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● *Historical Review*

FORTY YEARS OF OBSTETRIC ULTRASOUND 1957–1997: FROM A-SCOPE TO THREE DIMENSIONS

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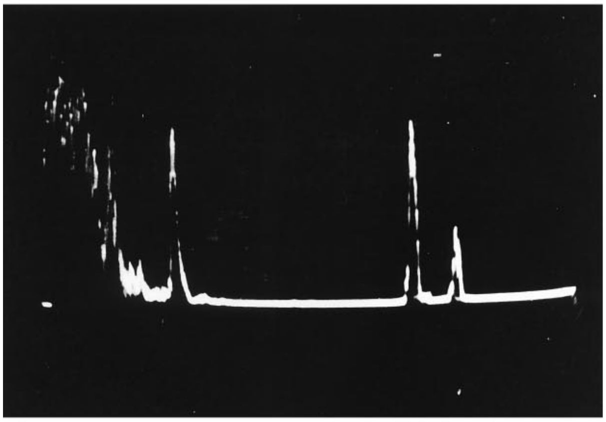

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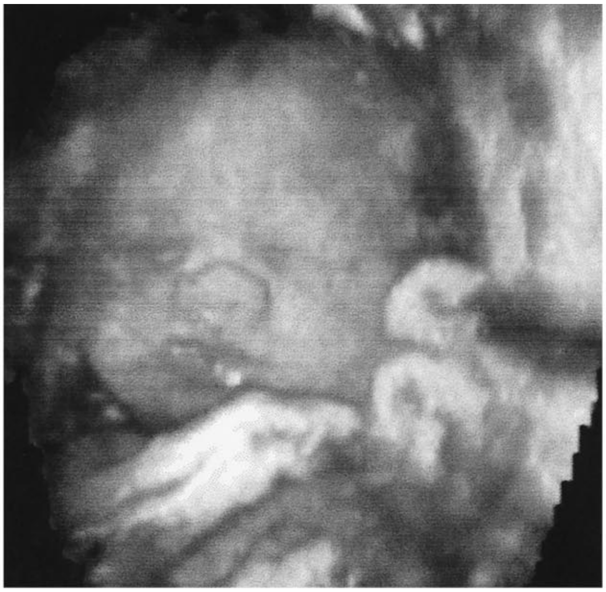

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Fig. 1. (a) An A-scan trace of fetal biparietal diameter. (Courtesy of Dr. J. Willocks.) (b) Three-dimensional image of a fetal head, taken in 1998. (Courtesy of Sonotron Ltd.)

"For thee....to whom
No sound is dissonant which tells of Life"
—Coleridge

Abstract—In this article, we record the history of obstetric ultrasound as it developed worldwide in the second half of the twentieth century. The technological advances during this period saw the evolution of equipment from the original adapted metal flaw detectors producing a simple A-scan to the modern, purpose built, real-time colour flow machines with three-dimensional capability (Fig. 1). Clinically, ultrasound began as a research tool, but the poor quality of the images led to the ridicule of many of the early investigators. However, because of their perseverance, ultrasound developed into an imaging modality providing immense diagnostic capabilities and facilitating with precision many invasive procedures, diagnostic and therapeutic, both of which have made significant contributions to patient care. In this history, we recall the people, the personalities, and the problems they encountered during the development of ultrasound and how these problems were resolved, so that

ultrasound now is available for use in the care of pregnant women throughout the developed world.

***Key Words:* History, Ultrasound imaging, Diagnosis, Obstetrics, Fetus, Fetal measurement, Fetal abnormality, Fetal therapy, Color Doppler.**

INTRODUCTION

The evolution of a new technology cannot be viewed in isolation, but is the result of complex interactions and circumstances. There must be a need, in this case the diagnostic problems that might be resolved with a new imaging technique; and there must be the means, the availability of the necessary people, their expertise, and the tools and equipment that can be adapted or purpose built for the project. In addition, the social and political climate must create an appropriate environment to facilitate, or at least not hamper, the research. All of these factors have had a major influence on the development of ultrasound imaging.

A record of the history of obstetric ultrasound should provide a systematic account of the origin and progress of its development. In trying to achieve this goal, we have perused the letters and papers in the archives of the British Medical Ultrasound Society (BMUS) and the American Institute of Ultrasound in Medicine (AIUM). In the latter are letters and records from many of the pioneers in ultrasound from around the world. They were solicited and collected by Joseph Holmes who, in the late 1970s, recognised the need for an historical record to be made. After Holmes' death, Barry Goldberg continued to gather information and organised "The Symposium on the History of Medical Ultrasound" in Washington in 1988. At that time, the opportunity was taken to interview many of the international researchers from the early days who were able to attend the meeting. Copies of the papers presented and the interviews are kept in the archives. The Wellcome Unit for the History of Medicine at the University of Glasgow made available to us taped interviews with several of the early British investigators. These sources have provided much of the material for this article, particularly from the pioneers from countries where English is not the first language. In addition, there are the many publications on obstetric ultrasound. For practical reasons, selection has been necessary; as a result, the majority of the papers and texts quoted are in English.

Obstetrics and gynaecology is a combined specialty, and there is considerable overlap in the early history of each. Dr. Levi already has written an article on the history of ultrasound in gynaecology, in which he describes many of the early events that cover both areas of our specialties. We shall try to avoid repetition but, in view of our close association with so many of the people and events that took place in Glasgow and our wish to include their contribution in some detail, inevitably there will be some duplication.

It cannot be denied that ultrasound has made a major contribution to changes in obstetric practice. Without the combined input of all the pioneers, these changes would not have occurred, and, on a personal level, neither of the authors would have experienced the opportunities and challenges in their own careers. J.E.E.F. has worked as an electronics engineer with ultrasound in Glasgow since 1962 and M.B.M. as a clinician since 1978. Therefore, this article has been written from a technical and clinical viewpoint. We would like to dedicate it to all those who contributed to the development of ultrasound.

The article is arranged so that the reader may dip into a section of interest. The layout is chronological, but we have had to be flexible to allow for events overlapping. Developments in technology, although influenced by potential diagnostic use, preceded the clinical application. The first part of this history is concerned mainly with describing the progress that was made in adapting and constructing the equipment; the second part covers many of the clinical applications using that equipment. The two parts cannot be viewed entirely separately, because the history of each is closely interwoven with the other.

Ultrasound pre-1955

The history of ultrasound as a diagnostic imaging technique belongs to the second half of the twentieth century, but its earlier beginnings may be traced back to the first description of the properties of sound and ultrasound and its applications in detecting underwater objects and flaws in metals. Ultrasound was utilized in medicine first for therapeutic purposes before the potential for diagnosis was considered. A brief summary of the names of the key figures and their achievements prior to the introduction of ultrasound to obstetrics follows.

1842: Doppler published his observations on the change of pitch when a source of vibrations is moving toward or away from an observer, now known as the Doppler effect.

1877: Rayleigh (1877) published "The Theory of Sound."

1880: The Curie brothers described the piezoelectric effect, initially regarded as a scientific curiosity but subsequently found to be of major importance as the

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means of producing acoustic waves in sea water (Curie and Curie 1880).

1912: The Titanic sank. Richardson, a British meteorologist, suggested that sound be used for the detection of icebergs (Richardson 1912). In 1914, Fessenden (Hackman 1984), an American electrical engineer, successfully demonstrated this idea.

1914–1918: The First World War. In 1917, Langevin (Biquard 1972) constructed the first piezoelectric ultrasound transducer in the effort to detect submarines. ASDIC—the anti-submarine detection committee—was established.

1929: Sokolov proposed that ultrasound might be used for imaging flaws in materials (Sokolov 1929).

1937: Dussik suggested that ultrasound might have applications in medicine and further developed his ideas during the 1940s (Dussik 1942). He described a transmission method for sending ultrasonic waves through the intact skull. He called the resulting display a hyperphonogram.

1939–1945: Prior to the Second World War, sonar (sound, navigation, and ranging) development increased and work on radar (radio detection and ranging) began. During the war, major advances in the equipment and instrumentation took place.

1945: Firestone published his work on the "Reflectoscope," an A-scope instrument for inspecting the interior of solid parts by means of sound waves (Firestone 1945).

1946: Wild, trained as a surgeon in England, moved to the US, where he developed his interest in ultrasound at the University of Minnesota, leading to his first publication, "The use of ultrasonic pulses for the measurement of biologic tissues and the detection of tissue density changes" (Wild 1950). Wild's main interests were the measurement of bowel wall thickness and the study of breast lumps. He saw the potential of ultrasound for breast screening and, in this respect, was extremely farsighted. Wild, Reid, and their collaborators were to make an important contribution to ultrasound imaging.

1948: Howry, in Denver, Colorado, as a young physician training in radiology, developed his interest in ultrasound, completing his first A-scope in 1949. In collaboration with Bliss, an engineer, the Somascope was constructed, a B-scan instrument that produced very good images but was extremely cumbersome and unsuited for use with sick or pregnant patients. Howry and Bliss published in 1952, "Ultrasonic visualization of soft tissue structures of the body." Howry's aim was primarily to obtain good anatomical sections. He was joined in 1950 by Holmes, also a radiologist, and together they worked toward obtaining clinically useful images.

1949: Ludwig worked at the University of Pennsylvania and the Naval Medical Research Institute, where he demonstrated that gallstones within the body gave a different reflected echo pattern than soft tissue (Ludwig and Struthers 1949). He then moved to the Massachusetts Institute of Technology (MIT), where he collaborated with Ballantine, Bolt, and Hueter, and with Dussik from Austria. At MIT, their main interest was in intracranial pathology.

1949: Uchida constructed the first A-scope in Japan at the Nihon Musen Company in Tokyo. He then collaborated with many clinicians in the development of equipment and application of ultrasound in clinical practice. In 1952, the first report entitled "Ultrasonic flaw detection in the human body" was published in Japan. Uchida later became president of the Aloka company (Uchida 1988).

1954: Edler, a cardiologist, and Hertz, a physicist, in Lund, Sweden, introduced echocardiography, publishing their first report on "The use of ultrasonic reflectoscope for the continuous recording of movements of heart walls" (Edler and Hertz 1954).

The summary of the achievements of these early pioneers, in different specialties and in different countries, provides an overview of the groundwork that had taken place and upon which future clinical developments would be built. Ultrasound imaging has had a huge impact on clinical practice in obstetrics, and the story of its early development is a fascinating one.

THE 1950s: THE CONCEPTION AND BIRTH OF OBSTETRIC ULTRASOUND

The first reports of the use of ultrasound in obstetrics and gynaecology came from Glasgow, Scotland.

The main character—Ian Donald, 1910–1987

Born in 1910, the eldest of four children, his mother a musician and his father a doctor as his father before him, Ian Donald was educated in Britain and South Africa, obtaining a B.A. in Classics and Music at the University of Cape Town, followed by his medical degree at St. Thomas' Hospital, London. In covering more than 20 years of his life in so few words, we fail to convey the changes and challenges Ian Donald had to face: first, his father's ill health, which necessitated the family's move to the warmer climate of South Africa; then his own illness (only realized in retrospect to be rheumatic fever); and the subsequent loss of both his parents when he was only 16 years old. These events surely influenced the character of the man.

Ian Donald was a very "big" man in every sense. He was physically commanding, with a powerful presence, able to show compassion to his patients but ruthless in the pursuit of his goals. He also has been described as a man of faith and courage, not only in facing three major cardiac operations but in having the courage of his convictions and being prepared to stand firm and speak out for what he believed was right. To these attributes can be added a man of culture, wit, and vision. It is the realization of his vision of ultrasound as an imaging modality in obstetrics that will be described.

Following his training in obstetrics and gynecology in London, Donald was appointed Reader at St. Thomas' Hospital and then at the Hammersmith Hospital, where his main research interest was in respiratory problems of the newborn. In 1954, he was appointed Regius Professor of Midwifery in the University of Glasgow. During his 22 years' tenure of that chair, he established ultrasound as the diagnostic imaging modality we know today. For this he received many accolades, including a CBE. He was awarded many prizes, but there was a feeling among his colleagues and admirers that he deserved more, perhaps even a Nobel prize, such was his contribution to medicine. At the memorial service held in Glasgow after his death, James Willocks included the following words, "*If you seek his memorial, look around you. In every maternity hospital you will see ultrasound in use. A great discovery by a great man.*"

The early years in Glasgow

The A-scope. Glasgow was a city rich in pathology, partly a result of poor nutrition together with the slum areas of poor housing and inadequate sanitation, a legacy of the industrial revolution. The National Health Service (NHS), introduced in 1948, made medical care available to all at no cost at the point of delivery. However, patients often did not seek medical attention until symptoms and signs were well advanced because of the still prevailing pre-NHS attitudes, primarily concern about cost, together with a fear of the unknown, which was a prominent feature of the social climate of the time. Therefore, it was not uncommon to see a woman with a grossly swollen abdomen from which might be removed an ovarian cyst or fibroid weighing many pounds. Differentiating these benign gynecological tumors from other conditions was difficult, and there was a real need for a safe method to investigate the enlarged abdomen.

It was against this background that one should view the subsequent developments. The environment was ready for research to proceed. What was needed was the man with the vision. Ian Donald was that man. Much of the following account is taken from his article, "Sonar—the story of an experiment" (Donald 1974), in which he described himself as "*having a continuing childish interest in machines, electronic or otherwise.*" The combination of this interest, some elementary knowledge of sonar and radar gained as an RAF officer (awarded the Military Cross for gallantry) in the Second World War, and an introduction, while still working in London, to John Wild from whom he learned of the early applications of ultrasound in medicine led Ian Donald to

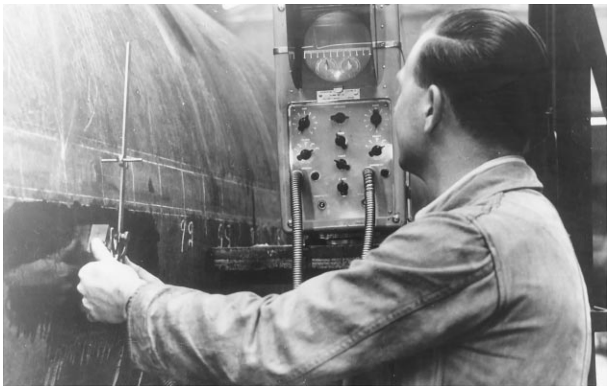


Fig. 2. Mk4 Flaw Detector manufactured by Kelvin Hughes Ltd., London, in use by the late Mr. J. Davis at Babcock and Wilcox Ltd., Renfrew. (From BMUS Collection.)

consider the potential for ultrasound imaging in differentiating cystic and solid masses. The seed was sown and would grow and flourish in his fertile mind following his move to Glasgow. There is nothing in Ian Donald's papers to indicate that there was a sudden or dramatic realisation by him of the potential for ultrasound imaging. This was no conversion such as of Saul on the road to Damascus. Rather, this seems to have been more akin to the seed, planted beneath the surface of the soil, where it germinates and struggles to find the light. Once exposed, it is able to grow and flourish.

