unconventional requirements of the receiving equipment for capsule transmitters can best be achieved in specially designed panoramic receivers. These may be built around a bank of sharp-tuned filters which are swept across the operating band of the transmitter by voltage-sensitive capacitors or they may be based on a sharp-tuned heterodyne system with an oscillator and input stage that can be swept in the same manner as the filters. In both cases the voltage at which response occurs is a measure of the frequency deviation. This may be measured by a horizontal slit in front of a camera observing an oscilloscope trace or by a voltage sampling arrangement triggered by the pulse passed through the sharp-tuned circuits at the transmitter frequency.

(iv) Digital frequency meters.

If discrimination against other signals can be made by keeping the receiving antenna close to the transmitter, very accurate frequency determinations may be made using digital counter circuits that respond directly at radio-frequencies up to about 10 Mc/s. These meters may be used for calibration spot checks or in applications where information is required only intermittently.

3.4 <u>The detecting equipment.</u>

(i) Design and construction.

At the beginning of the work when the design of the receiver was first considered it was not known how serious the problem associated with movements/

Figure 18

The first version of the detecting equipment.

A single channel pen recorder is on the right of the receiver, beneath is the single loop antenna.

movements of the capsule within the bowel was likely to be and a simple loop antenna was adopted to pick up the radio signal. Best results were obtained using 35 turns of 32 s.w.g. enamelled copper wire mounted in a 4" diameter plastic former (Fig. 18). The relatively fine wire gave a Q-factor sufficiently low at 450 kc/s to pass 100 kc/s without serious attenuation of the signal. The centre of the pass band could be moved over the range 400 - 500 kc/s by adjusting a 500 pF variable capacitor.

The carrier signal, after being passed through a two-stage RC-coupled amplifier was mixed with the output from a reaction-type oscillator so as to change the nominal450 kc/s centre frequency to an intermediate frequency of 1,600 kc/s. The maximum possible frequency deviation in the carrier signal of about 10% is reduced to less than 3% at the higher frequency enabling transformer coupling to be used in the I.F. strip, and the higher frequency is easier to reject in the filtering necessary before the discriminator circuits. Filters that would pass the 100 - 200 kc/s band and reject 450 kc/s would be extremely complex but with a frequency of 1,600 kc/s the situation was much better and a simple low-pass circuit was sufficient. At 210 kc/s the filter output was reduced 6 decibels (dB's) and at 330 kc/s it was reduced 20 dB. The amplified signal was mixed with the output of a second oscillator producing a second nominal supersonic frequency of 150 kc/s, filtered and then passed through an overdriven amplifier stage which acted as a low-level amplitude limiter.

A simple pulse-counting type of discriminator, consisting of a diode pump and a pulse integrating circuit, was used to produce a voltage output proportional to the frequency deviation. This controlled a valve voltmeter circuit which was used to drive a standard pen recorder. Both the sensitivity and the linearity of the discriminator depend on the values of/

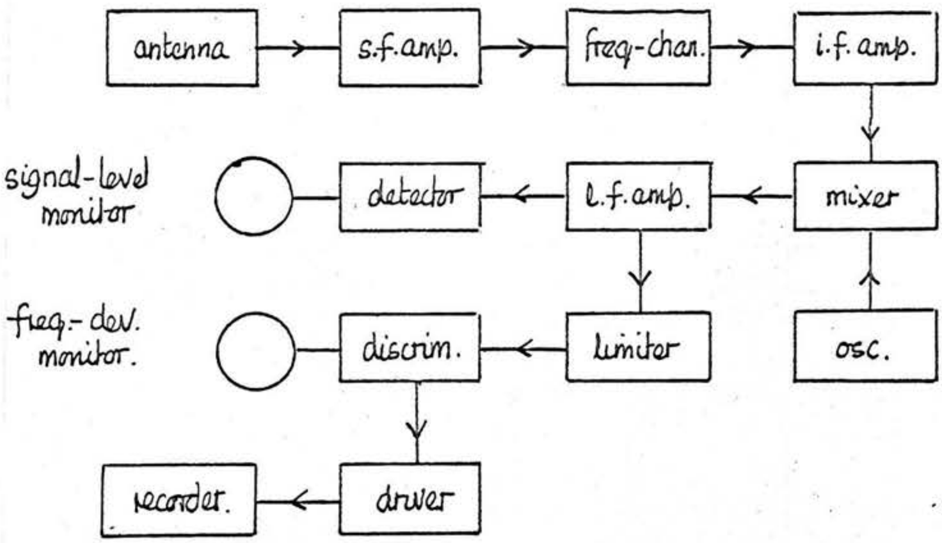


Figure 19

A block diagram of the first version of the detecting equipment

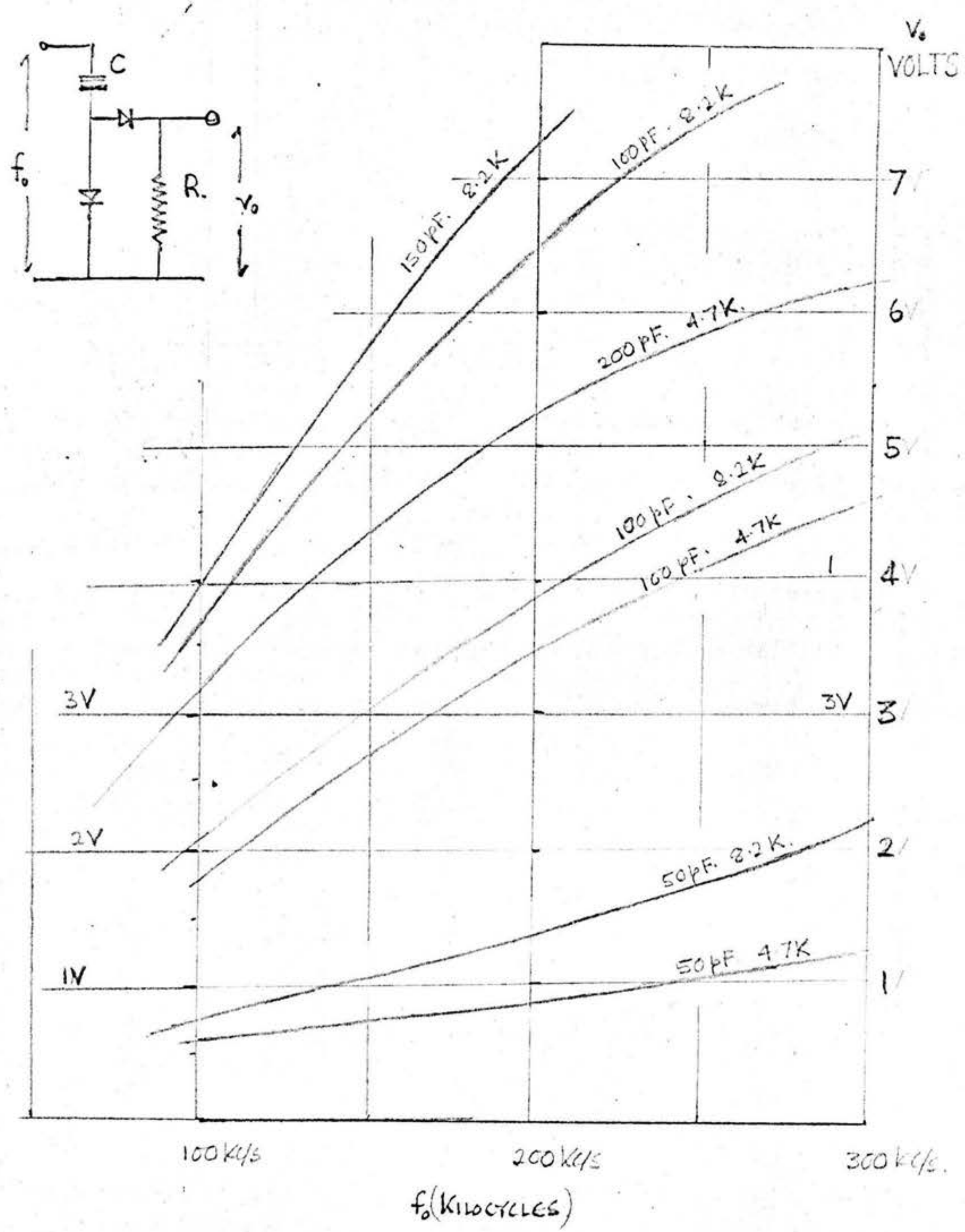


Figure 20

The voltage response obtained using different combinations of component values in the diode pump discriminator.

of the resistance and capacitance chosen for the diode pump circuit. I found that a centre frequency of 150 kc/s could be conveniently obtained from the filter after the amplifiers, and at this frequency good linearity could be obtained using values of 8.2 KΩ and 150 pF (Fig. 20). A change of 1 milliamp is obtained for 15 kc/s swing and this can of course be reduced for more sensitive capsules by including series resistance in the output circuit. There are no sharp bends in the characteristic, so only slight distortion is introduced into the output. Other more conventional discriminators were found to be unsuitable for this application; the Round-Travis circuit using two tuned circuits does not have a good wide-band characteristic; the ratio-detector is more sensitive but it is also very sensitive to amplitude variations, whereas a Foster-Seely discriminator is stable with respect to amplitude changes, but does not have such a good wide-band characteristic as the pulse-counting type. It requires a similar threshold level of signal to the pulse-counter which needs about 2 volts r.m.s. signal.

An examination was also carried out on the change of signal level tolerable before the error in the indicated frequency becomes serious. It was found that there was an ambiguity in the indicated frequency which increased with deviation from the nominal frequency of 150 kc/s. It reached a maximum of 6% error at the maximum anticipated frequency deviation of 45 kc/s if the signal level was increased from 2 volts r.m.s. to 20 volts r.m.s. This represents the maximum possible error in the discriminator under the worst conditions of change in signal strength.

With this ambiguity in mind and because the response of the pulse-counter falls off very quickly below this value, a signal level monitor indicating the actual signal passing into the discriminator was included in

the/

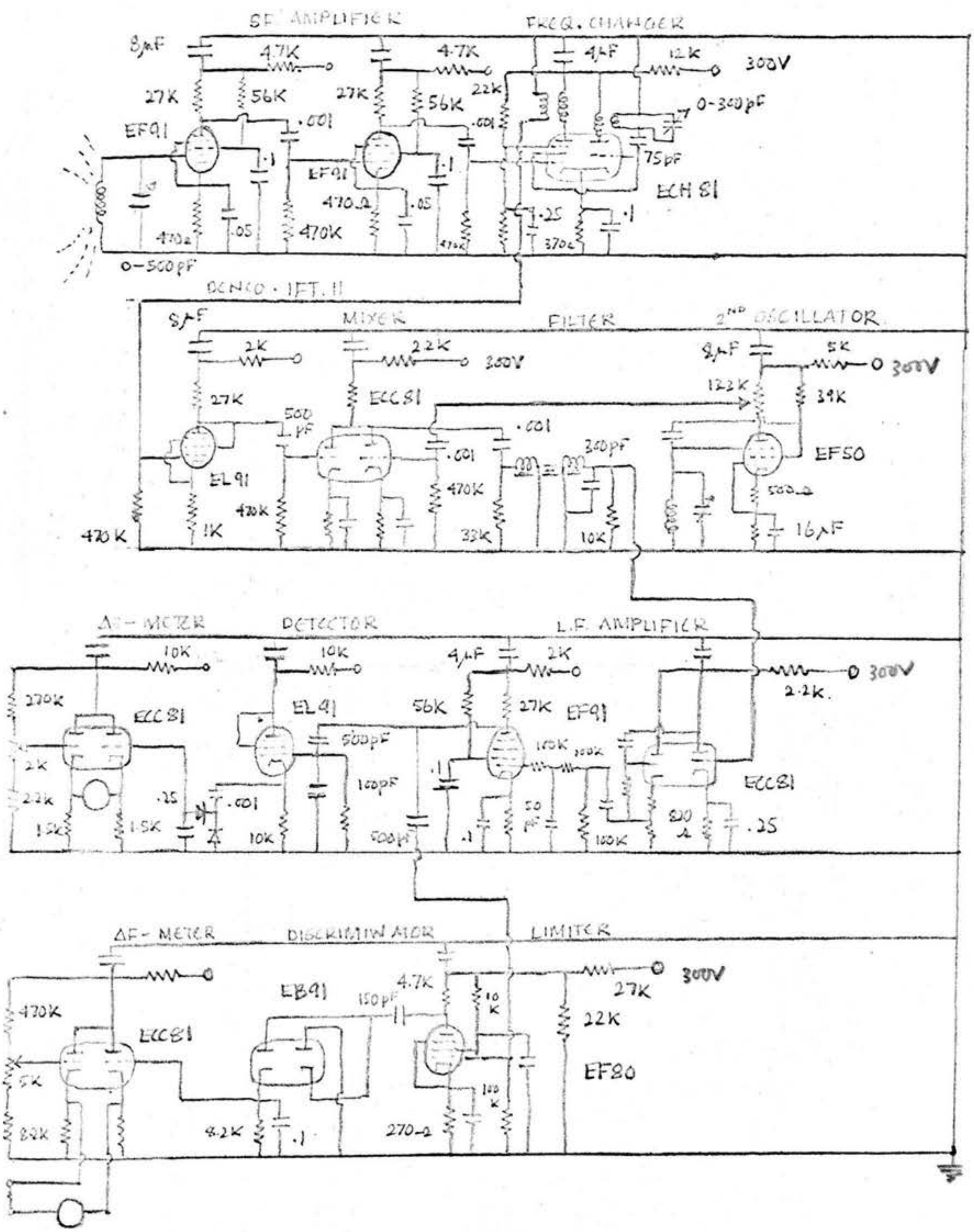


Figure 21

The circuit diagram of the first version of the detecting equipment.

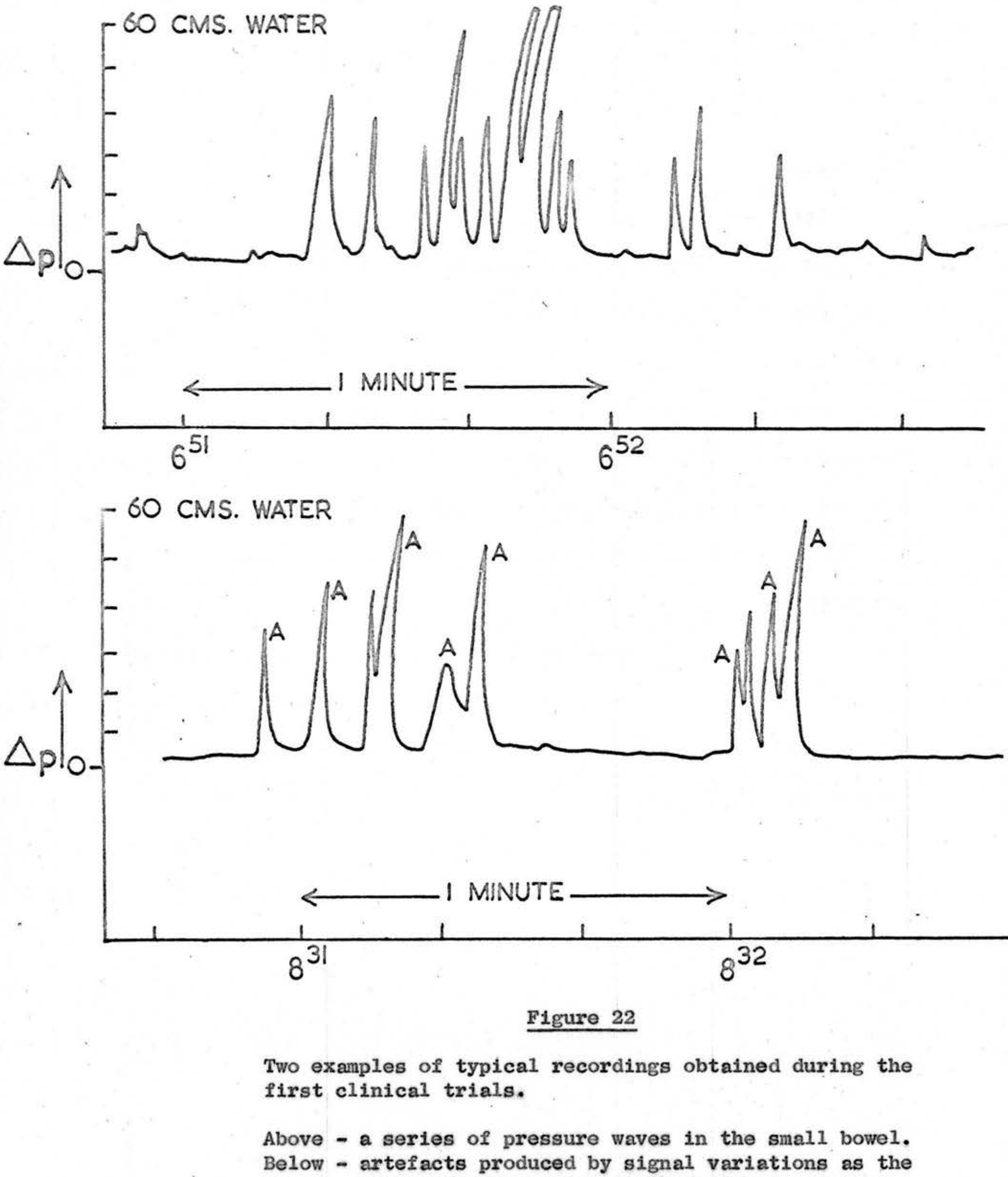


Figure 22

Two examples of typical recordings obtained during the first clinical trials.

Above - a series of pressure waves in the small bowel.
Below - artefacts produced by signal variations as the capsule turns in the body.

the first receiver constructed (Fig. 21).

(ii) First series of clinical trials.

In spite of two oscillators being used in this first receiver the overall frequency stability proved to be better than 2% of full scale deflection over the periods of use, which varied between 8 and 12 hours. Oscillator frequencies on opposite sides of the nominal values were used so that drifts due to thermal changes would tend to shift the nominal frequency in opposite directions, this helped to reduce spurious frequency changes. The gain and the bandwidth of the receiver proved to be adequate for most of the capsules used during this period, although some had nominal frequencies rather near to the limits of the tuning range. Trouble was occasionally experienced with intermittent interference, but this appeared to be the result of inadequate screening between the various amplifying circuits.

A more fundamental disadvantage which became apparent during the tests was the appearance of artefacts resulting from movements of the capsule within the bowel. When a 'null' position was presented to the antenna the signal entering the discriminator fell below its critical value and the pen tracing the output returned towards its zero or rest position. This meant that a temporary excursion appeared on the pressure trace and it was usually extremely difficult to distinguish these excursions from normal pressure activity (Fig. 22). A constant watch had to be kept on the signal monitor so that these artefacts could be marked (A) as artefacts, and it was clear that if further use was to be made of single loop antennae the discriminator would have to be protected against the signal from the amplifiers falling below the critical level for correct limiting.

(iii) Subsequent modifications.

A/

Figure 23

The second version of the detecting equipment with the double-channel pen recorder on the left of the receiver.

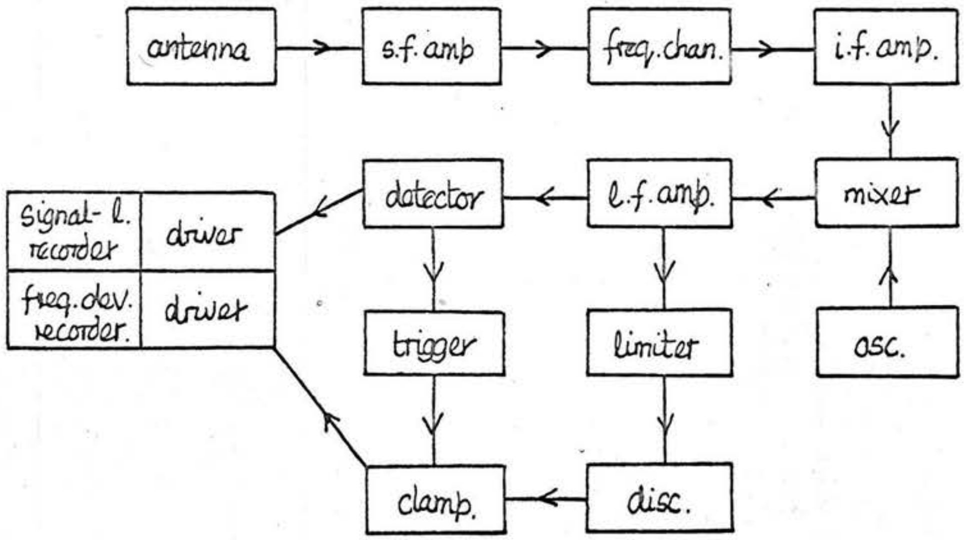


Figure 24

A block diagram showing the circuit of the second version of the detecting equipment.

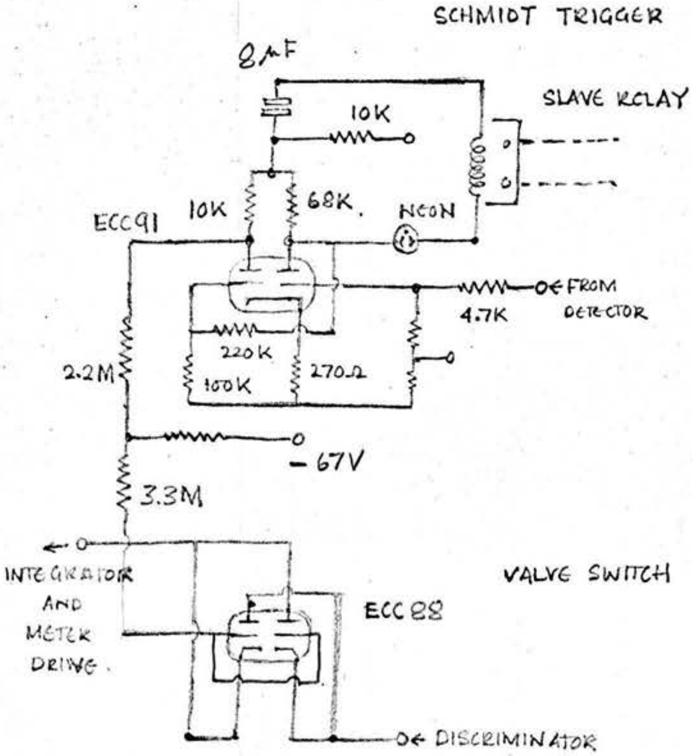


Figure 25

The circuit modifications showing the Schmitt trigger, the isolating valve, between the discriminator and the meter, and the neon controlled slave relay.

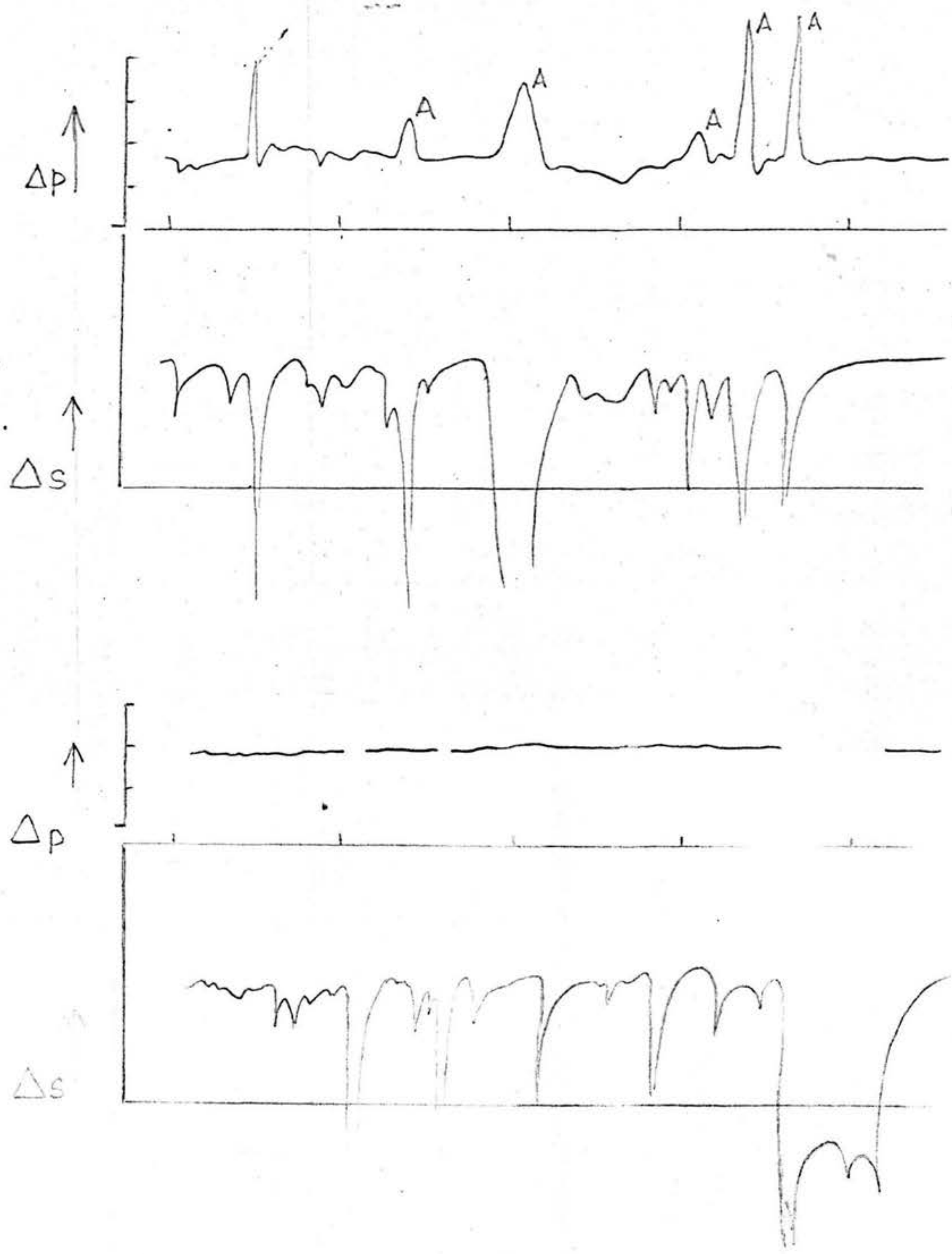


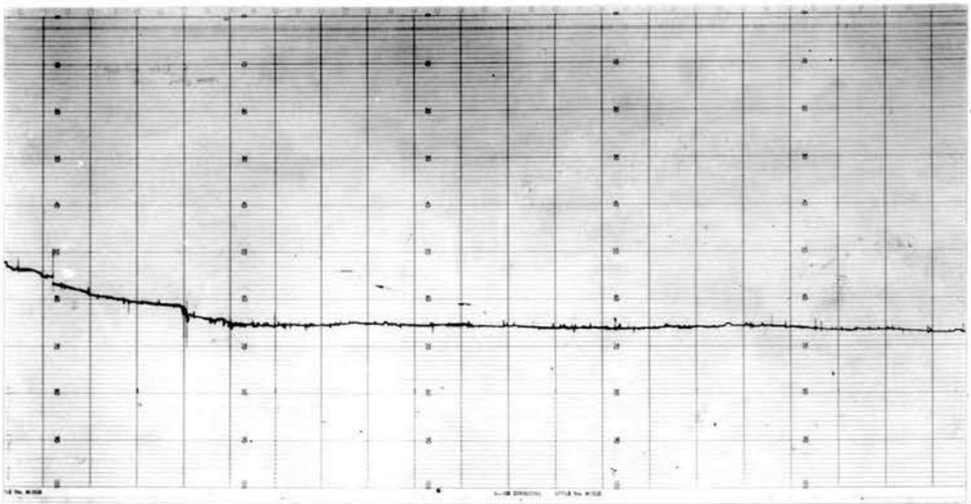
Figure 26

Above - movement artefacts, produced in vitro with the clamp circuit disconnected

Below - a recording to show how the clamp effectively removes the movement artefact from the pressure tracing (Δ p)

The markings along the time axis are minutes.

