Conclusion

Such is a very rough-and-ready sketch. I am profoundly aware that already a few courses organised on these lines exist and that much may be learned from them. I am also aware that the best results of such a course could be obtained only if it interlocked with the teaching in the clinical years far more closely than does the present preclinical course. Such interlocking is implicit in the structure of the new course's third year: much of the sociology, for example, would be taught by medical men from the fields of social medicine and of the psychology of industrial and group relations. Doubtless some crusading zeal could be lavished on the last years of our present curriculum too! But I am trying to be very strictly practical; everything I have suggested could actually be put into practice—as an experiment—without too much trouble with regulations, I believe, at any of a number of medical schools in the United Kingdom.

The General Medical Council in its 1957 *Recommendations as to the Medical Curriculum* has removed its previously rather detailed recommendations about the teaching of particular subjects. The present recommendations have been drawn up specifically to foster experimentation with the curriculum: they " refrain from specifying the period of time to be allotted to particular subjects or the sequence in which they should be taught . . . and from specifying subjects in which separate examinations should be held ". The Council make a particular point of asking schools not to regard their activities as " in any way limiting their own right, which may equally be described as a duty, to experiment with different courses and various methods of teaching ".

The present proposals should be viewed in the light of this recommendation. Summing them up one could say they imply a three-year preclinical course covering all the present ground of 1st M.B., 2nd M.B., and general pathology, but reorientated in consecutive courses entitled Cellular Biology, Organisation of Mammals, and Organisation of Man. Biochemical genetics enters the course at the start; ethology is part of it all along. The growth process is used to introduce anatomy and physiology and at the same time behavioural development. The concepts of maturation and learning introduce normal psychology, family studies, sociology, and finally a discussion of the role of the doctor—or various sorts of doctors—in our society.

I am sure much more thought and a great deal of experiment must go towards making a real course in human biology for doctors; but I think we ought to face squarely the implications of the modern nature of medical practice in our society. I believe we should seriously consider giving thought to the reorganisation of the curriculum from the point of view of the human biologist. We might further invite the views upon this of a variety of disciplines outside our own to see what their representatives conceive of as the doctor's role and his training for it. In this way we would gradually work towards the time when we could envisage setting up an experimental training in line with these emerging conceptions, and in which studies of human biology would exert their true usefulness in the training of medical men.

This essay has benefited much from the constructive criticism of a number of persons who have long thought about problems in medical education. In particular I would like to thank Dr. C. F. Harris, Prof. A. A. Moncrieff, Prof. J. Z. Young, Sir Geoffrey Vickers, and Dr. J. S. Weiner. Needless to say, however, the views above are not to be imputed in whole or part to anyone but myself.

INVESTIGATION OF ABDOMINAL MASSES BY PULSED ULTRASOUND

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VIBRATIONS whose frequency exceeds 20,000 per second are beyond the range of hearing and therefore termed " ultrasonic ". One of the properties of ultrasound is that it can be propagated as a beam. When such a beam crosses an interface between two substances of differing specific acoustic impedance (which is defined as the product of the density of the material and the velocity of the sound wave in it), five things happen:

(1) Some of the energy is reflected at the interface, the amplitude of the reflected waves being proportional to the difference of the two acoustic impedances divided by their sum (Rayleigh's law). Therefore the greater the difference in specific acoustic impedance between two adjacent materials the higher will be the percentage of energy reflected. This fact makes a liquid-gas interface almost impenetrable to ultrasound and is important in relation to gas-filled intestine within the abdominal cavity.

(2) Much of the energy which is not reflected is transmitted into the second medium but is somewhat attenuated.

(3) Some refraction may occur, particularly when the ultrasonic beam is not at right-angles to the plane of the interface.

(4) Some of the energy may be absorbed and produce heat. The ability to absorb ultrasound varies with different tissues —e.g., that of bone is considerable.

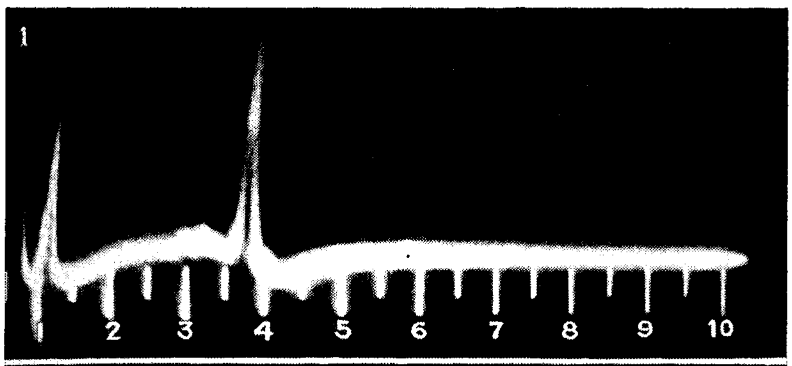
(5) Cavitation may be produced if considerable energies are present at the lower ultrasonic frequencies. This phenomenon, whose mechanism is not yet fully understood, can develop when the negative sound pressure exceeds the ambient hydrostatic pressure, giving rise to small temporary voids in the material. Cavitation becomes increasingly difficult to produce as the frequency of the ultrasound is raised, and usually develops only when the ultrasonic energy is applied continuously or in pulses of much greater duration than those we use. Nervous tissue is more susceptible than other tissues to cavitation (Fry et al. 1950).

For diagnostic purposes reflection and transmission are the important phenomena. Transmission is ruled out in our type of investigation because of the multiplicity of interfaces within the abdominal cavity and the impenetrability of tissue-gas boundaries. The recording and mapping of echoes from the reflecting interfaces is therefore the method of choice, which has been extensively used for many years in industry for detecting flaws in homogeneous materials, particularly metals, and the information so obtained may in some instances be superior to radiography, even with 2,000,000-V X-ray machines.