Coincidence and circumstance also played their part in the story. In his early days as a professor, Ian Donald performed a hysterectomy on a patient whose husband was a director of the company Babcock and Wilcox, boiler makers in Glasgow, a city whose predominant industries at that time were steel and shipbuilding. After meeting the patient's husband, Donald was invited to Babcock and Wilcox to see their industrial flaw detector (Fig. 2). This was an A-scope, Kelvin Hughes Mk4, and Donald saw in the resulting traces possibilities for clinical application. His enthusiasm and energy must have been infectious, and he was able to return to the factory, the boot of his car filled with pathologic specimens of fibroids and ovarian cysts, recently removed at laparotomy. Babcock and Wilcox provided a piece of meat as a control, and so the first A-scan images of human tissues in Glasgow were obtained. Donald described the results as "*beyond my wildest expectations. I could see boundless possibilities in the years ahead.*"

The factory artist apparently made sketches of the day's events, but sadly there are no visual records remaining of that notable day, 21 July, 1955. Some 40 years later, under the aegis of the Wellcome Unit for the History of Medicine at the University of Glasgow and with the help of the departments of Obstetrics and Gynaecology and Veterinary Anatomy, it was possible to recreate the original experiments and obtain visual recordings of what Ian Donald would have seen. With the advantage of hindsight, it is possible to say that the images did provide convincing evidence of differences in the signals obtained from solid and simple cystic tissues. In truth, interpretation of the A-scan traces from tumors and multilocular cysts was less clear, and a lesser man than Donald might well have gone no further. It is entirely to his credit that he withstood the ridicule of many of his colleagues who failed to see the potential of these early traces. In this respect, Donald is no different from pioneers in many fields who remain unrecognized by their peers in the early days of their research.

Encouraged by the events of the summer of 1955, Donald secured an introduction to Professor Mayneord at the Royal Cancer Hospital, now the Royal Marsden in London. Douglas Gordon, probably the first radiologist to be interested in ultrasound in medicine in Great Britain, seems to have been responsible for the introduction. At the Royal Cancer Hospital, they were attempting to investigate the brain through the intact skull with an ultrasonic metal flaw detector, but they were so discouraged by their results that they abandoned the project. Ian Donald was introduced to the manufacturers, and it was agreed that the Mark 2B "supersonic flaw detector," built by Henry Hughes, should be transferred from London to the Western Infirmary in Glasgow. It is of interest that the firms of Henry Hughes, London, and Lord Kelvin's company (James Thompson, Glasgow) merged to become Kelvin Hughes, and it was they who would provide such valuable assistance in the forthcoming research in Glasgow.

This Mk2b instrument originally was designed for use with a double transducer, but it had been poorly modified to use a single transducer and so had a long "paralysis time," meaning that no echoes were seen within the first 8 cm. Donald did not know that this could be reversed, so instead he tried to overcome the problem by other means. He used a perspex bucket with a flexible latex rubber bottom, which was placed on a thin layer of grease on the patient's abdomen. The bucket was filled with water and then the transducer was lowered into the water. As one can imagine, more often than not the end result was a soaking for everyone! Perhaps, it was thought, using a balloon or condom would be better. The professor was keen to retain his anonymity in obtaining the latter, so at least one visitor was asked, because he would not be recognized, to purchase some condoms, but, not knowing whether they should be plain or teat-ended, the story is told of the visitor who ran out of the shop to ask the professor and, needless to say, Ian Donald's cover was blown.

By chance, in 1956, a young engineer, Tom Brown, who was working at Kelvin Hughes in Glasgow heard about Ian Donald and, with the self-assurance of youth, looked him up in the directory and telephoned him at home that evening. Brown (1988) has said, "*It was the most fateful call I ever made.*" He was invited to see the equipment in action and found the old, battered Mk2b with its modifications. He immediately recognised the problem with the long "paralysis time" and, through his connections at Kelvin Hughes, a Mk4 A-scope, as shown in Fig. 2, was borrowed together with a 35-mm oscilloscope camera. Having the right person in the right place at the right time made all the difference.

The acquisition of this equipment and Tom Brown's continued interest were to make a huge difference to the development of ultrasound imaging. That same year, 1956, John MacVicar joined the team, as a registrar, training in obstetrics and gynaecology, in Professor Donald's unit. MacVicar (1997) has described his colleagues in the following terms: "*Ian Donald had the vision, Tom Brown the expertise, and I was the dogsbody. I was young enough and ambitious enough to see that if I do this work there may be something in it for me.*"

There certainly was "something in it," but that was only achieved by an enormous amount of hard work, involving long hours, often with little to show for it at the end of the day. The hard work paid off for MacVicar who, after his training, became a senior lecturer with Donald and then was appointed as Professor of Obstetrics and Gynaecology at the new medical school in Leicester, England, where he was very supportive of the use of ultrasound although not directly involved himself.

In the early days, Tom Brown would come along to the hospital after his day in the factory to join Ian Donald and John MacVicar after their day in the clinic or operating theatre. The techniques used were clumsy and time consuming and involved fairly primitive photographic methods, necessitating development of film in a portable darkroom. If the film was dropped accidentally, light got in and several hours' work was ruined. No doubt all researchers face setbacks at different times, and when one hears of the difficulties encountered by these three one wonders that they had the energy to continue. The equipment was large, unwieldy, unreliable, and messy, and the end result was pictures that were difficult to interpret and ridiculed by colleagues.

It is unlikely that any one of the team on their own would have continued, but each must have given strength to the other. Donald (1974) has given due credit to both his colleagues in describing Tom Brown as "*the real genius behind the massive technical developments,*" and saying of his registrar, "*had it not been for John MacVicar's determined assistance I might well have wilted from further effort.*"

Wilt they did not and one of the high points recalled by Ian Donald was being asked by his medical colleagues to use the A-scope to examine a very sick woman who was thought, clinically and on x-ray examination, to have carcinoma of the stomach with portal obstruction and gross ascites. Versions of this story vary, but the message from each is the same. The echo pattern produced by the metal flaw detector was consistent with the diagnosis of a large cyst rather than ascites. John MacVicar, with the imprudence of youth, was quick to point out the diagnosis, warranting a subtle kick on the ankle from his professor who, displaying the wisdom of maturity, wanted to avoid direct criticism of his colleagues' judgment. Discussion followed, with each side modestly accepting that they could be wrong. The end result was agreement that the patient should have a laparotomy. Much to the team's relief and to the considerable benefit of the patient, a truly massive mucinous cystadenoma of the ovary was removed.

Diagnostic success with direct patient benefit such as this served to encourage the researchers who, as they progressed, were discovering new information that today we take for granted. They found, to their surprise, that the higher the frequency of ultrasound the less the penetration of the tissues, and, even with the A-scope, they rapidly became aware of the effect of tissue density on reverberation, the beginning of tissue characterization.

All the very early work was on gynecological patients. Prior to laparotomy, an abdominal mass would be imaged and pictures taken. After surgery, the mass would be rescanned in a water bath and the pictures compared, thus correlating the findings pre- and postoperatively. In 1957, the first known studies of the fetus were made—hence, the title of this history. There is no record of the exact day or of the details of the first case. MacVicar and Donald (1963) stated that visualization of the fetus "*had been found more or less by accident when examining a case thought clinically to have uterine enlargement due to fibromyomata.*" The fetal head in later pregnancy lent itself to identification, the strong echoes from the skull producing marked deflections when the A-scope was applied to the mother's abdomen. This initially was utilised to clarify fetal position in cases where this was uncertain, particularly in the obese patient of whom there were many as a result of the high fat and carbohydrate diet of the Glasgow population.

It is interesting at this point to note the climate in which the early work took place. Glasgow as a city had a strong engineering background and a well-respected medical faculty, but one in which obstetrics and gynecology were not noted for their research activity. The climate was right for new developments, and the patients were there to take part. If they were told there was a new machine to be tried out, they were very keen to be involved. There was greater clinical freedom in proceeding with research. There were limiting factors such as money, equipment, laboratory space, and the collaboration of colleagues needed to facilitate research, but these constraints were not specifically ethical restrictions. There was no such thing as a Local Research Ethics Committee (the UK bodies from whom approval for research must now be obtained). The Declaration of Helsinki, the international guidelines governing medical research, was not drawn up until 1964.

Obstetrics and gynecology has been described as a fairly crude specialty, more so in the 1950s than today. There were large cysts, large fibroids, and large wombs making an ideal starting point for using fairly basic equipment. There is no doubt that the traces from the first A-scopes were rather crude, and it soon became evident to the Glasgow team, particularly Tom Brown, that this was a very limited method of investigation. Hence, the decision was made to try two-dimensional (2D) scanning. This change in philosophy mirrored the thoughts and ideas of other pioneers who followed a very similar path.

The contact scanner. Interestingly, Brown was aware of the work of Wild and Reid, but at that time did not know of Howry. If he had, Brown might well have been persuaded to go forward with water bath imaging. He realised, however, that it would have to be a very large tank to overcome reverberation, and this would prove totally impractical as far as elderly and sick patients were concerned. Brown, albeit an engineer, was well aware of the patient's condition, and he could not see any technique being well received that involved disturbing these sick old ladies any more than was absolutely necessary.

And so the contact scanner was developed by Brown (Fig. 3). He describes the project being done on a "*fairly stout shoestring.*" The following is his own account, extracted from his presentation at The Historical Symposium in Washington in 1988. "*It was a case of scrounging for parts wherever I could, and generally I could count on goodwill, or at least tolerance on my raiding expeditions.*

"*To measure where the transducer was in space I chose the simplest system I knew, an X-Y orthogonal measuring frame. This remained the basis of all subsequent scanners from the Glasgow 'stable,' and is in marked contrast to most other machines. It led to high potential 'registration' accuracy with relatively inexpensive measuring elements, and consequently little degradation of resolution by machine inaccuracies. This was at the expense of relatively cumbersome but simple, mechanical mechanisms to support and adjust the position of the measuring frame over the patient with the necessary five degrees of freedom of adjustment. However, we believed we were developing something which*

Fig. 3. Tom Brown with the first contact scanner in the development laboratory at Kelvin Hughes Ltd., Glasgow, 1957. This machine commonly is referred to as the "bed table machine," as a hospital bed table was used to support the scanning mechanism. (From BMUS Collection.)

would ultimately go into X-ray departments, where people were accustomed to that sort of thing, and in any case why should our machines deny their ancestry, and not be a little 'Clyde-built.'

"*However, back in 1957 the best we could do was a borrowed hospital bed-table.* [Authors' comment: This table subsequently was recalled by the administration so that the equipment currently on display in the BMUS collection does not include the original table. "Plus ca change, plus c'est la meme chose."]

"*The ultrasonic pulser and receiver were from the Kelvin Hughes Mark 4 A-scope, which was a double-transducer machine. Later we were to use single-transducer operation with amplifiers designed for the job.*

"*From the outset we were cautious about the possibility of biological effects, and we followed an unvarying policy of controlling the overall sensitivity of the apparatus by reduction of the transmitter output by means of an attenuator, and let the amplifiers run at full, noise-limited sensitivity. The pulse repetition rate was only 50 per second, and though we could have increased this, we did not, for the same reasons.*

"*From the very outset we attempted to provide brightness modulation of the display screen which was a continuous function of echo amplitude. We knew that we were seeing a very large dynamic range of echo signals, and put a great deal of effort into the signal processing system to handle this. We were particularly anxious to preserve little echoes which would otherwise be buried and not seen, in the 'tails' of larger ones.*

"*Because we used photographic integration of the results virtually up to the point when scan converters became available, we always had some degree of 'grey-scale' in our pictures. We avoided the use of bi-stable displays, and when we did use storage displays for monitoring purposes, these were always variable-persistence, 'semi-grey-scale' ones.*"

Brown's comments on the large range of echo amplitudes is an early recognition of the importance of dynamic range and the desirability of a grey-scale display. It has to be acknowledged that the full importance of this only became recognized widely with the work of Kossoff et al. in the 1960s, which is described later.

Patents were filed by Kelvin Hughes in April 1958, naming Tom Brown as the inventor. In keeping with normal practice, commercial rights were assigned to the company.

So the first 2D scanner took shape in 1957, but the initial results were still quite crude. Often weeks would pass without a decent picture, but progress was being made, albeit slowly, and within a year the team were able to demonstrate the fetal head and an intrauterine pregnancy if it was over 12 weeks and the uterus was intra-abdominal. These were still difficult times and support from immediate colleagues was in short supply, but Donald did receive encouragement from his old chief in London, Joe Wrigley (of forceps fame), and from his surgical colleagues in Glasgow, who asked him to demonstrate his equipment to a meeting of the American College of Surgeons who were visiting the city in the summer of 1958.

That same year, 1958, was the watershed when the *Lancet* accepted and published the report by Donald, MacVicar, and Brown entitled "Investigation of abdominal masses by pulsed ultrasound." This article ranks as the most significant in the development of ultrasound in obstetrics and gynaecology. Illustrations showing the fetal head, twins, polyhydramnios, early pregnancy, fibroids, and ovarian cysts were included.

Two new members joined Ian Donald's team in the late 1950s, and each made his own contribution to further developments. Their inclusion in the research group reflected the need for both technical and clinical input. James Willocks, a young obstetrician and gynecologist in training, joined Donald in 1958. He began scanning at the Western Infirmary where the gynecology wards and the ultrasound equipment were situated and only later was an A-scope taken across the city to the Royal Maternity Hospital for use on patients in more advanced pregnancy. The A-scope was on a small trolley that was pushed around the wards—an early portable scanner although it weighed over 30 kg! Willocks' interest in measuring the fetal head stemmed from his knowledge of the problems of obstructed labour, due to a contracted pelvis that resulted from rickets. Obstructed labour was by no means uncommon in Glasgow and, in the late nineteenth century, had led to some of the earliest recorded cases of caesarean section. Willocks' main contribution to ultrasound was in establishing fetal cephalometry for clinical purposes. He was a respected clinician who subsequently became one of Donald's consultant colleagues, pursuing his clinical interests primarily but always very supportive of developments in ultrasound.

The second new member of the team was Tom Duggan, a physicist, who joined in 1959. He later learned from Donald that the source of his salary was a Scottish Hospital Endowment Research Trust grant for neonatal respiratory studies, which had been awarded on the understanding that it would not be used for ultrasound! But Duggan did work in ultrasound, and during 1961–1962 he developed the original fetal cephalometry equipment that was used by Willocks. Duggan then joined Kelvin Hughes, where he was involved with transducer developments, moving on to an academic post at the University of Strathclyde and then to the West of Scotland Health Boards' Department of Clinical Physics and Bioengineering, where he was closely involved with the introduction of the ultrasound teaching and development laboratories and supervised the ultrasound maintenance service.