A second version of this receiver was built into a more robust chassis which would stand up better to routine use and the frequent movement about the hospital (Fig. 23). Besides more effective internal screening, two new features were included in the circuitry (Fig. 24); provision was made for recording the signal amplitude in a second channel on the continuous tracing, and an electronic clamp system which isolated the pressure-indicating meter from the amplifier during poor signal conditions was also added (Fig. 25). A Schmidt-trigger circuit monitoring the level of signal at the amplifier output was set to operate when the signal fell below the critical level of two volts r.m.s., necessary for undistorted frequency discrimination. When this happens and the first triode in the trigger cuts-off, the second triode begins to conduct. The rising anode voltage of the first triode causes a neon lamp, visible on the front panel of the receiver, to strike and the current drawn through the tube operates, by means of a Carpenter slave relay, a Post Office Type 3000 relay which lifts the pen from the pressure tracing. Two triodes coupled 'back to back' act as an isolating switch between the discriminator and the meter circuit; a negative potential derived from the second anode of the trigger and applied to the grids of the triode switch prevents the valve from conducting when the signal level falls below the critical value. During transient changes, therefore, the meter is effectively clamped and the pressure pen is lifted from the tracing; the warning lamp indicates a prolonged loss of signal (Fig. 26). The pressure trace is, therefore, an interupted record, but all the values marked represent pressures sensed by the capsule and clinical interpretation is made much easier. The second channel was intended to be used to observe the periods of interuption of the pressure record before the mechanical arrangement was completed, but it has been found to be useful for indicating the periodicity of capsular movements/



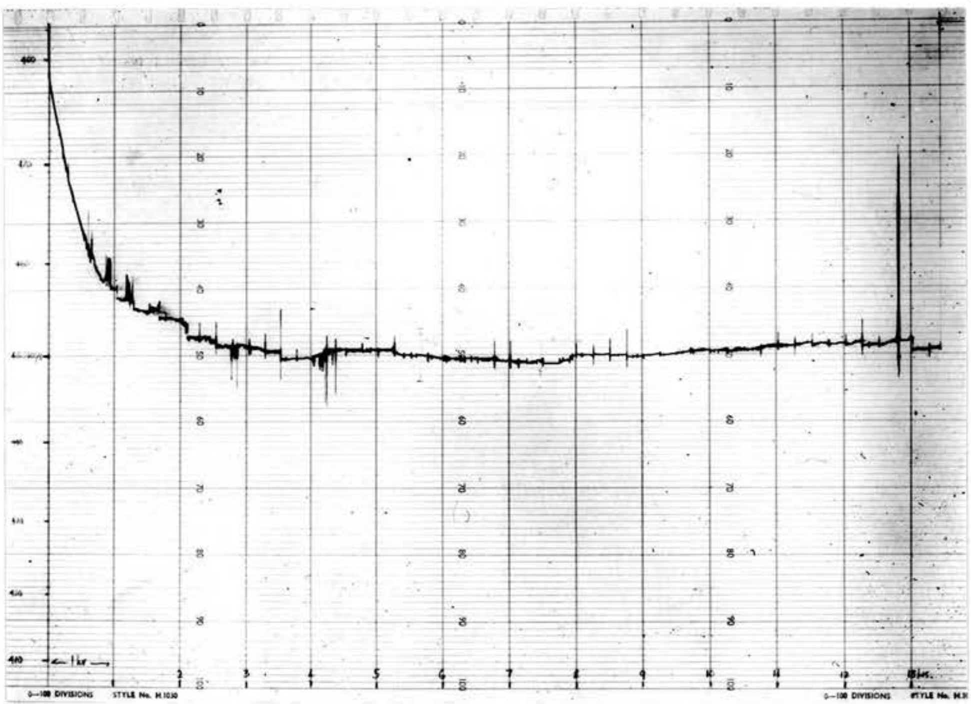


Figure 27

The long-term frequency stability of the detecting equipment, above - at a typical sensitivity, and below - warming up from complete cold at maximum sensitivity. Each large division on the horizontal scale represents one hour.

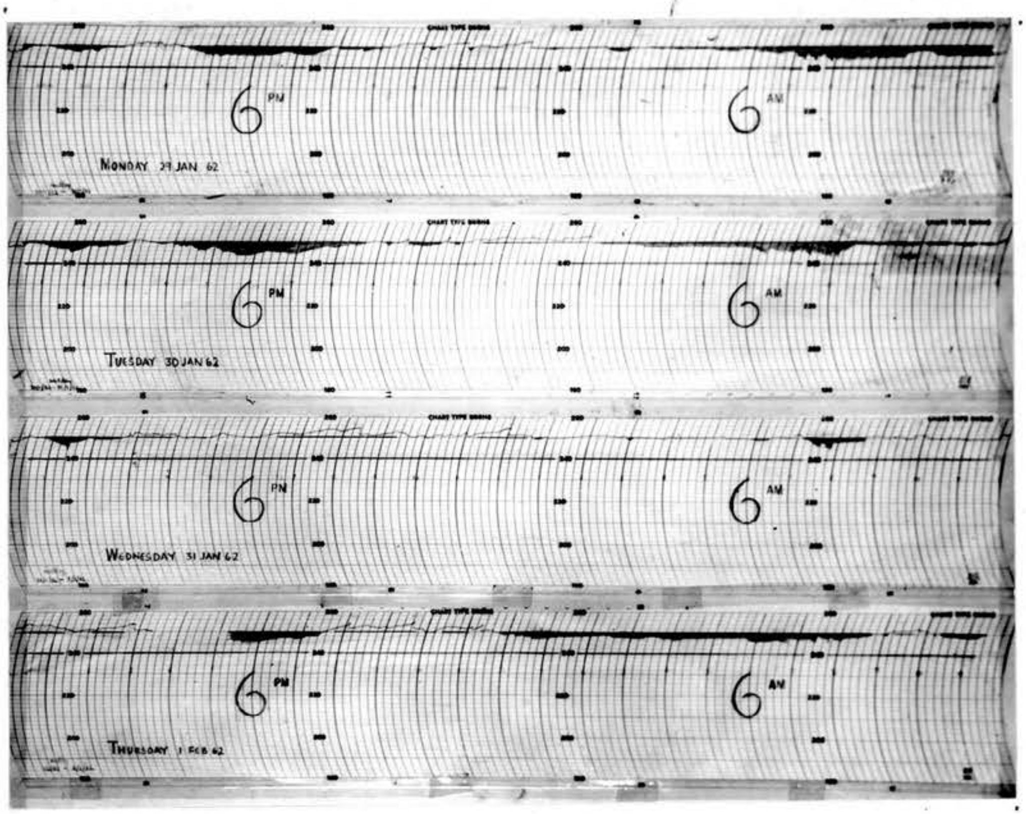


Figure 28

The variation of the mains supply voltage in the laboratory where the investigations were carried out over a period of four days.

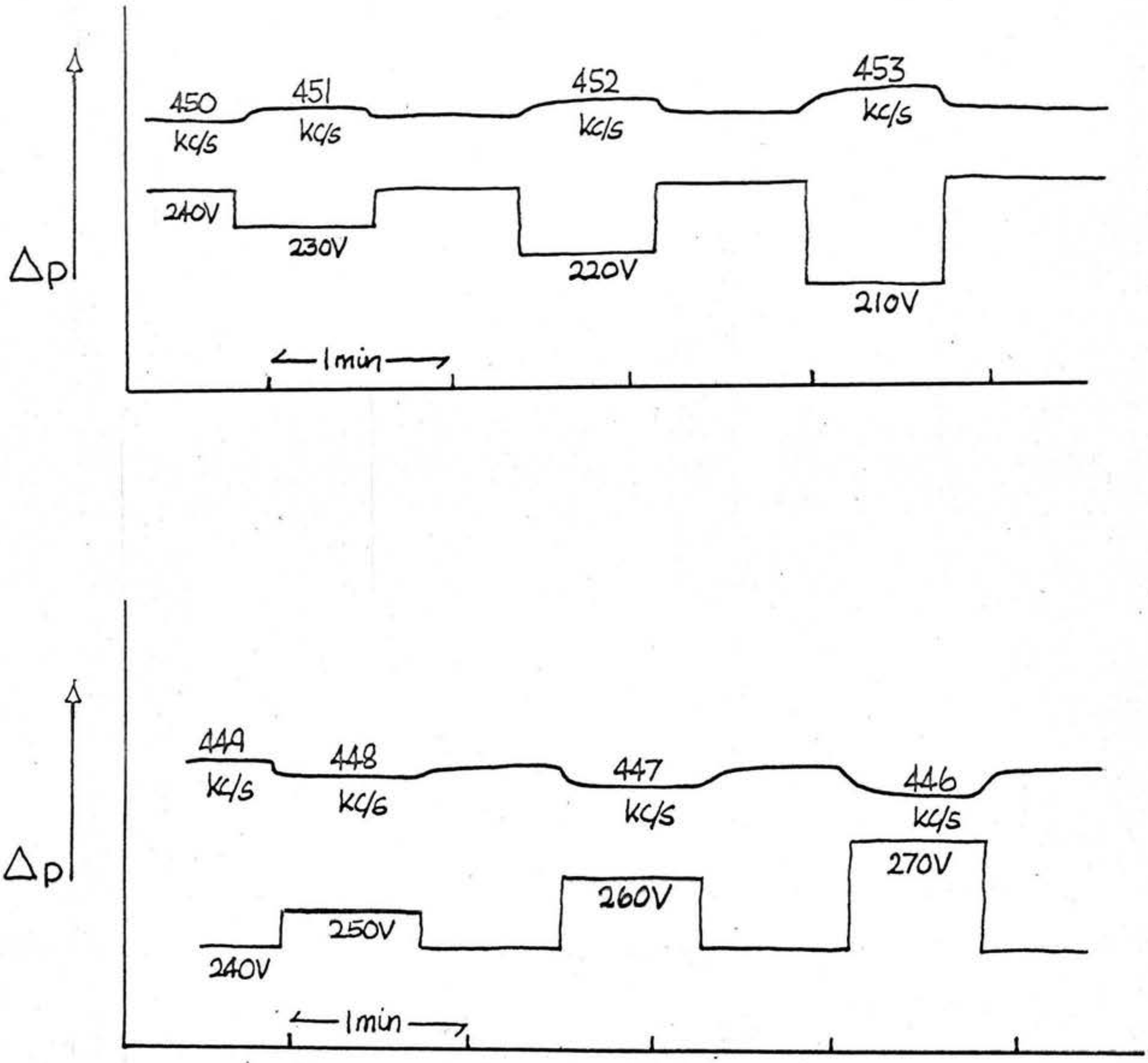
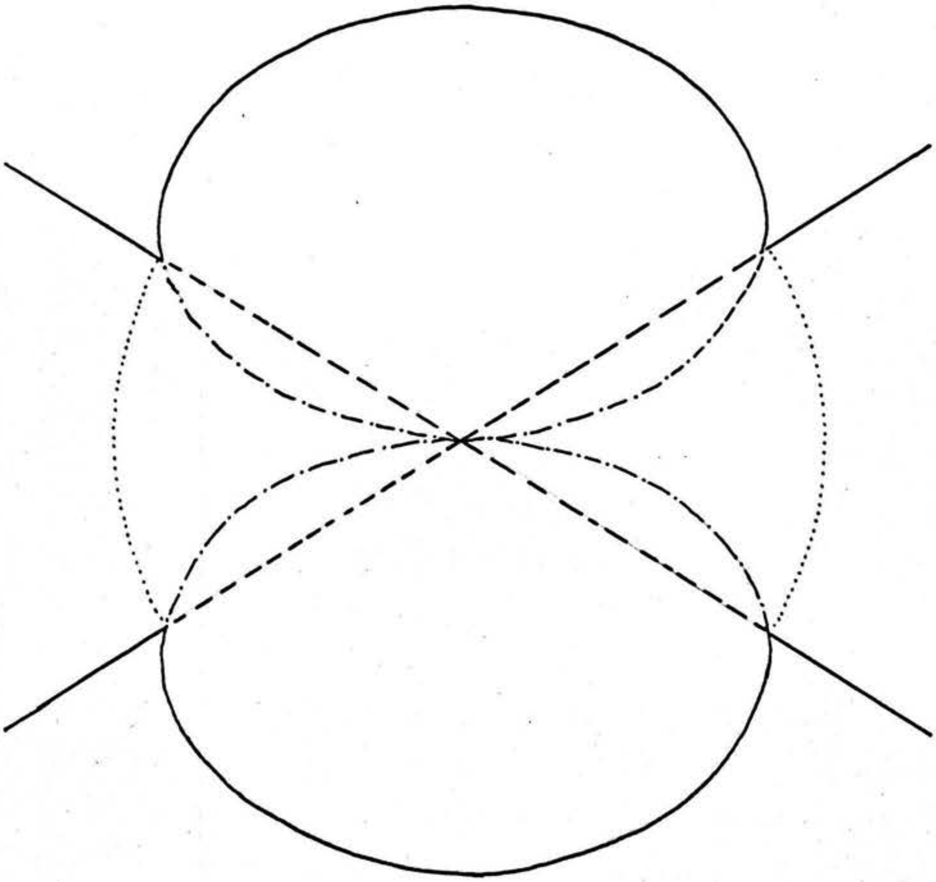


Figure 29

The short term stability of the detecting equipment shown by the effect of variations in the supply voltage on the basal level.



<u>Figure 30</u>

A polar diagram showing 'null signal' angles of about 65^{o} where the signal falls below the critical level as the capsule is rotated.

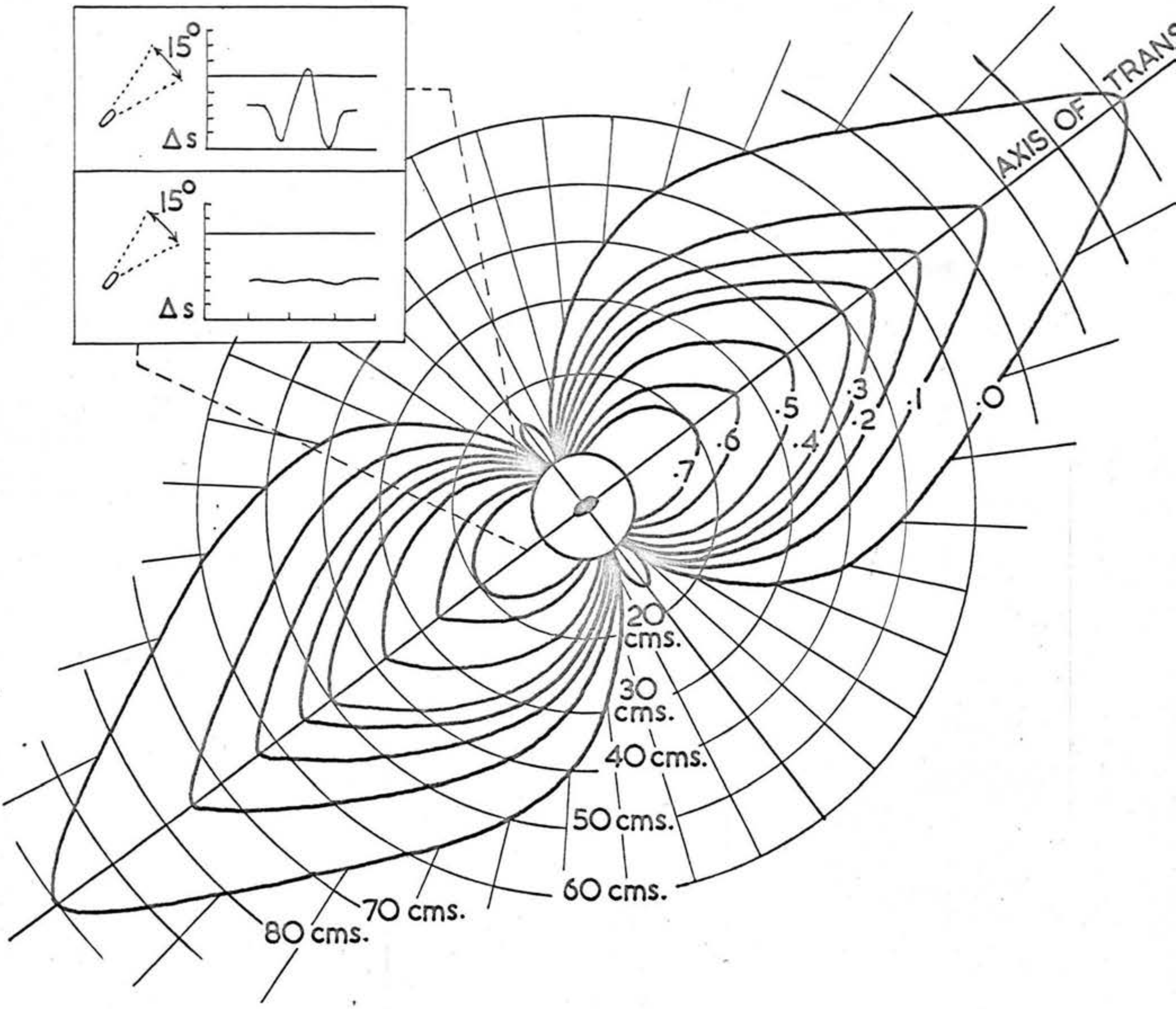


Figure 31

A polar diagram showing the variation of signal strength with inter-axial angle. The antenna loop is maintained with its axis towards the transmitter.

movements at certain sites.

(iv) General performance.

One of the results of increasing the internal screening was to change the ventilation characteristics so that the receiver took longer to reach complete thermal equilibrium. From complete cold in a cold environment the basal level took two to three hours to become steady, but this did not prove to be inconvenient because the equipment could be switched on at a pre-set time by a simple time-switch. Running the equipment at a temperature above the usual room temperature ensured that it was not sensitive to slight ambient changes. The long-term frequency stability was good enough to maintain the base line within 1 kc/s over periods of 24 hours or more (Fig. 27). Short-term changes resulting from fluctuations in the mains supply voltage were not serious. The regulated power supply built into the receiver gave good protection against the voltage fluctuations, which were not generally excessive in the laboratory and observation rooms used for the experiments (Fig. 28). Changes of 10v in the mains supply line caused a basal shift of not more than 1 kc/s. (Fig. 29).

At a distance of 25 cms. in air, the capsules showed null signal angles of 40 - 60^{o} (Fig. 30) and the dipole field is such that this angle of poor coupling becomes greater as the distance between the transmitter and the antenna loop increases. The gradients of signal level for simple rotational movements of the capsule (Fig. 31) show how small rotational movements of the capsule can be detected by moving the antenna loop to different parts of the field. The application of this 'edge' effect will be discussed in Chapter 5.

Two attempts at the construction of a non-directional antenna system, which were made during the period that the equipment was being used for clinical/

clinical experiments were abandoned. An attempt to use the action of the clamp circuit to trigger a uniselector powered by a simple pulse generator, which would then scan a system of differently orientated coils automatically, could not be made to work satisfactorily because the long response time of the pen recorder in the signal level circuit was usually longer than the period of the transient changes in the signal level.

An attempt to use the principle of the variometer to obtain a non-directional antenna, which would have an equal response to all frequencies within the working band, was not completed because it became mechanically too complicated to use near to a patient. It was made up of three coils wound into the shape of a truncated cone so that they were equi-spaced and more or less mutually at right angles. A fourth cone wound in series with the other three and of a similar size and shape was to be rotated within the cone so that the mutual inductances between a high and a low value as similar and opposite sides came into juxtaposition. In this way each of the three perpendicular coils would be tuned in turn through the frequency range as the fourth coil rotated. Only a rough working model had been completed when we decided that it would be unsuitable for clinical use because of the short distance between the patient and the rotating aerial, necessary to intercept sufficient signal.

CHAPTER 4

A review of previous work on systems for telemetering from the human alimentary tract

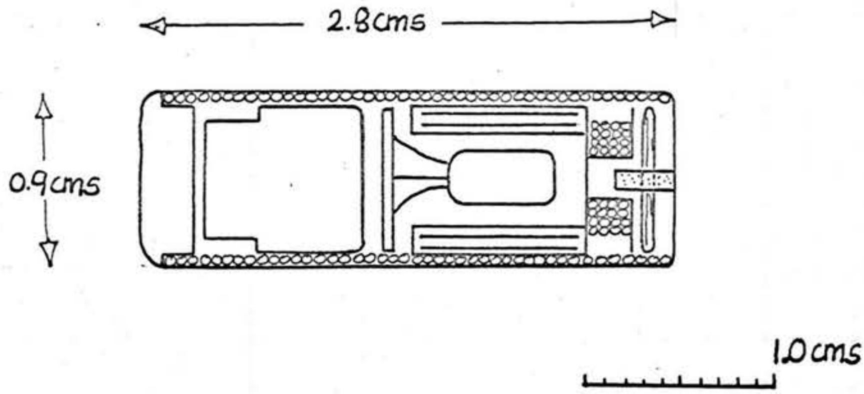
4.1 First reports

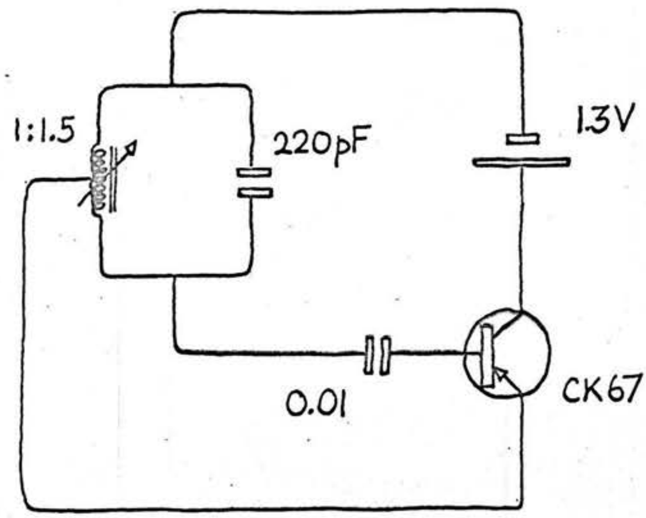
In 1957, when small transistors had been generally available for a number of years, two groups of investigators working quite independently reported the invention of capsule transmitters small enough to be swallowed. Both were designed for studies in the alimentary tract - B. Jacobson and R. S. Mackay working in Stockholm described two different 'endoradiosondes', one for telemetering pressure and temperature simultaneously (Mackay and Jacobson, 1957) and a 'pH endoradiosonde' for acidity studies (Jacobson and Mackay, 1957) - and another investigator J. T. Farrar working in New York with V. K. Zworykin of the Rockefeller Institute had developed a 'radio-telemetering capsule' for measuring intra-luminal pressure variations and applied it to one or two clinical cases (Farrar et al., 1957). Both groups emphasised that the reports were made on preliminary equipment designed to assess the clinical value of such apparatus and that no attempts had been made to improve the technical performance of the systems. Previously Mackay had spent some time at the University of California Medical Center attempting, unsuccessfully, to develop a system whereby a capsule in the human alimentary tract containing a tuned circuit sensitive to pressure or to some other biological variable, could be be monitored by an absorption grid-dip meter from outside the body.

(i) The pressure-temperature sensitive 'endoradiosonde'.

The 'sonde' produced by Jacobson and Mackay was described as being of cylindrical shape, 2.8 cms. long, 0.9 cms. diameter and weighing 2.2 gms. A Hartley type oscillator (Fig. 32) powered from a cell within the capsule and working at a nominal frequency around 400 kc/s produced the basic signal for

the/





<u>Figure 32</u>

The 'endoradiosonde' described by Jacobson and Mackay;

above - a cross section showing the mechanical design, and
below - the electronic design.

the transmissions. Two forms of modulation were impressed on this signal; the movements of an iron dust core within the tuning inductance changed the frequency of the oscillator and a blocking capacitor in the base circuit of the transistor caused the oscillator to 'squegg' or block so that the transmission was pulsed. The biased-off period was in part dependent on the temperature-sensitive back resistance of the transistor junctions and the movements of the iron-dust slug were varied by means of an elastic diaphragm by the pressure surrounding the capsule. Little else about the technical specification of the capsule transmitter or about the external detecting system was given in the original publication, although subsequent reports indicate that the diaphragm to which the slug was attached was of a thin rubber material bonded across one end of the capsule casing. The original power source appears to have been a specially constructed dry cell reported as providing the transmitter with an active life of some two or three weeks. This figure, however, is not borne out in subsequent reports which quote a figure of one to three days. Experiments using body fluids to activate the capsule proved unsuccessful because a steady voltage is essential for frequency stability.

This early model was considered unsuitable for clinical applications and the data obtained would probably prove to be inaccurate for a number of reasons. Unwanted frequency changes might be expected from the effects of gravity and other accelerating forces on the rather heavy ferramagnetic tuning slug from the voltage variations in the crude battery and from stray capacitance effects. Stability may also have been affected by the chemical action of the digestive fluids on the thin rubber membrane. The frequency deviation with pressure was probably not very much greater than the modulation due to these spurious effects although the intra-luminal pressure changes would be of much shorter/

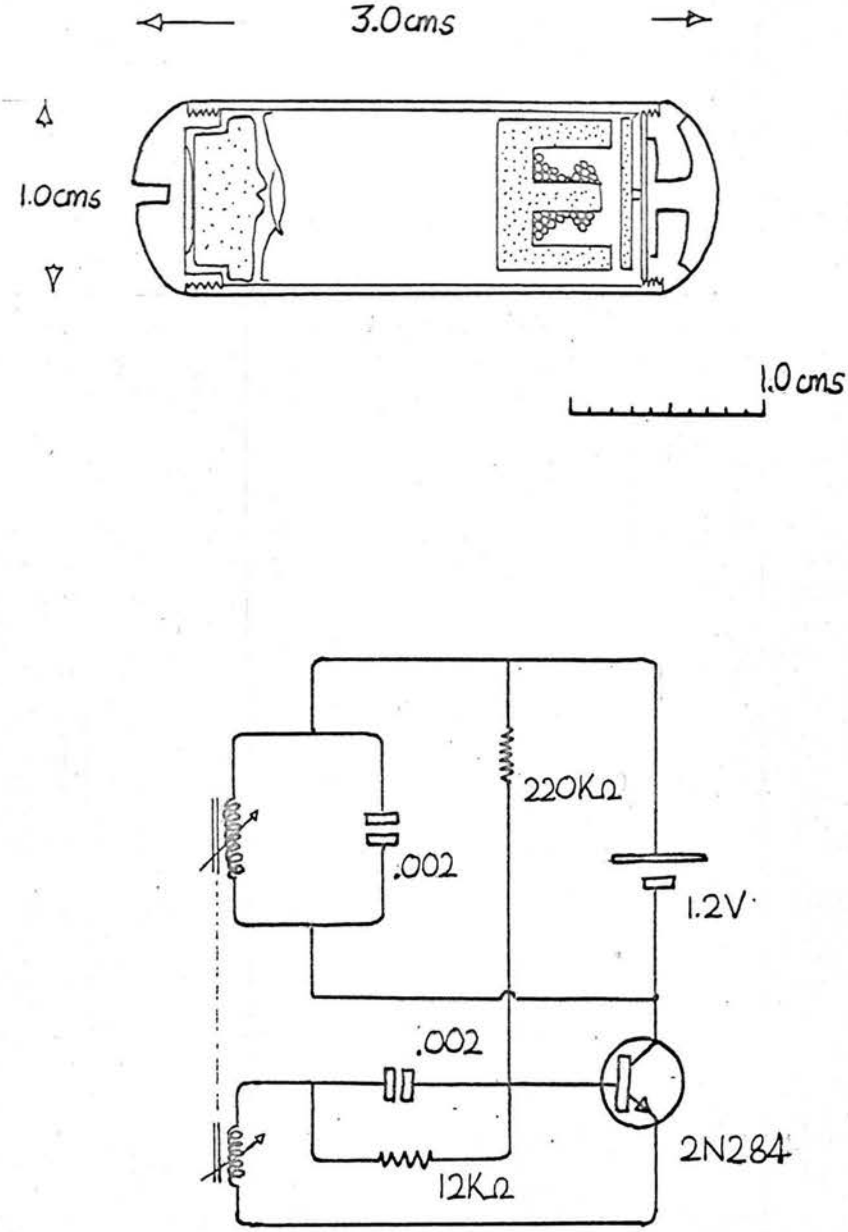


Figure 33

The capsule described by Farrar and his co-workers; above - the mechanical design, and below - the electronic design.

shorter periods. The most fundamental objection, however, seems to be that the period when the oscillator was biased-off did not give an unambiguous indication of the ambient temperature of the capsule. It is dependent on the value of the inductance of the tuned circuit and on the battery voltage as well as temperature characteristics of the transistor. The blocking effect can be removed by simple changes in the values of the components and more refined versions of this original design have been used extensively for routine clinical investigations by Mackay (Mackay, 1959) and for some time by Jacobson, although he has since stated that the clinical data obtained by these 'sondes' must be considered unreliable (Jacobson, 1960)(2). The small frequency deviations were easily accommodated by a tuned-loop antenna feeding a slightly modified communications receiver.

(ii) Farrar's 'radio-telemetering capsule'.

The capsule described by Farrar (Farrar et al. 1957) was cylindrically shaped, 3.0 cms. long, 1.0 cm. in diameter and weighed 5.6 gms. It was built for assessment by Farrar's group by the Advanced Development Department of the Radio Corporation of America (Haynes and Witchey, 1957). The greater volume of this capsule accommodated the rather large number of components used in the complex reaction-coil circuit (Fig. 33). The oscillator was powered by a small, commercially produced nickel-cadmium cell and transmitted for between 15 and 30 hours at a nominal frequency of about 900 kc/s. Modulation of less than 1%, with a maximum frequency deviation of about 6 kc/s, was impressed on the carrier signal by the pressure dependent movements of the lid of a ferrite pot-core. The tuned coil and the feedback coil of the oscillator were wound inside the pot core. The pressure sensing element was a neoprene diaphragm, protected from the action of the digestive juices by a limp polyethylene/

polyethylene membrane.

Random frequency drift and the sensitivity of the capsule to small variations in the ambient temperature limited the usefulness of the system and it could not be used with certainty to study pressure variations which take place over periods greater than about five minutes. The greatest disadvantages as far as clinical studies were concerned appeared to be its very high density and the shortness of its active life.