The use of ultrasonic echoes in studying human tissues promises to be much more complicated because of the great variety of tissues concerned and, it is believed, the not very large differences in specific acoustic impedance between them. It is therefore not surprising that results so far do not appear to have matched the technical ingenuity which has been shown in recent years.

A-scope Presentation

To confirm that echoes were obtainable within the body we started modestly with this method of presentation,



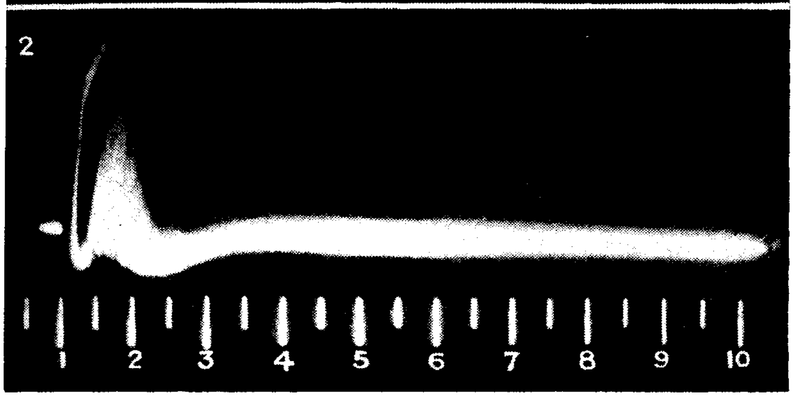


Fig. 1—A-scope presentation of acute retention of urine, showing bladder walls separated by gap representing urine.

Fig. 2—Same bladder as in fig. 1 after having been emptied by catheter, showing bladder walls no longer separated by gap.

which is standard practice in industry. By this method any echoes picked up are represented by vertical blips on a cathode-ray oscilloscope screen on a horizontal linear time-base sweep, the propagating source of ultrasound being represented by the left-hand end of the sweep. Since the velocity of propagation of ultrasound is very nearly the same in the various soft tissues encountered, the distance to the right along the base-line at which an echo blip is shown gives a measure of the distance of the reflecting interface from the propagating source. Figs 1 and 2 illustrate the principle of A-scope presentation. The patient from whom these figures were obtained had acute retention of urine following colporrhaphy, and the ultrasonic probe was placed over her distended bladder. The clear space in fig. 1 between the two blips represents the urine within the bladder. A catheter was then passed, and the blips closed up together as the bladder emptied (fig. 2). The apparatus used was the standard ' Mark IV ' Kelvin Hughes flaw-detector, with which we had considerable experience, making 165 A-scope records of various solid and cystic swellings both in vivo and postoperatively in vitro.

It was not long before we discovered that the pattern of the blips is altered considerably by changing the angle of incidence of the ultrasonic beam, and it appeared that only the simplest reflecting interfaces could be diagnosed by conventional A-scope technique.

We were using at that time a standard frequency of $2\frac{1}{2}$ megacycles per second, and we compared the quality of echoes from the same subjects at $\frac{5}{8}$, $1\frac{1}{4}$, and 5 megacycles as well, but we appeared to obtain the best results at $2\frac{1}{2}$ megacycles. The higher the frequency and therefore the shorter the wavelength the greater can be the resolution; but attenuation within the transmitting medium also increases with the frequency, as does " scatter ", which confuses the picture, and therefore range is restricted for a given power. Reid and Wild (1952), using a higher frequency of 15 megacycles, were restricted to a range of about 2 cm. only, but they suggested that this could be extended by the principle of time-varied sensitivity, in which the receiver gain is increased as a function of the elapsed time between propagating signal and echo. A compromise has to be reached between frequency and resolution and depth of penetration.

The use of A-scope presentation has been applied in ingenious ways, especially by Effert et al. (1957), who studied the movements of the left atrial walls of the heart simultaneously with electrocardiography and phonocardiography in the relative assessment of mitral stenosis and incompetence. They also demonstrated pericardial effusion.

B-scope Presentation

In this arrangement the direction of the probe is kept constant, and the area is scanned by moving the probe sideways along a line at right-angles to the ultrasonic beam. The display on the cathode-ray tube is made to follow this sideways movement of the probe. If the size of the echo is represented by variations in brightness of a spot on the cathode-ray screen instead of as a blip, it is possible to build up a composite picture on a long-persistence screen or on a photographic plate.

A variant of this method was used by Wild and Reid (1951) using a hand-held instrument in which a propagating crystal scanned to and fro over a range of 6·5 cm. within an elliptical water-chamber. Another variant is to place the test object in a water-tank round the outside of which a probe travels directing a radial beam inwards. Similarly, in Japan, Kikuchi et al. (1957) graduated from A-scope presentation to a type of B-scope scan, which they call " ultrasono-tomography ", for the exploration not only of the abdomen but also of the cranial cavity, as much of the head as possible being placed in a water-tank. The method appears to be still under development.

Our experience was like that of Howry (1955), who noted that even quite small angular displacements from the perpendicular in the incidence of the ultrasonic beam produced very great differences in the amplitude of the reflected echo. Howry calculated that an angle as small as 6° off the perpendicular reduced the amplitude of the detected echo to a tenth, and 12° reduced it to a hundredth. Howry and his colleagues have done a lot of fundamental work with simple geometrical test objects in water-tanks and have used ultrasonic lenses to narrow the beam and to improve penetration and resolution. They have also attempted three-dimensional and stereoscopic observations of body structure by building up two composite pictures taken from angles differing by 10° in respect of each other and studying them in a stereoviewer (Howry et al. 1956).

Radial Scan or Plan-position Indicator

A plan-position-indicator (P.P.I.) display is produced by rotating the probe about a fixed point in or near the area being scanned and causing the time-base sweep to follow the angular movement of the probe while originating from a fixed point on or off the face of the cathode-ray tube. If the origin of the display is off the face of the tube, the display is known as a " sector scan ". None of the aforementioned methods is sufficient by itself to produce a satisfactory echo pattern of a deep-seated structure within the body, because echoes are only detected by the receiving crystal if the reflecting surfaces from which they originate are at right angles to the incident energy beam.