Much of the work by Willocks and Duggan was with the A-scope, but they also were involved in using the prototype contact B-scanner. This scanner was by no means easy to operate, and Tom Brown, particularly, was uncertain whether apparent inconsistencies in the results were due to equipment variations or caused by the operator. Brown (1988) wrote, "*There was no way in which the Victorian establishment of the Western Infirmary, in the middle fifties, would ever countenance me, a young layman, laying hands directly on patients, especially gynaecological ones. Therefore, if I was going to take control of the examination conditions, I would have to use some other stratagem. This was the real reason for developing the automatic scanner.*"

The automatic scanner (Fig. 4). "*The business end of this machine had a transducer mounted in a 'silver ball' reminiscent of the soap dispensers once common in public lavatories. It would walk its way across the surface of the abdomen, keeping a constant pressure, and rocking back and forwards through an angle of about plus and minus 30 degrees to the perpendicular to the skin, carrying out a thorough and quite consistent compound scan. It even rang a bell when it finished to recall its attendants.*

"*If the patient pulled away from the silver ball, it would of course follow, and this sometimes gave the impression that it was trying to burrow its way through to the couch behind, especially on some of the very fat Glasgow ladies. This machine was in use from 1959 to 1967, working safely and surprisingly reliably, considering its complexity, and with it Donald and his colleagues [Fig. 5] amassed a very substantial bank of clinical data.*"

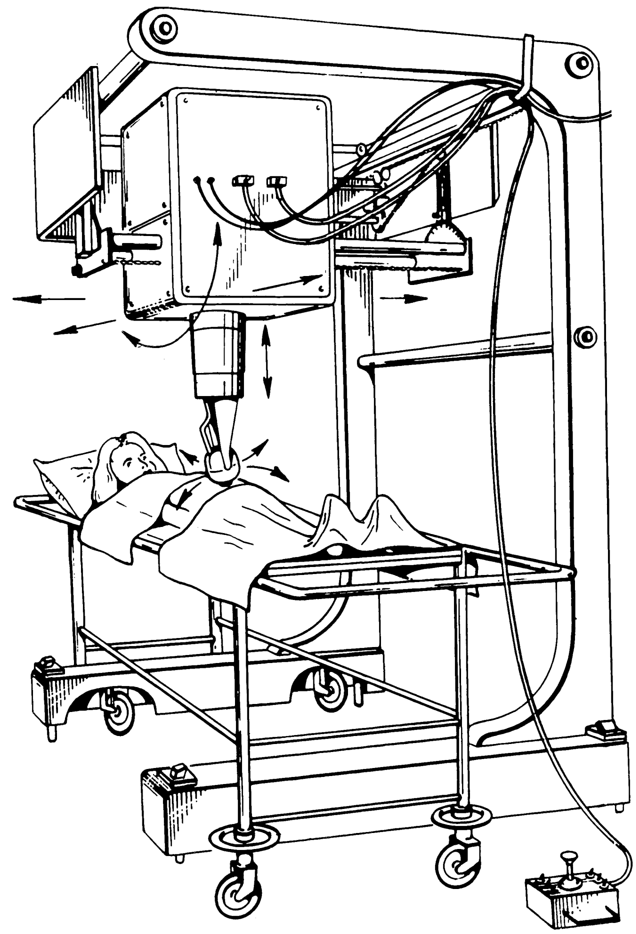


Fig. 4. Drawing of the automatic contact scanner, designed by Tom Brown, and used for many years by Professor Ian Donald and Dr. John MacVicar in the Western Infirmary, Glasgow. (From BMUS Collection.)

Fig. 5. Professor Ian Donald (left) and Dr. John MacVicar in the Western Infirmary, Glasgow, operating the automatic contact scanner, designed by Tom Brown. On his second day as a junior engineer working with Tom Brown at Smiths, J.E.E.F. assisted with the operation of this machine. (From BMUS Collection.)

Funding of the early research work

Tom Brown was an employee of Kelvin Hughes who began cooperation with Ian Donald informally in 1956. It soon became clear that the approval of the company was needed, and Donald wrote to one of the sales personnel he knew through a shared love of sailing. As a result, meetings took place involving the deputy Chairman, Mr. W.T. Slater, and the chief scientist. Mr. Slater is described by Tom Brown as a formidable gentleman, but one who backed his hunches, and he chose to back the development of ultrasound in Glasgow. The chief scientist gave a cautious blessing, and the company provided an initial budget of £500. This turned out to be a very elastic sum of money. Brown gives all credit to Slater for his support. Without it, the project would not have continued. Slater kept it going by whatever means he could, sometimes in near defiance of the rest of the board and the chairman himself. It is doubtful if the early development would have taken place had Slater not been behind it. Who knows? Slater eventually had to inform Donald in 1959 that funding could not continue, because the firm was already out of pocket to the tune of several thousand pounds, and there seemed no likely prospect of a financial return in the immediate future. Donald responded by hastening to see the principal of the University of Glasgow, Sir Hector Hetherington, whom he described as a wonderful and wise old man, and from whom he negotiated a sum of £750 to enable the research to continue. Donald also was advised to see the Advisory Committee of Medical Research and the Scottish Hospital Endowments Research Trust who, to his delight, gave him a grant of £4000 and advised him to approach the National Research Development Corporation in London, from whom an additional £10000 eventually was forthcoming to put the project on a more secure footing. This supported the design and construction of the auto scanner.

Safety aspects. We already have seen reference made by Tom Brown to concern about possible harmful effects of ultrasound and to the prudent use of control of power output and of a low pulse repetition frequency in the contact scanner. Donald and Brown were well aware of the biological effects of ultrasound, which were used therapeutically, and they also were aware of the association between maternal exposure to x-rays during pregnancy and subsequent childhood cancer (Stewart et al. 1956). Before he began his research on patients, Donald asked Dr. Bacsich of the Department of Anatomy at the University of Glasgow to suggest an animal experiment that would establish the safety of the techniques he was proposing. Bacsich suggested that kittens' brains would provide suitably sensitive experimental tissue, as the myelination of the optic tracts had not taken place and that any susceptibility to damage was greater. The experiment consisted of anaesthetizing four newly born kittens. Two were exposed to ultrasound continuously for 1 h and two acted as controls. At 8 to 10 h later, all four were returned to their mothers. At 24 h and 21 d, one test and one control kitten were killed and their brains sectioned. No abnormalities were found. The results of this experiment, reported by Donald et al. (1958) in their *Lancet* article, together with a review of the existing literature on biological effects of ultrasound, led Donald and his team to conclude that, at the diagnostic levels they were proposing to use, there was no evidence of harmful effects of ultrasound. All three initial members of the Glasgow team and those who joined them later allowed themselves to be scanned during the course of their research.

Summary of the 1950s in Glasgow

The 1950s had seen the birth of obstetric scanning and as, with any infant, there had been many ups and downs, but by the end of the decade there was no doubt that the Glasgow team had reason to be optimistic about the future. The cynics remained, but time would prove them wrong. Highlights of the events that occurred in the 1950s in Glasgow are listed in Table 1.

Developments in Japan, Australia, and the United States in the 1950s

The preceding sections have been devoted entirely to the early developments in obstetric ultrasound in Glas-

Table 1. Highlights of the 1950s in Glasgow

Year	Event
1955	The first A-scans of fibroids and cysts using metal flaw detectors.
1957	The first two-dimensional contact scanner designed by Tom Brown.
1957	The first images of the fetus.
1958	Publication of "Investigation of abdominal masses by pulsed ultrasound" by Donald MacVicar, and Brown in the *Lancet*.

gow. The reader should not infer that Glasgow was the only center. Research was progressing in several other centers but, partly because methods of communication were more primitive in the 1950s, publications were far fewer and travel between centers was far less easy. Each group of workers tended to pursue their own path from their own standpoint. We use the word "group" deliberately, because we are not aware of any individual developing clinical applications of ultrasound imaging on his own. Each group consisted of a combination of medical and nonmedical personnel. It is interesting to record the reasons behind the initial involvement in obstetric scanning of each group and the different approaches adopted.

Japan. In Japan, in the 1950s, early developments in ultrasound imaging proceeded along remarkably similar, albeit independent, lines to those in the West. Most of the early work was published in Japanese journals, restricting the availability to researchers in the rest of the world. Similarly, journals in English were not readily available to the Japanese. Hence, each group tended to work in relative isolation. There were exceptions and a limited amount of interchange took place. One amusing incident apparently occurred in 1956, when this headline was attributed to Professor Firestone: "Dr. Wagai thumbs ride to ICA Congress from Japan." This was a reference to the way the young surgeon, Dr. Wagai, had managed to negotiate his travel to the International Congress of Acoustics held in Boston in 1956—"*a rare and precious opportunity for a young and ambitious investigator*" (Fukuda 1986).

Toshio Wagai was working as a clinical resident in 1951; his chief was Professor Kenji Tanaka. Wagai had a friend in a shipbuilding firm where ultrasound was used for detection of flaws in metals—a familiar story? And so, in another country, a very similar sequence of events was about to take place. Tanaka and Wagai were introduced to Rokuro Uchida, then an engineer with the Nihon Musen Company, later president of Aloka. He adapted an early A-scope metal flaw detector and then began the group's clinical applications of ultrasound, together with several studies on biological effects. A comment made by one of the later workers (Fukuda 1986) reflects once more the scepticism of colleagues, "*In spite of their very active pioneering works, genuine ignorance governed the medical profession in these early days and the pioneers in ultrasound had to struggle against ignorance and indifference expressed by the medical authorities.*"

In 1959, the Japanese researchers, Wagai, Yamanoi, and Yoshimito, published their article, "Application of ultrasonic diagnostic methods in obstetrics and gynaecology," in *Journal of the Japanese Obstetric and Gynaecological Society* (Wagai et al. 1959). This was to be the first of many publications in this specialty emanating from Japan.

Australia. In Australia, the Commonwealth (later National) Acoustic Laboratories were established in 1948 by the Australian Department of Health, and the first investigations into ultrasound were undertaken in the early 1950s. An Ultrasonic Committee was set up in 1955. In May 1958, it recommended that the field of medical ultrasound had developed sufficiently to justify the appointment of a full-time research physicist, so George Kossoff was appointed in 1959. His remit was threefold (Kossoff 1975). These were, first, to conduct research into medical ultrasound; second, to provide a centre of technical expertise in the field; and third, to set up joint research programs with suitable organizations for the clinical evaluation of newly developed techniques. It does seem, in retrospect at least, that the Australian Department of Health was much more organised than any other in addressing the issues of ultrasound in medicine.

The first joint clinical program began in September 1959 with Professor B. T. Mayes of the Department of Obstetrics in the University of Sydney. Dr. W. J. Garrett was appointed medical consultant to the project and there began one of the great partnerships, Garrett and Kossoff, in obstetric scanning. David Robinson was to join them in 1961 and David Carpenter in 1968. Together they made a major contribution to the development of ultrasound imaging, which is described in the section on the 1960s.

United States of America. In the US, several groups of investigators were developing ultrasound during the 1950s. These included the Fry brothers and Elizabeth Kelly Fry in Illinois; George Ludwig, Theodor Hueter, Richard Bolt, and Henry Ballantine in Boston at the Massachusetts Institute of Technology; John Wild and John Reid in Minnesota; and Douglas Howry and Joseph Holmes in Denver. These pioneers are all recognized as having made, each in their own way, an enormous contribution to the development of ultrasound imaging. The clinical applications varied, but it was the 1960s before the first publications from the Denver group describing ultrasound imaging in obstetrics and gynaecology (Taylor et al. 1964; Thompson et al. 1965).

Summary of the 1950s

And so by the end of the 1950s the concept of obstetric scanning had been established in just a few centres. Delivery of the new technique followed a lengthy and somewhat troublesome gestation, but it was succeeded by a new generation of equipment and manpower. In the decades to follow, we witnessed a veritable explosion of technological development and clinical application.

THE 1960s: OBSTETRIC ULTRASOUND'S CHILDHOOD

Continuing the Glasgow story

The 1960s were a time of great activity in Glasgow, both on the engineering side and in the clinical applications. The automatic scanner was in use and, in 1960, was shown at a medical electronics exhibition in Olympia, London. The breadth of application of ultrasound imaging in obstetrics was widening. The first cases of placenta praevia were recognised and fetal cephalometry was being developed. Both of these were to have considerable impact on patient welfare.

The first visitor from overseas, or, as Ian Donald called him, "*our first disciple from abroad,*" came to Glasgow to spend a month learning the art of ultrasound imaging. He was Dr. Bertil Sunden (Fig. 6), an obstetrician from Lund, a more than able student. His story and the development of obstetric scanning in Sweden are told later. Sunden purchased a scanner from Kelvin Hughes, their first sale of an ultrasound machine for medicine. This was a most significant event. Soon after this, the firm's resources were improved further by a merger with the much larger Smiths Industries from England and became known as Smiths Industrial Division. This made expansion of the ultrasound project possible, and in 1963 John Fleming and Angus Hall, both electronics engineers, joined Tom Brown. Fleming has remained since then; Hall left in 1980 to become head of the Department of Medical Physics at St. James' Hospital in Leeds. Both Fleming and Hall were very involved in the technical developments of the ultrasound equipment, especially the measurement facilities. But their first task was to work with Brown on the development of a machine for production. Orders were received for 12 of these Diasonographs, which went to places as far apart as Aberdeen and Baghdad. Importantly, the Ministry of Health placed an order for four machines for research in the clinical application of ultrasound in centres in Great Britain.

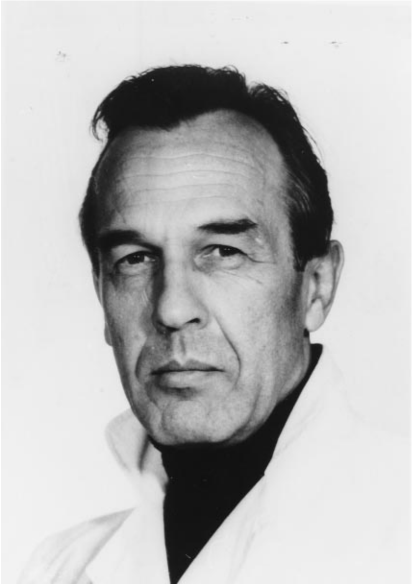


Fig. 6. Dr. Bertil Sunden, Lund, Sweden, whose thesis "On the diagnostic value of ultrasound in obstetrics and gynecology" was published in 1964. (Courtesy of Dr. Bertil Sunden.)

An example of the clinical application of ultrasound with immediate benefit for the patient was its use in determining the lie of the fetus. It had become accepted practice for a particular young midwife, Miss Marjory Marr, to scan, using the A-scope, everyone in whom the presentation was uncertain prior to the Professor's weekly grand round at the Royal Maternity Hospital. Her enthusiasm and abilities were rewarded in due course by her appointment as matron of Ian Donald's new maternity hospital, The Queen Mother's Hospital (Fig. 7). This was opened in 1964 and was probably the first maternity unit to have a scan department, although the initial plans for the hospital apparently did not specify a separate area, ultrasound being referred to as a research activity. The development of ultrasound was such, however, that by the time of the official opening by Her Majesty Queen Elizabeth the Queen Mother on 23 September 1964, the diagnostic department on the ground floor included radiology, clinical photography with dark room facilities, and the sonar department for ultrasonic diagnosis. The clinical report of 1964–1965 refers to the apparatus being in use from the summer of 1964. We should note here that Ian Donald always preferred the term sonar to ultrasound, but common usage has determined that ultrasound be the chosen name.

Into the new hospital came new blood. First, Dr. Usama Abdulla arrived from Baghdad as a research assistant, and he concentrated on using ultrasound for

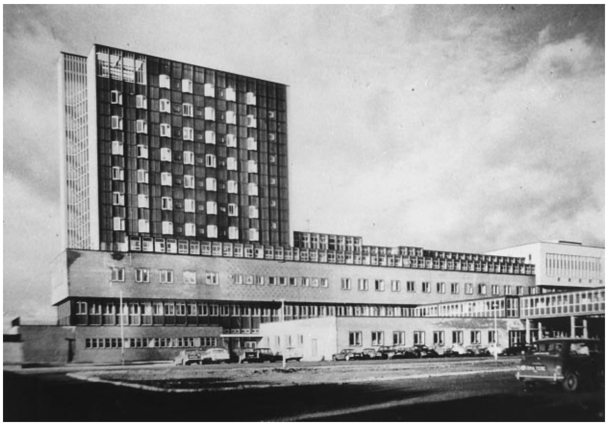


Fig. 7. The Queen Mother's Hospital in 1965. The first patients were admitted 11 January 1964, and the hospital was officially opened by Her Majesty The Queen Mother on 23 September 1964. (From BMUS Collection.)