4.2 Subsequent development of Jacobson's system.

After the preliminary studies with pressure-temperature and pH-sensitive 'sondes'. Jacobson decided to concentrate his development on the pressure-sensitive units alone. This would allow measurements both for physiological studies and for diagnostic investigations in body organs which could not be so easily obtained by other methods.

(i) Capsule-transmitter.

A smaller and more refined version of the original capsule design measuring 1.8 cms. by 0.8 cms. was developed. This capsule which used a specially constructed nickel cadmium cell had an active life of about 50 hours. This cell, however, proved to be inferior to the commercially constructed Mallory RM312 cell and he decided to re-design the capsule in order to accommodate this slightly larger battery. In fact two new capsules were developed, a larger and more ruggedly constructed capsule suitable for use in animal experiments designated the 'Pl-sonde'; and the 'P2-sonde' for use in human applications. The small capsule had an active life of about 3 weeks whilst the 'Pl-sonde' using a larger mercury cell lasted approximately 3 months. Care was taken to investigate every conceivable source of spurious frequency drift in the transmitters and every precaution which would not involve an appreciable increase in the size or density of the capsule was taken. Specially designed rubber/

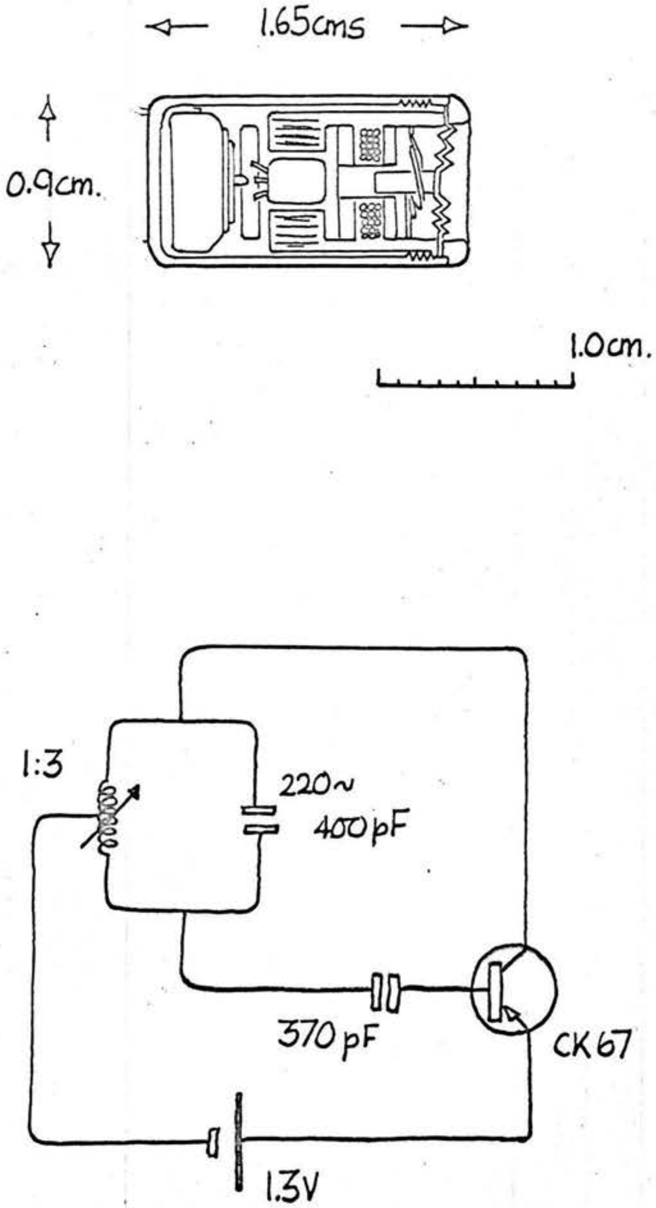


Figure 34

The P2-sonde described by Jacobson; above - in cross-section showing the mechanical design and below - the electronic design.

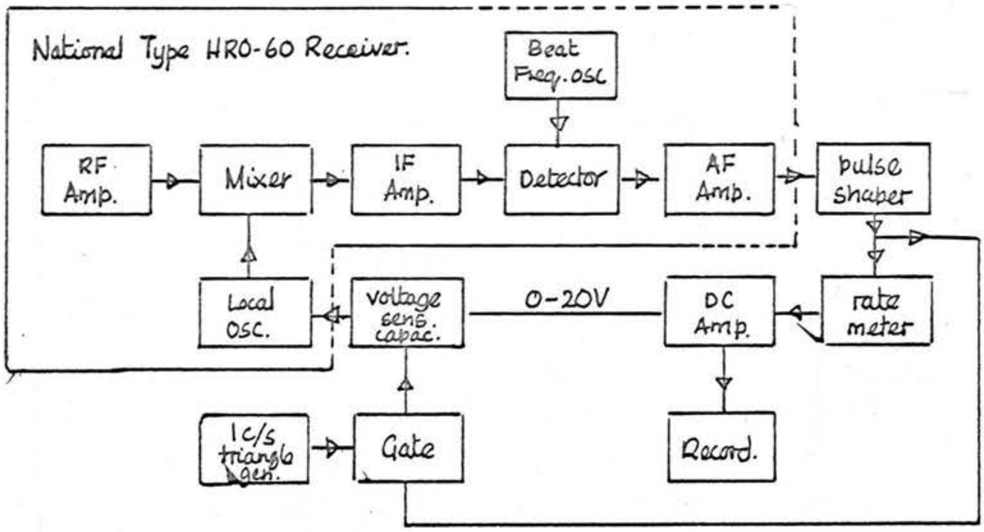
rubber membranes were vulcanised in order to reduce the large changes which resulted from the action of body juices on the unvulcanised diaphragms when they were exposed for long periods. The sensitivity of the transducer was determined by the stiffness of the suspension spring which was mounted behind the diaphragm and it was usually chosen to give a deviation of about 30 kc/s for a pressure change of 300 cms. of water. The improved geometry of the ferrite slug and the tuning coil resulted in a maximum departure from linearity over the full scale deflection of less than 4%, compared with errors up to 20% in the original design. He also showed that by adjusting the volume of air trapped inside the capsule and filling the remaining space in the capsule with silicone oil it was possible to balance the different temperature effects over a small temperate range and in this way the frequency drift in the capsule transmitter was reduced to not more than about 2 kc/s per week.

(ii) Detecting equipment.

Jacobson developed special external apparatus which although it was extremely complex, could accommodate the large frequency deviations necessary for accurate telemetering and detect extremely small signal levels. This enabled him to use smaller supply currents in the transmitter and achieve a much longer active lifetime from a Mallory cell. The SFG-receiver which he developed later showed a much better frequency stability than conventional communications receivers and it was not sensitive to orientational changes of the capsule.

The Automatic Frequency Control Receiver

This equipment consisted of a standard super-het type communications receiver with a beat-frequency oscillator and a frequency meter, modified so that a voltage feedback loop from the output of the detector to a voltage-sensitive/



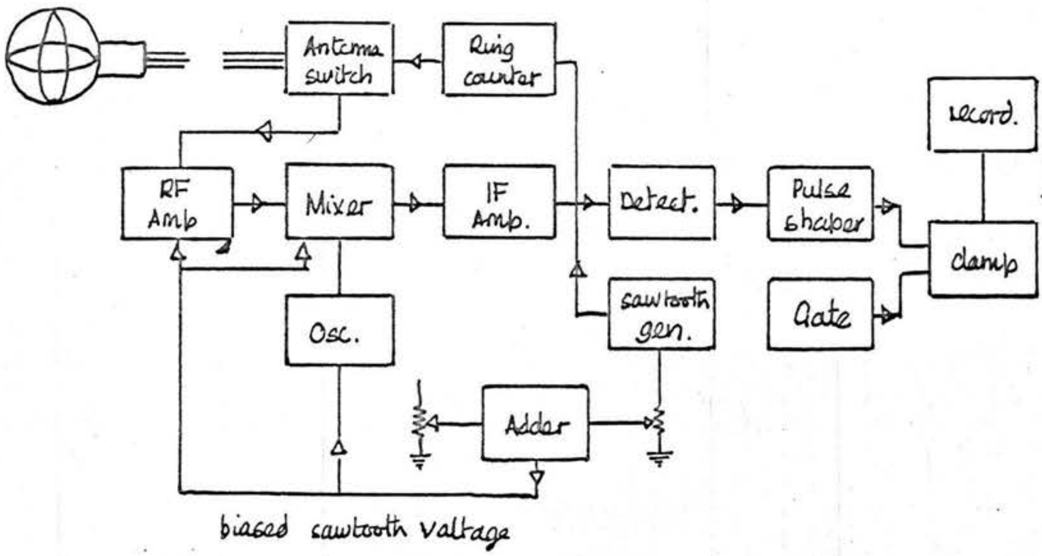


Figure 35

Jacobson's receiving equipment:
Above - the A.F.C. system and below -
the S.F.G. receiver.

sensitive capacitor in the local oscillator caused it to continually retune to the capsule transmitter frequency (Fig. 35). This control voltage was proportional to the frequency deviation of the transmitter, and a 1 c/s triangular wave generator swept the oscillator in the receiver over its working band if the signal from the capsule was lost. The system could operate over a wide range of frequencies and it showed a fast response to changes, but the additional circuitry was complex and the overall performance was limited by the long-term drifts in the communication receiver (Jacobson, 1959).

The Swept-Frequency and Gated Receiver

The stability of the SFG-receiver was so precisely maintained that pressure changes causing a frequency deviation of one fiftieth of a Kilocycle (0.02 kc/s.) or more, with a period of up to two or three days could be recorded accurately. The antenna system had omnidirectional sensitivity; each of three co-centred, perpendicular loops being connected in turn to the input of the receiver. The upper frequency limit was 3 c/s. During the period that each loop was connected, voltage-sensitive capacitors in the RF stages and the local oscillator were swept across the operating band of the transmitter by a sawtooth voltage (Fig. 35). At the instant when the receiver was tuned to the signal from the capsule, a pulse of energy from the transmitter was passed through the very sharply tuned intermediate-frequency stages, detected and after shaping made to operate a valve 'gate'. A sample of the sweep voltage at that instant, forming a second pulse, was passed to an integrating circuit and a steady voltage level proportional to the frequency deviation obtained.

The receiver could be tuned to the nominal frequency of the capsule transmitter by changing the voltage bias on the output from the sawtooth generator/

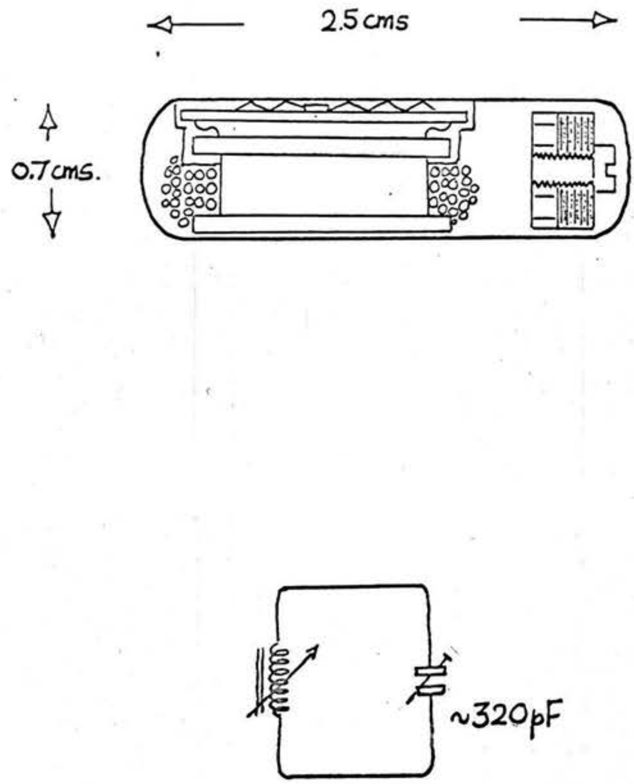


Figure 36

The capsule built for use with R.C.A.'s 'passive' system, showing its mechanical design and very simple circuitry.

generator and the sensitivity could be varied by changing the amplitude of the sawtooth. A mechanical filter in the intermediate frequency stages enabled the system to be made very selective and 6 microvolts of signal at the input operated the receiver satisfactorily. A signal 30,000 times greater than this only caused distortion equivalent to 0.02 kc/s. The coil and capacitors of the Clapp oscillator were enclosed in an oven which was maintained steady at 55°C (Jacobson and Lindbergh, 1960). The most serious practical disadvantage with this very precise instrument was its extreme electronic complexity and the need for careful mechanical design to avoid errors which might arise from mechanical distortion of the components.

4.3 Equipment developed for Farrar's group.

Although the original capsule built by RCA had been used quite extensively to study a series of patients with gastro-intestinal symptoms and also a number of normal control subjects, it had several features which were not ideal; the diameter of 1.0 cms. was slightly larger than was desirable and the short length of the transmission period which varied between 8 and 30 hours, prevented studies of complete transits through the bowel. The large number of components in the circuit also made the specific gravity of the capsule undesirably high. They decided to try to circumvent these technical difficulties by resorting to the entirely different principle of energising the capsule from outside the body. A 'passive' type of system was built for Farrar by the Advanced Development Department of R.C.A.

(i) "The externally-energised wireless capsule".

The capsule was a cylindrical shape, but had one side slightly flattened to form the pressure-sensitive diaphragm. It was made of plastic

known/

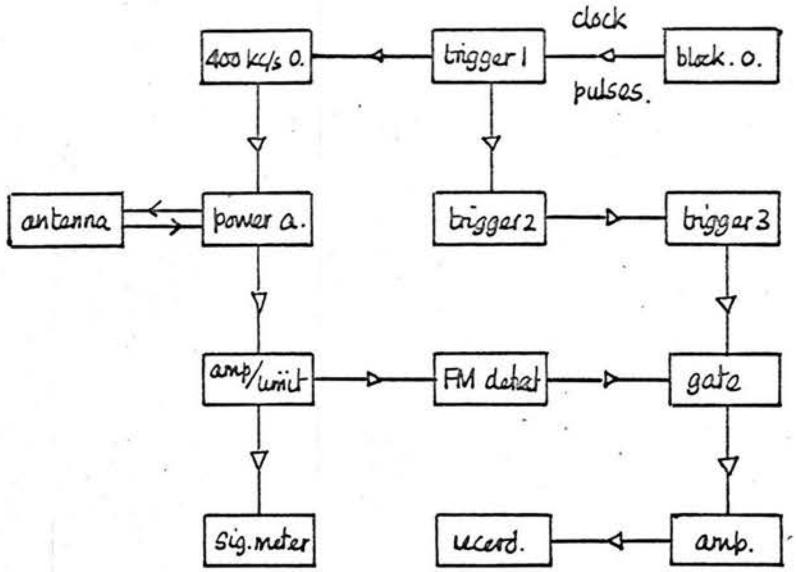


Figure 37

A block diagram of the external circuit of the 'passive' system.

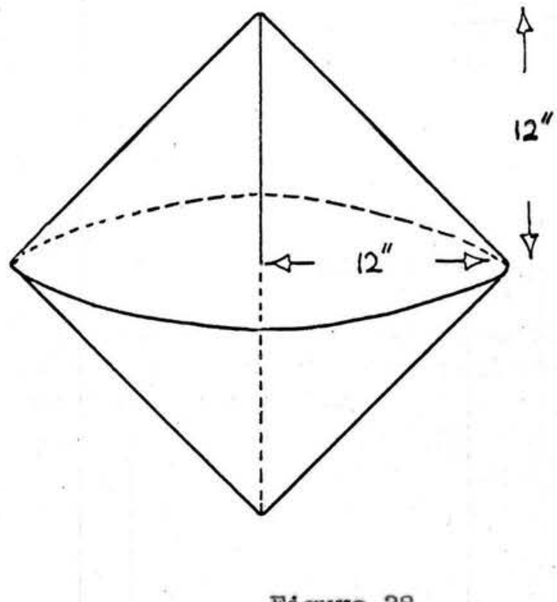


Figure 38

The effective range of the capsule with the single antenna loop.

as Textolite and was 2.5 cms. long with a maximum diameter of 0.7 cms. - appreciably smaller and because of the very simple nature of the encapsulated circuit, less dense than the battery-powered capsule (Farrar et al. 1960). It contained a capacitor made up from 12 silvered-mica discs and a variable inductor that had a ferrite armature attached to a 'Mylar' diaphragm which ran along the length of the casing (Fig. 36). In the original form of the apparatus a 24 inch diameter coil was placed around the patient after the capsule had been swallowed; short bursts of energy at about 400 kc/s were passed into this coil at a rate of 3,000 pulses per second. Some of this energy was transferred to the pressure sensitive circuit in the capsule through the inductive coupling between the capsule and the antenna. In the 'quiet' periods between bursts the energising oscillations were quickly damped out by applying a load to the antenna, whereas the oscillations induced in the capsule circuit continued, dying away relatively slowly because during construction special care was taken to keep the Q-factor of the components as high as possible. Throughout this period of 'ringing' the oscillations in the capsule circuit induced small alternating voltages in the external antenna loop, not necessarily at the original excitation frequency, but at its own slightly different resonant frequency which is dependent on the deflection of the pressure-sensitive diaphragm. After amplification this signal was demodulated and recorded directly as a measure of pressure (Fig. 37).

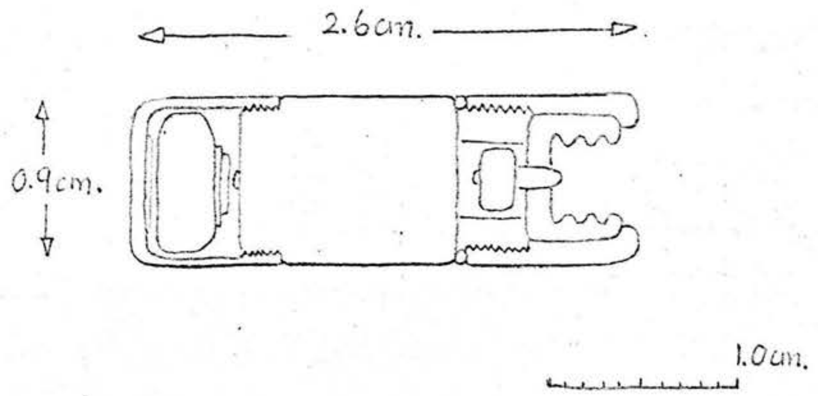
A blocking oscillator supplied 3 kc/s pulses which switched the 400 kc/s oscillator off and on. Alternating voltages of about 80 volts, peak to peak, were passed at this frequency into the electrostatically shielded antenna loop from the power amplifier. Rapid damping of the excitation during the 'off' period was achieved by a non-linear diode which had a much smaller/

smaller damping effect on signal received back from the capsule. Both signals, that from the capsule and the small remainder of the excitation voltage, were amplified and detected and the unwanted part of the discriminator output due to the original signal was excluded from the record by a 'gate' valve operated by the 3 kc/s clock pulses. The remainder of the output was integrated in a capacitor and applied through a direct current amplifier to the recorder (Haynes and Witchey, 1960).

Although this 'passive' system possessed the great advantage that the effective life of the capsule was virtually unlimited, difficulties arose during the clinical experiments from the orientation changes that the capsule made during active periods of motility. The effect of these coupling changes is much more serious in passive systems of this type because the energy induced into the circuit is very critically reduced as well as the passage of signal from the capsule to the external equipment being affected. To overcome this problem an aerial system consisting of three orthogonal loops was constructed and built into a cylindrical jacket about 50 cms. long which was placed around the abdomen of the subject. In operation the loops were switched sequentially until a signal was received which exceeded the amount required for complete limiting action. If the capsule was within the volume enclosed by the aerial jacket this occurred before three switchings. A complete search through all three loops took about one-tenth of a second so that the loss of information during switching could be neglected.

The simplicity and lightness of the capsule, its unlimited life and its only slight sensitivity to temperature, suggest that this system has a significant potential for the detection and transmission of physiological information from many different organs and cavities in both animals and in man. The theoretical frequency limit due to the pulsing of the information, not the antenna switching, is 1,500 c/s.

(ii) .../



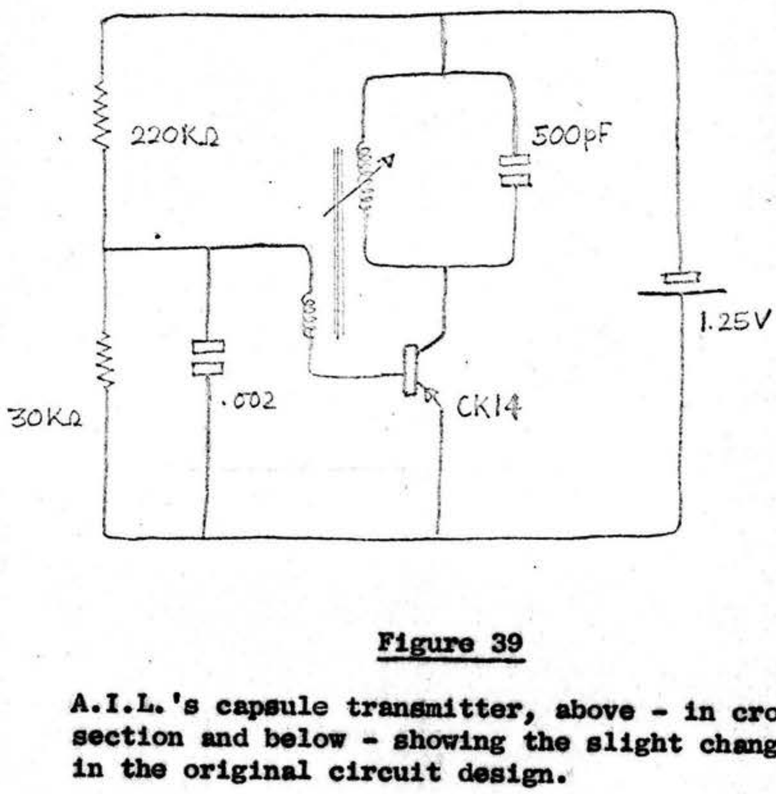


Figure 39

A.I.L.'s capsule transmitter, above - in cross section and below - showing the slight change in the original circuit design.

(ii) The 'Pressure Transenser'

Further development of the original battery-powered capsule was undertaken by the Airbourne Instruments Laboratory in New York. Using higher frequencies, around 2 Mc/s, they produced a capsule 2.6 cms. long and 0.9 cms. in diameter (Fig. 39). The rugged casing, made from epoxy resins, could be repeatedly sterilised in chemical solutions without becoming deformed and the pressure transducer used a small plastic coated nickel bellows which was likewise resistant to the action of both digestive and sterilising fluids. By changing to a solenoid type of armature they made the transmitter operate for about 70 hours from a Mallory cell which could be replaced after it was exhausted, so each capsule could be used for a considerable number of clinical experiments. The frequency drift was claimed to be less than 1% per day of full scale deviation, which was about 50 kc/s, and the non-linearity was also said to be small. Thus some of the disadvantages of the original capsule appeared to have been overcome although the specific gravity of the capsule was said to be still rather too high for physiological investigations. These units are commercially available in the U.S.A. and they cost approximately 250 dollars each (Horowitz and Farrar, 1962).

4.4 von Ardenne's 'Swallowable intestinal transmitter'

Telemetry systems which appear to be based on thos described in 1957 by Farrar's group have been built in East Germany by M. von Ardenne of Dresden.

(i) Capsule transmitter.

The capsule was cylindrical, 2.8 cms. long and 0.9 cms. in diameter. The pressure sensitive diaphragm consisted of the end wall of a small rubber bag that enclosed the whole body of the capsule and which was tied at the non-sensing/

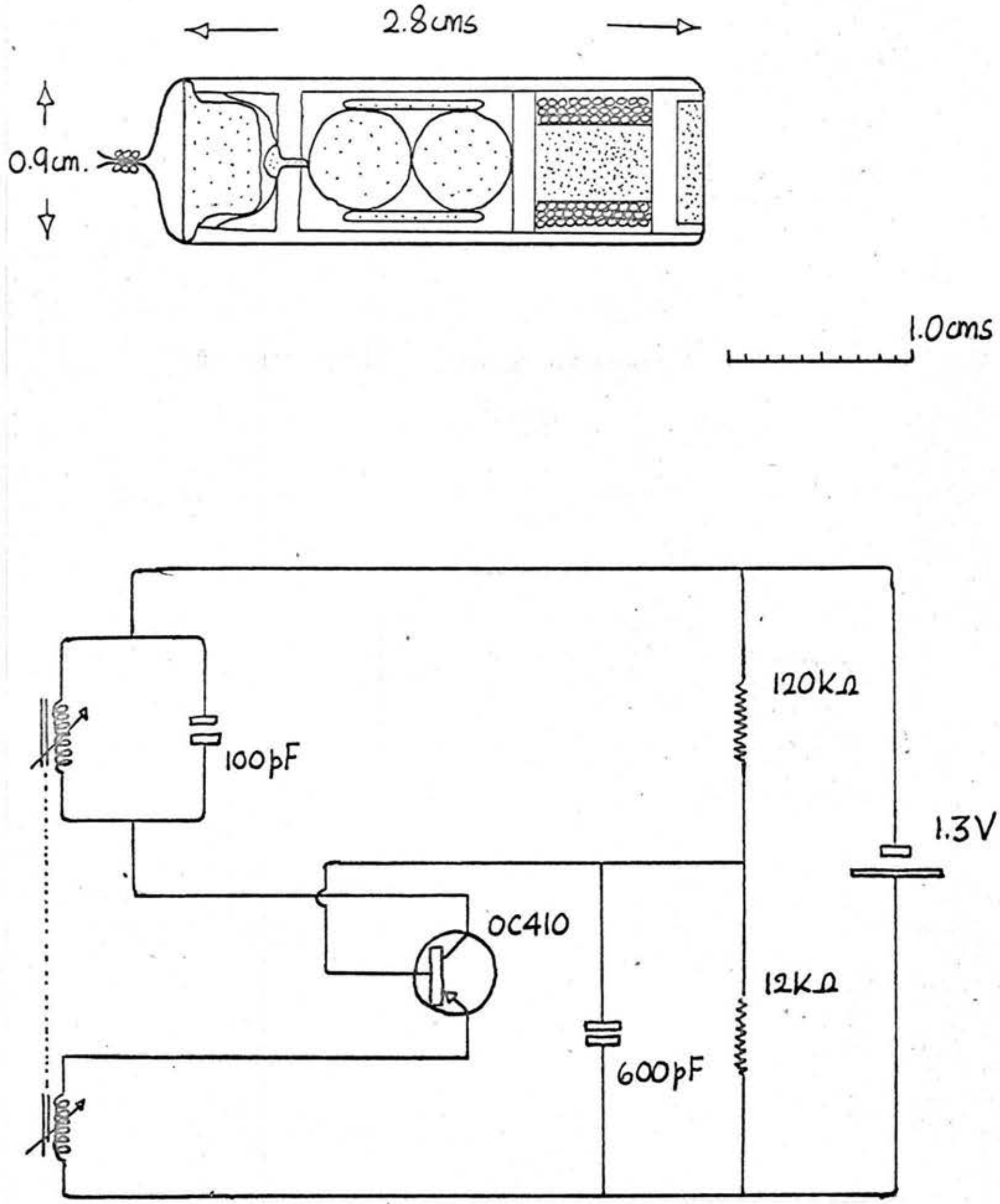


Figure 40

The capsule described by von Ardenne. Above - the mechanical design and below - the design of the transmitter circuit.

sensing end. The transmitter circuit oscillated at about 1,800 kc/s and was modulated about 10 kc/s by the movement of a small ferrite plate which was separated from the ferrite-cored coils of the oscillator by a wafer of expanded plastic (Fig. 40). The transmitter was powered by a nickel-cadmium cell which was said to last for about 48 hours at a drain of 0.05 milliamps (von Ardenne, 1957).

(ii) The external equipment.

Very sensitive receiving apparatus was used to detect the signals from the transmitters enabling them to drain a very small current from the battery. A special solenoid-shaped antenna or 'Hemdantenne', sewn into a loose-fitting bedjacket, was used encircling the subject's abdomen. Since the coupling between the transmitter and the receiver is greatest when the loops are coaxial the variation in amplitude of signal picked up on the 'Hemdantenne' loop indicated certain types of movement within the body and the signal strength was recorded along with the pressure-dependent frequency deviation as a second source of clinical information.

The greatest frequency deviation obtained from the transducing system in the capsule was so small that conventional receivers were at first employed. The nature of the 'Hemdantenne' was such that large changes in the signal level were seen at its output, particularly when the capsule was lying across the axis of the coil and a special receiver was constructed to accommodate the big changes in signal level. Pulse techniques were employed to avoid distortion due to this coupling effect, though little else of the technical specification was described (von Ardenne, 1959). Many clinical investigations were made with this equipment and with a similar pH-sensitive capsule.