For these reasons it was decided to attempt to produce a scanning and plotting mechanism which, so far as possible, would enable each individual part of the surface of the structure under investigation to be scanned by the

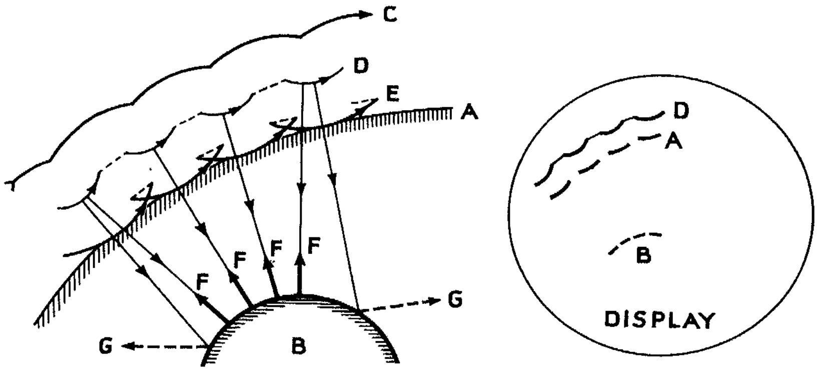


Fig. 3—Diagram of method combining B-scope and P.P.I. presentation: A, patient's skin; B, reflecting mass; C, D, E, paths traced by probe spindle, transducers, and probe face respectively; F, paths of echoes returning to receiving transducer (where reflecting surface is at right-angles to incident ultrasonic beam); G, paths of useless reflections (where beam strikes surface obliquely).

ultrasonic beam from a large number of different angles, all, however, lying in the plane of the cross-section to be represented. In this way we have sought to reproduce a composite cross-sectional view of the parts of the body examined, " collecting " echoes on the one picture from as many angles as possible, registering simultaneously not only the echoes and their strength but also the position of the probe and the angle of the incident beam. Our

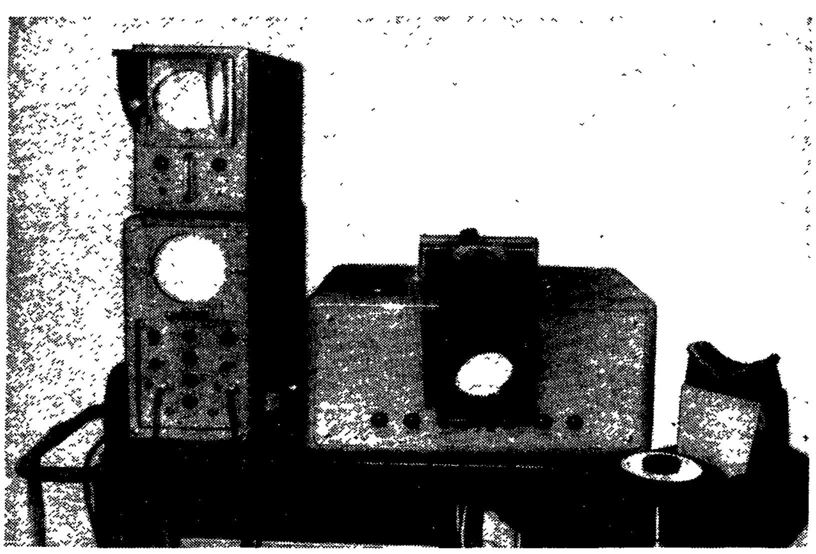


Fig. 4—Recording apparatus, showing three cathode-ray tubes with camera folded back over cathode-ray tube on the right.

apparatus thus combines B-scope and P.P.I. presentation (fig. 3).

Apparatus

A probe containing both transmitting and receiving transducers is mounted on a measuring jig, which is placed above the patient's bed. The probe is free to move vertically and horizontally and, as it does so, operates two linear potentiometers, which give voltage outputs proportional to its horizontal and vertical displacements from some reference point. The probe is also free to rotate in the plane of its horizontal and vertical freedom, and transmits this rotation via a linkage to a sine-cosine potentiometer. The voltage outputs from this system of potentiometers control an electrostatic cathode-ray tube, so that the direction of the linear time-base sweep corresponds to the inclination of the probe, and the point of origin of the sweep represents the instantaneous position of the probe.

The apparatus is so calibrated that the same reflecting point will repeat itself in exactly the same position on the cathode-ray tube screen from whatsoever angle it is scanned, and likewise a planar interface comes to be represented as a consistent line.

The probe mounting and measuring jig have been built on to a standard hospital bed-table, which is placed over the patient's bed. The patient's abdomen is smeared with olive oil to establish acoustic coupling by excluding intervening air, and the probe is applied directly to the abdominal skin. We have been able to dispense with the water-tank or water-column transmission system of other workers; this enables us to scan far larger areas. The echoes picked up by the probe are displayed on three oscilloscope screens: an A-scope display; a combined

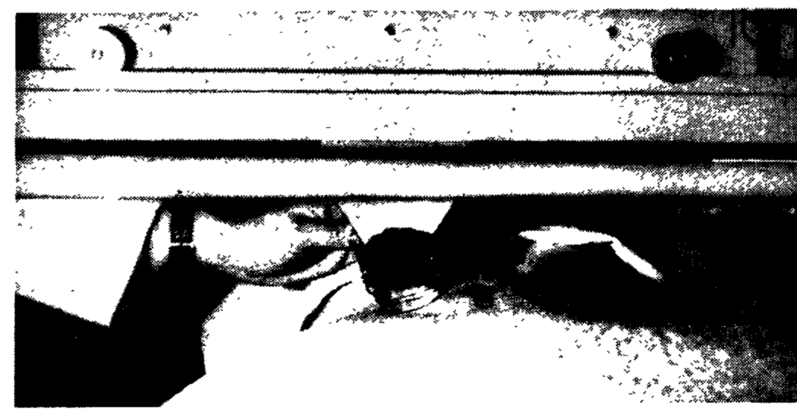


Fig. 5—Rotating probe applied to abdomen.