Fig. 8. Dr. (later Professor) Stuart Campbell, scanning using an NE4102 at Queen Charlotte's Hospital, London. (Courtesy of Professor Stuart Campbell.)

placental localisation. His early experiences in Glasgow clearly had a major influence on him, and he has remained in Great Britain as a consultant obstetrician and gynaecologist, furthering his ultrasound interests mainly in the area of infertility. Stuart Campbell joined Donald in 1964. Little did he know that he would become one of the best known and most respected scanners of the next generation. At that time, Campbell, a junior doctor, was, in his own words (Campbell 1997) "*in awe of Donald because he was a towering figure, always amusing, giving you a challenge just to keep you on edge*." Campbell (Fig. 8) began to scan first with the A-scope measuring biparietal diameter (BPD), then with the B-scan looking at early pregnancies, and, with Abdulla, looking at the placenta. Campbell then combined A- and B-scan, making significant advances in BPD measurement. He liked to stand to scan, because that way he could move the transducer more quickly than if he had been sitting. Therefore he could "catch" the mid-line echo of the fetal head on the longitudinal scan and swing the gantry round to the transverse before the fetus changed position. Campbell moved to London in 1967, and it was there he made his major contributions to diagnostic imaging. These will be described in the clinical section.

Ian Donald visited the US in 1961, on the first of several lecture tours he was to make over the next few years. During these lecture tours, he made many new friends, particularly in Denver, where Dr. Holmes and his group were making early advances into obstetric scanning. The contribution of the Denver group and the other American centers is described later.

In 1963, quite by chance, Ian Donald had a stroke of luck. He noticed that, if the patient had a really full bladder, it was possible to get a good view of the uterus, even though it was confined to the pelvis. Hitherto, it had only been possible to study the pelvic organs if they were sufficiently enlarged to be intra-abdominal and approached directly through the abdominal wall. The full bladder displaced the intestines out of the way and provided a built-in "water tank" through which the uterus was visible. With great excitement, the team observed an early pregnancy of 6–7 weeks' gestation in a patient with a history of recurrent abortion.

In Donald's own words, "*1964 was indeed a good year*." The potential application of ultrasound in obstetrics was really expanding: pregnancy could be identified from the early stages (Fig. 9), multiple pregnancy could be recognized, blighted ovum diagnosed, fetal growth monitored, and the placental site determined. The list was growing by leaps and bounds.

The team were optimistic. Progress was being made. Ultrasound gradually was gaining recognition. Donald was seeing the realization of his vision, but his dream was to be shattered when, as Donald (1974) described, "*For commercial reasons Smiths Industries decided to pull out of Scotland, not because I was ruining them, in fact they were now beginning to sell ultrasonic machines under the trade name of Diasonograph, but because the Glasgow factory as a whole was not paying its way. Sonar as a subject, at least in this country, seemed finished and it looked as though America would inherit the lot, and we ourselves would be faced with the dust-sheet.*" Ian Donald must have been very much aware of a similar situation in other areas of development where original ideas had been born in Great Britain, but their later development, and most of the plaudits, took place in America. An example would be the jet engine.

Disaster was, however, averted in Glasgow and could be said to have been a blessing in disguise, as the principal of the university instructed Ian Donald to set up, in 1967, the Department of Ultrasonic Technology at

Fig. 9. Mid-line longitudinal static scan of early pregnancy from the automatic contact scanner in the Western Infirmary, Glasgow, 1964. Transducer was 2.5 MHz. (From BMUS Collection.)

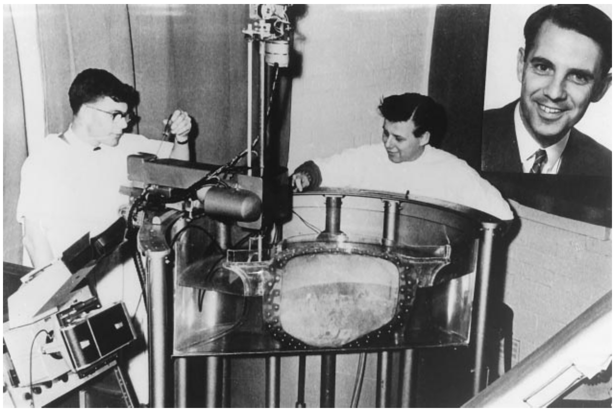


Fig. 10. David Robinson (left), George Kossoff, and Bill Garrett (inset) with the original water path scanner developed in Australia, 1962. (Courtesy of Dr. G. Kossoff.)

The Queen Mother's Hospital. Two of Smiths' key electronics engineers, John Fleming and Angus Hall, who had been involved with the project for some time, moved to the new department. Nuclear Enterprises (NE) in Edinburgh took over the manufacture of medical ultrasonic equipment from Smiths, with Brian Fraser who had been in charge of all ultrasound development at Smiths. He was later joined by Tom Brown, who had spent some time in another area of medical electronics. Thus, continuity of development was maintained at NE. Brown remained there for several years before moving on to undertake research into three-dimensional (3D) scanning systems at the University of Edinburgh. He then moved to Sonicaid Ltd., where he led the team that developed, in 1972, the first commercial 3D scanner.

In the late 1960s, the future of ultrasound technology in Scotland seemed assured. Meanwhile, developments were proceeding apace throughout the world.

Australia—Kossoff, Garrett, and Robinson

George Kossoff and Bill Garrett came together in 1959 as already described. They were concerned by the report by Alice Stewart and her colleagues (Stewart et al. 1956) suggesting an association between childhood leukaemia and x-ray examination in pregnancy. As there was no evidence of any adverse effects of diagnostic ultrasound, they set about designing ultrasonic equipment specifically for the examination of the pregnant uterus. Their primary aim was placental localization. Garrett (1988) described the early days thus. "*Starting in the antenatal clinic with a tape measure and in the laboratory with a plaster anatomical model of the pregnant uterus, we built first an A-mode probe to determine the type of echo information which would be available, and secondly, with the assistance of David Robinson, a B-mode water-path system*" (Fig. 10).

An amusing incident is described from the early days. "*The first echoscope with its vacuum tubes glowing a gentle orange, had a latex rubber membrane against which the patient, while standing, held her abdomen. On one occasion, the rubber membrane burst. Fifty gallons of water hit the floor. David Robinson and I jumped up on chairs to avoid the wild electricity, and the patient said that she thought her membranes had ruptured!*"

"*The B-mode system followed the principles established by Howry and Bliss (1952) but differed from them by the development of a weakly focused transducer to achieve a narrow beam width. Each parameter of the system was optimised for the pregnant uterus [(Kossoff 1963; Kossoff et al.1964, 1965a, 1965b)] and as a result we were able to obtain good quality pictures and outline fetal anatomy with a considerable degree of confidence. It seems strange to say that the fetal spine was not demonstrated echographically until 1962 and then it was only as a white blob on a black background. Nevertheless it was a blob which allowed the fetal head to be distinguished from the fetal trunk and prevent a 'biparietal diameter' being measured from the fetal abdomen in a case of anencephaly.*

"*A refinement of this machine gave clearer detail*

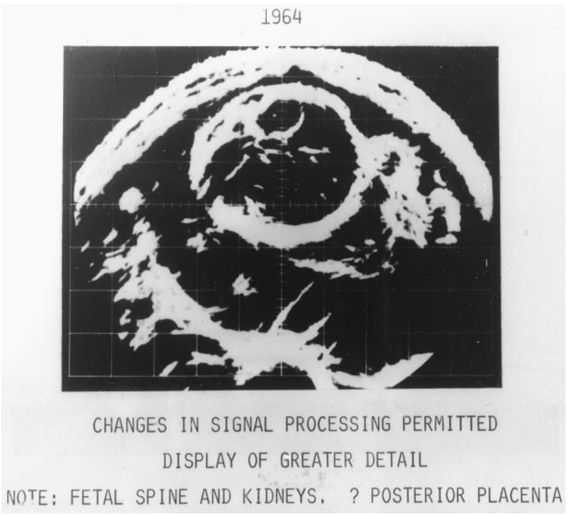


Fig. 11. Cross-section of fetal abdomen showing spine and kidneys, 1964. (Courtesy of Dr. G. Kossoff.)

and by 1964 something resembling a modern echogram was obtained. The spine [(Fig. 11)] was no longer a blob but was now clearly seen in cross-section complete with its paravertebral muscles. The lessons learnt in the construction and application of this early equipment were then applied. A new machine with a wide aperture transducer was built allowing fetal anatomy to be easily displayed. The fetal kidneys and bladder became regular landmarks and other organs became obvious one by one [(Garrett et al. 1966; Robinson et al. 1967, 1968).]

"*The quality of these early echograms was attributed in some quarters to the use of a water-delay system but this was not so. The essential ingredient was George Kossoff's transducer design and signal processing. To confirm this point, David Robinson built a contact system with an articulated arm which, apart from difficulty in the near field, closely approximated the water-delay system in resolution.*

"*The old machine then became rickety, and a new one was on the way in 1968 when the original machine literally blew up, and went to the scrap heap. The new echoscope did a much smoother job altogether. In 1969, under George Kossoff's aegis, its bi-stable system was changed to film echoscopy, or grey scale as we now know it.*"

Grey scale. Up until this time, the bi-stable system was in use. Garrett described the limitations of that system and the change to grey scale thus, "*Two-dimensional echograms in black and white were built up on a persistence screen before being photographed, the so-called bi-stable system. Only high level echoes were recorded and the system was suited to displaying outlines of major tissue interfaces but gave little information as to the parenchyma of an organ. It was known from A-mode studies that there was much information contained in the low level echoes which was then being lost, [(Kossoff et al. 1976)]. To retrieve this information, it was necessary to record the small echoes, and for this George Kossoff suggested direct film recording from a standard oscilloscope.*

"*Our echoscopes were converted to grey scale in November 1969. Such grey scale was easily applied to mechanical scanners with a water delay system but required considerable skill on the part of sonographers where a contact transducer and articulated arm were used. The open shutter technique also had the disadvantage that the picture could not be seen until one minute after it was taken and retakes were often necessary. This phase was however short lived as scan converters became available and greatly simplified the procedure. It is important to remember that with the introduction of the scan converter a slight degradation of the picture quality followed and that this difficulty was compounded by a further loss of clarity with the change from analogue to digital systems.*"

The resulting images of fetal anatomy were truly remarkable and a clear demonstration of the importance of grey scale (Fig. 12). In time, everyone would change over to this technique, abandoning the storage tubes, both the bi-stable that showed only black and white, and the variable persistence ones (used by Brown) that produced only a few shades of grey.

The Australian group deserves due credit for all their early work in constructing purpose built equipment for obstetric use and developing it as they did. There is no doubt that the picture quality of the images they obtained was far superior to those produced by the converted metal flaw detectors. In a letter to Kossoff, Donald wrote, with just a hint of envy, "*I fairly drooled over some of your pictures. My congratulations.*" Donald's machine had proved itself indispensable in getting scanning off the ground, but the way ahead was to have purpose built equipment.

Highlights of the events that occurred in the 1960s in Australia are listed in Table 2.

United States of America

Denver. Dr. Joseph Holmes rightly was given the accolade of "father of ultrasound" in the US, and the following paragraphs are taken in part from a description by him of the early work in Denver (Holmes 1981). He wrote, "*The construction of a contact-compound scanner was finished in early 1962. The transducer moved in a mechanical sector scan, 30 degrees to each side of the perpendicular, while the transducer carriage was moved over the pregnant abdomen. Mineral oil was used to*

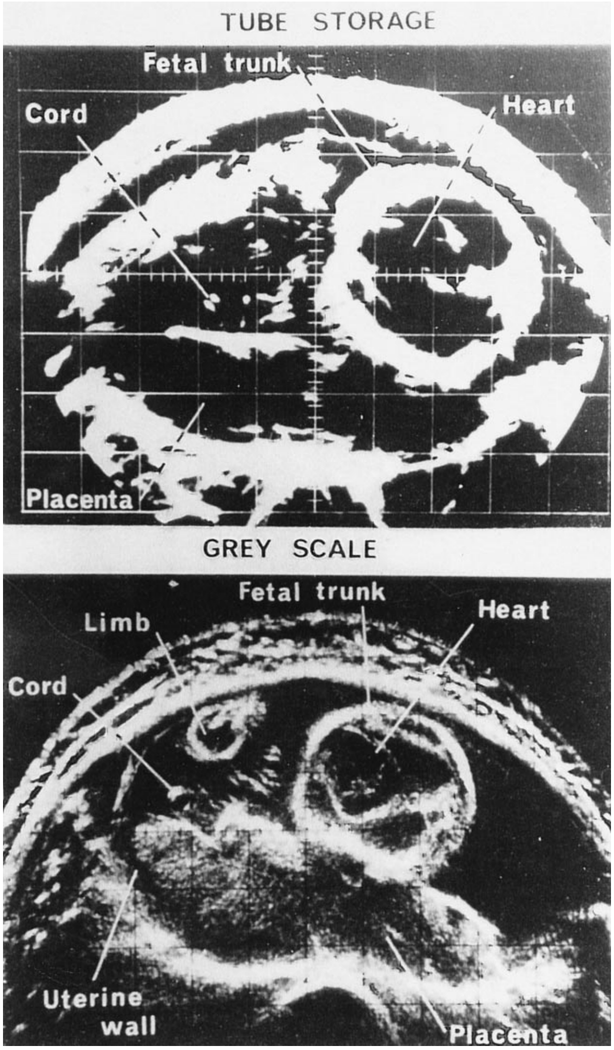


Fig. 12. The improvement obtained with grey scale is shown clearly in these images, 1969. (Courtesy of Dr. G. Kossoff.)

achieve ultrasonic coupling. During the construction of this scanner, Douglass Howry, Ed Meyer, Bill Wright, Jerry Posakony and I all held frequent conferences to discuss and design this equipment. The new scanner was immediately effective for examination of pregnant patients and diagnosis of obstetric problems and, by chance, the right person was in the right place at the right time to take forward the clinical applications."

Dr. Horace Thompson had studied medicine in Denver, graduating in 1948, the year after Douglass Howry. Thompson moved away from Denver to pursue his training in obstetrics and gynecology but returned there about 1957. He recalls that he had read and heard about the early uses of ultrasound and, on his return to Denver, its use was being discussed at a Journal Club meeting. Thompson became quite fascinated and wrote Ian Donald for additional information before becoming aware that equipment was available right in town! He then contacted his friend, Dr. Taylor, the head of the Department of Obstetrics and Gynecology at the university, and that was the beginning of Thompson's long involvement with obstetric scanning.

Table 2. Highlights of the 1960s in Australia.

Year	Event
1962 (June)	Acquired the first obstetric echogram.
1962 (September)	Clearly distinguished the fetal spine.
1966	First international publication, "Ultrasonic echoscopic examination in late pregnancy" by Garrett, Kossoff, and Robinson.
1968	First description of the fetal heart and other fetal anatomical details in "Fetal anatomy displayed by ultrasound" by Robinson, Garrett, and Kossoff.
1969	Grey scale introduced.