4.5 ../

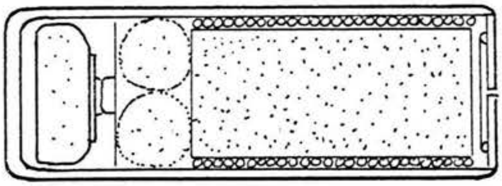
4.5 'The Heidelberg Probe'

Telemetering apparatus using very small capsule transmitters has been developed on a commercial basis by the Telefunken Company for H. G. Nöller of the Universitats Kinderklinik in Heidelberg. One report claims that he has used pressure and temperature sensitive capsules in routine studies on the digestive processes of small children (Nöller, 1959) although he appears to have concentrated on pH-sensitive units that might be used instead of the chemical tests which require materials to be aspirated from the stomach by tubes. These intubation methods are often impossible to carry out on small children whereas he claims that they can pass capsules up to 0.65 cms. in diameter without any trouble. The latest pH-sensitive version for use with new-born babies is 1.7 cms. long and 0.4 cms. in diameter (Nöller, 1960). Unfortunately very little technical or critical information has been given in his reports and in spite of his claims it is difficult to form an opinion of how accurate are his methods.

(i) Capsule transmitter.

The capsules which are made of Plexiglass (Perspex) appear to have been constructed in various sizes. Generally they are quoted as being 1.8 cms. long and 0.8 cms. in diameter and the smallest 1.0 cm. by 0.45 cms. The smallest units oscillated at about 3.7 Mc/s though later versions used lower frequencies around 1.9 Mc/s. A Colpitts type oscillator appeared to form the basic unit, pressures being sensed by a capacitive metallised diaphragm and pH by an external antimony electrode. The temperature coefficient of the transistor was used to detect temperature changes. The transmitters were powered by small 1.5 volt electrolytic cells using magnesium and silver chloride electrodes activated by physiological saline just prior to being used. The pH capsules were not used again after the experiment because of the contamination of the electrode and they appear to be active for only two or

three/



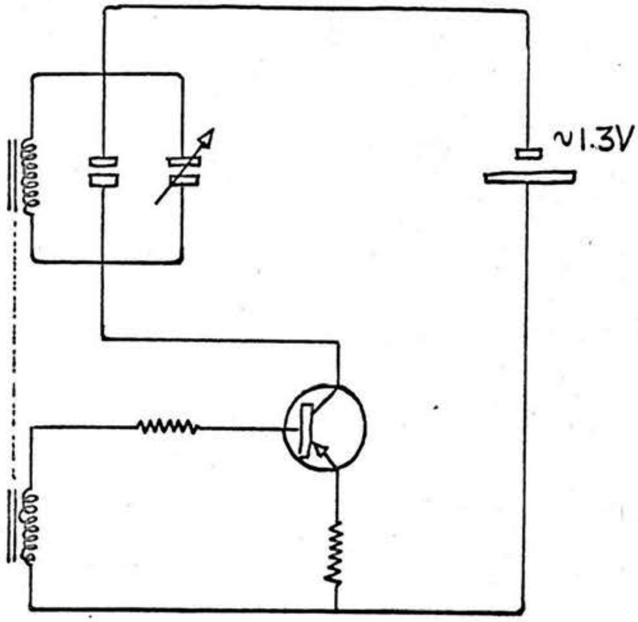


Figure 41

The mechanical design of the externally-switchable capsule, and below, the probable electronic design.

three hours.

(ii) Receiving equipment.

The greatest frequency deviation obtained from the transducers was only of the order 1% and sufficient bandwidth could be obtained using conventional heterodyne radio-receiving techniques. A clamp arrangement was incorporated into the earlier apparatus to prevent recording false signals when the capsule assumed an unfavourable orientation. Later a triple loop antenna was used.

4.6 The externally-switchable endoradiosonde.

A very brief specification of an externally switched capsule transmitter was given recently by F. Lepri and M. L. Ramorino of the University of Rome.

(i) Capsule transmitter.

The pressure sensing element consisted of a brass disc with a small hole in the centre to conduct the pressures to a membrane of silvered mica cemented to the back of the disc. The varying capacitance between these two elements formed part of the resonant circuit of the transmitter. The oscillator circuit was described as 'of conventional design' and probably similar to that shown in Fig. 41. The 'tank' coil and the feedback coil were wound together on a 1.5 cm. ferrite core. The direct connection through the feedback coil between the base and the emitter of the transistor meant that the oscillator did not start spontaneously, and in this resting state the only drainage from the battery was the leakage current of the transistor - about 4 microamps. Oscillations were induced into the 'tank' circuit from a third coil which was outside the body. Since the oscillation was also

induced/

induced into the feed-back coil the regeneration factor of the circuit became greater than unity and the circuit was made to oscillate. The oscillation could be stopped by saturating the ferrite core coupling the feedback loop to the collector circuit reducing the amount of feedback. This was achieved by discharging a large electrolytic capacitor through the external coil. The battery drain during oscillation was about 100 microamps, and it was stated that intermittent operation enabled a life of up to 10 months to be achieved (Lepri and Ramorino, 1960).

(ii) Receiving equipment.

A three-channel receiving system was used to detect the signal from the capsule when it was transmitting. The antenna consisted of a 10 cm. square coil surrounding two coils mounted on crossed ferrite rods and was therefore flat and convenient for clinical applications. The receiver had three input stages, three convertor stages, one oscillator, three intermediate-frequency stages and three discriminators. The outputs from these stages operated a power amplifier driving a low-inertia servo motor which tuned vernier capacitors in the local oscillator and the three antenna tuning circuits. The servo voltage also drove the chart recorder.

The temperature coefficient of the capsule due to the air trapped in the transducer was balanced by a ceramic capacitor with a negative temperature coefficient in the 'tank' circuit. No estimates were given of the reliability of the calibration for pressure over long periods, but the method seems to have a very great potential for long term studies not only in the alimentary canal, but in other organs or body cavities.

PART II

THE APPLICATION OF A PRESSURE TELEMETERING SYSTEM TO A STUDY OF BOWEL MOTILITY

CHAPTER 5

Methods of recording and clinical techniques

Although the technical performance of the equipment had not yet reached the stage where absolute pressure values could be inferred from the recorded data, a series of preliminary clinical studies were started in October 1960 at the Gastro-Intestinal Unit of the Western General Hospital, Edinburgh. The purpose of those studies was to provide a basis for more efficient clinical routines and to establish the technique with the nursing staff of the hospital.

5.1 Clinical procedure.

Particular care was taken when selecting subjects for study to avoid those likely to have abnormal or narrowed segments which would prevent free passage of the capsule. The nature of the investigation was always explained to the subjects in order to gain their co-operation in the study and also to prevent anxiety on their part.

The human stomach, when empty, is small and relaxed, but the middle part, which is often termed the body, can distend to accommodate food without increasing the muscular tension, or tone, of the stomach wall. After a meal, food lies in the body of the stomach in distinct layers, which generally are not completely mixed together until gastric emptying is almost complete. Weak rings of contraction pass over the wall of this part of the stomach, but these do not have much direct effect on the gastric content until they become stronger in the narrower and more muscular parts near the pylorus.

The ingested capsule has a density which is slightly greater than normal gastric contents and it eventually settles against the lower surface where it is acted on by the weak contractions and slowly moved towards the pylorus.

If/

If the capsule was swallowed in the morning before any food was taken, it usually passed into the small bowel without any delay. There were, however, occasional lapses when the capsule was held back for many hours and sometimes all or part of the small bowel activity was missed because recording had been temporarily abandonned to allow the patient a break from the monotony of constant observation.

At first these delays were not serious because they enabled us to make one or two lengthy records of gastric activity, but later when we attempted to standardise the recording conditions, the simple technique of giving the capsule 'on an empty stomach' proved to be too variable. It is not surprising that delay should occur at this point because one of the natural functions of the mechanism guarding the outlet from the stomach to the small bowel is to prevent the onward passage of the larger food particles in the stomach.

The complete absence of subjective sensations once the capsule had been swallowed, meant that, compared to other methods, long periods could be used for observation without tiring the patient. They could read or listen to the radio as they lay in bed, but it was always better to allow intermissions every two or three hours if the patient was well enough to be allowed up, to ease the monotony of enforced physical inactivity. The occasional delays at the pylorus led to a considerable waste of those periods when the patient was settled, and the more interesting periods, e.g. when the capsule was passing through the small bowel, could not be arranged to occur conveniently throughout the day and night. Sometimes, in spite of reassurances to the contrary, the concern of the clinician with detecting the onset of small bowel activity caused the patient to suspect that something fairly serious had gone wrong with the investigation.

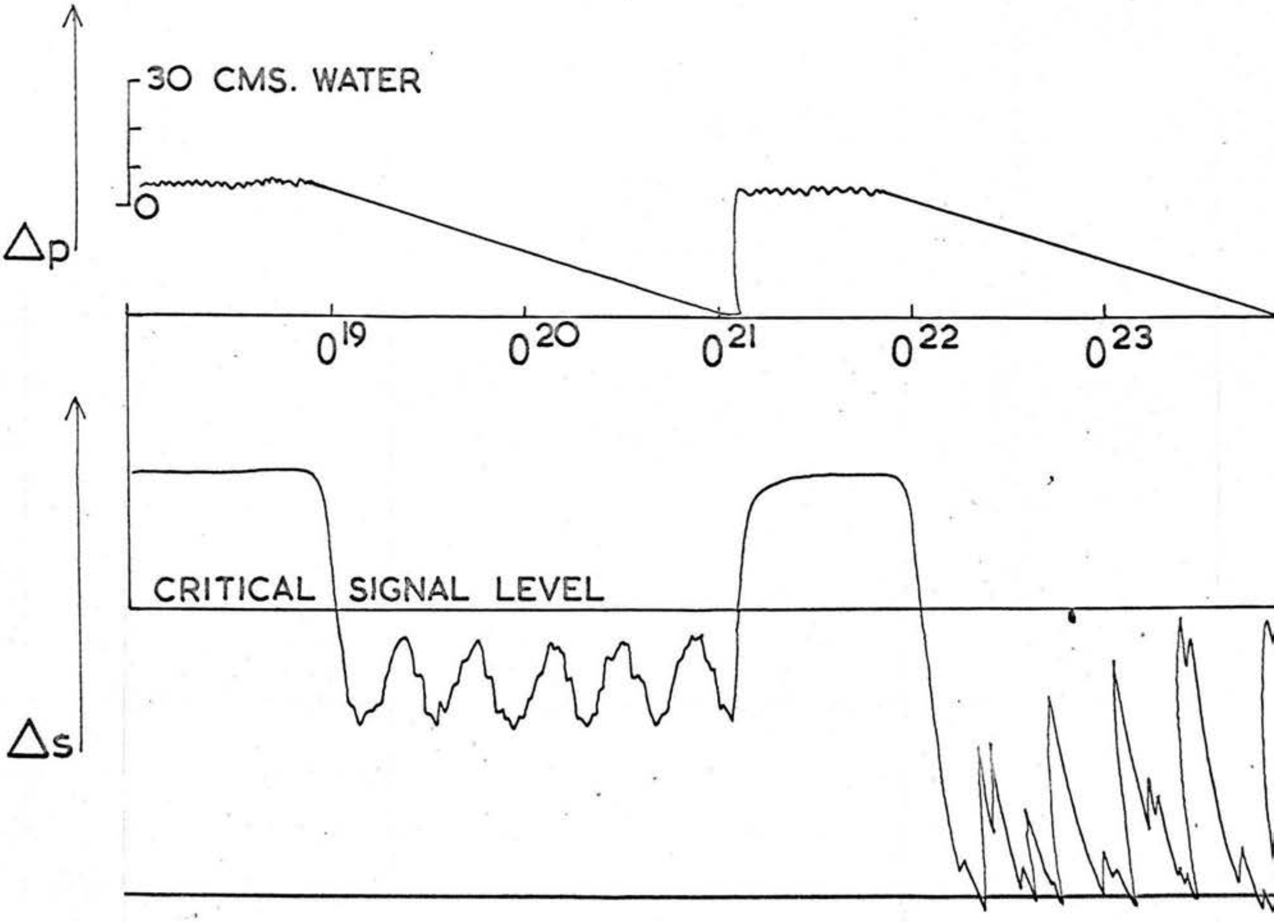
To/

To ease these problems a more systematic approach was adopted for the later experiments whereby the capsule was swallowed in the late evening just before the patient went to sleep. A piece of soft thread of sufficient length to allow the capsule to pass out of the stomach, but not beyond the distal part of the duodenum, was attached to the capsule and fastened securely to the collar of the patient's bedjacket; between 70 and 80 cms. was usually allowed from the lips, depending on the build of the patient. On one occasion the subject complained that the thread had led to discomfort during the night; this was apparently due to the capsule being allowed to pass too far beyond the pylorus.

If a tracing had been made overnight the change from gastric to duodenal pressure activity could usually be seen, but a radiograph was taken as a matter of routine to establish the exact point from which the capsule started its transit.

Only on one occasion out of the fourteen experiments did the capsule not pass the pylorus overnight. In this case the thread was divided to prevent irritation and it was passed into the small bowel during the course of the day.

After the thread had been divided, recordings could be made either intermittently or continuously as the capsule made its way through the small bowel. The activity of the large bowel could be recorded overnight and during the following day, sometimes right up to the time that the capsule was passed. Whether or not this was done depended on the nature of the experiment and the willingness of the patient to be studied for long periods. Once the capsule had passed into the large bowel each evacuation was collected in special black plastic bags which could be sealed. Identification was easy if the capsule continued to transmit after it was passed; on these occasions it was re-calibrated/



<u>Figure 42</u>

Weak gastric contractions at the typical rate of three per minute shown on the signal level tracing (Δs) by the 'field edge' effect. Evidence of these contractions cannot be seen on the pressure (Δp) tracing.

The time scale is marked at minute intervals.

re-calibrated for pressure to estimate the drift of the transmitter. If the battery was exhausted before the capsule was recovered, the plastic containers were kept until the capsule had been positively identified. The soft containers minimised the problem of locating the capsule.

5.2 Recording technique.

(i) 'Field edge' effects.

Quite soon after the clinical trials had started we discovered that the absence of significant pressure activity on the tracing did not prove that muscular activity in that particular organ was absent, or that the capsule was not being moved along the bowel. Rapid and marked changes in the amplitude of the recorded signal strength indicating quite vigorous changes in orientation often occurred spontaneously, even when no pressure changes were recorded. These changes were seen sometimes for periods of an hour or more. The channel recording signal strength which had been added originally to help in distinguishing the artefact due to excessive coupling variations, was often found to produce tracings of great interest during these periods.

The nature of the inductive coupling between the capsule and the antenna loop is such that a quantitative calibration of this 'amplitude modulation' effect would be extremely difficult to carry out, but the effect may be exaggerated or minimised by changing the relative position of the antenna loop (Fig. 31). If the 'steep gradients' of signal level change at the edge of the field where the capsule and antenna coils are almost at right angles, were used, even the small movement of the abdominal contents with the respiratory excursion of the diaphragm could be seen (Fig. 42). It was also possible, during all but the most vigorous movements, when the capsule/

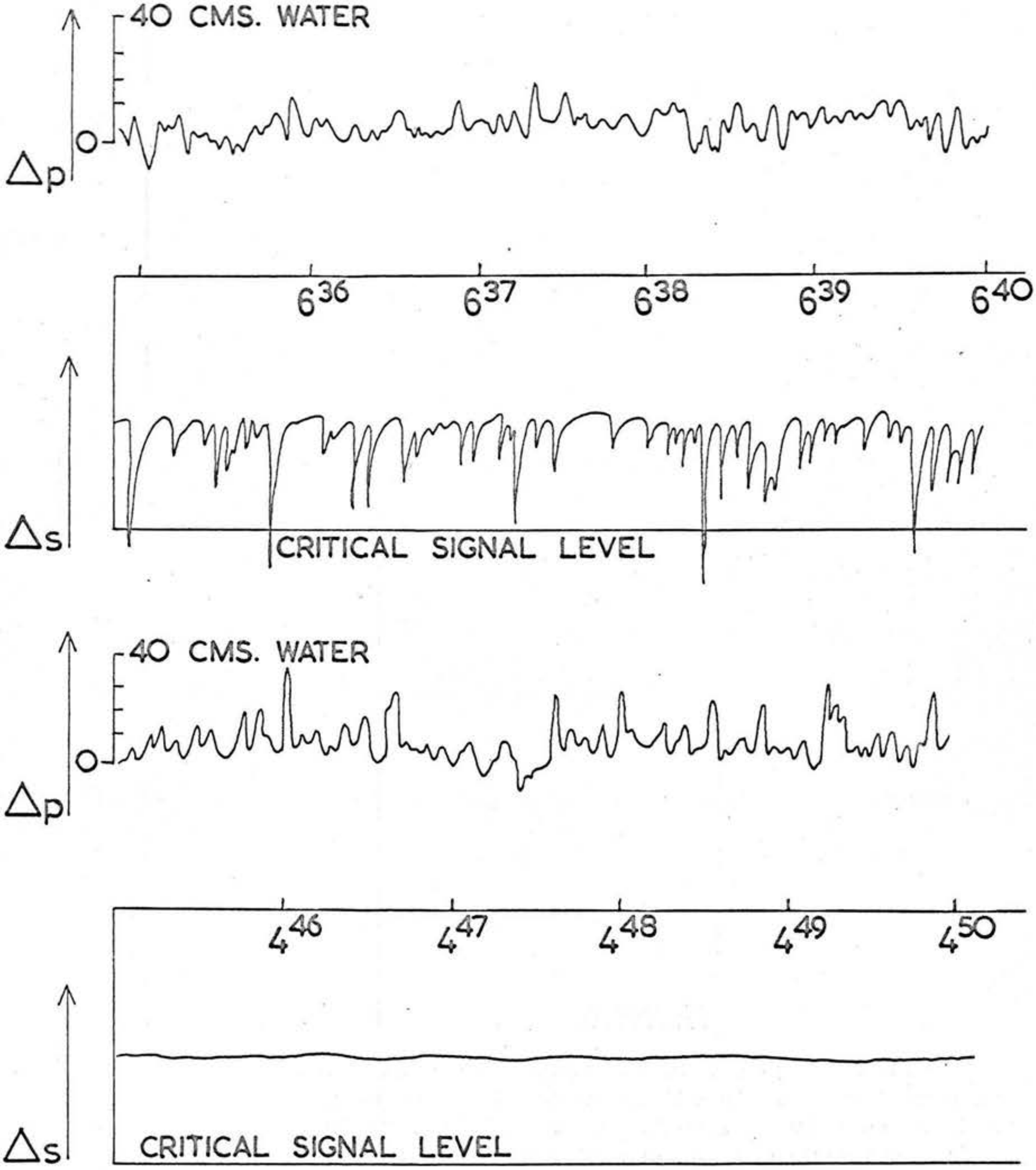


Figure 43

Pressure activity in the small intestine. Above - at a loop position where the movements associated with the pressure can also be recorded.

The time scale is marked at minute intervals.

capsule was being constantly re-orientated through wide angles, to find a loop position where the amplitude effects did not cause serious discontinuity in the pressure record. Occasionally it was possible to find a site where both pressure variations and orientation change could be recorded simultaneously (Fig. 43). Besides recording pressures we were thus able to record periods showing pressure and movement, and also periods showing movement alone.

A method using this variation in coupling to deduce information about orientational changes between the capsule and the external antenna loop has been described by Sprung (1959). He used a totally enclosing antenna loop encircling the abdomen of the subject in order to be able to detect the weak signals from the capsule-transmitters that he used. It appears from his reports that he was able to record pressure variations and orientation changes simultaneously for most of the time. Using an antenna loop which has a fixed orientation to the abdomen removes the ability to make use of the properties of different parts of the capsular field except for the occasions when the capsule itself happens to turn into the appropriate position relative to the antenna loop. Best use can be made of this coupling effect if a small mobile antenna loop is used.

(ii) Multiple loop antenna.

It seemed an obvious expedient when using the mobile antenna loop to arrange a number of other similar loops around the patient's abdomen as he lay in bed. Four loops mounted in a strip of soft expanded plastic material were connected to the receiver through a simple manual switch mounted at the side of the bed, underneath the receiver unit (Fig. 44). This light belt of antenna loops could be pinned under the top fod of the bed cover and positioned conveniently across the patient's abdomen without restraining his freedom of movement or allowing the loops to slip about the bed. Any one of these/

Figure 44

The double-channel recording system with the manually switched multiple loop antenna seen on the bed. The reference-frequency generator, seen beneath the recorder, could also be switched to the input to check the basal levels of the capsule and the receiver.

these four fixed loops could be switched to the input of the receiver or a fifth mobile loop could be selected and positioned in a part of the capsular field not incident on any one of these loops. The regular use of this simple array of aerials led us to discover other qualitative features which frequently helped to complete our estimates of the capsule's position and its rate of progress. For instance, we found that the outlying loop on the right side of the abdomen gave the most steady level of signal when the capsule was approaching the ileo-caecal valve or when it was in the caecum or the right colon; whereas the outer loop to the left was used most frequently when the capsule was in the distal transverse colon. These observations gave only approximate information, but they were often found to be helpful if the deduced movement could be judged to be anatomically reasonable in relation to the radiographs.

5.3 Localisation of the capsule.

The clinical value of the intra-luminal pressure data is limited unless it can be associated with a particular segment or length of the bowel. Activity that might be considered normal in one organ may well be indicative of an abnormal or pathological condition if it is seen at some other site. A continuous and permanent record of the change of site as the capsule moves along the digestive tract would be the most satisfactory solution, but the technical complications of such a system are considerable. Location either by radio-direction finding methods or by radiography only fix the position of the capsule within the body space, or in relation to its bone structure; for this particular problem its position must be related to the anatomy of the alimentary tract. A continuous recording of the movements of the capsule in two, or preferably three, dimensions would be the best solution to this problem because/

Figure 45(i)

The capsule in the small bowel.

because the general picture of progress down the bowel is fairly well known from radiological studies. Simple radiographic location is, however, possible in every hospital and these methods have been used almost exclusively up to this time. A continuous radiographic method is, of course, not possible in human applications because of the dangers of excessive exposure to ionising radiations.

(i) Spot determinations.

Localisation by radio direction-finding methods requires a small, non-directional antenna. Manual tracking with such an antenna is tedious and over the periods of many hours such as would be required for correct estimations, completely impracticable. Simple location in the body space can be ambiguous at many sites, particularly in the mid-abdominal region where the convolutions of the small bowel generally overlap not only on itself, but also on the stomach and on the transverse part of the colon. Spot radiographic determinations, although simple to carry out, can be ambiguous unless care is taken to plan the spacing of the radiographs.

There are several established techniques which may be applied to resolve these uncertainties. Contrast media can be used to outline parts of the bowel and it has also been suggested that two exposures could be used to obtain a stereoscopic projection. We have preferred the first method using only a single exposure because we were interested only in identifying the part of the bowel in which the capsule is lying. The information that can be deduced from the characteristics of the pressure patterns already known from previous intra-luminal pressure studies sometimes helps except during the periods when no characteristic activity is seen. We tried to establish a simple routine which would make it easier to compare the records that we made during the different experiments.

The/

Figure 45(ii)

The capsule in the stomach.

The subject was at first asked to swallow the capsule in the early part of the morning, whilst fasting, to exclude as far as possible, retention of the capsule in the stomach. Unless it was obvious that the capsule had not yet passed out of the stomach, a localisation radiograph was taken about four hours after the capsule had been swallowed. Two small doses of bismuth carbonate in half a glass of water, were given to the patient, one in the morning before the test started and one just before the first radiograph. These 'meals' outlined the terminal ileum and the caecal region and also the stomach at the time when the X-ray was taken. In every case the faint bismuth 'shadows' enabled unambiguous 'fixes' to be made (Fig. 45i). Generally the capsule was found to be in the upper or mid small bowel at this time, although on two occasions during the first six experiments it was found to be still in the stomach (Fig. 45 ii).

A second radiograph was taken after a further lapse of two or three hours, or when the capsule was thought to have passed into the large bowel. At the time of the first radiograph if the capsule was in the small bowel, it was 'trapped' between two doses of the radiopaque marker fluid and the relative positions of these shadows on the second picture enabled us to make an estimate of the overall motor activity of the bowel as well as having a continuous record of the pressure activity (Smith and Ridgway, 1961).

It has been claimed that X-ray apparatus with an electronic image intensifier system would enable the total routine dose of irradiation to the patient to be reduced (Connell, 1961a), but we have been guided by experienced radiologists who are of the opinion that the estimation of the site would be more difficult, even with contrast techniques, because of the smaller area covered, and the saving in X-ray dose would not be appreciable because of the preliminary/

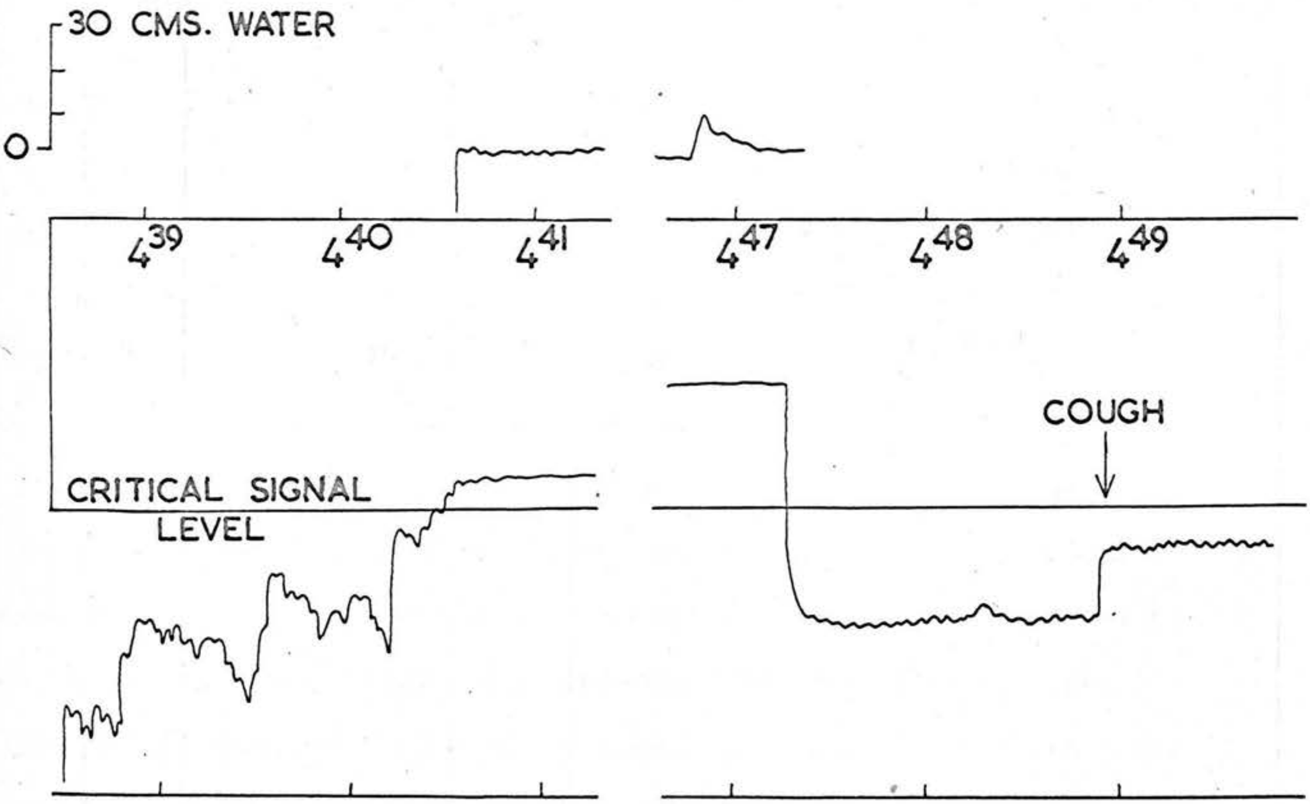


Figure 46

Two short sections from a recording six minutes apart showing passage of a capsule into the caecum.

The time scale is marked at minute intervals.

preliminary exposure required to find the approximate site of the capsule. Screening apparatus of this type, if it were available, could be used at interesting moments, say when the capsule was being passed into the caecum, but impromptu use in this manner would probably lead to a greater total dose than a fixed programme of simple abdominal radiographs.

(ii) Interpolation.

From our occasional studies with image intensifying apparatus the capsule appears to make steady progress all the time that it is in the small bowel until it reaches the distal parts near the ileo-caecal valve where it sometimes comes to a complete halt for periods up to an hour or more. Other workers have also reported complete stasis of the capsule in the terminal ileum for similar periods. The capsule often remains in the caecum for long periods and we have come to associate lack of activity at this stage in a clinical experiment with a site in the caecum, particularly if respiration artefact is prominent. Onward movement in the large bowel appears to be much more occasional than in the small bowel and the capsule seems to move considerable distances across the abdomen during relatively short bursts of activity. The structure of the large bowel is such that location of the capsule within the body frame gives a good indication of its position within the organ. Simple timing is, therefore, quite a reliable means of interpolating the capsule position between radiographic fixes when it is in the small bowel, whilst a measure of the level and steadiness of the signal strength can be used to aid location, even with a directional aerial, when the capsule is in the large bowel.