B-scope and P.P.I. display on a long-persistence screen for monitoring; and a similar screen and display of short persistence with a camera mounted in front of it (fig. 4).

The probe is moved slowly from one flank, across the abdomen, to the other flank, being rocked to and fro on its spindle the whole time to scan the deeper tissues from as many angles as possible. At present this is done by hand, but we have plans for mechanical scanning, which should produce far more consistent results. Thus the entire cross-sectional picture is composed of a large number of overlapping sector scans, and each potential reflecting surface within this cross-section is " seen " by the probe from a great number of angles (figs. 3 and 5). The process usually takes between $1^1/_2$ and $2^1/_2$ minutes, and the patient experiences no discomfort whatsoever. Several cross-sectional views are taken thus at different levels between the symphysis pubis and the xiphisternum.

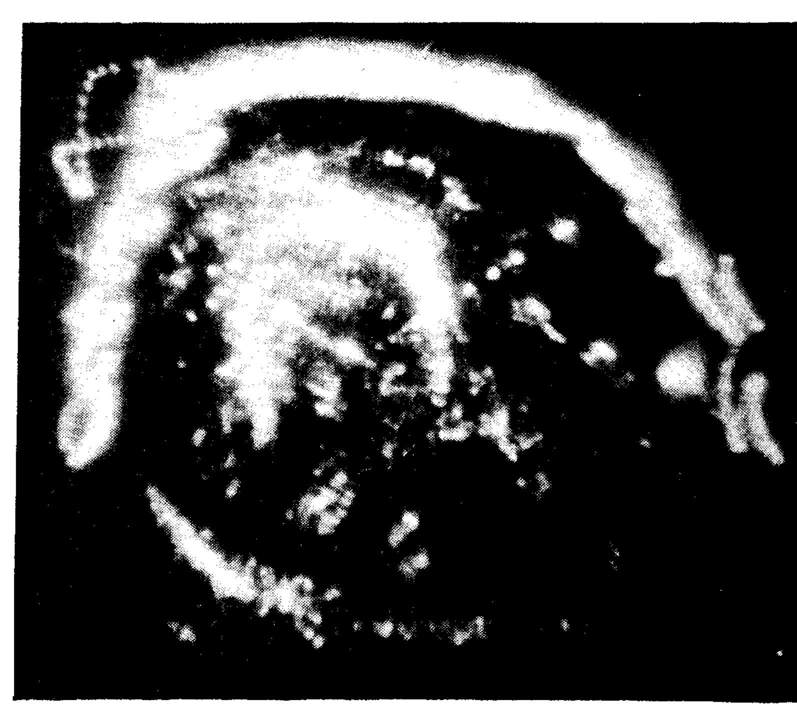


Fig. 6—Transverse section of anterior half of thigh showing femur.

Fig. 7—Unilocular ovarian cyst of moderate size.

Fig. 8—Large simple ovarian cyst with posterior surface indented by vertebral column and posterior abdominal wall.

Probe System

We use separate piezo-electric transducer crystals, one for transmitting and one for receiving. Each is a barium-titanate rectangle 10 mm. × 7 mm., and the two are placed with their 7 mm. sides adjacent. These dimensions were chosen empirically as likely to give the best compromise between beam divergence and beam diameter. The transducers lie on a conducting layer on a ' Perspex ' block 1 in. thick, whose opposite side is in contact with the patient's skin. The transmitting transducer is " air-backed " and is electrically pulsed fifty times a second. At each pulse it vibrates mechanically for a very brief interval at a frequency determined by its elastic properties and its thickness. For a frequency of $2\frac{1}{2}$ megacycles, such as we use, the thickness is about one millimetre.

Transmitting System

A 100 pico-farad capacitor is charged to about 1400 V through a high resistance and is then discharged by a thyratron through the primary winding of a pulse transformer. The transmitting transducer is connected across the secondary of the pulse transformer in parallel with a damping resistance of 50 ohms. The amplitude of the transmitted acoustic pulse rises from zero to its maximum value in 0·3 microseconds and has decayed to 10% of this value after a further 1·8 microseconds. Fifty such pulses are transmitted each second.

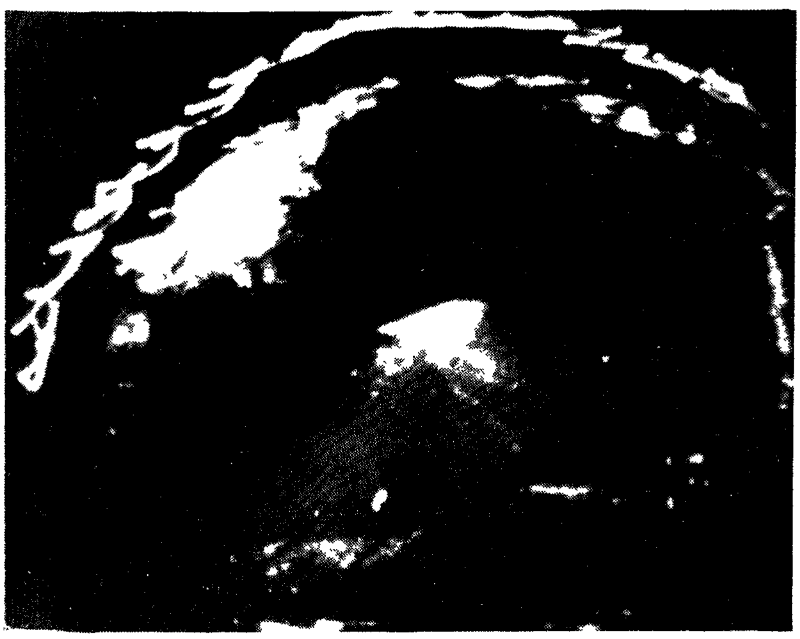


Fig. 9—Bilateral ovarian cysts. At operation left cyst's diameter was 26 in. and right cyst's $12\frac{1}{2}$ in.