Dr. Kenneth Gottesfeld began his residency training programme in obstetrics and gynecology at the University of Colorado in 1963 at the time when Drs. Holmes and Taylor were seeking an enthusiastic young person to join Dr. Thompson in the early application of ultrasound imaging in obstetrics. Dr. Gottesfeld proved an excellent choice, and he and Dr. Thompson together became experts in the field of ultrasound imaging in obstetrics.

On being asked about the relationship between the Denver group and Ian Donald, Thompson is reported as saying that "*Donald was probably ahead of us by two or three years but our work was complementary and we were in touch from the time I started. I visited with him, he visited with us, we compared notes. Yes there was competition but it was a friendly competition because there were never any harsh feelings regarding what we were doing.*"

Holmes continued, "*Thompson and Gottesfeld concentrated on the diagnostic use of our ultrasonic equipment in obstetrics and gynecology. As designed originally, this equipment was particularly effective in demonstrating the echo pattern of the placenta which had not been previously described. The two were also interested in the rate of fetal growth, diagnosing hydatidiform mole and determining fetal death.*

"*The initial contact scanner was remodified and reconstructed in 1964 and it continued as a very effective diagnostic scanner until 1967/68. Wright and Meyer left the University of Colorado and formed a small company called Physionics Instruments where they constructed the Porta-Arm scanner whose principles were incorporated into most scanners over the next 10 years. At first this scanner did not give as good pictures as the mechanical scanner but later after installation of improved electronics, it proved to be very effective although much* *depended on the understanding and skill of the operator. The clinical programme in Denver expanded rapidly thereafter.*"

Before this move into obstetric scanning, there had been a number of visitors to the Denver laboratory to see the early applications of diagnostic scanning in general. One of these visitors was the Australian, Dr. Murray, who was responsible for the appointment of George Kossoff. In 1961, Kossoff himself visited Denver and was impressed by the pictures obtained with the water bath system. His own subsequent contribution has been described already.

There were many other foreign visitors to Denver, in part due to the exciting developments taking place there and, no doubt, as the result of improved travel facilities. The huge increase in transatlantic air traffic began in the 1960s, making overseas trips from Europe much easier. Communication systems also were improving, and this had an impact on scientific development as well as on both social and political life.

In 1965, Joe Holmes was the prime mover in applying for funding to host an international symposium on diagnostic ultrasound, which was to take place in Pittsburgh that year. Papers were given by many of the early pioneers in obstetrics, including Donald from Great Britain, Kossoff, Garrett, and Robinson from Australia, and Mizuno, Takeuchi, and Nakano from Japan, in addition to the American workers Thomson, Gottesfeld, von Micsky, Evans, Stauffer Lehman, Brady, Smyth, and Hart (Grossman et al. 1966). A Diasonograph, weighing over 1 ton, was airfreighted in pieces to the US and reassembled there by Fleming for use in demonstrations by Donald. Dr. Horace Thompson later said of that meeting, "*I think in terms of the American history of ultrasound, it was the turning point. That was the meeting that really put us on the map here.*" Prior to this meeting, there was a great deal of scepticism, but thereafter there was a gradual acceptance of the technique.

The following year, the first postgraduate course in diagnostic ultrasound was held at the University of Colorado Medical Center. Also that year, approval was obtained from Blue Cross and Blue Shield for the acceptance of charges for ultrasonic diagnostic studies. Other insurance companies were to follow their lead. This was an important change in policy for these companies and was evidence of the recognition of ultrasound as an imaging modality.

The emphasis in Denver, as in the other pioneering centers, was on the equipment because this was the key to progress. The technology had to be in place before clinical applications could be made—another example of the productive interaction among engineering, physics, and medicine.

Table 3. Highlights of the 1960s in Denver.

Year	Event
1962	Contact scanner used in obstetrics.
1964	Physionic Porta-Arm scanner introduced.
1964	Publication of "Ultrasound diagnostic techniques in obstetrics and gynecology" by Taylor, Holmes, Thompson, and Gottesfeld.
1966	Blue Cross/Blue Shield accepted charges for ultrasound studies.
1966	Publications of "Ultrasound placentography: A new method for placental localization" by Gottesfeld, Thompson, Holmes, and Taylor.

Highlights of the events that occurred in the 1960s in Denver are listed in Table 3.

New York. Lajos von Micsky was Hungarian by birth. After his medical training in his native country, he worked in Puerto Rico for some time. Thereafter, he completed his residencies in obstetrics and gynecology in the US and became an attending physician at St. Lukes Hospital, where he began working with ultrasound in 1964. His first publication came in 1965 (von Micsky 1965), the same year as the Pittsburgh meeting in which he took an active part. He recognized the technical progress made in the pioneering centers, and he implemented the techniques in his clinical practice and contributed to further developments. This was the beginning of the spread of ultrasound imaging throughout the country from the original centers. von Micsky collaborated with Uphoff on the construction of a compound water bath scanner and an intracavitary scanner (for bladder and rectum) that, sadly, was not tested clinically at the time of his early death and was never marketed.

Another person who was influenced by the pioneers was Lou Hellman, who was working at the Downstate Medical Center in Brooklyn. Donald visited there in 1964. The next year Hellman went to Glasgow to spend a few weeks with Donald, learning how to use the ultrasound equipment. Hellman was so impressed with the diagnostic potential of ultrasound in obstetrics and gynaecology that he organized the setting up of his own department in Brooklyn. Initially, he tried to use a Diasonograph, but it never worked properly, so he changed to the Physionics Porta-Arm scanner. Hellman and Donald remained friends and collaborated on several projects, notably safety aspects, on which they published jointly (Hellman et al. 1970). One of Hellman's fellows in training was Dr. Kobayashi from Japan, who proved himself a "*superb phonocardiographer*." Together they are probably best remembered for their "*Atlas on Ultrasound in Obstetrics and Gynecology*" (Kobayashi et al. 1972). This was one of the earliest textbooks on ultrasound imaging in the specialty.

Yale, New Haven. An interesting anecdote is the story of Ernest Kohorn's early involvement in ultrasound. His first interest was in oncology and, after studying in London (he was British), he planned to pursue his training at Yale. Both his mentors, Professor Nixon in London and Professor Buxton in Yale, realised the potential for ultrasound and arranged and encouraged young Kohorn to visit Donald in Glasgow for a period of training in scanning before traveling to the US. At Yale, in 1965, he found that the only machine was an A-scope, which he made use of during the next year prior to his return to London. There he found one of the Diasonographs that had been acquired for testing through the Ministry of Health. Kohorn wrote to Holmes, "*Nothing could have suited me better, and we set about to do a great amount of clinical work.*" Stuart Campbell moved from Glasgow to London in 1967, and he and Kohorn collaborated for a little while (Campbell and Kohorn 1968; Kohorn et al. 1969) before Kohorn returned to Yale, where he continued his involvement in ultrasound before moving wholly into his main interest of oncology. John Hobbins would take over the ultrasound department at Yale in due course, and the major clinical contributions from there will be described later.

Sweden, Dr. Bertil Sunden

Research had started at the University of Lund on the use of ultrasound as a diagnostic tool in cardiology and neurology in the 1950s. Talk over the lunch table stimulated the Professor of Obstetrics and Gynaecology to consider the potential use of this echo method in obstetrics. As a result, he encouraged his younger colleague, Bertil Sunden (Fig. 6), to investigate a number of pregnancies with the Krautkramer echoscope, which was being used successfully by Leksell in neurology to diagnose mid-line shift. This instrument was an A-scope and provided limited information. It was only after reading the article by Donald et al. in the *Lancet* in 1958 that further interest was stimulated. Bertil Sunden was sent by his professor to Glasgow to learn from Ian Donald. As a result of this visit, application was made to the Swedish Medical Research Council for funds for similar equipment that was to be built by Smiths Industrial Division and delivered to Lund in the autumn of 1961. This machine (Fig. 13) was the first ever produced in response to a commercial order rather than as part of a research project. Although based on the experience gained developing the auto scanner, Sunden's machine was manually operated. Building the auto scanner had been a very worthwhile exercise, but its complexity and need for frequent maintenance militated against building another, particularly when the new machine was to be used so far away from the factory. This was probably the first example of the realisation of potential difficulties with maintenance influencing the choice of equipment. The influence of the industrial designer, Dugald Cameron (now Professor and Principal of Glasgow School of Art), led to the ergonomic design and overall appearance of the Swedish machine being a great advance on its predecessors. The cost of all these improvements meant, apparently, that no profit was made on the sale, the machine being sold for £2500.

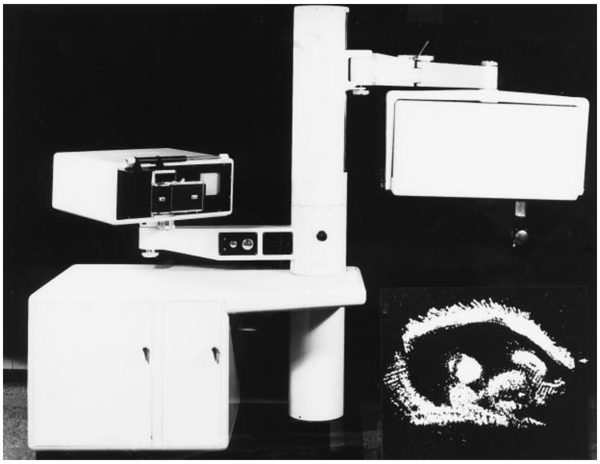


Fig. 13. The scanner built by Kelvin Hughes, Glasgow, for Dr. B. Sunden. At lower right is an image of an anencephalic fetus at 31 weeks' gestation. (Courtesy of Dr. B. Sunden.)

Sunden began his studies, investigating the usefulness of ultrasound in more than 400 patients (Figs. 13 and 14) and, most importantly, making extensive studies of possible harmful effects of ultrasound on the gonads of male and female rats and on the fetuses of pregnant rats, with observations in the first and second generations of their offspring. No adverse effects were recorded. Sunden's results were published in his thesis in 1964. Ian Donald was invited to be the examiner for this thesis—an event that took place in public, in the English language, although in Sweden, in full morning dress, and lasted several hours—an ordeal for both the examiner and the examinee.

It is interesting to note the following comments made by Edler and Hertz (1977), the cardiologist and physicist from Lund, who were the pioneers in the development of ultrasound in Sweden. "*We think that facts peculiar to Sweden and Lund during the 1950s played an important role. First of all the attitude of the government and the general public towards the advancement of science generally and medical science in particular was very positive during those years. Also it was recognized by many members of the medical faculty that a closer cooperation between physicians and physicists might be very rewarding. Lund was small enough that doctors of all medical specialties met daily, were well informed*

Fig. 14. Longitudinal scan of a breech presentation, head to the left, at 36 weeks' gestation, obtained using a 2.5-MHz probe. (Courtesy of Dr. B. Sunden.)

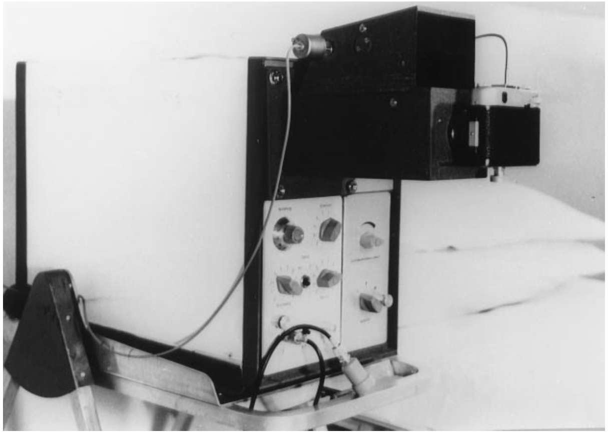


Fig. 15. Kretz 4200 A-scan for obstetrical and gynecological use. An instrument of this type was used by Dr. A. Kratochwil, 1966. (From AIUM Archives, courtesy of Professor B. B. Goldberg.)

about each other's research, and collaborated closely. Scientific work progressed freely, unencumbered by bureaucracy and so-called planning of scientific research in the interest of society."

Austria, Dr. A. Kratochwil

In 1964, Alfred Kratochwil, a young obstetrician and gynacologist, was preoccupied with the question of how to localise the placenta most accurately while avoiding the hazards of radiation. By chance, he attended a lecture by a neurosurgeon on the diagnosis of cerebral bleeding with ultrasound at the Society of Doctors in Vienna. He realised that this method could be applied to placental localisation. The very next day, the wife of one of his neurosurgical friends was admitted in labour and, while awaiting the arrival of the baby, the two doctors discussed the lecture and where one could obtain the necessary equipment. Kratochwil learned of a local ophthalmologist who had started scanning the eye using an A-scope from Kretztechnik in Upper Austria. Immediately Paul Kretz, the owner and founder, was contacted and persuaded to provide an instrument (Fig. 15), complete with the user's manual indicating how to detect inclusions in cast steel and how to check the quality of welds.

So began the clinical applications in Austria. This is a familiar story of metal flaw detectors being adapted for clinical practice and concern about the safety of x-rays for placental localization leading different workers to look for an alternative method.

Kratochwil began using the A-scope to look at the placenta in a water bath after delivery to see what might be the expected appearance *in utero.* Then, all patients to be delivered by caesarean section were scanned before surgery. The position of the placenta was noted at operation and the findings correlated. With great joy, he was able to observe that his findings were 90% correct (Kratochwil 1966). Prior to this, colleagues had thought of him more as an astrologer. Here is another example of the ridicule that early workers had to endure.

Following the placental studies (Kratochwil and Rachmat 1969), work proceeded on measurement of the BPD and on identifying fetal heart pulsation. It would appear that the full bladder technique had not been recognised, and the vaginal approach (Figs. 16 and 17) was chosen to visualize the uterus in the early weeks of pregnancy. The Kretz company designed special transducers just for this purpose. This was still an A-scope, but it enabled Kratochwil's group to identify fetal heart

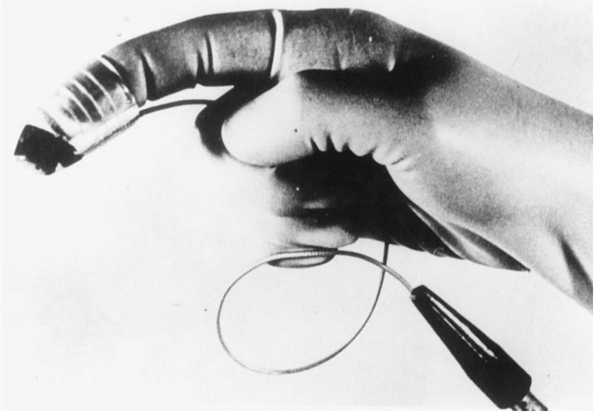


Fig. 16. Thimble-like transducer for combination sonography and bimanual examination, used with A-scan by Dr. A. Kratochwil, 1966. (From AIUM Archives, courtesy of Professor B. B. Goldberg.)