When use was made of the 'field edge' effect the appearance of three per minute contractions of the stomach served as a reliable indicator that the capsule had not yet passed into the small bowel, enabling us to delay the first radiograph/

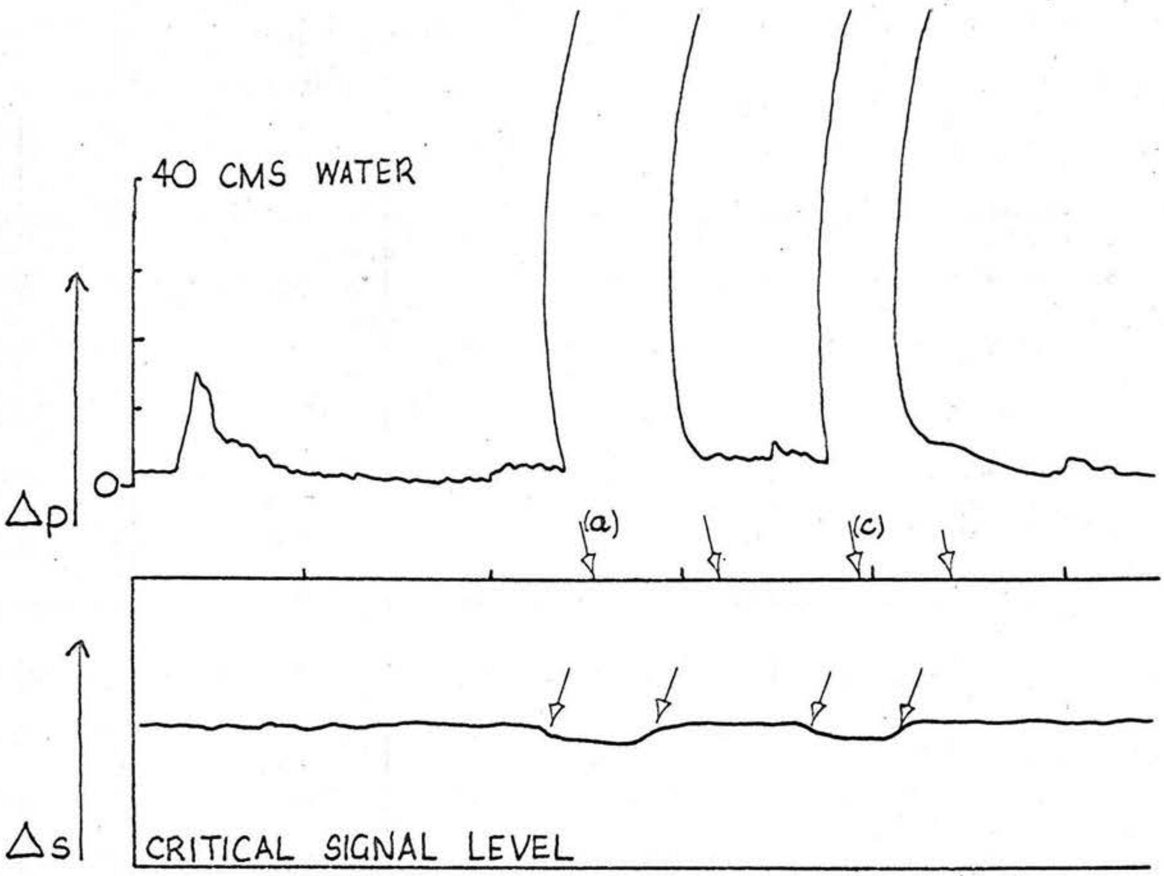


Figure 47

The effect of switching at (a) and (c) to an 'overcoupled' loop.

radiograph. Frequently evidence of these contractions could not be detected on the pressure trace (Fig. 42). Sometimes this method could also realise additional information on the capsule's behaviour. For instance in Fig. 46 recordings of the signal level taken from two parts of the continuous tracing, six minutes apart, show distinct differences in the capsule's movements. The tracing on the left shows the capsule undergoing gentle back and forward movements as it approached the aerial loop, which was on the right-hand side of the abdomen near to the ileo-caecal junction. No significant pressure activity was seen on the recording during the next six minutes, until a single small wave suggested that the capsule might have passed into the caecum. Recording the signal level from a position at the edge of the field showed that the capsule appeared to be stationary, consistent with it lying in the caecum. This conclusion was also supported from the way that a cough displaced the capsule nearer to the antenna loop, as it might do in a relatively large organ.

The overcoupling effect discussed in section 3.1 (ii) locates the capsule to within two or three centimetres which is often adequate to fix the position of a capsule in the large bowel, where it is usually near to the surface of the abdomen. Fig. 47 shows this effect and how, by switching between loops at different sites, it can be seen to be a function of the loop position.

(iii) Tracking.

The methods of making spot determinations by manual antennae and radiography are essentially temporary methods devised to enable us to make useful clinical recordings until such times as a simple method of automatic localisation is developed. Jacobson has recently described an automatic system which follows the path of the capsule as it moves through the body, marking the movements on a chart supported on a plastic table across the patient's/

patient's abdomen (Jacobson, 1962). The method uses an omnidirectional antenna rotated at a rate of 1 c/s about an axis at right angles to the surface of the chart and almost perpendicular to the abdominal surface. If this point of rotation does not coincide with a point of symmetry in the dipole field surrounding the capsule, then the level of signal incident on the antenna varies at the frequency of rotation, i.e. at 1 c/s. These variations in the signal level were made to operate two small servo motors which moved the axis of the system until it arrived at a point of symmetry in the field. This point is approximately the shortest distance from the point on the chart to the capsule. The marker pen, mounted on the antenna axis makes a two dimensional tracing following the movements of the capsule within the body. The system is continuous and automatic in operation and if the speed of response can be made fast enough the movements of the capsule, in two planes at least, can be correlated with the pressure changes. This sort of application will probably be as important as its use in following the long-term progress of the capsule through the alimentary tract.

5.4 Application to the study of various organs.

although this new technique of telemetering information from the natural cavities within the body is a major advance in methods of making clinical measurements, it cannot be applied with equal advantage to all the digestive organs.

(i) Oesophagus.

In the oesophagus, although the capsule could be held stationary, by means of a thread, somewhere between the upper and lowersphincter zones, approx. 25 cms. from the loop, it is poorly adapted for measuring pressures in the sphincter zones themselves because of its large diameter. The tube methods commonly/

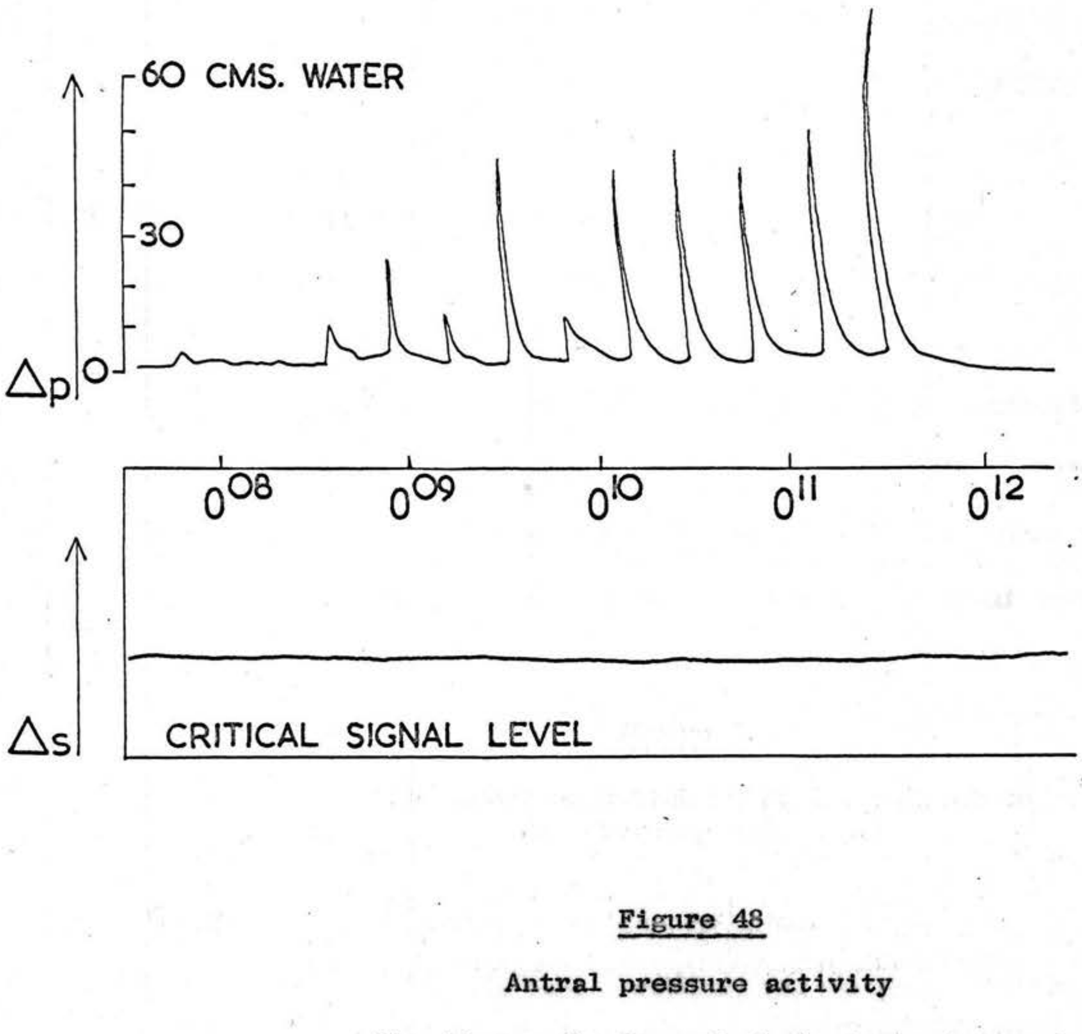


Figure 48

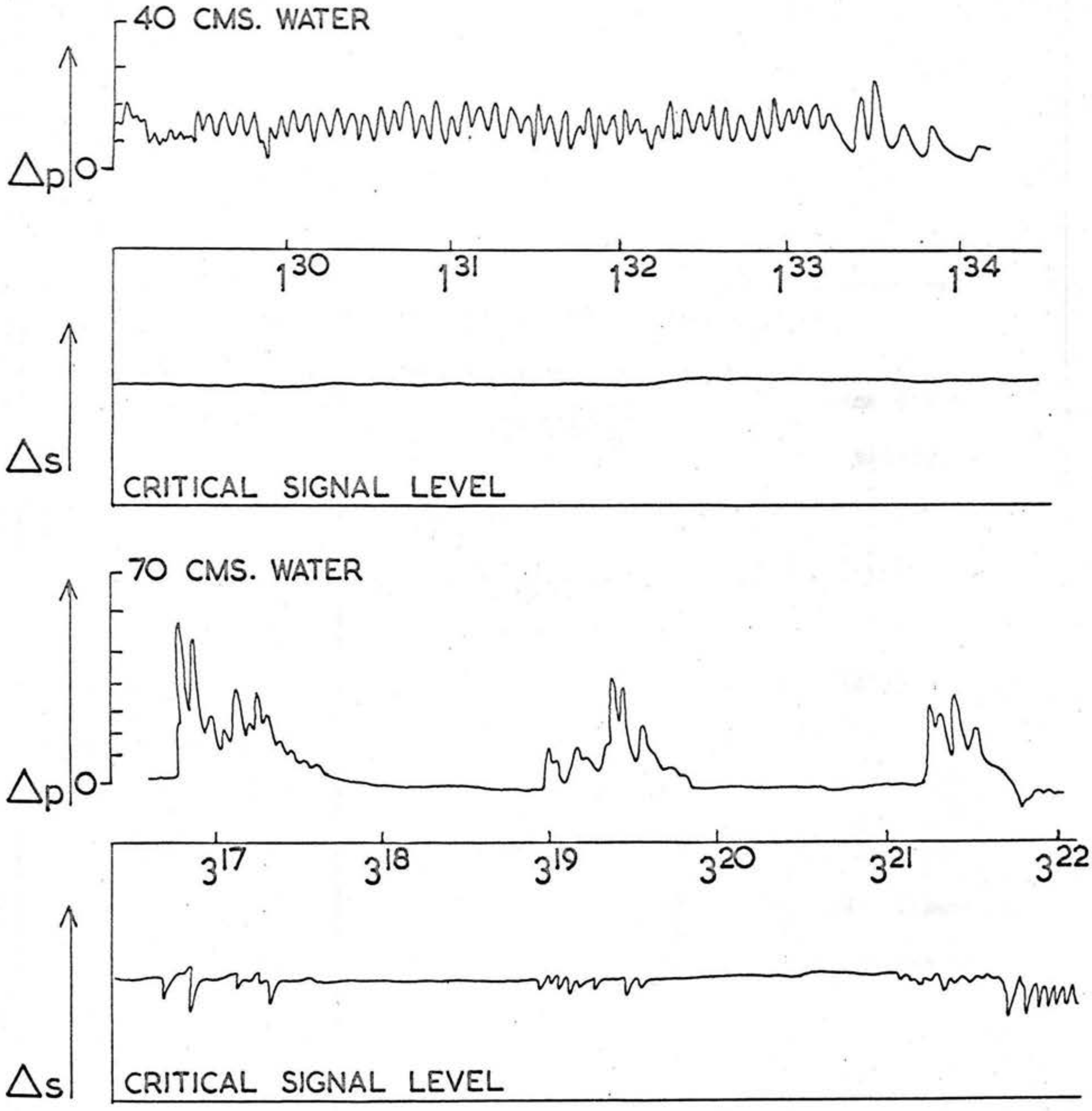
Antral pressure activity

The time scale is marked at minute intervals

commonly used are simple and reliable and they enable more useful information to be gained about peristaltic action because they allow simultaneous measurements at many points. The connecting tubes can be made of very small diameter without restricting the frequency response of the system because of the short distance to the external recording equipment. Moreover, I consider it to be a misuse of the technique to employ a capsule with a restraining thread even for mid-oesophagus studies, where small transducers would obviously be more reliable. We did not, therefore, carry out any clinical studies in the oesophagus.

(ii) Stomach.

Recordings of the pressures and movements associated with the muscular activity of the stomach were obtained in eighteen of the clinical experiments. The very constant periodicity of the contractions, at approximately three per minute, was a most striking feature of all the records, sometimes being displayed continuously for many hours. In the light of our experience, it appears that the capsule with its specific gravity slightly greater than other gastric contents was moved about more as a result of postural changes by the patient than by the muscular action of the stomach itself. It also became clear that pressure 'activity' could be present at one site within the stomach and not detected at another, so the recorded incidence of pressure activity is probably related more to the restlessness of the patient than to the actual muscular activity of his stomach. Long periods were often seen when no significant pressure fluctuations could be detected on the manometer tracing, yet the presence of the three per minute movement could be demonstrated using the 'field edge' effect. This confirmed that the capsule lies for long periods against the lower surface of the body of the stomach where the shallow contractile rings do not compress the contents of the organ, but merely change its shape. Only on rare occasions/



<u>Figure 49</u>

Rhythmic pressure changes recorded from the upper small bowel

The time scale is marked at minute intervals.

occasions when the capsule was known to be in the stomach, could this three per minute activity not be demonstrated and this must have been either when the capsule was lying in the fundus of the stomach, above the level of the origin of these contractions, or possibly when the organ was at rest.

The mobility of the capsule and the consequent uncertainty in the position of the capsule within the stomach makes it difficult to draw conclusions about the incidence or significance of gastric pressure activity. The Type II pressure waves, obviously associated with the more muscular parts of the antrum and the pre-pyloric regions (Fig. 48) were usually seen at intervals throughout the gastric phase but the positional uncertainty associated with this technique made the quantitative study of these patterns pointless. The method is, therefore, less effective for studying gastric activity than the intubation techniques.

(iii) Small bowel.

Our objective in all forty of the clinical experiments that we undertook between October 1960 and June 1962 was to make as complete a record as possible of the pressure activity along the length of the small bowel. We expected to be able to judge when the capsule left the stomach by the onset of multiperiodic waves which were thought to be characteristic of the pressure activity in the upper part of the jejunum. We found, however, that a capsule could complete its journey through the small bowel into the colon without giving rise to any significant or recognisable pressure wave-forms. Sometimes this happened in control studies on subjects without any clinical symptoms, but more frequently it occurred in patients who suffered from 'intestinal hurry' or diarrhoea. For some of the time we usually saw the regular patterns which are so often described in the literature (Fig. 49), but there was a wide variation in almost every aspect of these patterns.

The/

The frequencies which are often quoted in the analysis of this type of activity were often obscured by irregular changes and the greater part of the recorded activity could not be easily described in precise terms.

The time that the capsule took to travel through the small bowel varied from about four to eight hours although again there appeared to be a wide variation. The figures could not be determined precisely because of the difficulty encountered in making an accurate diagnosis of when the passage, into and out of the small bowel, occurred. Transit times for the head of a barium meal moving through the small bowel are sometimes quoted as being as low as fifteen minutes. These estimates with heavy pastes are probably unrealistic since the essential processes of absorption in the small bowel must require contact between the mucosa and the bowel contents for much longer periods. There seemed here to be a topic worthy of further investigation, but the nature of the study requires the interest of a radiologist who has access to a large number of patients having routine radiographic examination.

The fact that we were able to study each of these cases with a minimum of interference, shows the undoubted advantage of the telemetering method over the tedious and upsetting procedures of intubation, but the positional uncertainty resulting from the freedom of the capsule made it difficult to establish a steady basal level of activity such as would be required for the testing of drugs.

On one occasion we restrained onward movement of the capsule for a short period in the small bowel with a length of thread, in an attempt to study the effect of certain drugs. The thread, however, cannot remove the possibility that the longitudinal muscle of the bowel may have moved the bowel over/

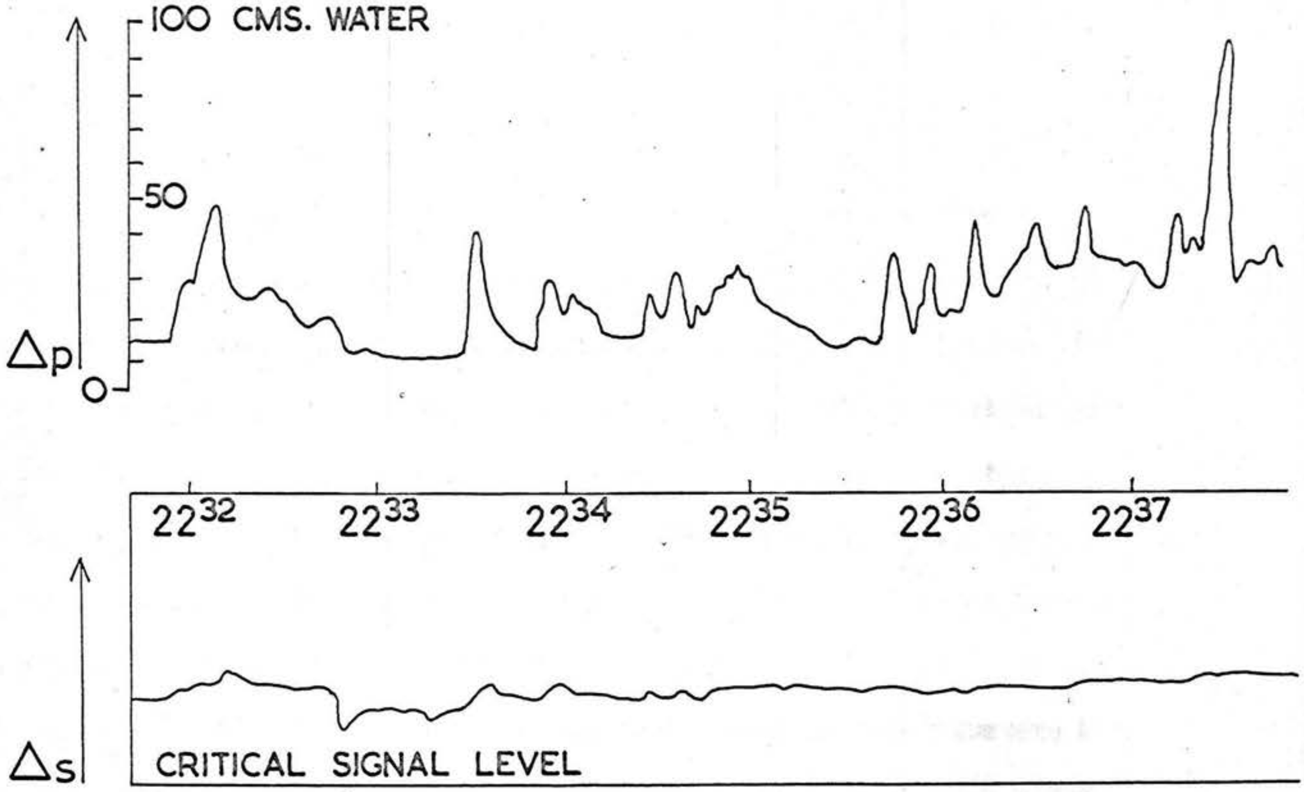


Figure 50

Typical build up of pressure in the distal large intestine

The time scale is marked at minute intervals over the capsule. The method cannot be considered to be satisfactory or conclusive for this purpose.

(iv) Colon.

Activity can be recorded very easily by the capsule system from all parts of the colon. The latest units are capable of transmitting for five or six days so that it is possible to make a complete recording even from constipated patients. Localisation in the colon is not such a serious problem as it is in the stomach and the small bowel, because of the relatively long periods that the capsule remains at one site. In the distal segments the question arises as to whether it is valid to interpret the intra-luminal pressure as an accurate measure of the muscular activity of the organ or whether the dominant effect is that of the change in the nature of the bowel content. Long periods of quiescence were commonly recorded from the colon and pressure changes when they occurred, tended to be complex though more clearly defined than in the other organs (Fig. 50). The latter did not seem to be directly related to movement of the bowel content.

5.5 Physiological artefacts.

Measurements of intra-luminal pressure have a 'background' of pressure variations not originated by the muscular action of the organ being studied, which limits the accuracy of such measurements more than the present technical limitations of the capsule transducing and transmitting system. The wall of the bowel is not completely rigid and so a certain part of the intra-abdominal pressure changes must be conducted to a pressure-sensing capsule within the lumen of the bowel. We have termed changes on the record due to this effect, physiological artefacts.

(i) ..../

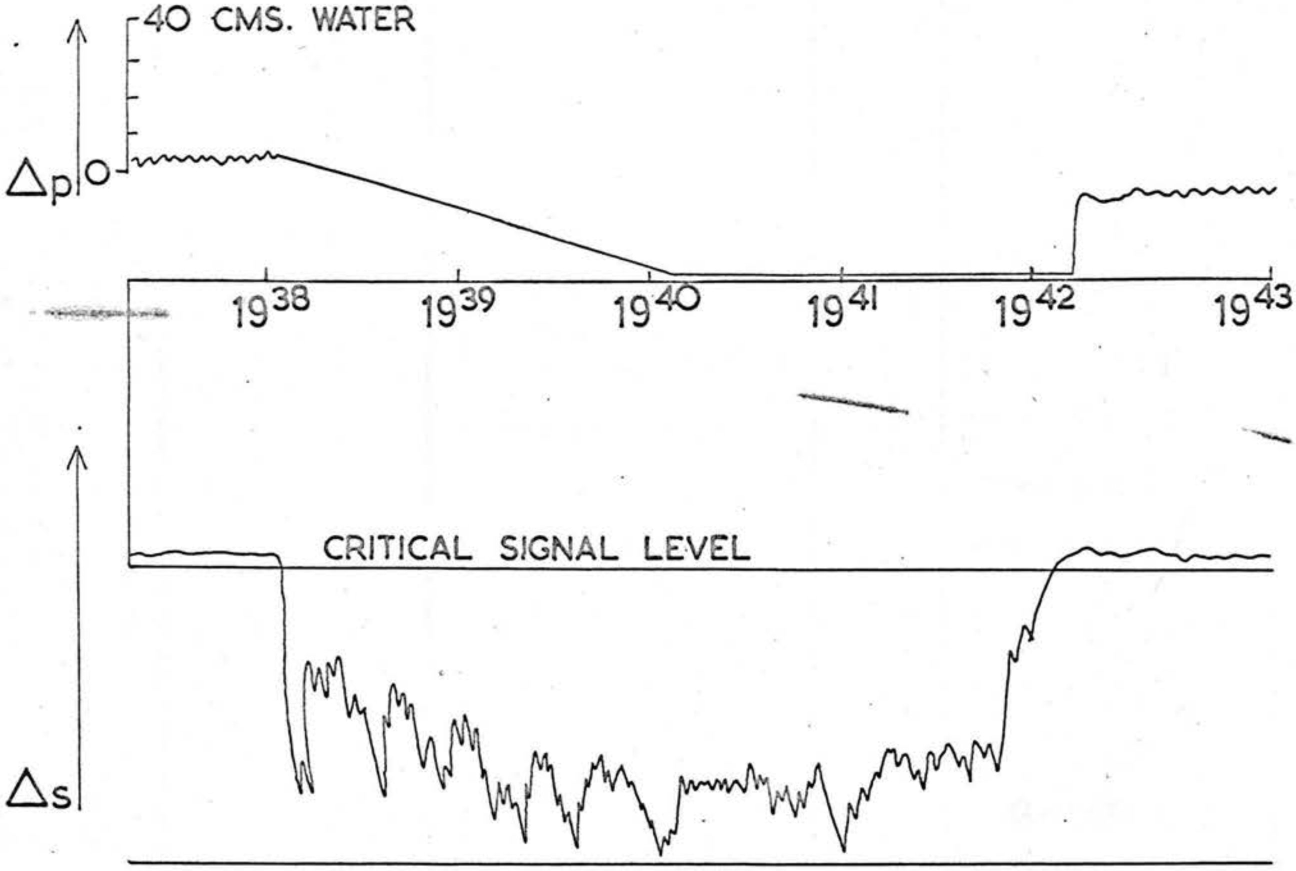


Figure 51

Movements of similar periodicity to gastric contractions seen when the capsule is lying in the large intestine. The smaller superimposed excursions are caused by the regular movement of the diaphragm.

The time scale is marked at minute intervals.

(i) Respiratory artefact.

The rise and fall of intra-abdominal pressure with the excursion of the diaphragm could usually be recognised on the recordings by its regular rhythmic nature. In certain areas of the abdomen the forward movement of the abdominal wall dominates the influence of the diaphragm and the phase relationship to the rise and fall of the chest can, therefore, vary. The effect on the intra-luminal pressure records amounts usually to only two or three centimetres of water and it does not lead to any uncertainty in the gastric and colonic pressure patterns. Occasionally if the pressures are small the patterns in the small intestine can be confused with the respiratory rate, which varies between twelve and twenty-four per minute, sometimes being of about the same frequency as the faster activity in the jejunum. Some subjects appeared to conduct intra-abdominal pressure artefacts much more prominently than others. The reasons for this are not clear but do not appear to be related to any specific physical characteristic.

(ii) Postural and transmitted effects.

Unless there is some muscular rigidity in the wall of the bowel, the weight of overlying body tissue and fluid forms part of the hydrostatic pressure at any point within the bowel. Unpublished work by Edwards and Rowlands, quoted by Connel (1961b) confirmed this by showing that the basal pressures in the small intestine of the cadaver were in the same range as in the living subject, and that the pressure recorded was directly related to the distance of the recording point from the body surfaces. This factor will, therefore, be modified by postural changes and also by movements of the capsule from one particular site to another deeper within the abdomen. Transient pressure changes occur when a subject moves from a standing to sitting position, but generally these effects are masked by the effects of traction in the abdominal muscles. Coughing causes large changes in the recorded pressures, often up to one/

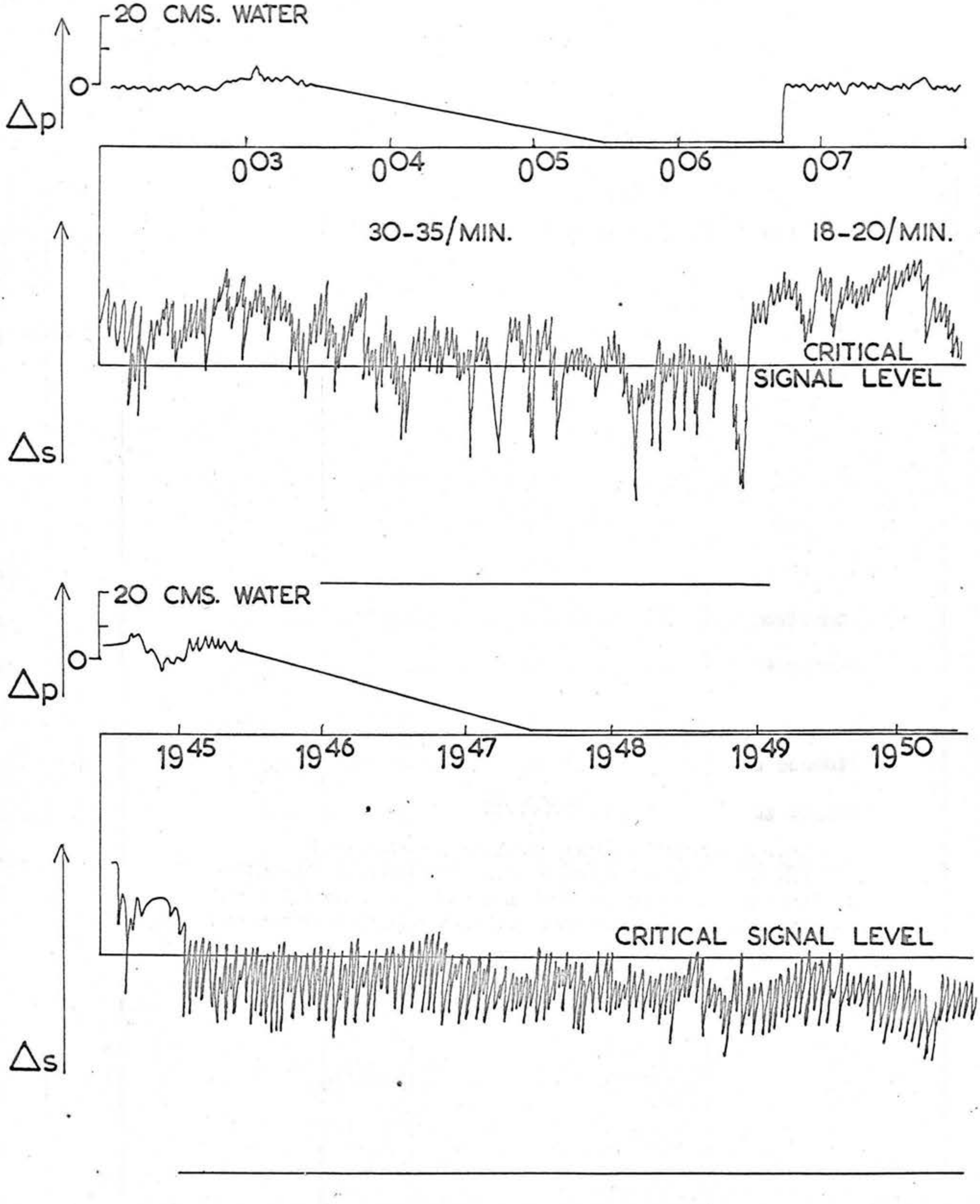


Figure 52

Capsule movements of high frequency exaggerated by the 'field edge' effect

The time scale is marked at minute intervals

one hundred and eighty centimetres of water or more, but these artefacts can usually be recognised by their typical sharp-fronted appearance.