Results

We have now investigated 100 patients and made 275 records by this scanning technique, in addition to the previously mentioned A-scope work. Most of the cases were gynæcological or obstetrical because we mainly investigated the routine clinical material of our own department. Our work therefore deals chiefly with various conditions of pregnancy, ovarian cysts, fibroids, ascites, and abdominal carcinomatosis.

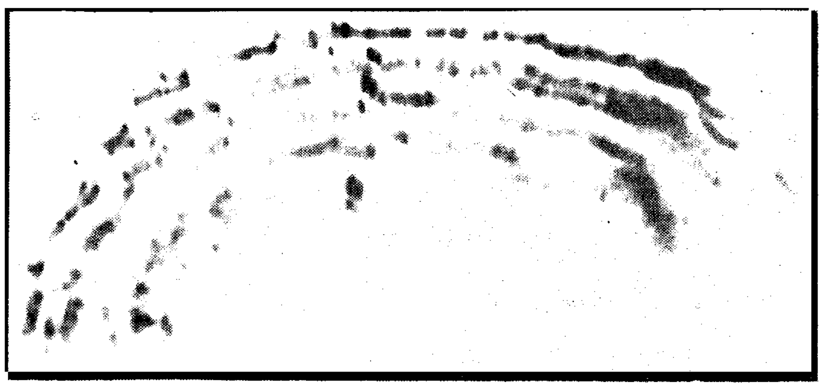


Fig. 10—Transverse section of healthy abdomen at level of umbilicus.

A transverse section of the thigh of one of us (T. G. B.) is shown in fig. 6. The outermost line represents the movement of the probe, and the wriggles in it represent the rotary movement applied to the probe. The femur appears crudely in cross-section.

A moderate-sized unilocular ovarian cyst is shown in fig. 7. The shadows below and behind it are believed to be due to displaced bowel, which gives very powerful echoes because of the tissue-gas interface which intestine provides.

A much larger cyst is shown in fig. 8, and the indentation of its posterior surface by the vertebral column is clear. The cyst was very tense and clinically diagnosed as a fibroid, but the ultrasonic characteristics of a fluid-filled cyst are here quite unmistakable.

Bilateral ovarian cysts are shown in fig. 9; only one cyst had been diagnosed clinically, but the outlines of both cysts can here be made out; two cysts were found at operation. The heavy collection of shadows in the centre of the picture and in the upper left part are believed to be due to coils of intestine.

Fig. 11—Gross ascites due to cirrhosis of liver. Ultrasonic beam can penetrate more deeply in random fashion because of fluid between coils of intestine.

By contrast the *healthy abdomen* of one of us (J. M.), scanned at the level of the umbilicus, is shown in fig. 10. We are not yet certain of the identification of the various layers of the abdominal wall shown here, but the noteworthy feature is that deep penetration into the abdomen is prevented by normally situated coils of intestine.

In *ascites*, however, the fluid intervening between the coils of gut allows the ultrasound to penetrate to a much greater depth, yet without producing the clearcut margins of an ovarian cyst. This is shown in fig. 11, taken in a case of portal cirrhosis in which the patient's abdomen was scanned at umbilical level in the presence of gross ascites. This film is almost certainly overexposed and probably exaggerates the picture.

Fig. 12—Very large complex ovarian tumour, which proved at operation to be a multilocular pseudomucinous cystadenoma with almost solid plaques of minute loculi.

A huge and structurally very complicated ovarian tumour is shown in fig. 12. This was a large pseudomucinous cystadenoma of ovary with many areas of very small loculi clustered together so as almost to give the macroscopic impression of areas of solidity. Histology showed the tumour, however, to be benign.

Multiple fibroids are shown in fig. 13. Our findings so far indicate that fibroids tend to absorb and scatter ultrasound, with the result that only faint echoes can be recorded from the posterior surface of the mass (as in this figure) or none at all, in contrast to a fluid-containing cyst, in which the ultrasound is readily transmitted and reflected from its posterior wall. Here the outline of the fibroids can be roughly seen and the thickness of the tumour gauged. Our tentative conclusions at present are that the ability of fibroids to transmit ultrasound depends on their vascularity.

The *pregnant uterus* offers considerable scope for this kind of work because it is a cystic cavity containing a solid fœtus. In fig. 14 a suprapubic scan is shown of a patient at the 34th week of gestation in whom placenta prævia was suspected; we were trying to see the placenta in the lower segment. We are not yet sure about this, but the outline of the fœtal head shows up very well.

Hydramnios is very vividly shown in fig. 15, in which the transverse section of the baby's body appears within the enormously distended amniotic sac. The period of

Fig. 13—Multiple fibroids, showing progressive attenuation of ultrasound, with only faint echoes from posterior surface of mass in contrast to ovarian cysts.

gestation in this case was 32 weeks, and the girth of the abdomen 44 inches.

Twins are shown in fig. 16. The scan was taken just above the level of the umbilicus at the 37th week of gestation. Both twins presented by the vertex, and what is visible here is the two breeches at the fundus.