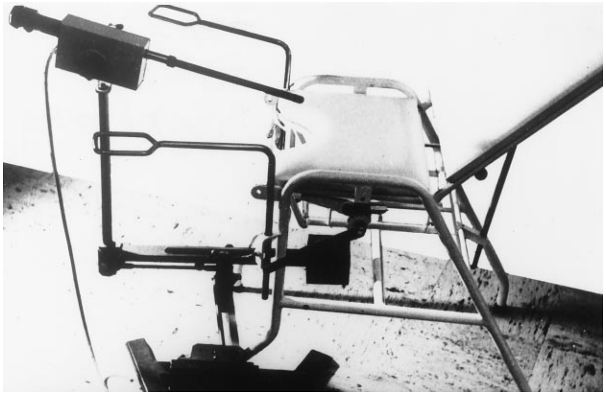
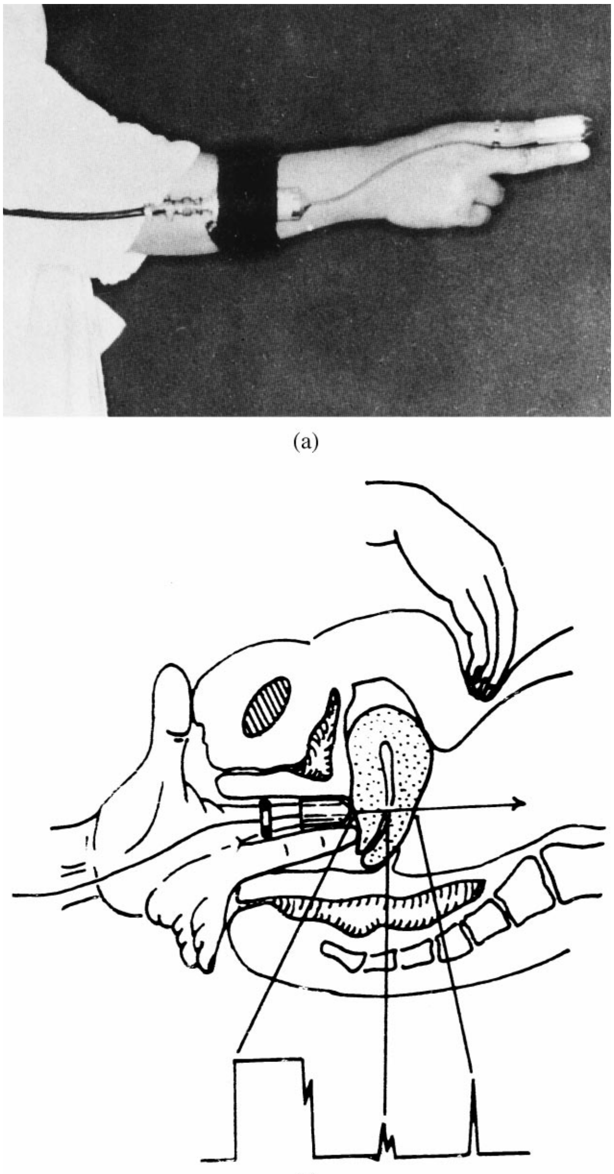


Fig. 17. Unit for transvaginal, rectal, and vesical examination mounted on a colposcopic tripod, 1969, used by Dr. A. Kratochwil. (From AIUM Archives, courtesy of Professor B. B. Goldberg.)



(a)

(b)

Fig. 18. (a) Photograph of the vaginal transducer on the tip of the index finger. (b) Diagram of its application and the resulting A-scan trace (Hayashi et al. 1965). (From BMUS Collection.)

pulsation after 42 day menstrual age (Kratochwil 1969). Another development of the A-scope was a special transducer with a central hole to enable amniocentesis to be carried out more safely.

After Kratochwil learned of Donald, MacVicar, and Brown's work, he persuaded the Kretz company to develop a B-scanner. This was transistorised and, like the American Physionic machine, had an articulated arm instead of the large X-Y measuring frame used on the Smiths' machine. It was, therefore, smaller and easier to manipulate than the Glasgow machine. The display was a 2D bi-stable image. This instrument facilitated additional clinical applications, which enabled Kratochwil to make a major contribution to the development of ultrasound imaging. Initial scepticism from his colleagues was replaced by enormous enthusiasm and interdisciplinary cooperation, which led to the foundation of an ultrasound diagnostic and training centre in Europe in October 1970.

Japan

The Japanese Society of Ultrasonics in Medicine was founded in 1961 with 209 members, biannually holding meetings at which papers were presented on the recent progress being made in each of the specialties in which ultrasound was being used. In addition, annual reports were published by the Ultrasonic Research Group in Juntendo University, Tokyo, where Wagai and his colleagues were based. Perusal of the reports and papers available in English from the early years together with the papers in the AIUM archives provided the information on the early developments.

Technical developments and clinical applications were reported throughout the 1960s. In 1963, detection of the position of the fetal head and measurement of its size using the A-scan and B-scan was noted. The transvaginal approach also was described, primarily for the diagnosis of gynaecological tumours, but also for the diagnosis of early pregnancy. A slender transducer with a quartz crystal 5–10 mm in diameter and frequency 5–10 MHz was used (Wagai et al. 1963). The following year, Hayashi et al. (1964) reported additional use of the vaginal probe (Fig. 18).

In 1964, the Juntendo group also reported that, although the fetal outline could be identified easily using B-scan, detail of the internal structures was poor. This was in contrast to cases of hydatidiform mole, where the inside of the uterus was acoustically almost homogeneous with a number of fine spots throughout (Fukuda et al. 1964). These appearances were in keeping with the reports of moles diagnosed in other centres. Tanaka et al. (1964) published their first report on “Early diagnosis of pregnancy” in the *Japanese Journal of Medical Ultrasonics.*

The use of ultrasound clearly was expanding in Japan the same way as has been recorded elsewhere. The report of the Japan Society of Ultrasonics in Medicine for 1964 extends to four pages on obstetrics and gynecology. There are sections on the diagnosis of early pregnancy that describe improvements in the vaginal transducer so that it fit onto the tip of the index finger; the diagnosis of placenta praevia by both the vaginal and abdominal route; and measurement of the fetal head. Later annual reports contain fewer references to obstetrics and gynecology. Most of the papers on these subjects were published in Japanese.

Japanese technology has had a huge impact on ultrasound imaging, as evidenced by the number of companies, such as Aloka, Hitachi, and Toshiba, which have produced literally thousands of machines for diagnostic use.

Additional international developments

The influence of the key workers in the countries already mentioned spread beyond national boundaries, and the evidence of the dissemination of their research was seen in the establishment of ultrasound facilities in many other countries and a “second generation” of researchers who would also leave their mark on obstetric ultrasound. As the ripples spread from the pioneering centres, increasing amounts of interest were generated, leading to the involvement of many people in this new imaging technique. We are including many examples of individual involvement, but recognise that this will not be comprehensive. Among the researchers, some names became better known than others, and we wish to acknowledge all who contributed in any way to improving the role of diagnostic imaging in obstetric practice.

As an example of the spread of interest across national boundaries, we know that, in the late 1960s, equipment became available from neighboring Vienna, and Kratochwil was able to demonstrate its uses to his colleagues in (the former) Yugoslavia. Asim Kurjak was among his enthusiastic audience. He was to be become a leading figure, particularly in the field of education, and one of the prime movers in establishing, in 1981, in Dubrovnik the Inter-University School of Medical Ultrasound, subsequently prefixed by the name “Ian Donald” in recognition of Donald’s pioneering work.

In 1966, in Leiden, The Netherlands, a young Dr. Wladimiroff was aware of the A-scope in his hospital’s neurology department and had read the Denver paper reporting various uses of ultrasound in obstetrics and gynaecology (Taylor et al. 1964). He was particularly interested initially in fetal cephalometry and wrote to Denver for additional information. In reply, Gottesfeld described his technique in some detail and provided both more information and encouragement to the young investigator. Wladimiroff’s early interest flourished, and he proceeded to make an enormous contribution to diagnostic imaging and training over the next 30 or more years.

Dr. Holm, a urologist, introduced ultrasound to Denmark in the early 1960s. He began with an old Krautkramer flaw detector from the Danish welding centre, but he soon was given a grant to purchase a Physionics machine with TM-mode. In 1965, he was joined by Jens Bang, a young obstetrician, and together they published their first report on the use of ultrasound in the detection of fetal heart movement (Bang and Holm 1968). Thereafter, one of their main interests was ultrasonically guided needle puncture, of which there will be further descriptions later in this article.

The first world conference in diagnostic ultrasound was held in Vienna in 1969, and the proceedings were published 2 years later (Bock et al. 1971). Many of the early workers were present in Vienna, where 19 papers were presented on the use of ultrasound in obstetrics and gynaecology. Among the delegates was Manfred Hansmann from Germany, who gave, with Hoven, their report on BPD measurement. This was to be the start of Hansmann’s major contribution to ultrasound imaging. Although some of his papers are in English, many are in his native German, and the authors’ access to these is limited by their lack of knowledge of that language. This is also true for many other workers, who may feel that they have not been given due credit for their contribution because we have included mainly English publications.

Dr. Levi, who wrote the article in this series on “The history of ultrasound in gynecology” (Levi 1997), has himself contributed to diagnostic imaging in no small way. Many of his own publications are in French and are referenced in his own article. Working in Belgium, he has been a major force in European ultrasound, his first publication on the subject being in 1967 (Levi 1967).

Professors Ai-Hong Zhang and Xu Zhi-Zhang have contributed to AIUM their recollections of the early work in China (Zhang and Zhi-Zhang 1988). Clinical applications began in 1958, in Shanghai, with A-mode equipment. The following year, the Shanghai Medical Ultrasound Research Group (the first in the country) was founded. In 1960, a manual type of contact compound B-scanner was constructed with a simultaneous A-mode display. This machine was the result of collaboration between the engineer Liu Jing-Zou and the clinician Xu Zhi-Zhang. M-mode followed in 1961. The first paper on diagnostic ultrasound was presented at the first National Conference in 1959. Language difficulties and the political situation both contributed to there being limited exchange of information between China and the West, and it has been only recently that details of the early work have become known.

Ian Donald made many overseas tours. In 1968, he returned to the country of his youth, the Republic of South Africa, as a guest lecturer and, needless to say, his topic was "The use and application of diagnostic ultrasound." Among the audience were Professors Dennis Davey and Leon van Dongen, both eminent figures in their specialty. Each apparently was fired with Donald's enthusiasm, making application to their respective authorities for ultrasound equipment. Leon van Dongen's request was turned down initially, the proposed venture being labeled a "*newfangled gimmick*" by the then professor of radiology who had been asked for his comments. Davey was successful, and the Cape Provincial Authorities provided equipment for Groote Schuur and Tygerberg. This was the beginning of obstetric scanning in South Africa. It is perhaps unfortunate that the incident for which that country is best remembered in connection with ultrasound imaging is in the report of the increased number of sister chromatid exchanges recorded in chromosomes exposed to ultrasound (Macintosh and Davey 1970). This was a major event in the history of the safety of ultrasound, making international news headlines and leading to widespread concern about safety. The research was repeated in several other centres without any adverse effects being identified, but it was some time before the authors of the original report withdrew their allegations (Macintosh et al. 1975).

In perusing the material in the archives at AIUM, the influence that the early pioneers had on the next generation became very clear. The following quotes illustrate the influence of the personalities of the pioneers, whose energy and enthusiasm were self-apparent in their papers, presentations, and demonstrations.

"*I first became interested in ultrasound during a trip to Vienna in early 1969 when I visited with Dr. Kratochwil.*"

"*I had the privilege of hearing Ian Donald give the Joseph Price Oration in 1968...and I remember thinking that his ideas were rather farfetched but have recognized now that he was only ahead of his time.*"

"*I was an intrigued and fascinated onlooker.*"

"*While reading Kossoff's article in the bathtub one evening I became intensely interested.*"

"*On many of the numerous on-call nights I found myself listening to the radiology resident describing the wonders and mysteries of diagnostic ultrasound. Each individual case was a brave new world.*"

"*Each scan was a work of art.*"

"*Those were exciting days.*"

Not everyone's first interest was generated by contact with medical pioneers. One radiologist recorded his interest stemming from 1962, when an Austrian veterinary surgeon used therapeutic levels of ultrasound on one of his parents' show horses. The treatment was successful and apparently neither the boy nor the horse ever looked back.

So many had become involved for whatever reason that, as Charles Hohler (1980) wrote, "*I'm really one small grain of sand on an enlarging beach now.*"

Diagnostic imaging was, as we have seen, a feature of the industrialized world. Equipment was costly and required a great deal of maintenance. It was, therefore, impractical in areas where resources were limited. Priorities had to be established. In the 1960s, diagnostic imaging was not a top priority in less developed countries. It was only later, when equipment became more easily available, less expensive, and required less maintenance, that ultrasound was introduced to these countries.

Summary of the 1960s

By the mid-1960s, obstetric ultrasound was well established in many centres, and from these the ripples were spreading such that increasing numbers of individuals were setting up their own scanning departments. Interestingly, these were situated not in the same location in each hospital, but were dependent on the specialty of the clinicians involved. Thus, the strength of ultrasound might lie in the obstetrics department of one hospital while it would be in radiology in another.

FURTHER TECHNOLOGICAL ADVANCES

Technological development continued, and the areas of particular significance in obstetrics were image display and recording, measurement, real-time scanners, transducer design, needle guides, Doppler, and 3D scanners. To understand the significance of the advances in these areas, one has to know what it was like to scan before these technologies were available.

Image display and recording

In the early years, ultrasound images were recorded as a white image on a black background, using 35-mm film, a slow and fraught process. The introduction of Polaroid film in 1959 reduced the time and effort required to produce permanent records. At first, the film was in roll form and sometimes would leak in the developer, resulting in a mess. The later flat pack was a great

Fig. 19. Author J.E.E.F. checking the brightness and contrast settings of a video monitor used to record images from an NE4102 on a Polaroid flat pack camera in The Queen Mother's Hospital, 1975. (From BMUS Collection.)

Fig. 20. Tom Brown demonstrating to Barry Goldberg the method of recording patient and other data on the first contact scanner. This photograph was taken at The Symposium on the History of Medical Ultrasound, Washington, DC, 1988. (From BMUS Collection.)

improvement. Even so, the process of loading, developing, and cleaning cameras was an undesirable maintenance burden, and the critical setting of brightness and contrast of the display monitor was of continual concern to the operator (Fig. 19). One way of trying to overcome this difficulty was to record images as black on a white background. This was more commonly seen in the US, whereas white on black remained more popular in Europe. White on black now is used virtually universally.

Another difficulty with displays was that they could not easily be viewed directly. The camera was placed in front of a short persistence tube, which could be viewed if the camera shutter was closed, but it was very difficult to see the image. Long persistence tubes were used, but even when looked at in the dark the images were far from satisfactory. There really was no alternative to taking a photograph to appreciate fully the scan. The availability of cathode-ray tubes able to store an image was an interesting development. The first type was the Tektronix bi-stable tube. It was only able to show black or white, no grey scale at all. Some improvement was offered by the limited grey scale of the Hewlett-Packard variable persistence tube, but this had poor spatial resolution.

An additional problem was recording of patient and other information on the image record. The rather cumbersome method used by Donald's group to record patient data, ultrasound frequency, sensitivity and scan location is shown in Fig. 20. These are remembered by J.E.E.F. as causing a great deal of frustration and, on occasions, an outburst from Ian Donald!