The changes in atmospheric pressures which commonly amount to twenty or thirty centimetres of water over periods of a day or more, must also effect the pressures recorded by an ingested capsule. Attempts to correlate these changes with the basal pressure levels recorded from six subjects were unsuccessful, probably because of the smallness of the effect in relation to other changes after it has been conducted through the body tissues to the capsule.

In the ascending colon the phasic pressure activity is quite variable from subject to subject in both nature and duration. Faster movements were seen on several recordings which appeared to indicate a relatively rapid muscular action, apparently not reported by workers using intubation methods. Evidence from movements seen in the transverse colon showing the typical stereotyped three-per-minute rhythm of the stomach (Fig.51), together with the periodicity of the changes and the fact that no radiological evidence appears to have been documented about such colonic activity led us to suspect that these fast movements may have been effects transmitted from the rhythmic activity of the small intestine. They were seen only intermittently and this also supports the idea that they were transmitted effects occurring as the position of the capsule against the gut wall changed.

(iii) Cardiovascular pulsations.

Very rapid movements, presumably caused by the capsule lying against pulsating arterial vessels were seen occasionally when the capsule was lying in the stomach near to the aortic vessels and in the recto-sigmoid region where it was presumably lying alongside the iliac vessels (Fig. 52). These effects appear to be random and only cause sufficient movement to distort the pressure trace if the recording antenna happens to be lying near to the

'edge/

'edge of the field'. The movements are generally too rapid to be traced clearly by the recorder.

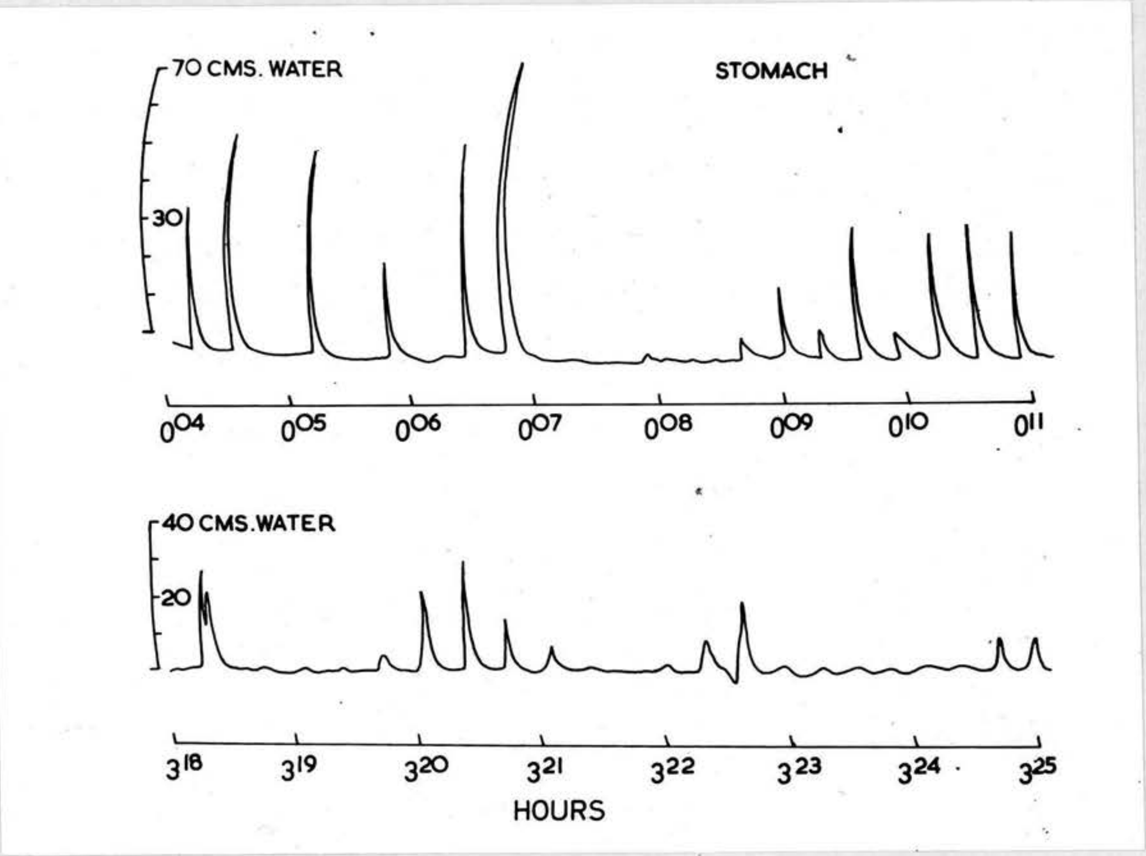


Figure 53

Typical gastric pressure activity.

CHAPTER 6

The control studies

The introduction of tubeless techniques to pressure measurements in the alimentary tract immediately made it practicable to carry out routine studies of intra-luminal pressure patterns on hospital wards. One of the objectives of our clinical experiments was to establish if such studies could be used to obtain quantitative expressions for any of the variables associated with the clinical symptoms of common gastro-intestinal disorders.

Previous documented studies of intra-luminal pressure patterns in humans, because they depended on difficult intubation methods, which are often unpleasant procedures for the patient, seem to have been confined to limited experiments in the physiological laboratory. Our findings did not differ very much from those of the 'tube' experiments and we found it convenient to adopt the methods of describing the patterns as those used in the literature, although they did not prove to be completely satisfactory.

6.1 Classification of intra-luminal pressure patterns.

All the authors segregated the waves into at least two groups, depending generally on either the periodicity of rhythmic waves, or the duration of waves which occurred singly. The most widely accepted scheme, that proposed by Code and his co-workers (1952), is based on the methods used by Templeton and Lawson (1931) to classify colonic motility in dogs and describes the pressure patterns in terms of four different wave types.

Type I waves are simple monophasic changes of low amplitude, between 5 to 15 cms. of water, and lasting from 5 to 20 seconds. They occur singly and also in groups, when their rhythm is that which is characteristic of the part of the bowel in which the capsule is lying.

Type/

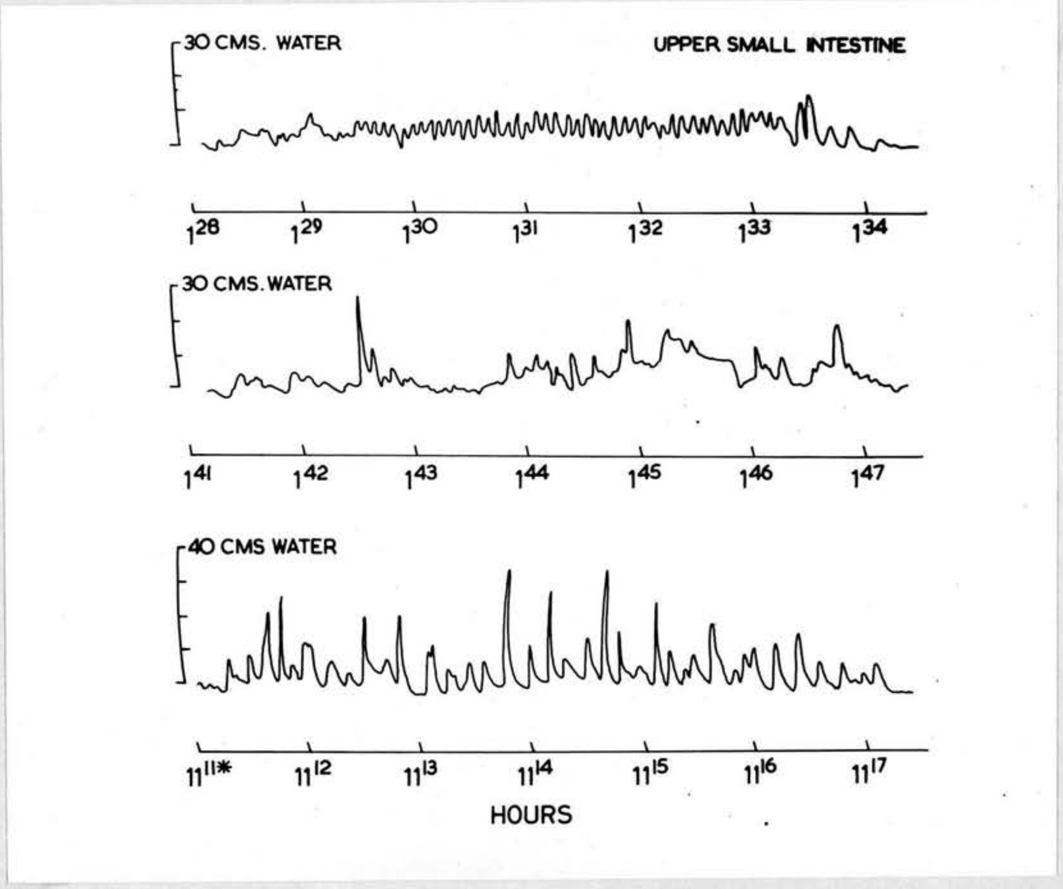


Figure 54

Typical pressure activity in the upper small bowel.

Type II waves are simple changes, not necessarily monophasic, and of greater amplitude than Type I waves, usually between 15 and 80 cms. of water; each wave lasts from 12 to 60 seconds. In the stomach their rhythm is the same as Type I waves, but in the colon they are usually slower.

Type III waves are complex formations whose most important characteristic is a rise in base-line lasting from a few seconds to some minutes. This rise is less than 20 cms. of water in the stomach and usually between 25and 40 cms. of water in the small bowel. Often Type I or Type II waves are super-imposed on this elevation of base line.

Type IV waves occur only in the terminal ileum and the colon; their rate when rhythmic is one every 2 to 4 minutes. The wave rises to a pressure of 70 to 100 cms. of water in about 30 seconds and falls more slowly.

The gastric activity seen in Figure 53 shows how the pressure waves may occur either at the fundamental human gastric rhythm of 3 per minute or in a non-rhythmic sequence with each wave separated from the preceding one by some multiple of 20 seconds. Gastric Type I and Type II waves show this same basic rhythm and they may occur in series or they may alternate (as seen in the period 0^{09} to 0") The sequence between 3^{23} and 3^{25} in the lower tracing shows a short period of typical gastric Type III activity.

The uppermost tracing in Figure 54 shows jejunal Type I waves in a rhythmic sequence at the characteristic frequency of 11 per minute. A more typical recording with an irregular mixture of jejunal Type I, Type II and Type III waves is shown on the middle tracing; recordings such as this cannot be analysed easily into simple components. The lowest tracing shows a sequence of ileal Type II waves occurring with a frequency of about 6 per minute,/

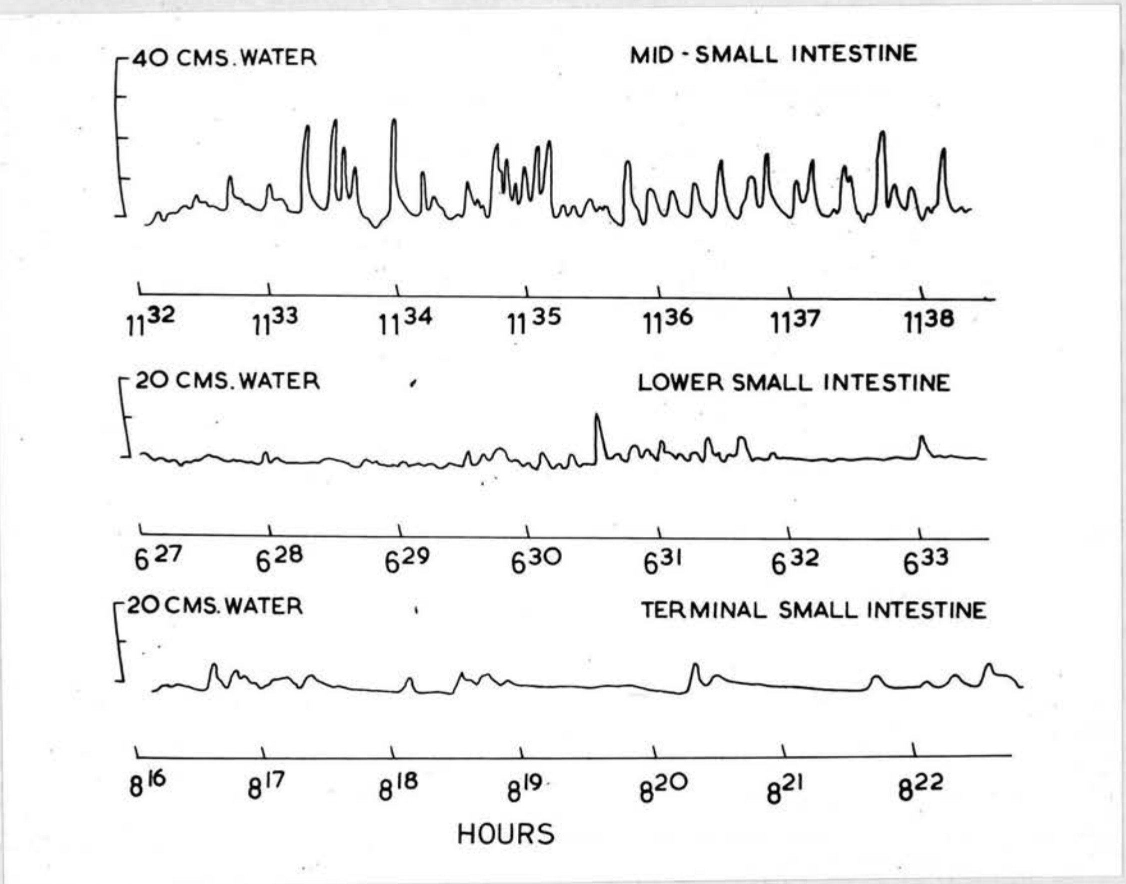


Figure 55

Pressure activity in the lower part of the small bowel.

minute, recorded in this case from a patient with diarrhoea.

Another series of ileal Type II waves, shown in the uppermost tracing of Figure 55, demonstrates again the complexity which is characteristic of many of the small bowel recordings. The two tracings below show the type of low amplitude activity which is often seen for long periods as the capsule approaches the ileo-caecal junction.

The waves shown in the upper tracing of Figure 56 are of the same form as the waves that Code classifies as Type IV. We have commonly seen this type of wave in the caecum and in the ascending colon, but not, as far as we can estimate, in the terminal ileum. Nearer the hepatic flexure rhythmic sequences of Type II waves such as those shown in the middle tracing, become more common whilst the complex type of pressure activity seen in the lowest tracing is often seen for long periods when the capsule is lying in the descending colon.

As I have already mentioned, we found that for long periods the pressure patterns, particularly in the small bowel, were very irregular both in form and amplitude. This made them very difficult to describe even in a simple qualitative manner; methods of classification based on the recognition and characteristics of specific waveforms could, therefore, only be successfully applied to the periods when there was regular pressure activity. We have not yet succeeded in finding a way to extract all the useful information from these extensive recordings or even of reducing them to a length at which they can be handled conveniently. These are difficult problems that will be discussed more fully in a later section.

6.2 The Clinical Trials.

It was difficult to find normal subjects who were willing to act

as/

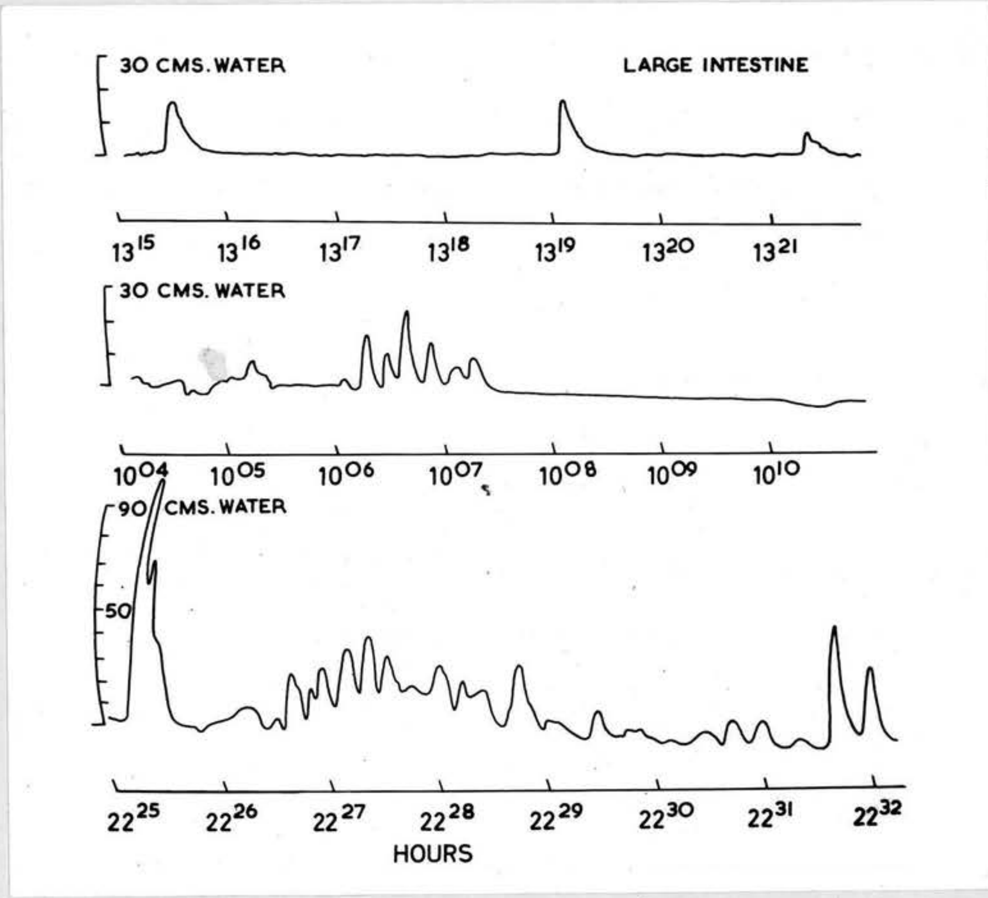


Figure 56

Colonic pressure patterns.

as controls for experiments requiring them to give up considerable amounts of time. We had, therefore, to rely mainly on volunteers either from patients who were in hospital with complaints that did not affect their digestive processes, or from those about to be discharged after the treatment of minor complaints. The recording methods underwent modification at intervals, particularly during the earlier experiments when we were trying to find solutions to the various clinical problems associated with the method and this also made comparisons between the recordings much more difficult.

(i) Initial series.

These first experiments, carried out in 1960, were used primarily to establish the method and to assess the performance of the equipment under clinical conditions. With the exception of myself (M.R.) the subjects were all volunteer patients from the Gastro-Intestinal wards who had mild conditions that were in the final stages of treatment. They are tabulated below in chronological order. The figures refer to the approximate period, in hours, that the capsule spent in each of the major organs;

S - stomach S.B. - small bowel L.B. - large bowel

and T the total transit time. The length of record (in hours) obtained from each experiment is also tabulated (L).

		S.	S.B.	L.B.	T.	L.
12.X.60	C.R.(F) - 60 yrs.	1-2	4-6	40-43	48	2 hours
19.X.60	J.W.(M) - 47 yrs.	-	2-3	41-42	44	3 hours
25.X.60	K.W.(M) - 35 yrs.	-	3-6	15-18	21	-
2.XI.60	M.R.(M) - 24 yrs.	2	4-6	31-33	39	16 hours
18.XI.60	W.S.(M) - 20 yrs.	>6	?	?	37	5 hours
30.XI.60	P.M.(F) - 25 yrs.	6	>3	>10	34	5 hours

In each case the capsule was swallowed and subsequently retrieved without any complications or difficulty. The capsules transmitted for periods of between 20 and 40 hours, but none were recovered whilst still active. In one experi ent (K.W.) the capsule failed complete shortly after the beginning of the test. Records were made at intervals either on the ward or in a separate observation room. In each case we asked the patient to swallow the capsule in the early morning whilst still fasting and we were troubled with retention in the stomach in only one case (W.S.).

In the series, recordings of pressure patterns were obtained from all levels of the bowel although the quality of the tracings varied from time to time. Sometimes we were troubled with artefacts caused by the loss of signal when the capsule was moved about in the body. For this reason it was impracticable to make extended observations and we decided to modify the receiving equipment, as described in Chapter 3, to enable us to record pressures without the need for constant supervision.

In the course of these experiments we had devised a useful routine for localising the capsule using three serial radiographs taken at intervals of about 4, 8 and 24 hours after the capsule was swallowed.

6.3 First control series.

Between June 1961 and March 1962 a series of eight 'normal' males were studied; all but myself (M.R.) and a post-graduate worker (R.H.) were volunteer patients; four had undergone hernia operations, one (J.G.) was recovering from a minor form of gastritis and the other (J.H.) was in hospital with a suspected ulcer. Some details of the experiments are tabulated below; as before the figures refer to the approximate time, in hours, that/

that the capsule spent in each of the major organs;

S - stomach S.B. - small bowel L.B. - large bowel

and T the total transit time.

		S.	S.B.	L.B.	T.	L.
9.VI.61.	D.P.(M) - 22 yrs.	1	4	47	52	18 hours
8.XI.61.	M.R.(M) - 25 yrs.	20	6-8	32-34	60	21 hours
22.XI.61.	J.H.(M) - 37 yrs.	<1	4-6	9-16	20	5 hours
6.XII.61.	R.H.(M) - 32 yrs.	10-17	?	?	>36	12 hours
19.XII.61.	J.T.(M) - 58 yrs.	-	5-6	?	<24*	8 hours
9.I.62.	F.C.(M) - 40 yrs.	-	6-8	?	>24*	7 hours
30.I.62.	J.G.(M) - 54 yrs.	-	6-8	22-24	30*	22 hours
12.III.62.	B.H.(M) - 54 yrs.	6	3-6	27-30	33*	22 hours

* - the total transit time is measured from the pylorus, not the mouth.

In the first four experiments the capsule was swallowed free, but the other four patients swallowed it on the evening prior to the day of the test with a length of soft thread attached, to prevent it from passing beyond the upper part of the small bowel. This was to enable us to make a more precise study of the small bowel.

The first subject (D.P.) was a young man who had been admitted to the Gastro-Intestinal Unit for investigation. He had complained for two years of periodic cramping pains in his abdomen, but a long series of tests and a previous laparotomy had failed to show up any lesion or abnormality. The pressure patterns that we obtained from all levels of his alimentary tract compared very well with our previous records.

The capsule passed into his small bowel about an hour after it was swallowed/

swallowed, just prior to his lunch. Irregular jejunal Type I activity was seen for only a short part of the period that the capsule was in the small bowel. Evidence of movements at the regular small bowel frequencies of 6 to 8 per minute was recorded using the 'field edge' technique and large pressure complexes were recorded in the evening, after the capsule had passed into the colon, from the region of the hepatic flexure. At one stage the onset of each of the pressure waves coincided with deep inspirations as the patient smoked a cigarette. The recording was continued overnight, but during this period there was very little evidence of either pressure activity or movement of the capsule until about 4.30 a.m. when apparently large movements of approximately the same frequency as the respiration rate were recorded. Pressure activity was seen at 7.30 a.m. when the patient woke, but it died away as he went off to sleep again. At 9.00 a.m. we woke the patient with his breakfast; the pressure activity started again and continued throughout the morning. Later the capsule was determined radiographically to be in the rectum, and was passed the following day.

I made myself (M.R.) the subject of the next experiment and swallowed the capsule in the early part of the morning whilst still fasting. The capsule remained in the stomach for the whole of the first day. Gastric Type I and Type II waves were recorded during about a third of this period. I could find little evidence of any activity that might have taken place as I slept, but the capsule must have passed into the small bowel during this period. There was a little evidence of movements at typical small bowel frequencies, but no significant pressure fluctuations. Colonic pressure activity was just seen after lunch on the next day and it was recorded at intervals thereafter until the capsule was passed.

The third subject (J.H.) had been admitted for investigation of a suspected ulcer which was in remission at the time of the experiment and probably/

probably healed. By the mid-afternoon on the day of the test, we had seen so little evidence of any form of motility that we resorted to screening him, at which time we found the capsule to be in the terminal part of the ileum. Three hours later we again screened the patient and found that the capsule had moved almost the complete length of the large bowel into the pelvic colon, a move which, in most subjects, takes between 20 and 30 hours. We were able to record a brief period of colonic Type II pressure activity, but the capsule had been passed by the next morning. We could find no reason for this very short transit period.

We were again troubled in the fourth experiment by the capsule not passing into the small bowel; the whole of the first day of the investigation being taken up by the prolonged gastric phase. We tried lying the subject on his right side for long periods, but this did not help. The delay was particularly inconvenient in this experiment because the subject (R.H.) was being studied as an out-patient and we could not continue the recording overnight. In the morning the capsule was found to have passed into the colon. We recorded for a short period, during which we saw a series of regular colonic Type II waves.

Because of these lapses when the capsule failed to pass the pylorus for sometime, we decided to try keeping the capsule on a piece of soft thread until it had passed into the small intestine. This would enable us to give the patient a break from the test, or even allow him home if he was an out-patient, without the danger of missing the period in which the capsule traversed the small bowel. We carried out investigations using this method on four volunteer patients from the general surgical ward. They were all in the final stage of recovery after hernia operations. We asked the subjects to swallow the capsule in the evening prior to the test and allowed sufficient

thread/

thread to be swallowed to permit the capsule to pass the pylorus, but not beyond the fourth part of the duodenum. We made a recording of the overnight period in one of the experiments. On that occasion the capsule passed into the small intestine shortly after the subject fell asleep in the late evening.

The experiment was successful in that, in all four cases, the capsule had passed into the small bowel by the morning and the test was started with the capsule at the upper end of the jejunum. The first subject (J.T.) was a heavily built man and we noted that in his case postural changes caused much bigger artefacts than usual on the pressure recording. Regular pressure fluctuations were not seen at any time during the small bowel phase but there was a noticeable decrease in the activity as recorded both on the pressure tracing and on the movement channel, using the 'field edge' effect, when he fell asleep during the afternoon. Vigorous colonic Type II waves were recorded later in the evening and by the following morning the capsule had been passed.

The next two subjects (F.C. and J.E.) showed records of small bowel pressure that were very similar to those we had obtained from the first subject. Characteristic rhythmic movements were recorded more frequently than pressure variations. We did not, in these cases, make extensive recordings of the motility of the colon. The fourth patient (B.H.) in this series anticipated the beginning of the test by accidentally dividing the restraining thread in the morning whilst shaving. His small bowel record showed much more vigorous Type II waves than the others in the series and he also passed the capsule into the large bowel in a shorter time.

We often found it difficult to determine the exact time of transit through the small bowel in these experiments, because often the change from ileal/

ileal to caecal activity coincided with the period that the patients were allowed to rest and take their evening meal. The length of these tests involved much co-operation from the nursing staff on the wards and it was not always convenient to continue recording at this part of the day.

The thread did not cause any discomfort to the volunteers or lead to anomalies on the record, as far as we could judge, although for routine studies in the hospital we still prefer to allow the patient to swallow the capsule free.