Fig. 17 is very interesting. The patient had had three months' irregular vaginal bleeding and a very hard enlargement of the uterus corresponding in size to about 14 weeks' gestation. A year previously a fibroid had been found within her uterus, and she was now admitted to hospital for myomectomy. A scan taken one inch above the symphysis pubis showed, however, a very different picture: a cystic cavity containing in its left half a mass which is clearly a very early fœtus. The result of the Aschheim-Zondek test ordered was awaited with considerable excitement since clinically the diagnosis was con-

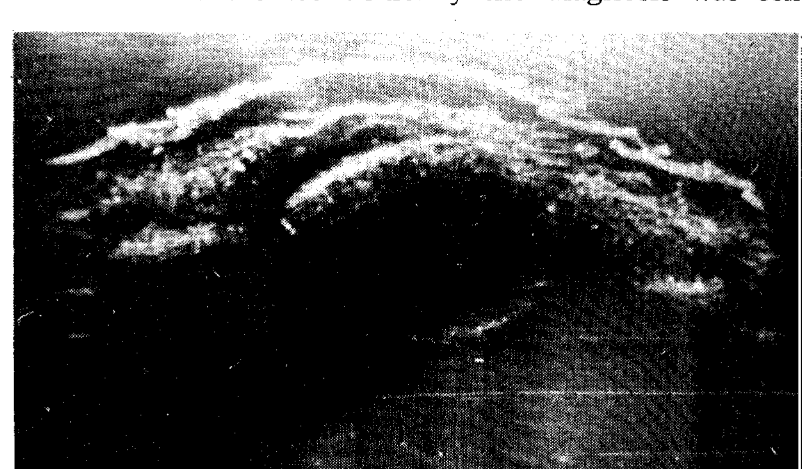


Fig. 14—Outline of fœtal skull in utero at 34 weeks' gestation (suprapubic scan).

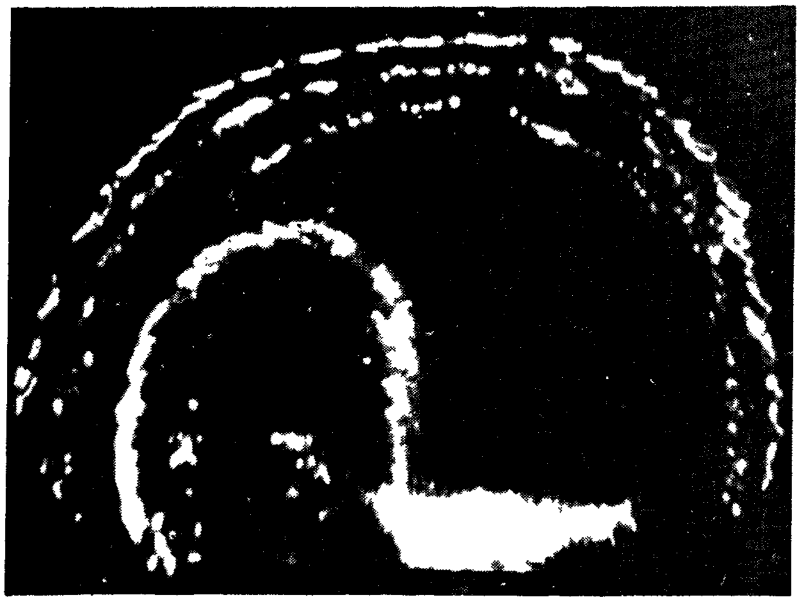


Fig. 15—Hydramnios, showing outline of transverse section of fœtal body within enormously distended amniotic sac.

Fig. 16—Twins: both breeches shown on scanning across fundus uteri.

vincingly that of fibroid. The test was positive; and with rest in bed the patient's bleeding ceased, and she was discharged home with the pregnancy continuing. She has since been safely delivered.

In another instance, in which, unfortunately, we did not secure a permanent and satisfactory record, the usefulness of ultrasound in diagnosis was well shown. A woman, aged 64, was admitted to a medical ward with gross abdominal distension believed to be due to ascites. She had severe vomiting and had rapidly lost weight. Carcinoma ventriculi with secondaries at the portal fissure was provisionally diagnosed, and one of us (I. D.) was asked to see her to exclude malignant disease within the pelvis as an alternative source of her ascites. Her general condition was very bad, and the abdominal examination was very difficult owing to distension, but the diagnosis of ascites was agreed, and the pelvis was found to be clear of any palpable malignant deposit. The ultrasonic apparatus was applied and indicated unequivocally a very large cyst, which we were unwilling to believe. At laparotomy, however, a very large pseudomucinous cystadenoma was removed, and the patient continues well to this day.

Possibility of Harmful Effects of Diagnostic Ultrasound

Ultrasound, being a form of mechanical energy, can be expected to inflict and make apparent its injuries, if any,

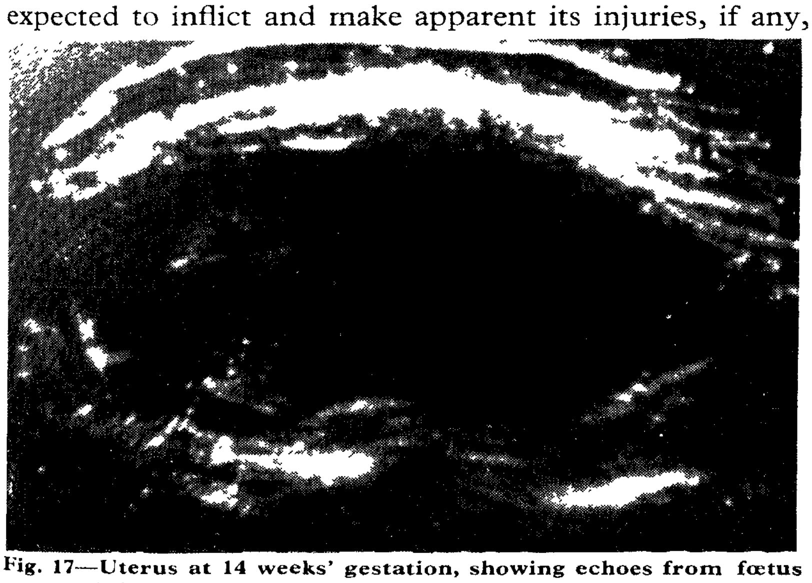


Fig. 17—Uterus at 14 weeks' gestation, showing echoes from fœtus towards left half of uterus. Provisional clinical diagnosis had been that of fibroid.