These unsatisfactory features were overcome with the development of scan converters. These devices were seen at first as a means of providing storage of images with a wide grey-scale range, but it was the fact that their output was in television (TV) format that allowed the use of bright, large-screen TV monitors and this made their impact dramatic. It also was possible to take advantage of other developments in the TV industry. Video recorders were used to record particular scans, such as cases where a fetal abnormality was suspected. The recording of data was simplified as character generation devices had been developed, which made it possible to overlay data onto the image. This technique also allowed improvements to the measuring facilities, as will be described. Video printers became available. These devices, with rolls of paper sufficient for 200 frames, largely overcame the problems with photography and presumably resulted in a significant reduction in the use of Polaroid film. Thus, scan converters led to a range of improvements. However, it should be recalled that this advance was not without problems, as initially scan converters were analogue devices based on the Princeton Inc. Lithicon tube. The adjustment of these complex pieces of electronics required considerable skill and experience and, as they tended to drift out of adjustment, patience in resetting them. Fortunately, as a result of advances in digital memory for computers, digital scan conversion became possible. This removed all the drift and adjustment problems. Now, scan converters, video recorders, and printers are merely components of the whole ultrasound system, taken for granted by many.

Measurement

The first measurements made were linear. They are described in the clinical section, as they were very much an integral part of the development of the clinical application of scanning. With improvements in image quality, other types of measurement, such as circumference and area, became feasible. These measurements were made

Fig. 21. The first electronic area and perimeter measuring device for ultrasound images (Fleming and Hall 1978). (From BMUS Collection.)

Fig. 22. Author M.B.M. using a Diagnostic Sonar XL, 1982. (From BMUS Collection.)

from Polaroid photographs either by using mechanical calipers to measure two orthogonal diameters, from which circumference and area could be calculated, or by using a map measurer and planimeter. The latter instrument was expensive, delicate, and difficult to use. Taking measurements from Polaroid photographs was prone to error, because the photos were shiny and mechanical measuring tools tended to slip during measurement. Additionally, as the photographs were only 100 × 80 mm and the area of interest occupied only a small part of the picture, small errors of measurement were magnified. With the coming of the scan converter, an electronic solution was possible. A joystick unit developed by Fleming and Hall (1978) that could be used to trace the outline of the section of interest and upon which the area and perimeter values appeared on the digital display is shown in Fig. 21.

Improved devices soon followed, including the Echo Computer (Diagnostic Sonar Ltd.), which used a light pen to interact with the image and was programmed to convert measurements into clinically important estimates, *e.g.,* relating crown–rump length (CRL) to gestational age and abdominal circumference to fetal weight. Similar systems later were incorporated into the company's real-time systems (Figs. 22 and 23). An alternative approach was the "Sonicomp" Computerised Obstetric Measuring System (Sonicaid Ltd.), which used a graphics tablet. These devices were superseded by the "track ball" and, at the less expensive end of the market, by the less convenient key pad. It is now common to find a variety of methods for delineating a cross-section, *e.g.,* a continuous line may be traced, a series of crosses can be positioned individually, or a pregenerated but adjustable ellipse can be fitted to the cross-section of interest. The area and perimeter values and corresponding clinical estimates then appear on the screen and, if desired, in a database containing all the patient's details.

Having such measurement and other data in digital form naturally led to investigation of computer-based

Fig. 23. Measurement of the abdominal circumference using a Diagnostic Sonar XL, 1982.

systems to deal with the large amount of data generated by obstetric ultrasound examinations. The earliest commercial approach to this was the Sonicaid "Sonicomp," which could store such data on a 5.25-inch floppy diskette. This system and later ones typically displayed a "screen" onto which measurements and specific observations could be recorded throughout a given pregnancy. These facilities became an integral part of scanning machines, and the most recent developments are in the integration of these with hospital information and support systems (HISS).

Real-time scanning

Ultrasound was becoming more widely used as a diagnostic technique in the late 1960s, and the availability of real time scanning had a major effect on the increase in sales of equipment worldwide. As sales rose, prices fell and interest grew both clinically and commercially. Although there were sceptics initially, it was the introduction of real-time scanning that led to diagnostic imaging becoming wholly accepted.

Although one thinks of real-time development as a feature of the 1970s, there is evidence of earlier research dating back to Wild in 1951, and a film was made (copy in BMUS Collection) showing cross-sections of the neck being scanned with a transducer oscillating at a few sweeps per second. Further development of this "real-time" technique does not appear to have taken place, but there were several workers, the authors included, who used a rapid movement of the transducer of the "static" scanner to give a "real-time" image. The first "real-time" transducer as we think of it today was a 10-element concave array for eye examination that was constructed in 1965 in association with Kretztechnic of Austria, but it was not developed further at that time. The Siemens Vidoson was the first commercially available real-time machine in 1966. A transducer rotated at the focus of a parabolic mirror in a water-filled enclosure to produce images at 15 frames per second. It was cumbersome and difficult to use, but it sold in large numbers in continental Europe. One of the authors (J.E.E.F.) first saw obstetric images from a Vidoson at an ophthalmic meeting in Munster, where he was most impressed on seeing fetal movement demonstrated. In those early days, with fewer people being involved, there was greater opportunity for interaction with different specialties.

The return to the array principle and away from the unwieldy Vidoson arose from an interest in improved cardiac imaging. In 1968, Somer started experimental work on phased arrays, then Bom et al. (1971) developed small arrays specifically for cardiac work. In 1974, the first commercially available linear array scanner was produced by Advanced Diagnostic Research Corporation (ADR). This instrument used 64 elements operating in groups of four and displayed 40 frames per second. For some time, cardiology was the only specialty where the technique appeared to have a place.

The acceptance of real-time scanning in obstetrics was delayed, if not actually resisted, because of its shortcomings. A limited field of view, poor resolution, poor beam shape, and gaps in the image made array systems unattractive compared with static scanners. Even Winsberg, in 1979, although recognizing the outstanding potential of real time scanning, expressed some concern for the loss of the static scanner's large image area. A Diasonograph scan could encompass the whole length of a term fetus. Changes in technique and the use of curved arrays have provided answers to this criticism and the new Siemens Siescape is capable of an unlimited length of scan. Other, gladly forgotten, features of many early array transducers was the stiff and heavy connecting cable and the rather heavy and bulky transducer, which made scanning far more tiring for the operator than the modern lightweight transducer connected by a highly flexible cable. The early real-time machines were smaller, lighter, portable, and easier to use than the static scanners. These features, together with improvements in technology leading to better resolution, paved the way for their general acceptance. Perhaps most important of all has been the development of the transducers, somewhat uninteresting looking devices, but without which real time imaging would not exist.

The review by Winsberg (1979) gives us some idea of the effort put into the development of transducers. He described 11 forms that had been, or were about to be, introduced commercially, using electronic scanned arrays or a range of mechanical methods in which a transducer or an acoustic mirror was moved, with or without a water path. Since then, more have been developed with the aim of improving resolution and reliability. Better resolution was the reason for the re-emergence of the vaginal transducer. This approach had been recognised by the early investigators, particularly the Japanese and then by Kratochwil, as offering a direct view of the pelvis. These workers were using an A-scope, and it was the advent of real-time scanning that led to the widespread use of the vaginal probe, especially for use in infertility work and in early pregnancy.

Three-dimensional ultrasound

The development of 3D scanning also is considered by many to be a product of the 1980s and 1990s but, just as with real-time scanning, the very early researchers were aware of the possibilities of 3D. Both Howry and Brown considered the possibilities, and Brown incorporated a 3D capability in the design of the automatic scanner already described. The problems of displaying the images inhibited its use, but Brown later designed the

Multiplanar scanner in 1972 while working at Sonicaid Ltd. This was the first commercially produced 3D machine, but it failed to become accepted for various reasons. Many people felt that the easy-to-use 2D real-time equipment provided all the information required. With increasing clinical demands, the potential benefits of viewing in three dimensions have become clearer. At the same time, changes in technology have made generation of a 3D image easier. The net result is an increasing acceptance of this technique, which is reflected in the organisation of the first congress on 3D in obstetrics and gynaecology in 1997.

Doppler

The development of Doppler, color flow imaging, and power Doppler are included in the clinical applications section on Doppler.

Summary of technological developments

From the early work around the world, ultrasound imaging machines have developed from a few pieces of crude laboratory equipment to complex, reliable, and sophisticated systems in widespread use. Of particular relevance to obstetrics has been the work on image quality and display, real-time, image measurement, Doppler and colour flow mapping, and 3D scanning. The direction and timing of these developments have been determined by the interaction of medicine, physics, engineering, and commerce. Progress in ultrasound should be seen against the broad background of rapid technological development, particularly in electronics.

CLINICAL APPLICATIONS OF OBSTETRIC ULTRASOUND IMAGING—ITS COMING OF AGE

Having recorded the major technological advances that led to more widespread acceptance of obstetric scanning throughout the world, we now shall describe the clinical developments that were many and varied, with pregnancy lending itself to ultrasound examination for very practical reasons. It was realized very quickly that, once intra-abdominal, the pregnant uterus distends the maternal abdominal wall, and the convex surface provides good contact with a transducer. Maternal bowel is pushed to the side, so that its gaseous contents do not interfere with the passage of ultrasound and there is no air or gas in the fetal lungs or bowel to obstruct the sound waves, which are transmitted easily through the amniotic fluid.

In the late 1950s and early 1960s, the perinatal mortality rate in Glasgow was in excess of 50 per thousand births. The principal known causes of stillbirth were fetal abnormalities, placental abruption, toxaemia, and rhesus incompatibility, with nearly one fifth unexplained. Prematurity was the main factor in neonatal deaths. Facilities for monitoring the fetus at that time were very limited, and ultrasound offered tremendous potential for fetal assessment. Just how much ultrasound would contribute to antenatal care was not realised in the early days, but as technology developed so the clinical applications broadened. In the 1990s, perinatal mortality rates in developed countries are in the single digits. The reasons for this are complex, but there can be little doubt that ultrasound has played its part and has been of tremendous benefit to many patients.

As clinical applications spread, the literature was flooded with publications. It would be impossible to avoid missing out the names of some who were involved in the early days, but this is almost inevitable as the numbers of investigators increased. As one would expect, there was an enormous amount of overlap in the way ultrasound was used in clinical practice. We have chosen to describe the applications in turn, referring to the key research, mainly in the English language, rather than listing individuals and their contributions.

It is clear from the section on technological developments that a wide range of people were involved, and this continued to be the case with its application in clinical practice. At first, the majority of those using ultrasound clinically were medically trained, either obstetricians or radiologists, although some nonmedical personnel, particularly physicists, undertook clinical investigations. As equipment became more widely available and easier to use, a range of people of various backgrounds started scanning. Local arrangements tended to be made informally. Gradually, as the role of ultrasound expanded, it became necessary to consider more formal arrangements for training. Scanning in obstetrics particularly lent itself to a variety of personnel being involved, especially obstetricians, midwives, radiologists, and radiographers. Each had something different to offer in addition to their ability to scan. The evolution of scanning, therefore, led to different arrangements being made in different countries for the training and certification of those scanning. These issues have been addressed elsewhere.

The following account of the clinical applications falls into three main areas. First, we review the role of ultrasound in fetal biometry and biophysical assessment; second, we consider multiple pregnancy and placentography; and third prenatal diagnosis and therapy. Ultrasound in early pregnancy is covered by Dr. Levi in his article on gynecology.

FETAL BIOMETRY AND BIOPHYSICAL ASSESSMENT

It is well recognized that uncertainties regarding gestational age are associated with higher rates of perinatal mortality and morbidity (Hall and Carr-Hill 1985). Similarly, poor intrauterine growth is associated with an adverse outcome (Bard 1970; Drillien 1971; Hill et al. 1984; Usher 1970), but detection rates by clinical means are notoriously poor (Galbraith et al. 1979; Thomson et al. 1968). Prior to the availability of ultrasound, obstetricians relied on their clinical judgement with occasional recourse to x-ray examination to assess maturity. Ultrasound, as a painless, noninvasive, and apparently safe technique, afforded the early investigators the opportunity to try to measure different aspects of the fetus. Measurements were correlated with gestational age, growth, and overall size. Errors, both systematic and random, were to be expected and were found to be dependent on factors such as the growth rate of the dimension under consideration.

Because the image of the head was the most easily recognized part of the fetal anatomy, it was the subject of the initial reports on measurement. Thereafter, as image quality improved, other areas of the body became equally easy to visualize and they, in turn, were measured. The availability of equipment, static or real time, also played a role in the choice of measurement. Size alone was recognized as providing only limited information on fetal growth. Assessment of the biophysical status of the fetus later was included in the monitoring of overall development.

Following the first publications relating to biometry in the early 1960s, a gentle trickle of reports became a veritable flood of information on the assessment of gestational age and fetal growth. Opinions varied widely, and continue to do so, on the place of routine scanning for the estimation of gestational age and the prediction of growth retardation. In this section, we first will describe individual dimensions, the development of a suitable measurement technique, and the assessment of gestational age. A section on growth and biophysical assessment then follows, and finally we review the role of ultrasound in clinical practice.

Measurement of fetal dimensions

Biparietal diameter. Once the fetal head was recognized by the echo pattern from the skull, it became clear that the head could be measured ultrasonically. This potential was reported in the first paper by Donald et al. in 1958. Subsequently, a series of experiments in Glasgow using the A-scope and a fetal skull in a water bath showed that equal echoes from the two sides of the head were obtained simultaneously only when the beam of ultrasound went through the BPD at right angles to the sagittal plane. In the pregnant patient, the BPD initially was measured using a water tank comparator and making a correction for the speed of sound through water as compared with a fetal head. Measurements were made on the photograph of the A-scan trace. Donald presented this rationale to the British Institute of Radiology in 1961 and, later that same year, Donald and Brown (1961) published their results in the *British Journal of Radiology*.

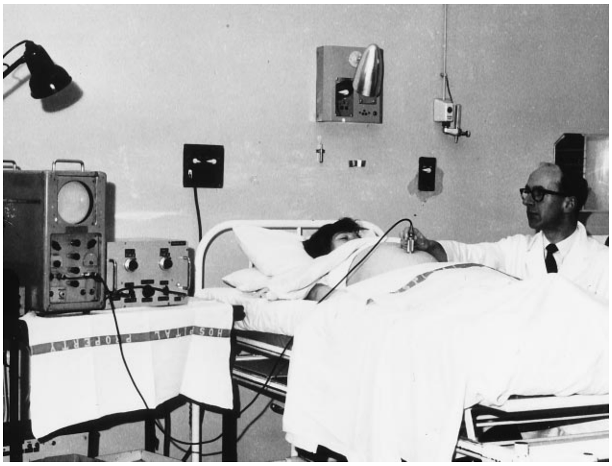


Fig. 24. Dr. James Willocks measuring biparietal diameter using Kelvin Hughes' Mk4 flaw detector and electronic caliper unit designed by Tom Duggan. (From BMUS Collection.)

Willocks (Fig. 24) developed the technique of BPD measurement with Duggan, who designed an electronic caliper unit that superimposed on the A-scan trace a pair of bright dots. Their position along the trace could be adjusted and the distance between them was controlled using a dial calibrated in centimeters and millimeters. This simplified the process of making accurate and reproducible measurements. These early studies of fetal growth were to be the basis of Willocks' MD thesis (Willocks 1963) and later publications (Willocks 1962; Willocks et al. 1964). The article in 1962 followed a presentation at the Royal Society of Medicine by Donald, MacVicar, and Willocks; Donald having risen from his sick bed to travel to London, such was the importance of the occasion. This anecdote typifies the character of the man who was so determined to be there in person that he would let nothing prevent him from going, least of all his recuperation from cardiac surgery.