Summing up this series; the activity of the small bowel was in most cases represented by irregular Type I pressure changes, generally of very low amplitude. The frequencies of these changes, when they could be determined, were similar to the frequencies of the characteristic movements, that is between 6 and 12 per minute, slowing as the capsule moved down the bowel. Frequently there appeared to be some delay before the onset of colonic activity and radiography was the only way in this period of deciding whether the capsule was lying in the terminal ileum or in the caecum. If a radiograph was not taken until regular colonic Type II waves had started, the capsule was invariably found in the ascending colon. Respiration artefact became more prominent on the pressure tracing when the capsule moved into the transverse colon although the movements induced by the respiratory action could be seen on the signal channel, using the 'field edge' effect, as soon as the capsule passed into the caecum. Colonic Type II waves were recorded in almost all the experiments; they were usually of large amplitude and they often continued for periods of an hour or more. Colonic Type III waves appear to be characteristic of the descending and pelvic colon.

6.4 .../

6.4 Second control series.

A short series of control studies, using three male medical students who had each volunteered to give up one day to the experiments, was carried out in March 1962. They were all final year students, in good health and without any history of gastro-intestinal disorders. The capsule was swallowed in the evening prior to the day of the test and they were brought into the hospital the following morning. We allowed them to sit at a desk during the recordings and they spent most of the day studying; we allowed them to walk about if they wished. Lunch was brought to them and since they did not suffer from boredom during the continuous recording sessions, we made a continuous tracing until 6.00 p.m. Some features of these experiments are tabulated below. The figures refer to the periods that the capsule spent in each of the major organs and T represents the mouth to anus transit time. The length of record made during each experiment is tabulated under L.

		S.	S.B.	L.B.	T.	L.
22.III.62.	R.B.(M) - 23 yrs.	-	6	>6	?	10 hours.
27.III.62	W.F.(M) - 24 yrs.	-	8	>4	?	13 hours.
29.III.62	J.P.(M) - 24 yrs.	20	>6	<9	34	13 hours.

When the first subject (R.B.) was X-rayed on the morning of the test, the capsule was confirmed to be in the upper jejunum and the thread was divided. Almost continuous irregular pressure waves and periodic movements were recorded during the next six hours, as the capsule passed through the small bowel. The amplitude and the periodicity of the activity changed from large pressure waves at 11 or 12 per minute in the morning to small waves at 5 or 6 per minute in the late afternoon. No Type III waves at all were seen when the capsule was in the small bowel. The recording was/

was continued in the evening, after a short break for a meal. Colonic Type II waves were seen as the capsule neared the hepatic flexure. There was also a distinct increase in the respiration artefact on the pressure tracing.

The second subject (W.F.) showed a very similar record. The capsule was released in the morning after a radiograph had showed the capsule to be distal to the pylorus. Shortly after the thread had been divided we did, however, record a burst of very high amplitude pressure activity with waves occurring at about 14 per minute. This activity was very intense for about 10 minutes and it was only slowly replaced by the type of activity more commonly seen at this site. The period of transit through the small bowel was longer than in the first experiment and small amplitude ileal Type I waves were recorded almost 8 hours after the beginning of the test.

In the third experiment the capsule was not passed into the small bowel overnight and it was not seen when a radiograph was taken the next morning. The activity indicated that it was still in the stomach and it must have been lying high in the body of the stomach or the fundus. To exclude the possibility of irritating the pharynx we cut the thread and continued the recording as usual. Bursts of antral Type II activity were occasionally recorded and the capsule finally passed into the small bowel late in the afternoon. The pressure activity was found to be very similar to the records from the two previous experiments. The capsule was still in the ileum 6 hours later at midnight when we took the subject home. The capsule had been passed by the next morning. The most striking feature of this short series was the difference between each of the colonic records, although the full colonic phase was not recorded in any of the experiments.

We/

We had noted similar wide variations in the first control series. The small bowel recordings were superficially very similar, particularly in the characteristic rhythms seen at different levels, but the complex nature of the pressure fluctuations made it difficult to carry out a detailed comparison.

6.5 Discussion.

The 18 control experiments reported in this section represents almost half of the total number of clinical investigations that we completed during the two years. Experiments of this type are very time consuming; we found that two workers could comfortably undertake only one experiment per week. The discovery of better techniques and improvements in the apparatus meant that the design and conditions of the clinical experiments were constantly revised, making comparisons with previous recordings much more laborious. The co-operation of the ward staff was also difficult to maintain during extended studies when the capsule was sometimes not passed for a number of days. The patients whom we studied were usually very co-operative and sometimes even enthusiastic about the 'tubeless' features of the test; particularly if they had previous experience of the usual gastro-intestinal ward tests. All of them found swallowing the capsule alone to be an extremely easy procedure but a restraining thread should not be used if continuous recordings can be made because it arouses slight apprehension in some patients. We have no conclusive evidence that the thread causes any artefact in the recording by a direct reflex, but we have not investigated this possibility very thoroughly.

The recordings made from capsules sited in the small bowel fell short/

short of our expectations in that we often found ourselves unable to form any helpful conclusions when we compared one record against another. The tracings did not show any clear characteristics or obvious variations which we could positively associate with the transit rate of the capsule, or any other clinical feature.

(i) Serial controls.

At first we feared that perhaps the form of the tracing was completely random, but we were able to show that this was not so by studying recordings that had been made at intervals from the same subject. When innovations were introduced into either the method or the management of the investigations, it often proved most convenient to establish the value of the changes by using myself as the subject of the experiment. From the point of view of obtaining objective physiological information it is often considered poor practice to do this, but I considered it to be more ethical and it was certainly more convenient when trying to find the best of several different arrangements than using a volunteer patient. I recorded pressures from my own alimentary tract on three different occasions. I have tabulated some of the statistics of each experiment below. The figures refer to the same measurements as before.

	S.	S.B.	L.B.	T.	L.
2.XI.60	2	4-6	31-33	39	16 hours.
8.XI.61	20	6-8	32-34	60	21 hours.
14.V.62	5	8-9	58-59	72	32 hours.

Each recording was made using a slightly different technique; the first was made at the very beginning of the clinical studies when the recording had to be supervised continuously; the second was a free swallow made after the apparatus had been improved and the third was made using the thread/

thread technique. A very careful comparison between the tracings has satisfied me that the patterns seen at all levels of the bowel compared very well on all three occasions - certainly they are not as grossly different between themselves as they are when compared with recordings made from comparable levels in other subjects. The magnitude and incidence of the various physiological artefacts also appeared to be similar on each occasion.

Similarity between repeated records made from other individuals has been noted in two experiments where we undertook 'within-patient' trials, using the patient as his own control. These will be reported in the next chapter.

CHAPTER 7

Application to clinical problems

In order to make the best use of the opportunity that we had to study patients who were undergoing routine examination in the Gastro-Intestinal Unit, we undertook the investigation of certain types of functional bowel conditions in parallel with our control studies. The motility of patients with such conditions might be expected to 'caricature' normal processes, so besides forming interesting and useful studies in themselves, the contrast between these and the control recordings might help us to resolve some of the complexities of the pressure patterns.

New clinical information about these conditions might also result from studying each of the major segments in sequence as formerly examinations have been confined to the suspected region of the bowel.

7.1 Chronic constipation.

Constipation is not necessarily the result of a pathological condition of the bowel; it can represent nothing more than one extreme of the normal variation in bowel habit. If this habit becomes persistently slow, the normal reflexes are dulled, resulting in a self-perpetuating constipated state. There are also bowel conditions involving obstruction or muscular disability of the colon which can delay the passage of material into the pelvic colon and rectum, but often these are presented as acute problems; chronic and intermittent states are more often of a functional origin. If the physician can show that the muscular action of the bowel is not impaired, and the sensory mechanisms prompting defaecation are still present, then he can set about breaking this 'vicious circle' with appropriate treatment, confident that the bowel can be 're-trained'.

We/

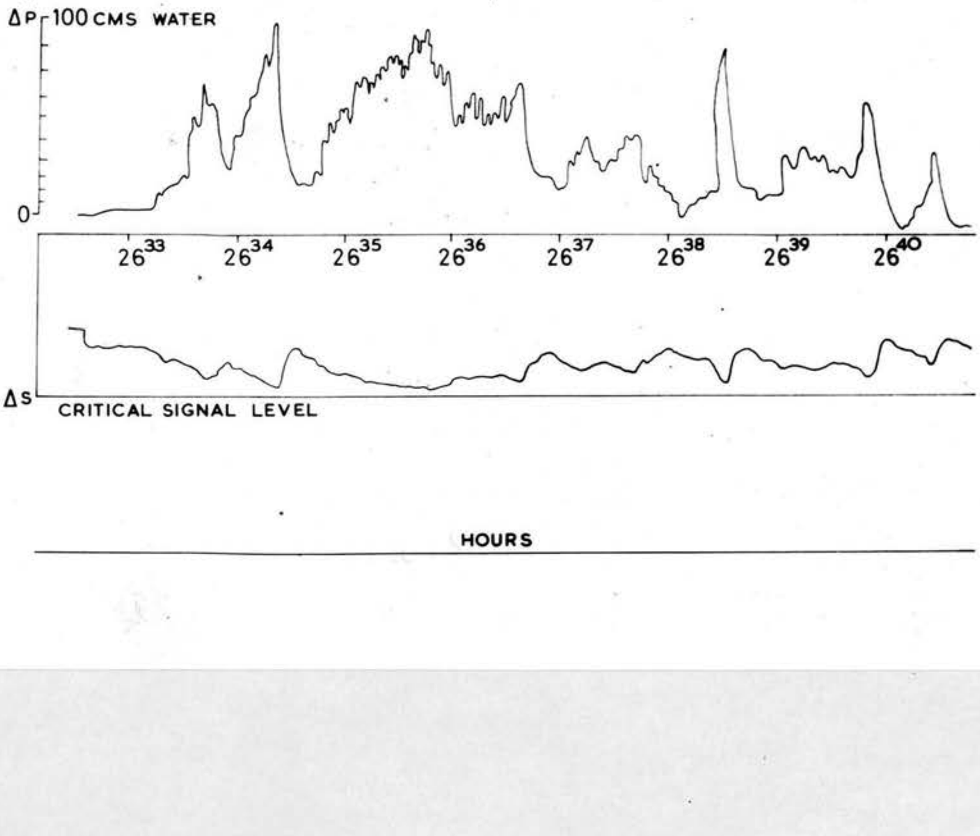


Figure 57

Complex pressure activity recorded from a patient with a distended colon.

We investigated the motility of four patients suffering from chronic constipation and were able to show in each case that a form of motility was still present. The table below shows some of the details of the recordings. As usual, abbreviations refer to the periods that the capsule spent in the major organs:

S - stomach S.B. - small bowel L.B. - large bowel

and T total transit time. L represents the length of the recording made from each patient.

		S.	S.B.	L.B.	T.	L.
25.X.61	J.C.(F) - 50 yrs.	>9	>3	90	117	37 hours.
16.I.62	J.B.(F) - 32 yrs.	1-2	10-15	85-90	93	61 hours.
20.III.62	C.R.(F) - 40 yrs.	5-6	6-8	58-61	72	67 hours.
22.V.62	Y.R.(F) - 44 yrs.	9-11	6-8	131-135	150	75 hours.

The first investigation was carried out on a female (J.C.) aged 50, who attended the hospital as an outpatient. She swallowed the capsule free and because we did not wish to make the study too long, we allowed her to go home that evening. When she returned in the morning the capsule was in the terminal ileum and a short period of normal small bowel activity was recorded. In the late afternoon we recorded normal colonic Type II waves from the ascending colon. During the next 24 hours the capsule remained almost stationary at the hepatic flexure and distorted Type II and Type III complexes were recorded almost continuously (Fig. 57). The long sustained pressure changes at this region in the colon indicated as might be expected that the transverse part, as well as the descending colon, was distended with semi-solid material. The capsule progressed slowly over the next few days into the pelvic colon and then into the rectum where normal Type II waves were again/

again seen. The capsule was passed after 117 hours.

The second patient (J.B.), a younger woman with a similar history of persistent constipation, swallowed the capsule with a restraining thread so we could make a complete recording of her small bowel activity. The thread was divided the next morning as usual, after the capsule had been confirmed radiographically to have passed the pylorus. Very soon afterwards, however, the small bowel activity was replaced by very characteristic antral waves which persisted for two hours. Small bowel activity returned just before lunch and low amplitude Type I pressure patterns were recorded. Twelve hours later a series of ileal Type I and Type III complexes were recorded, indicating either a very slow rate of transit through the small bowel or very prolonged ileal stasis. This abnormally extended period in the terminal part of the small bowel and retrograde movement are compatible features because reflux of material from the duodenum into the stomach is known to be most common in subjects with poor propulsive motility. Shortly after this activity we recorded distorted colonic waves, similar to those we had seen in the recording from the first patient. Long periods of extended and poorly formed pressure waves were also recorded. Normal activity eventually returned when the capsule was passed into the pelvic colon.

The third patient (C.R.) showed almost completely normal patterns during the test. There was a minimum of the 'lumpy' activity which we had associated in the two previous investigations with colonic distension, although the transit time through the colon was a little longer than normal.

During the investigation of the fourth patient (Y.R.), a married woman of 44, it was discovered that she had an abnormal psychiatric background which was very probably responsible for her condition. She showed very similar patterns to the results of the earlier investigations.

7.2 'Intestinal hurry'.

The variation between individual mouth to anus transit times for non-absorbed markers simulating normal food materials depends primarily on the length of the large bowel phase. In all cases of diarrhoea it is this phase which shows the greatest change in proportion to the normal transit period. It has been shown that the source of the water and electrolytes of diarrhoeal stool is the small bowel (Davenport) and it appears that the volume of fluid passed in these cases from this organ into the colon overwhelms its power to absorb. However, it is not yet known whether the fundamental cause of these conditions is excessive secretion, a disordered regulation of the small bowel or simply an impaired colonic function. It may be different combinations of these factors which causes the troubles in different patients. We examined six patients with three different forms of 'intestinal hurry'.

(i) Post-vagotomy diarrhoea.

In a modern version of the surgical treatment for duodenal and some forms of gastric ulcer, a branch of the vagus nerve supplying the stomach is divided in order to reduce the amount of acid subsequently secreted and, therefore, the chances of recurrence. Unfortunately in a small percentage of the cases treated, this procedure leaves the patient with persistent diarrhoea. The mechanism of this undesirable side-effect is not yet understood.

We investigated three subjects who had been left with this condition after ulcer operations. The figures again refer to approximate periods that the capsule spent in each of the major organs:

S - stomach   S.B. - small bowel   L.B. - large bowel

and T the total transit time.

.../

		S.	S.B.	L.B.	T.	L.
10.V.61	M.C.(F) - 35 yrs.	4	6	8	18	7 hours.
7.VI.61	E.M.(F) - 57 yrs.	2	7	9	18	10 hours.
14.VI.61	" "	2	?	?	28*	9 hours.
19.VI.61	" "	1	?	?	29*	8 hours.
29.VI.61	" "	2	6	9	17	3 hours.
28.VI.61	A.F.(M) - 49 yrs.	-	7	11	18	9 hours.
5.VII.61	" "	-	7	11	18	9 hours.

* - the capsule was restrained from onward movement for a period.

The recording made from the first patient (M.C.), a female of 35 who had suffered with this condition for two years, was not obviously different from many of the control studies. No significant pressures were recorded from the region of the hepatic flexure and the pelvic colon. The capsule was, however, passed after only 18 hours.

We studied the second patient in this series, a female (E.M.) of 57, on four different occasions within a month. The pressure patterns we recorded from her small bowel were very striking; the capsule did not appear to move quickly and steady rhythmic Type I waves were present for long periods. On the next two occasions that we investigated her the capsule was restrained from onward movement in the small bowel by approximately six feet of soft thread anchored externally. Intravenous injections of mechothane and atropine, drugs which are throught to stimulate and inhibit the smooth muscle of the bowel, were given over a period of a few hours, but there was no obvious change apparent in the pressure patterns. As I have stated previously, however, this method of testing the effect of drugs on small bowel motility cannot be considered conclusive because of the short term changes in the nature of the patterns which occur spontaneously and quite frequently. A system which measures/

measures the effect at a greater number of sites would be more satisfactory. We carried out a final examination on this patient after she had been treated for three days with Mebental, a drug which is thought to have a long lasting inhibitory action on the bowel, but again we could not detect any significant changes in the nature or incidence of the pressure variations.

The third case was a 49 year old male (A.F.) who had undergone a partial gastrectomy operation twelve years previous and five years later had an additional vagotomy operation performed to reduce the acid output from the cells in the stomach wall. The capsule passed into the small bowel almost immediately; this presumably was because of the altered structure of his stomach. Only short periods of phasic pressure changes were seen during the small bowel phase. Transit of the large bowel was rather quick and we did not record any significant activity, a characteristic we found with many, but not all, diarrhoea states. We repeated the test on this patient without using the bismuth carbonate powder to check any possible effect that it might have on the features of the recording, but again we could not detect any differences between the two tracings.

(ii) Carcinoid syndrome.

One of the symptoms of patients showing this syndrome is 'intestinal hurry'. It is thought that this is caused by a narrowing and spastic condition of the small bowel, producing a hosepipe-like effect pouring secretions from the small bowel into the colon.

We studied two patients suffering from this condition.

		S.	S.B.	L.B.	T.	L.
24.III.61	W.M.(M) - 65 yrs.	<1	?	?	14	6 hours.
29.III.61	" "	?	?	?	19	6 hours.
16.V.61	J.A.(M) - 65 yrs.	2	8	>20	>30	9 hours.

The/

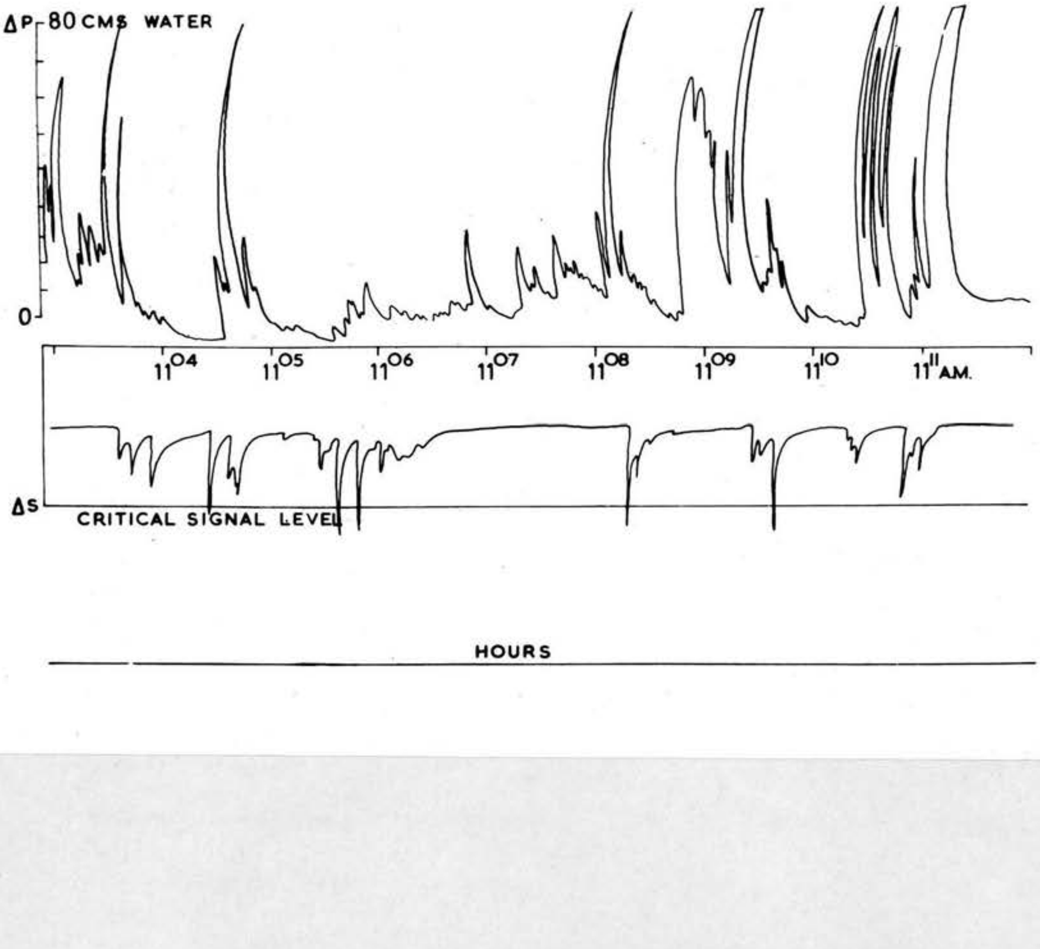


Figure 58

Recording made from the small bowel of a patient with thyrotoxicosis

The studies on the first patient (W.M.) were complicated, owing to the proximal part of his colon having been surgically removed some time earlier. This may account for the short transit periods which we saw on both occasions that he swallowed the capsule. No significant pressure activity was observed during the small bowel phase on either occasion, though we did record small colonic Type II waves from a site near the splenic flexure.

The second patient showing this syndrome (J.A.) did not appear to suffer 'intestinal hurry' when we carried out our investigations. Again we did not record very much activity from either the small bowel or the colon. The apparent transit time for the small bowel of 8 hours appears to be rather anomalous and we suspect that this rather high figure may be the result of an undetected period of reflux into the stomach. The results of the examination of these two patients are not really conclusive, although there was some qualitative evidence of quick transport through the small bowel.

(iii) Thyrotoxicosis.

One of the manifestations of the general increase in metabolic functions associated with over activity of the thyroid glands is an increase in the rate of transport of food materials through the bowel. We studied one patient (J.M.), a 43 year old male, with this condition before and after he was treated.

		S.	S.B.	L.B.	T.	L.
12.II.62	J.M.(M) - 43 yrs.	-	4-5	7-8	12	8 hours.
19.VI.62	" "	4	6-7	25-26	36	23 hours.

The nature of the record made after the patient had undergone iodine therapy was similar to that made before the treatment. Both records showed brisk/

brisk movements and very big pressures in the small bowel (Fig. 58). The original record had showed almost continuous Type II pressures in the colon which had resulted in a very fast transit time from the pylorus of 12 hours. This fast transport was obviously under control on the second occasion that he was studied and the colonic transit period of 25 hours was well within the normal range. Unfortunately we were unable to make a good tracing of the colonic pressures on the second occasion because of a fault which developed in the paper drive of the recorder.

7.3 Post-operative ileus.

One aspect of the surgical physiology of the bowel that has previously been difficult to study, is the return of motility following the trauma of an abdominal operation. The pressure-sensitive capsule seems well adapted to investigations of this sort, particularly since in the first instance we are concerned only whether or not pressure changes are occurring. We used the capsule to study the recovery of four patients after abdominal operations. They are listed below:

				Operation
11.I.62	J.D.(M)	-	65 yrs.	Gastro-jejunostomy
23.I.62	J.M.(M)	-	51 yrs.	Cholecystectomy
6.II.62	A.S.(F)	-	54 yrs.	Gastro-jejunostomy
16.II.62	M.S.(F)	-	55 yrs.	Gastro-jejunostomy with Vagotomy

In the first study (J.D.), the capsule was inserted into the small bowel during the course of the operation. It was placed 7 or 8 cms. distal to the site where the small bowel was sutured to the reconstructed part of the stomach. Recording started on the ward two hours after the operation had been completed, showed a 6 minute burst of vigorous pressure activity/

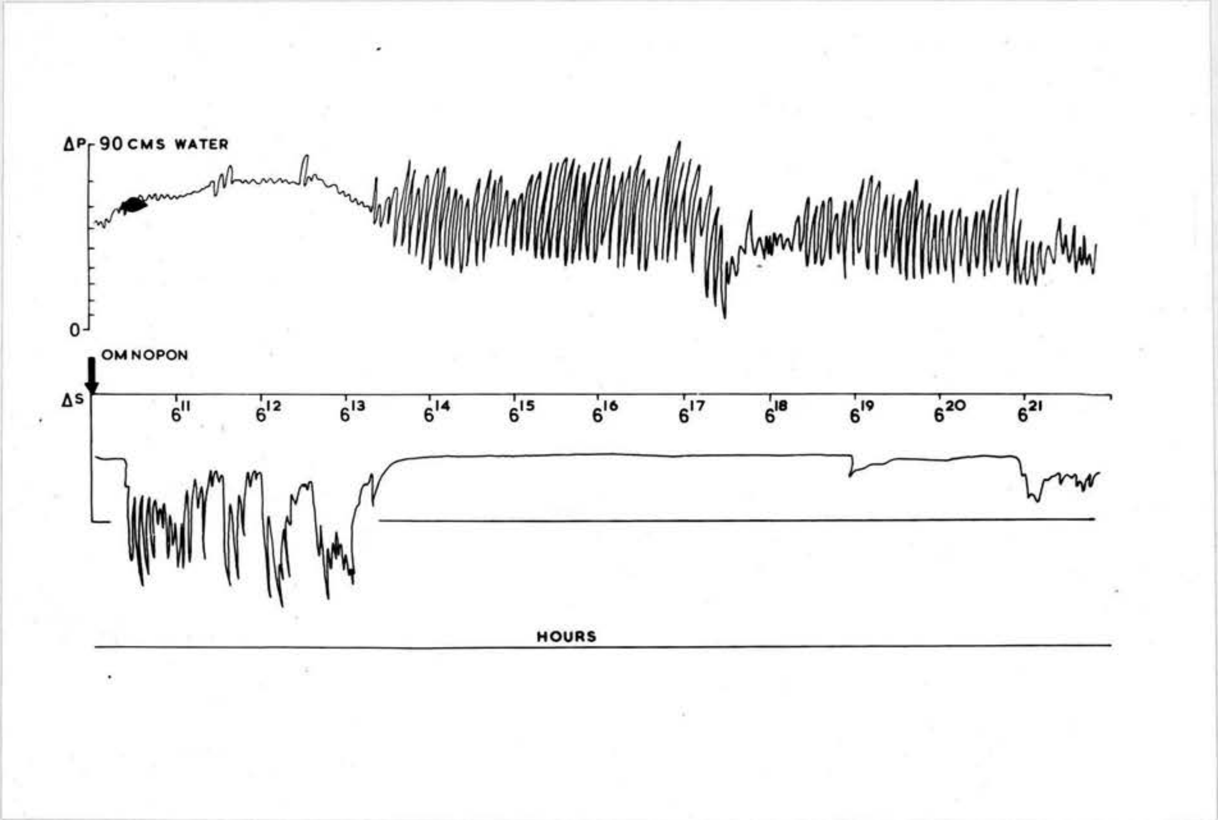


Figure 59

Burst of activity following an injection of Omnopon recorded from the small bowel of a patient recovering from an abdominal operation.

activity almost immediately. Longer periods of continuous activity with pressure waves up to 30 or 40 cms. of water rhythmically repeated 11 or 12 times per minute, were regularly recorded during the next 4 hours. Omnopon, a morphine-like drug is routinely administered to patients recovering after abdominal operations and examining the records in retrospect there appeared to be a correlation between the injections and the onset of each burst of activity (Fig. 59). The periodic activity continued during the following 7 hours slowing eventually to the rate of 2 or 3 excursions per minute. Normal ileal Type I activity was recorded the next day, 24 hours after the operation. The patient made an uneventful recovery and the capsule was retrieved from the stools one week after the operation.

For our second study we selected a patient (J.M.) who was to have his gall-bladder removed. In this case the bowel was not opened completely so we asked him to swallow the capsule in the morning just before the operation; it was then eased through the pylorus into the jejunum when the abdomen was open. Recording was started on the ward two hours after completion of the operation. No pressure fluctuations were recorded during the next five hours until we noticed a very slight undulation on the pressure trace at the respiration frequency. Weak gastric contractions appeared after 8 hours, confirming our suspicions that either reflux from the small bowel had taken place or the capsule had not been moved far enough through the pylorus. The period of 8 hours may not, in this case, be the true value for gastric recovery because of the uncertainty of the site in the stomach where the capsule was lying. Sustained periods of antral activity were recorded on the following day, and the capsule was passed five days later.

It is the modern practice to complete a gastro-jejunostomy operation by dividing that branch of the vagus nerve which passes to the stomach. This limits/

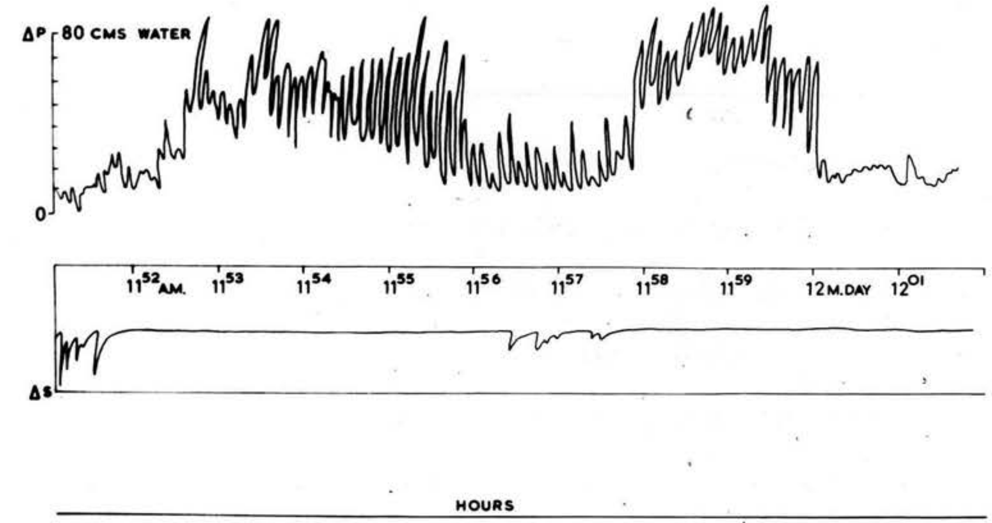


Figure 60

Pressure activity recorded from the small bowel of a patient one hour after a gastro-jejunostomy operation

limits the subsequent production of acid and thus reduces the probability of a recurrent ulcer. In rare cases an exception is made if the patient has a naturally low secretion rate and vagotomy is not performed. It seems very probable that dividing this nerve produces other effects beside limiting the production of acid and it was decided to compare recovery from both types of operation. Two female patients (A.S. and M.S.) one with a low natural acid secretion rate, had operations for similar ulcer conditions so we made use of the opportunity to carry out a comparative test.