at once, like other forms of mechanical trauma. In this it differs from ionising radiations. There are two possible means whereby damage might be inflicted by the passage of a beam of ultrasound: (1) the production of heat associated with the absorption of the energy of the ultrasonic beam, and (2) cavitation. There can be no doubt that intense ultrasonic energy can produce damage, especially from powerful machines using the principle of magnetostriction at lower frequencies. In diagnostic work, however, very high frequencies in the megacycle ranges and low-power outputs are used. One of us (I. D.), using continuous 1-megacycle ultrasound—i.e., not pulsed—with an intensity of 7 watts per sq. cm., made experiments in hæmolysing blood and observed that the rate of destruction of the red cells depended on the amount of heat generated within the sample of blood, because a similar degree of destruction could be achieved by heating the blood to the same temperature without ultrasound. Fry (1954), however, using intensities of 70 watts per sq. cm. and a 4-second exposure with multiple ultrasonic beams focused to a width of 2–3 mm. and working directly on animals' brains from which the overlying bone had been removed, produced immediate effects, particularly on the larger nerve-cells. He concluded that increased temperature was not the chief cause of damage, because the smaller nerve-cells would then have suffered as much as the larger.

Nerve-cells appear to be more susceptible to damage from ultrasonic energy than any other tissue, and Fry et al. (1950, 1951) showed that there was a linear relation, for a definite degree of paralysis in the frog, between the reciprocal of exposure time and the pressure amplitude of the sound-wave.

This structural damage was produced at intensities many thousand times higher than those used in diagnostic work. French et al. (1951), using Wild's 15-megacycle diagnostic apparatus, found no brain damage in four rabbits and a cat whose brains were directly exposed to diagnostic ultrasound. Wild and Reid (1952) calculated that the average intensity at the surface of their patients " was not more than 1·3 watts per square centimetre," a figure which strikes us as surprisingly high.

With our apparatus we have calculated that, even if we ignore the energy losses in the transmitting circuits, the greatest possible energy delivered to the transducer is $0{\cdot}5 \times 10^{-4}$ joules per pulse. If we take into account the efficiency of the transducer and the attenuation of the energy in its passage through the perspex block, the greatest energy which can be radiated into the patient is $0{\cdot}2 \times 10^{-4}$ joules per pulse. This is equivalent to an average power at the body surface of less than 1·5 mW per sq. cm. The cross-sectional area irradiated at any one time is about 0·7 sq. cm. Thus the energy is truly very small. Nevertheless it was vital to establish beyond all shadow of doubt that susceptible tissues would not suffer even from these dosages, and we are indebted to Dr. P. Bacsich, of the department of anatomy of this University, for the following investigations which he made for us on newborn kittens. His report is quoted in full below:

2 day-old male sibling kittens were used, two of them being controls.

Under pentobarbitone-sodium anæsthesia two kittens were exposed to pulsed ultrasound from the standard flaw-detector for an hour, the crystals being placed on the left temporo-parietal region after the scalp had been generously covered with olive oil; simultaneously the controls received " treatment " with a dummy crystal. All four kittens regained full consciousness within 9–10 hours and, after being put back to their mother, started to feed voraciously.

2 kittens (1 experimental and 1 control) were killed 24 hours after the start of the experiment. The other 2 were left under the mother's care for three weeks. During this period the experimental kitten showed no harmful manifestations of the treatment, in fact its development was considerably in advance of that of its sibling. It fed better and gained weight faster, its eyes opened a day earlier, and it left the mother's basket two days sooner.

At the end of this period the 2 kittens were killed with lighting-gas, and their brains were carefully removed and fixed in a 10% aqueous solution of formalin for three days. All 4 brains were embedded in celloidin-paraffin and sectioned serially in the coronal plane. The sections were mounted in four parallel " reduced " series as follows: after three consecutive 10-μ and one 20-μ sections had been mounted, the next 45 sections cut at 10 μ were discarded, and this procedure was repeated again and again. In every instance one series was stained with hæmalum and eosin, one with toluidine-blue, one with a modified ' Protargol ' method, and one with a modified Weigert method.

In the microscopical examination of the brain of the 24-hour experimental kitten signs of cavitation, coagulative necrosis, localised hyperæmia, hæmorrhages, and chromatolysis were looked for; and the brain of the 3-week kitten was examined for any evidence of patchy cell destruction, neuroglial scarring, axonal degeneration, and localised lack of myelination.

All these tests were completely negative, and the brains of the experimental kittens and their respective controls were in every way comparable.

On the basis of these findings one must conclude that exposure of the kittens to more than thirty times the dose of ultrasound necessary in its diagnostic use produced no detectable neuropathological change, or at least any possible lesion could not exceed 450 μ in extent.

Discussion

To be of any use at all to the clinician, the echo patterns obtained by pulsed ultrasound must be not only intelligible but also consistently reproducible at the same level in the same case. That this is not always so we attribute to inadequate scanning methods and technique —hence the development of our combined B-scope and P.P.I. presentation and scanning. Even so we are very far from satisfied with the crude results so far obtained. Other workers have made claims which, in many instances, are more striking than substantial, judged by some of the illustrations offered. The temptation to try to distinguish benign from malignant tissue by such simple, quick, and harmless means is well-night irresistible; but, being only too well aware of the difficulties which even the histologists on direct microscopy may have in assessing malignancy, we have not attempted this sort of assessment in the present state of crudity of an ultrasonic beam whose width is measurable in millimetres and whose wavelength is many times the diameter of any living cell, benign or malignant. Wild and Reid (1952) claim that it is possible to distinguish between a benign and a malignant tumour within the breast on the basis of positive differences observable on ultrasonic echography. The Japanese workers Kikuchi et al. (1957) have made the same claim; they also claim to have recorded echoes from human intracranial ventricles, as we have, in the newborn, and they make other claims which we have not explored. Howry and Bliss (1952) noted that fresh specimens in vitro differed in their sonic properties when compared with fixed specimens in formalin solutions. We also have noted differences between the tumour in vivo in a tank after removal from its host. We cannot explain this difference except by suggesting that blood circulating through a tumour alters its sonic properties.

Our experience of 78 cases in which diagnosis was quickly verified by laparotomy and subsequent histology indicates that ultrasonic diagnosis is still very crude, and that the preoperative diagnosis of histological structure is still far off, although such a possibility in the future is an exciting prospect. The fact that recordable echoes can be obtained at all has both surprised and encouraged us, but our findings are still of more academic interest than practical importance, and we do not feel that our clinical judgment should be influenced by our ultrasonic findings. Our most spectacular results have been obtained in dealing with fluid-filled cavities, which certainly show up well; but it is only fair to point out that the illustrations shown herewith are among the very best that we have so far been able to produce out of about 450. They do, however, encourage great efforts to refine our technique.

Summary

Large intra-abdominal masses, including the gravid uterus, pelvic tumours, and ascites, have been investigated by the echo patterns obtainable by pulsed ultrasound.

Masses containing fluid are easily but crudely demonstrated.

The possible identification of structures within the abdomen by their sonic properties is discussed.

A scanning mechanism is described whereby cross-sectional views of the abdomen are obtained, and illustrative examples are given.

The possible harmful effects of diagnostic ultrasound are discussed; they appear to be negligible.

The limitations of the technique so far developed in practical diagnosis are described, but further refinements in technique may provide a useful diagnostic weapon in cases in which radiological diagnosis with ionising radiations is either impracticable or undesirable.

Our apparatus was developed in the research department of the Hillington Factory, Glasgow, of Messrs. Kelvin Hughes Ltd., who cooperated in this research with generosity and enthusiasm, for which we are indeed grateful. One of us (T. G. B.) has been seconded by the directors of this firm for whole-time work in connection with this research. We also acknowledge, with thanks, the support received from the Scottish Hospital Endowments Research Trust.

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DIURETIC ACTION OF CHLOROTHIAZIDE

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IT has been claimed that oral chlorothiazide (6-chloro-7-sulphamyl-1, 2, 4, benzothiadiazine-1, 1-dioxide), synthesised by Novello and Sprague (1957), is effective in the treatment of certain types of œdema. Bayliss et al. (1958) have used it successfully in congestive heart-failure and premenstrual œdema, Slater and Nabarro (1958) in œdema due to the nephrotic syndrome (3 cases) and œdema due to hepatic fibrosis with portal hypertension (1 case).

The chemical structure of chlorothiazide suggests that it acts by inhibiting carbonic anhydrase, and Beyer et al. (1957) have shown that in vitro it is, in this respect, some thirty times more potent than acetazolamide (' Diamox '). Slater and Nabarro (1958) have tried to assess the effect of chlorothiazide as a carbonic-anhydrase inhibitor in vivo by giving 3000 mg. orally to a patient with rheumatic heart-disease and essential hypertension.

Despite fairly extensive investigations on dogs (Beyer et al. 1957, Ford et al. 1957) and on patients with incipient heart-failure (Ford et al. 1957) there is no information about the effect of chlorothiazide on the urine and the excretion of electrolytes in healthy people. The present investigation was an attempt to supply some of the essential basic information which cannot be deduced either from experiments on animals or from clinical trials. Consequently we sought to determine the effect of chlorothiazide on the composition and flow of urine in healthy adult males, to assess its action in vivo as a carbonic-anhydrase inhibitor, and to compare its effect with that of acetazolamide.

Methods

Investigations were made on 10 healthy males, aged 16–40, permitted normal activity and diet. The intake of sodium and potassium was not accurately standardised, but on the days of experiment the intakes of food and fluid were qualitatively and quantitatively similar.

Each man was studied during a control period of twenty-four hours. His bladder was emptied at 9 A.M., and his urine was collected under mineral oil in two-hour fractions for twelve hours. The urine passed during the subsequent twelve to twenty-four hours by 5 men was collected with similar precautions and pooled. The volume and pH of each sample were determined, and the urinary content of bicarbonate, chloride, phosphate, titratable acid, ammonia, sodium, and potassium during each period was measured.

On a subsequent day at 9 A.M. each man received chlorothiazide 2000 mg. by mouth, and the observations on the flow and composition of the urine were repeated. The experiment was repeated on 3 men under similar conditions but with acetazolamide 500 mg. instead of chlorothiazide. When this was done, at least a week was allowed to elapse between the administration of the drugs to allow fluid and electrolyte balance to return to normal.

The action of intravenous chlorothiazide 500 mg. was also studied by collecting samples of blood before and at half-hour intervals for four hours after the administration of chlorothiazide. The hæmatocrit, plasma-carbon dioxide, plasma-chloride, serum-sodium, and serum-potassium were estimated in each sample. Strict anaerobic precautions were observed in collecting the plasma for estimating carbon dioxide and chloride. Urine was collected and analysed, as in the previous experiment, before and each hour for four hours after the administration of chlorothiazide.

Chemical Methods

Sodium and potassium were estimated by flame photometry; urinary chloride by modified Volhard-Harvey titration (Peters and Van Slyke 1932); plasma-chloride by the open Carius method as applied by Van Slyke, Sendroy, and Eisenman (Peters and Van Slyke 1932); carbon dioxide in plasma and urine by manometric methods; and urine bicarbonate from the ordinate of the carbonic acid-bicarbonate curve according to pH (Peters and Van Slyke 1932). Urine pH was estimated with the glass electrode; ammonia by

Fig. 1—Average rates of excretion of water and electrolytes in 10 men after oral dose of chlorothiazide 2000 mg. compared with rates of excretion during control period. Note increase in excretion of sodium and chloride.

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