As in the first investigation the capsules were inserted into the small bowel at operation. Recording was started from the first patient (A.S.) one hour after the abdomen had been closed and complexes of Type II and Type III activity were seen almost immediately. The Type III waves, with a period of about 10 minutes, caused excursions from the basal level of 40 to 50 cms. of water. Type II activity of a similar amplitude and a frequency between 8 and 10 per minute was superimposed on the slower waves (Fig. 60). The activity continued for most of the day, steadily becoming slower. After 8 hours the activity was of lower amplitude and the frequency had slowed to 6 per minute. The activity continued for the whole of the 20 hours we recorded. The patient made an uneventful recovery and we retrieved the capsule after several evacuations six days later.

We started recording from the patient who had vagotomy performed (M.S.) one hour after the completion of the operation, and again pressure activity was seen immediately. The basal level remained steady, however, and only rhythmic Type I waves were seen during the long periods of continuous activity (Fig. 61). After 5 hours the frequency slowed to 2 or 3 per minute. The capsule was recovered five days after the operation.

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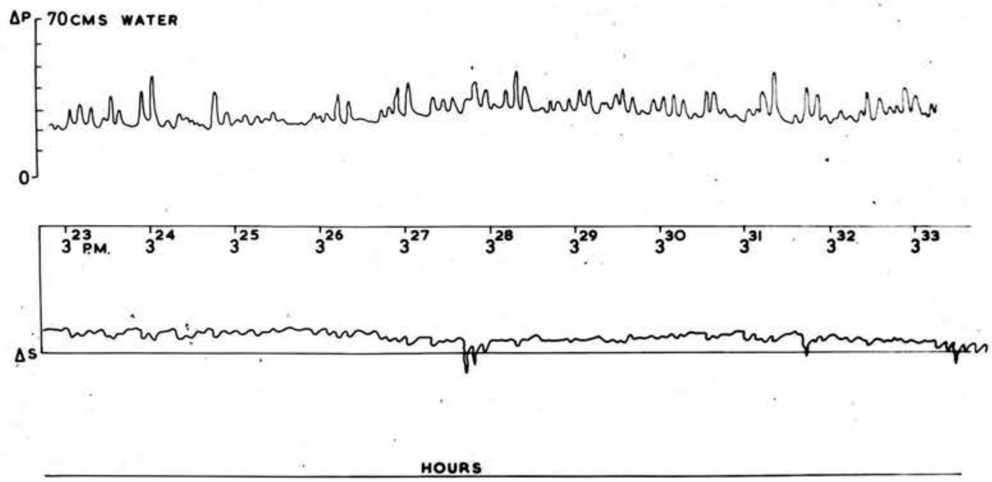

<u>Figure 61</u>

Continuous Type I pressure waves recorded from the small bowel of a patient recovering from a 'gastro-jejunostomy with vagotomy' operation.

From these few experiments it appears that there is muscular activity in the bowel even within an hour of surgery. Movements of the same periodicity as the pressures were observed in all the small bowel cases, but the waves do not appear to produce very effective propulsion because the transit time from the site of implantation into the large bowel is very much longer than normal. Perhaps these, apparently unco-ordinated, contractions are also responsible for the phenomenon of 'wind pain' which commonly occurs after abdominal surgery. We were also concerned whether or not these effects could have been produced by the respiratory excursions of the diaphragm impinging on a temporarily spastic bowel. After careful observation, however, we decided that they were probably not produced in this way.

The vagus nerve besides innervating parts of the alimentary tract, also carries the pace-making impulses controlling the rate of respiration, and the similarity between the periodity of the diaphragmatic excursions and these pressures tempted us to speculate that during the immediate post-operative period, this might be more than just a chance similarity.

CHAPTER 8

Interpretation and evaluation of the data

8.1 The problems of analysis

(i) Qualitative features.

Although in a few of the later experiments we succeeded in making a continuous recording of the complete small bowel phase, most of the records consisted of tracings made intermittently throughout the test period. We did not attempt to make more than a simple qualitative assessment of motility, based on the recognition of waveforms and patterns which have been described very fully in the reports on the many intubation studies that have been carried out. Samples of the pressure activity from different levels may prove to be sufficient to measure the muscular function of the small bowel, or the colon, when more accurate estimates can be made of the location and the short-term movements of the capsule, or perhaps when an effective method of analysis has been devised. At this time, however, we could only allow for the mobility of the capsule and its consequent positional uncertainty by making the periods of continuous recording as long as possible.

The pressure patterns recorded during the capsule studies were superficially very similar to those obtained by the 'tube' methods. In the stomach and in the large bowel, the freedom of the capsule to move in response to the pressure gradients did not lead to any apparent distortion of the tracing. Comparisons with small bowel records were not so easy to make, for two reasons; intubation studies were attempted less frequently in this organ because of the difficult, and sometimes dangerous, experimental procedures involved and the reports of these experiments usually described in detail only the short periods of rhythmic activity which are not frequently seen in the capsule studies, particularly/

particularly in the lower part of the organ. Other investigators (Farrar and Bernstein, 1958; Connell, 1960) have shown that when capsules are tied to the tip of catheter systems, the intra-luminal variations which they record are similar to those displayed by the external manometric recorders. The more realistic comparison, between the pressures recorded at different sites from a virtually stationary catheter tip and a completely mobile capsule in the same segment, would be extremely difficult to carry out. Farrar showed, however, that the capsule records of small bowel activity sometimes differed quantitatively from tube records in that they contained slight phase distortion. In a preliminary study on the application of computer techniques to analysis (Farrar, 1960) he found that a digital computer could be used to extract the basic rhythms from the more regular patterns obtained by intubating the upper part of the small bowel, but that it was not always successful when applied to capsule tracings which were superficially very similar to the 'tube' records. The areas of the bowel undergoing 'segmenting' activity sometimes move back and forward along short lengths of the bowel destroying the absolute periodicity which the computer demands.

(ii) Automatic analysis and data reduction.

If we had a large amount of intra-luminal pressure data in the appropriate form, and adequate computing facilities, there would be two ways of approaching the problem of analysis. We could either formulate a mathematical model from the accumulated information or we could attempt to select combinations of features in the patterns and correlate them with appropriate clinical data, using the computer to record the occurrence and characteristics of these features. For complete success, the first method requires a very large accumulation of data as a basis for the analysis, whilst the/

the latter procedure is a form of 'trial and error' requiring frequent changes in the computer programming.

Computing from large quantities of data is, however, completely impracticable without automatic systems to convert the recorded pressure variations into the appropriate digital form. Even the series of experiments we carried out, which was much too small for a good statistical evaluation, resulted in some 600 hours of recording and over 3,000 feet of tracing. Using manual methods or even some form of specially designed semi-automatic device, the reduction of these analogue records to a digital form would be a formidable undertaking and a very complicated process for routine experiments. A series of experiments intended for accurate, quantitative reduction requires a system with a more flexible output, such as magnetic recording. The expense of these systems would make the storage of the information for indefinite periods prohibitive unless an automatic closed loop method of reducing the data was used.

An automatic system could be built which would overcome the difficulty of reducing the characteristic variations of a large amount of intra-luminal pressure data but the complication and consequent expense of making the system capable of discriminating between meaningful variations and the artefacts that are so immediately obvious on the analogue records would be very considerable. Many of the earlier investigators carried out a very simple form of analysis which consisted of measuring the incidence, height and duration of each series of waves. Even for the less complicated measurements made with tubes these simple methods of reduction have not yet provided any conclusive clinical finding, so it may be that these obvious features on which the analysis is based reflect only a part of the information/

information contained in the data or, more likely, that these variations exhibit a variable relationship to the real physiological situation. The amplitude of intra-luminal pressures, for instance, is not a reliable indicator of muscular effort nor is the basal pressure level directly related to the 'tone' of the bowel wall.

8.2 Intra-luminal pressures.

It is not surprising that the complex muscular actions which result in effective mixing of masticated food materials with digestive fluids, the controlled progression and exposure of the solutions to the appropriate sites of absorption and the consequent passage of the waste materials to the rectum should be difficult to investigate experimentally and no matter how accurate and objective the recordings of intra-luminal pressures are made, the measurement of one single parameter can only reflect a part of the resultant of such intricate physiological situations. In trying to estimate these functions using simple experiments, we should be careful to balance the accuracy of any quantitative analysis applied to the results against possible shortcomings in the experimental method.

In parts of the bowel with a fluid content, a systolic contraction which completely obliterates a length of the bowel, ejects the fluid in both directions, but a pressure wave results only if a temporary closed cavity is formed or if the fluid shows resistance to flow. Contracted, or so-called peristaltic 'rings' moving along the length of the bowel, lead to pressure changes within the lumen, only if there is a relative velocity between the 'ring' and the bowel content.

(i) Closed cavity.

Let/

Let us consider, in the simplest terms, the development of pressures within a fluid-filled contractile cavity, such as that represented in Figure 62.

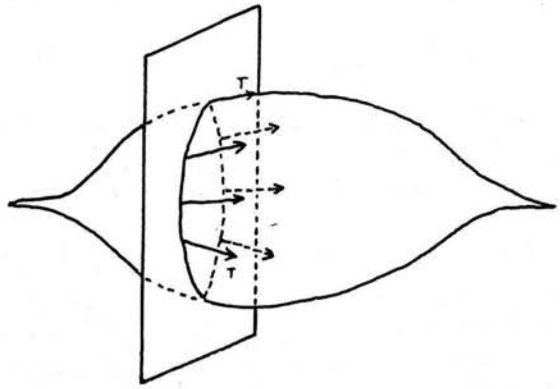

Figure 62

If we equate the tensional force in the wall (F_W); pulling one side of an imaginary plane surface passing through the cavity against the other, to the force (F_p) which develops the incremental pressure (Δp) inside the cavity, we have

$$F_p = \Delta p \cdot A$$

and $$F_W = \oint T \cos\theta \cdot dl$$

where T is the tensional force in the wall, normal to the curve of the section, of area A.

$$\Delta p = \frac{\oint T \cos\theta \cdot dl}{A}$$

This equation, representing the simplest theoretical situation that could lead to an intra-luminal pressure rise within the bowel, does not have a direct application, but Quigley (1943) used a similar argument to justify three generalisations/

generalisations about balloon probes passed into the bowel which are frequently assumed to relate to the development of intra-luminal pressures measured by other systems. They are as follows:-

(a) The pressure developed is directly proportional to the strength of the contraction (T).

(b) The pressure developed is inversely proportional to the linear dimension of the cavity.

(c) The pressure developed is not independent of the shape of the cavity.

The first conclusion is obviously not true except under the special conditions where the content of the cavity cannot 'escape'. Recording from natural cavities formed in the bowel, we do not have any way of differentiating between 'fluid escape' and a weaker muscular contraction. The other statements could apply to natural bowel cavities, but they only emphasise the difficulty of evaluating the experimental results, even from this simple basic situation, since the size and shape of the bowel lumen is constantly modified either by normal anatomical variation or as a result of muscular actions.

(ii) Cavity with 'fluid escape'.

The next step in this very simple treatment is to consider the situation where the natural lumen allows fluid to escape from the cavity in response to the muscular contraction. Some of the force of the contraction will be used to eject the fluid through the orifice and consequently the pressure developed at any instant within the lumen will be reduced. The difference between the pressures developed in these different situations will depend on the rate of outflow (Q) at that particular instant, which will in turn be dependent on the viscous resistance to escape. If we consider, for simplicity, that at this instant there is a steady escape of fluid and that the orifice/

orifice behaves as a pipe with a fixed diameter, then we can apply Poiseiulle's relationship that the 'driving' pressure is exactly balanced by the force of viscous resistance (R_v)

$$\Delta p = \frac{Q}{R_v}$$

If we assume steady flow, R_v will be given by the expression

$$R_v = \frac{\pi . r^4}{8 \eta l}$$

where r represents the radius of the outlet; l, the length of the outlet 'pipe' and η the viscosity of the fluid.

Modification of the expression obtained in (i) results in the following relationships:-

$$F_m = \oint T \cos \theta . dl$$

$$'F_p' = \Delta p . A + \frac{\pi . r^4}{8 \eta l}$$

and therefore $$\Delta p = \frac{\oint T \cos \theta . dl}{A} - \frac{\pi . r^4}{8 l A \eta}$$

Like the original expression, this last relationship is not directly applicable to any real physiological situation because of the over-simplification of the argument. McDonald (2) has shown that Poiseuille's relationship cannot strictly be applied where pressures are developed periodically. He presented a more rigorous solution to a similar situation in blood vessels showing that flow is still directly related to the pressure gradient, but that the inertia of the fluid leads a complex resultant relationship which is time dependent. The much more complicated conditions within the bowel make it difficult to derive a simple general statement, but the approximate relationship given above is sufficient to guide some simple reasoning.

The muscular action of the bowel manifests itself in two ways; i.e. either in the direct transport of the intra-luminal content or as intra-luminal pressures/

pressures if there is resistance to transport either of a viscous nature or as a direct physical barrier when a temporary cavity is formed. Until more is known of the exact mechanisms of bowel transport, the question whether these intra-luminal pressures are secondary effects, or whether they are a stage in the normal transport process, must remain open. It is, however, interesting to consider some of the bowel functions at different levels as they have been interpreted from the many routine and experimental radiological studies that have been carried out.

8.3 Motility and pressures within the bowel.

(i) Oesophagus.

The oesophagus provides a passage for the food materials from the pharynx through the thorax and into the stomach. Its function is primarily propulsive and at rest the walls remain flaccid and they generally lie in close apposition. The pressure recorded by an instrument passed into the lumen is, therefore, of approximately the same level as the thorax, 6 to 12 cms. of water below the ambient atmospheric pressure. Like the stomach the basal level within the oesophagus has a component related to the respiratory excursion of the diaphragm. On inspiration the oesophageal level falls a further 6 or so centimetres of water below the ambient level and the intra-gastric level rises by a similar amount; on expiration there is, of course, an exactly opposite effect. The oesophageal passage is closed off from the ambient pressure level at the pharynx by a tonically contracted muscular sphincter, and from the even higher intra-gastric pressure by a more complex valve mechanism at approximately the level that it passes through the diaphragm. If a pressure transducer or an open-ended tube is used to measure the basal level within these tonically contracted zones, pressures of between 10 and 30 cms. of water/

water above the ambient level are recorded.

When a bolus of food is swallowed, it is passed first into the pharynx which then contracts until the pressure rises to about 60 cms. of water above atmospheric. The upper sphincter then opens briefly and the bolus is projected into the oesophagus. This initiates a peristaltic 'ring' which forms behind the bolus, generating a pressure wave of 30 to 150 cms. of water as it moves down the oesophagus at a rate of between 2 and 4 cms. per second. It is not capable of exerting a strong force and an unusual bolus such as the capsule, may be overtaken by the contraction and left behind to be caught up by the contractions which always follow a single swallow. The contracted 'ring' usually takes about 9 seconds to reach the lower sphincter and it may involve a length of 10 or 20 cms. of the muscular wall. As far as we could estimate, the capsule completed the oesophageal phase in about 10 or 15 seconds. We only attempted to record this period in a few cases because of the danger of alarming the patient at the stage when he swallowed the capsule. On two occasions we detected a single brief pressure peak, presumably resulting from the initial contraction passing over the capsule. As I pointed out earlier, peristaltic functions such as this can be studied much more effectively with fine, multilumen tubes, held stationary at different levels in the oesophageal passage.

(ii) Stomach.

The stomach acts as a reservoir for ingested food materials, retaining most of the larger solid particles in the 'body' until they have been reduced in size or completely liquified by the acid and pepsin secretions.

When it is empty its volume shrinks to 50 mls. or less, yet the structure of its wall is such that even in this shrunken state it is completely relaxed. Phases of activity are less frequent when it is empty and much less vigorous./

vigorous. The motility of the 'body' which consists of shallow ripples of contraction, arising at a focal point on the lesser curvature, near to the cardiac sphincter, and involving a contracted ring around the organ, does not lead to very effective mixing of the contents. The waves of contraction, which in man occur at a very regular rate of three per minute, do not have an appreciable mixing action until they involve the muscle of the narrower pre-pyloric region. The viscous resistance of the gastric content is sometimes sufficient to lead to small local pressures of ten or twenty centimetres of water, sometimes called tonus waves, when the contraction is not strong enough to form a completely closed cavity. Some physiologists believe that the peristaltic waves travelling towards the distal part of the organ initiate systolic contractions of the whole antral muscle. These views are not widely held and there seems to be little evidence of any vigorous reflux into the body of the stomach such as would result from a completely simultaneous contraction.

It is now thought that the pylorus, the outlet from the stomach into the duodenum does not act in the same way as the muscular sphincters in the oesophagus. For most of the time it is not tonically contracted and experiments suggest that it is nothing more than the narrow terminal segment of the antral muscle. The investigators have shown that there is no physiological pressure barrier if a small pressure transducer or an open-tip tube is drawn through it (Atkinson et al. 1957). A balloon-probe of about 6 mm. diameter shows a zone of slightly raised pressure, 6 to 8 cms. long, indicating that it is a patent segment of 5 or 6 mms. diameter. When the peristaltic contraction involves the narrow and heavily muscled part of the antrum, proximal occlusion of the lumen displaces the antral contents/

contents towards the pylorus. A small amount passes into the duodenum, but before the greater part is swept onwards by the wave into the small bowel, the duodenal bulb, immediately distal to the pylorus starts to contract, forming a pressure gradient which prevents further escape of the intra-gastric materials. Gastric emptying is, therefore, stopped three, or four seconds before the pyloric sphincter is closed in the final phase of the gastric wave. Experiments have also shown that in laboratory animals there is a simple correlation between the rate at which the content escapes into the duodenum and the vigour of the gastric activity.

The observations we made on gastric motility during the course of the capsule studies were completely consistent with these theories, but because of our inability to make precise estimations of the site of the capsule and to record the short-term movements when it was in the stomach, we were unable to carry out a conclusive experimental study.

(iii) Small bowel.

As befits its digestive and absorptive function, the motility of the small bowel consists of orderly and regular movements which mix the liquified food materials with the many digestive secretions and repeatedly expose the mixture to the absorptive areas of the mucosal surface. Because of its characteristic appearance radiologically it is easy to differentiate this complex 'segmenting activity' from the usual peristaltic movements, but it is not easy to investigate quantitatively its more subtle nature. The following quotation from Davenport (2) is taken from the original description by Cannon (1911) of segmenting activity seen during the fluoroscopic examination/

examination of a cat.

> "Rhythmic segmentation is by far the most common..... mechanical process to be seen in the small bowel..... A small mass of food is seen lying quietly in one of the intestinal loops. Suddenly an undefined activity appears in the mass, and a moment later constrictions at regular intervals along its length cut it into little ovoid pieces.......A moment later each of these segments is divided into two particles, and immediately after the division neighbouring particles rush together, often with the rapidity of flying shuttles, and merge to form new segments. The next moment these new segments are divided, and neighbouring particles unite to make a third series, and so on."

The segmenting movements of the small bowel, which in man divide the intra-luminal column at a rate between 6 and 12 times per minute, appear at irregular intervals. During fasting they may be absent but they appear immediately after a meal, and it has been shown that as a result, the rate of propulsion of the fluids along the bowel becomes much slower. (Marker fluids usually take between 3 and 5 hours to travel through the 2 to 3 metres of small bowel, a mean rate of about 1 cm. per minute). Intra-luminal pressures will be developed in the segments formed between each of the simultaneously contracted zones and they will occur at the same rate as the segmentation. The amplitude of the pressure fluctuations will depend on the length of the segment/

segment, the vigour of the muscular activity, the rigidity of the bowel wall and the resistance to flow offered by the luminal content. Radiologists have also observed that the constrictions do not always divide the lumen completely, particularly if the material is viscous and they may, therefore, be quite small. We have also observed in the course of our studies of the small bowel with the capsule that normal, apparently regulated, flow often takes place without any obvious phasic intra-luminal pressures being detected, sometimes throughout a complete transit of the organ.

We have now formed the hypothesis that the incidence of large amplitude pressures during segmenting activity in the small bowel reflects not so much excessive muscular activity, although this will obviously lead to bigger changes, other things being equal, but a more subtle act of co-ordination between the contractions restricting the onward flow of the fluids. The pronounced rhythmic pressures seen in the small bowel, below the site of recent surgical interference could be evidence that this positive muscular effort is an attempt by the body to 'dam' the flow of material in the small bowel, thus preventing drainage past the wound. The very slow onward progression of the capsule in these studies shows that if this is the case, it is a successful mechanism.

In health, these contractions are co-ordinated so that there is regular back-and-forward movement of the bowel contents which leads to a very effective mixing, whilst changing the fluid in contact with each part of the mucosal surface. Code (1962) believes that small amounts of material are continually and progressively moved down the bowel by the small phase differences resulting from the gradually slowing rate of segmentation which exists along the length of the organ. If this mechanism is in fact responsible for onward movement, it would also explain very simply the occasional phenomenon of retro-

grade/

retro-grade transport of small bowel material. There is also radiological evidence of a tendency for these complexes to migrate down the bowel towards the colon, presumably resulting in a faster displacement of some of the bowel contents towards the terminal ileum and caecum.

The inertia of the capsule reduces its response to the more rapid changes in the direction of flow and as we would expect, if these theories are correct, results in it taking longer than fluids to pass through the organ. The usual transit time for the capsule of between 4 and 8 hours compared to the 3 to 5 hours for fluids therefore appears reasonable. We might also expect the capsule's inertia to lead to a slight artefact in the phase of the recordings made of small bowel pressure rhythms when the migrating complexes pass over the capsule. This effect should be less pronounced in the lower ileum where the segmentation rate becomes lower, but the movements also become weaker because of the thinner musculature of the wall and we found that the pressure patterns were still irregular. We saw direct evidence of these small movements using the sensitive 'field edge' recording technique, but as I have explained, we could not draw exact inferences from these changes. In its present form the tracking system used by Jacobson shows only the grosser movements and it does not resolve these small effects.

(iv) Large bowel.

The caecum receives daily, from the small bowel, between 300 and 500 mls. of fluid containing undigested and unabsorbed food materials. This fluid is 'kneaded and churned' by contractions of the caecum and ascending colon until much of the water has been absorbed through the bowel wall and it is reduced to a pasty mass. The muscle of the colon produces a series of simultaneous/

simultaneous annular contractions which, on radiographic examination, appear as the so-called haustra. The segments between these relatively slow, but powerful, contractions are not usually regular in size and the pressures are essentially local effects. The slow rise and fall of these pressure changes is a reflection of the increasing viscosity of the luminal content. Three or four times a day this pasty content is transported to the distal part of the colon by massive simultaneous contractions of the proximal segments. Fluoroscopic evidence shows that during this period sections of the colon shorten and form a smooth tube to facilitate the transport of this material. As in the oesophagus these contractions, which usually take place over a period of about 15 minutes, apparently manifest themselves completely in transport, and we did not detect any pressure effects that could be directly related to these processes. In some overnight studies of the colon we saw periods of prolonged and vigorous movements over 10 or 15 minutes during otherwise inactive periods, but we were not able to record any associated pressure changes.

SUMMARY AND EVALUATION OF THE EXPERIMENTAL METHOD

A considerable period at the beginning of this work was devoted to the design and construction of the miniaturised electronic and mechanical units required for the capsule part of the telemetering system. The initial difficulties with small components and the micro-manipulation techniques had been almost overcome and the prototype 'probes' were nearing a final state when it was discovered that a similar unit was soon to become available commercially. It did not seem worthwhile continuing work on the capsule at that time, but since I was able to anticipate the appearance of the commercial version, by the time that it appeared on the market, in October 1960, I had built an external detecting system so as to be able to estimate the effects of attenuation through the abdominal wall and movement of the capsule within the bowel; factors which at that time were unknown. As a result of these experiments the original receiving unit was modified and in March 1961, a series of clinical trials was started, in conjunction with a medical colleague, to establish the possible uses of the capsule telemetering method.

The instrument, which was developed for measuring pressures within the bowel using a mobile, rather than stationary, transducing system proved quite adequate both for assessing the immediate applications of the system and for estimating its potential for more comprehensive studies. Further refinements, such as a non-directional aerial array, which would have made the routine studies more convenient and a more elaborate receiver with better long-term stability which would have increased the accuracy of the system during extended experiments were put aside in favour of the clinical experiments. This uncertainty in the basal levels was not a serious limitation, however, because we did not attempt to make the complicated computations, involving variations/

variations in abdominal pressures and the hydrostatic effects of viscera overlying the bowel, which would have been necessary to deduce absolute pressure levels within the bowel.

We devised a method for localising the capsule, using contrast techniques and a series of two or three abdominal radiographs to enable us to make estimates of the long-term movements of the capsule. A method of monitoring the changes in signal intensity was also adopted to enable us to form some idea of the short-term movements of the capsule, as well as making a record of the intra-luminal pressure variations. Neither the method for localising the capsule, nor the monitoring of the short-term movements was sufficiently accurate to make really precise studies, but they allowed us to start the clinical experiments without further delay.

The capsule technique proved to be extremely successful in that the clinical procedures involved were simple and from the patient's point of view, completely atraumatic. The uncertain length of the gastric phase presented a practical difficulty which we were not able to solve satisfactorily and sometimes an interesting part of the experiment was missed on this account. The length of the transit periods through the intestine appeared reasonable compared to known rates of transport, although the inertia of the capsule prevented a direct comparison with the more realistic estimates using fluid markers. We were, therefore, satisfied that the capsule did not lead to direct stimulation of the bowel as previous intubation methods have been thought to do, although as I have explained earlier, the nature of the method is such that we could not prove this by a direct experimental comparison. The periods of complete quiescence which were recorded on many occasions from all levels of the major organs were also inconsistent with local stimulation.

We carried out 40 clinical experiments, each of which involved, on

the/

the average, 2 or 3 days of recording. The investigations included series of normal controls, a number of patients with abnormal functional conditions and a short series of post-operational studies. The large amount of data collected from each of these experiments was found to be something of a problem because the salient features were sometimes obscure and the records required a careful evaluation which we did not succeed in reducing to a concise, quantitative form. Because of this difficulty, the method did not yield as much information on bowel motility as we had anticipated that it would. The most successful application was found to be the 'all or none' type of experiment, such as the post-operational studies, where we were primarily concerned with showing only that pressure activity was present within a certain period of time and certain of the tests on patients with functional disorders where we were able to show that the affected parts of the bowel still had some muscular ability.

The mobility of the capsule sometimes led to uncertainty about the exact site at which it was lying, which was particularly troublesome at times when unusual phenomena were recorded. This uncertainty, which made it virtually impossible to extract meaningful information from motility studies in the stomach could only be removed by tracking the capsule as it moved through the alimentary tract. The simple, qualitative method we adopted to study the short-term movements of the capsule suggested very strongly that a much more comprehensive study of motility could be made if we utilised the mobility of a small capsule with low-inertia to make quantitative recordings of transport along the bowel, as well as the complementary study of intra-luminal pressure. It does not seem practicable to reduce the present form of the capsule, but a different approach using an externally energised 'probe' may provide/

provide the solution. Also the problems of interpreting the data might be simplified if a different type of measurement could be made which excludes variations from extra-luminal pressure fluctuations. A lighter capsule of about the same length as the present 'probe' with a differential pressure transducing system which transmitted a measure of relative changes between the ends of the capsule might prove to be a more potent instrument for examining motility, particularly in the small bowel. A differential measurement would also exclude the extra-luminal effects.

A few difficulties, therefore, remain to be solved before telemetering from within the human body can become a routine clinical procedure, and in conclusion I would like to express the hope that these studies will form a useful basis for the practical advancement of these 'tubeless' techniques.

In the course of this work the publications listed below were made jointly with Mr. A. N. Smith of the Department of Clinical Surgery.

April 1961. A paper describing the management of the clinical investigation and the elucidation of the localisation radiographs was published in the Journal of the Royal College of Surgeons of Edinburgh.

September 1961. A paper describing the double channel recording technique was presented at the Newcastle meeting of the Physiological Society.

July 1962. A paper describing the provisional findings was presented at the Aberdeen meeting of the Physiological Society.

Two papers describing our methods and results more completely are to be published shortly in Gut, the Journal of the British Society of Gastro-enterology.

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