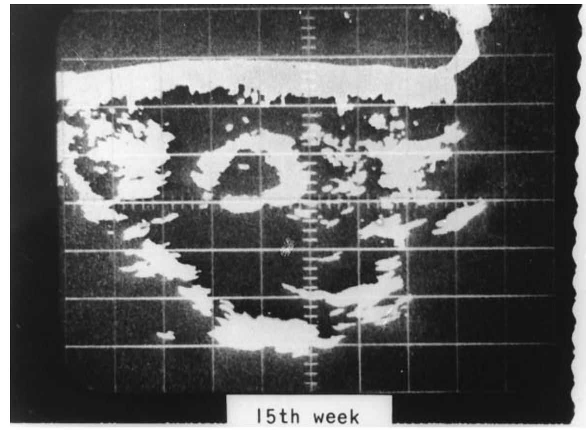
Cephalometry also was developed at other centres. In Denver, the A-scope also was used and measurements of the BPD were made, comparing them to the actual caliper measurement taken after birth. The maximum variation was reported as 3 mm (Taylor et al. 1964). Even at this early stage, it was recognized that obstetricians felt an estimate of fetal weight would be more meaningful; therefore, the late BPD measurements were correlated with the birth weight (Thompson et al. 1965). The B-scan had been introduced in 1962 in Denver and was used to visualise the head (Fig. 25), which was still measured by the A-scan technique as reported by Thompson (1966). Some of the patients in one early series on fetal growth apparently were unmarried mothers from a home in the city—an example of the social situation of the day providing readily available subjects for a project. Other investigators in the US, including Goldberg et al. (1966), also were using A-scope techniques. Reference to work in other countries has been made in the technology section.

By the time of the First International Conference in Pittsburgh in 1965, several of the pioneers, including Donald, Gottesfeld, Mizuno, Thompson, and von Micsky, were able to include reference to their experience with measurement of the BPD in their presentations. Details of these are included in the proceedings of that meeting (Grossman et al. 1966).

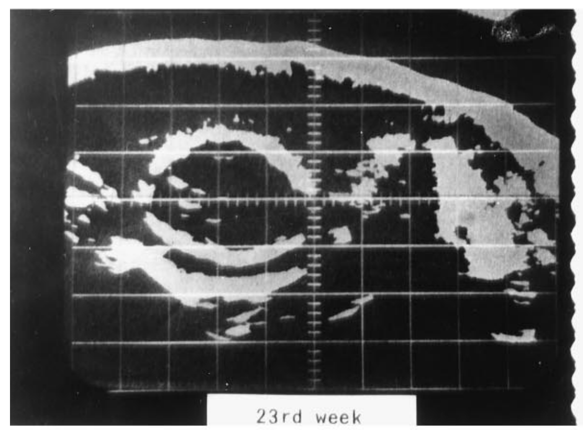
The technique of BPD measurement in the UK was improved by Campbell (1968, 1969, 1970), who combined A-scan and B-scan (Figs. 26 and 27). For readers who have never used an A-scan or a static B-scanner, it is both interesting and salutory to read a description from the early days of how to measure the BPD. This was a very different and much more time-consuming exercise than using modern real-time scanners, which display the detailed anatomy of the brain. The first step was to identify the fetal head on a longitudinal scan of the fetus and obtain a clear mid-line echo. The angle of asynclitism of the head was noted from the scale on the transducer assembly, which then was rotated at right angles to give a transverse view of the fetal head with the mid-line echo still present. Small adjustments of the transducer position were made until the maximum diameter was obtained. The proximal and distal echoes of the skull then were apparent on the A-scan, and calipers were positioned on the leading edges of each to enable a measurement to be made. Additional measurements were taken above and below the first scan plane to ensure that the largest diameter had been found. This whole process took several minutes. If, as happened quite frequently, the fetus moved, one had to start all over again.

Campbell and Newman (1971) described the normal growth pattern of the BPD as linear during the mid-trimester, with increases of approximately 3 mm per week, thereafter gradually decreasing to about 1 mm per week after 36 weeks.

The reproducibility of the technique was the subject of much debate. Comparison of the published data was difficult because of different workers using different calibration and correction factors in an effort to give a



(a)



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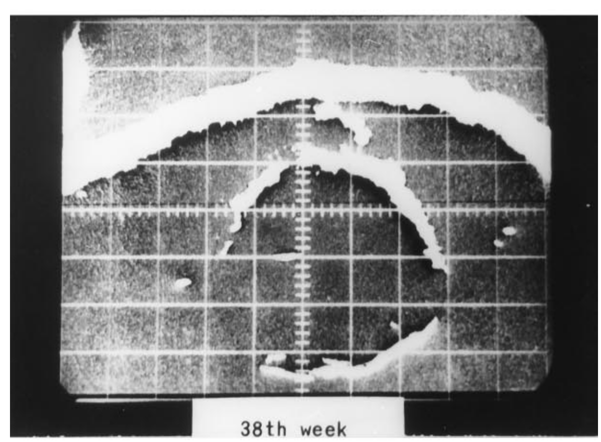

(c)

Fig. 25. Growth of fetal head at (a) 15 weeks, (b) 23 weeks, and (c) 38 weeks. Taken by the Denver group. (From AIUM Archives, courtesy of Professor B. B. Goldberg.)

reading, which represented the true outer diameter of the head. It was not always stated whether measurements were made from outer to outer or outer to inner aspect of the skull. There was no agreement on the use of com-

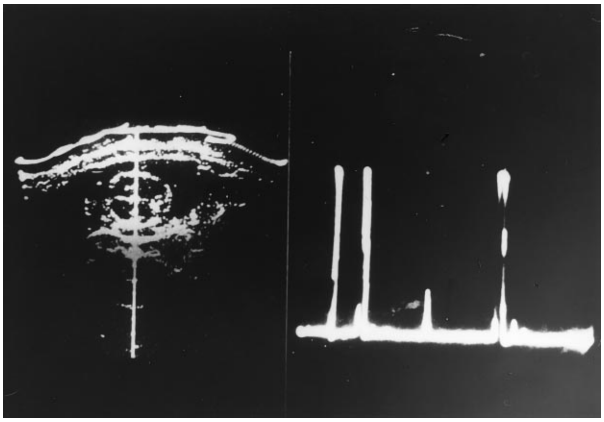

Fig. 26. Measurement of the biparietal diameter (BPD). On the left is the B-scan image taken prior to measurement of the BPD. The vertical line indicates the position from which the A-scan trace, shown on the right, was taken. (From BMUS Collection.)

pleted weeks or days for defining gestational age. Some articles reporting "diameter" measurements did not state the calibration factors and, therefore, were of little value. There was no agreement on calibration factors. From their work on neonates, Willocks et al. (1964) in Glasgow recommended using a value of 1600 m·s^{-1}), whereas Hansmann and Hoven (1971) in Germany favoured 1580 m·s$^{-1,}$ and in the US 1540 m·s^{-1} was preferred. It was to be 1975 before a meeting of the European Study Group for Ultrasonics in Obstetrics and Gynaecology, chaired by Kratochwil, agreed to recommend the adoption of 1600 m·s^{-1} as the calibration velocity for BPD measurement. Subsequently, there was general acceptance that the soft tissue value of 1540 m·s^{-1} should be used for all purposes, and this now is used universally for calibrating ultrasound machines. Those more recently involved in scanning take this totally for granted and probably never pause to consider this question, which was a real bone of contention in the early days.

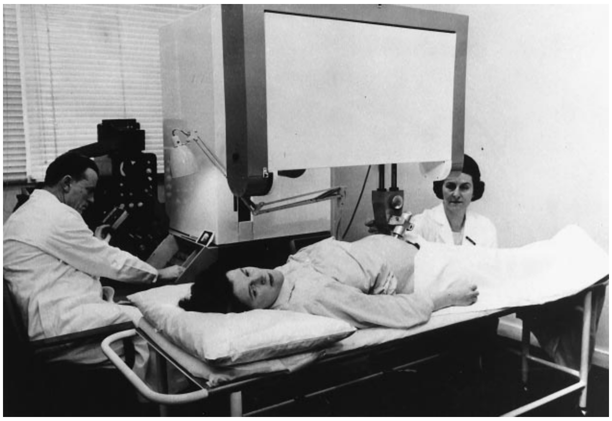

Fig. 27. A Kelvin Hughes Diasonograph and, in the background, a Mk7 flaw detector (A-scan) were used by Dr. Stuart Campbell in his early biparietal diameter studies. The combined system is shown here being used by Professor Ian Donald with the assistance of Mrs. Ida Miller in The Queen Mother's Hospital. (From BMUS Collection.)

Throughout the later 1960s and the 1970s, the technique of BPD measurement became widely used. A considerable body of literature became available, which described growth of the BPD during pregnancy and its clinical applications in determining gestational age and monitoring intrauterine growth. Numerous charts were published and used in different centers.

In the May 1974 issue of *Clinics in Obstetrics and Gynaecology*, an issue devoted to fetal medicine, Stuart Campbell was the author of the article on fetal growth. In his conclusions, he wrote, "*Ultrasonic measurement of the fetal biparietal diameter is the most precise fetal measurement which can be obtained antenatally. Single measurements are superior to abdominal palpation in the prediction of birth-weight at the extremes of the birth-weight range and when taken before 30 weeks gestation are a highly accurate method of determining fetal maturity. Serial measurements are valuable in detecting the growth-retarded fetus and would appear to have advantages over urinary oestrogens, especially in separating the small-for-dates fetus from the fetus whose maturity has been mistaken. Different growth patterns can be identified which seem to fit into two main groups: either a persistently slow growth rate from early in the second trimester (low growth profile) or a sudden slowing after a period of normal growth (late flattening). Cross sectional measurements of the fetal body are complementary to fetal cephalometry and may yield information as to the nature of the growth retardation.*"

Reading the preceding paragraph, we realise how limited the range of measurements was in 1974, some 17 years after the first fetal ultrasound images had been obtained. How different the next 17 years would prove to be when almost everything that could be measured was measured. Much of that subsequent expansion was related to the advent of real-time scanning and the progressive improvements in image quality. As a result of these various technological developments, organs and structures were recognized that previously had been seen only on dissection by the pathologist or anatomist. There was a need for obstetricians to reach for their anatomy textbooks to enable them to interpret all that was visible on the ultrasound image.

Details of the structures within the brain made particular impact on those scanning and, together with the easier technique of real-time imaging, led to changes in the manner in which the fetal head was measured. The

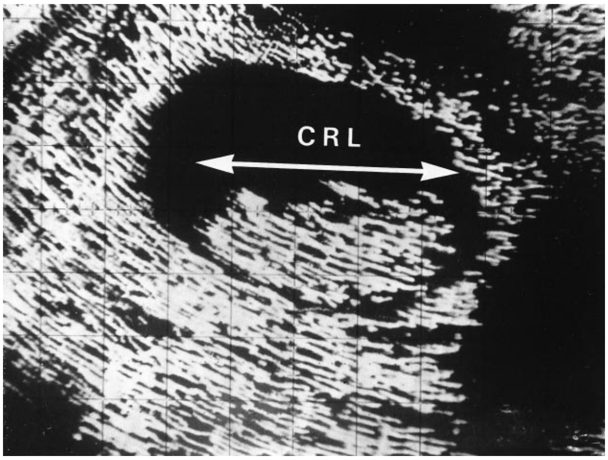

Fig. 28. Crown–rump length (CRL) of 42 mm corresponding to 11 weeks' gestation, taken using an NE 4102, at The Queen Mother's Hospital, 1964. (Courtesy of Dr. H. P. Robinson.)

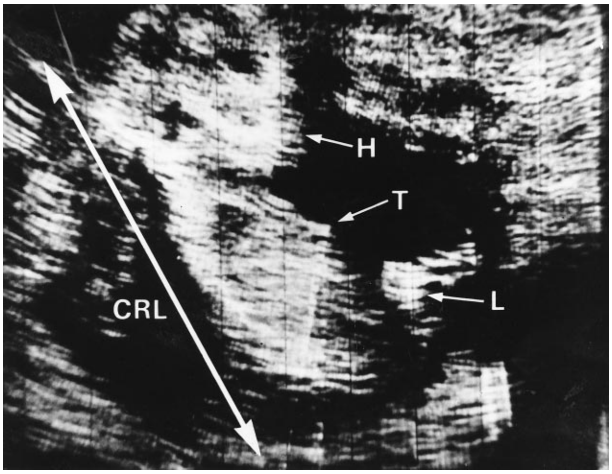

Fig. 29. Crown–rump length (CRL) of 80 mm corresponding to 14 weeks' gestation, taken on an NE 4102, at The Queen Mother's Hospital, 1964. H = head; L = leg; T = trunk. (Courtesy of Dr. H. P. Robinson.)

anatomical features that were seen in the BPD plane were the cavum septum pellucidum, the thalami, and part of the falx cerebri. These became the landmarks needed for the correct plane for BPD measurement.

Head circumference. The head circumference (HC) was measured on the same plane as the BPD. The advantage of HC over BPD was that the former is a 2D measurement that should not be influenced by alteration in the shape of the head in, for example, breech presentation, twins, or oligohydramnios. Charts relating HC to gestational age were introduced (Hadlock et al. 1982; Hansmann 1976), but in practice they confered little or no advantage over BPD in second-trimester dating. The value of HC measurement was primarily in assessment of growth in relation to the rest of the body in later pregnancy (see following).

Crown–rump length. The measurement of CRL in the first trimester was first shown to be practical by Hugh Robinson in Glasgow in the early 1970s (Robinson 1973). Using the Diasonograph, a static contact B-scanner, he made serial parallel longitudinal scans at small increments from one side of the gestation sac to the other, identifying the ends of the fetus and making a mark on the mother's abdomen to represent each end. The gantry then was swung around so that scans could be made along the line joining the marks on the abdomen. Once the longest length of fetal echoes was obtained, this was taken as the CRL (Figs. 28 and 29) and measured from a photograph of the image, which also showed the graticule on the display screen. This is a far cry from the present-day method. Scanning was a different sort of challenge in those early days, requiring an enormous amount of patience and skill.

Measurements made in the manner described are subject to systematic errors from a variety of sources, including the effects of scale factor, beam width, and calibration velocity, and random errors, such as those resulting from fetal movement and operator judgement. Despite all these potential errors, CRL measurement was shown to give very accurate estimates of gestational age. For a single measurement, an estimate could be given to ±4.7 d, with 95% confidence. If three independent measurements were made, the limits were reduced to ±2.7 d (Robinson and Fleming 1975). Similar data were obtained by other investigators (Bovicelli et al. 1981; Drumm et al. 1976; Kurjak et al. 1976; Pedersen 1982). Bovicelli et al. (1981) used real-time equipment (a Kretz Combison 100), whereas the others used static scanners. All their measurements were in remarkable agreement (within 2 mm at any stage) to those of Robinson and Fleming (1975).

The early data were obtained from "normal" pregnancies. Subsequently, evidence of differences in CRL growth rates was shown in diabetic pregnancies (Pedersen and Molsted-Pedersen 1979) and between the sexes (Pedersen 1980). Concern was expressed by MacGregor et al. (1987) regarding the reliability of the original data, suggesting an underestimate of 3–4 d in the calculation of gestational age. Christie (1981) felt that curvilinear measurements should be made, because the fetal posture tends to be curved. These concerns have not been borne out in practice. Parker et al. (1981) reported on the reproducibility of CRL measurements obtained with real-time compared with the static scanner. The data of Robinson and Fleming (1975) have proved robust and

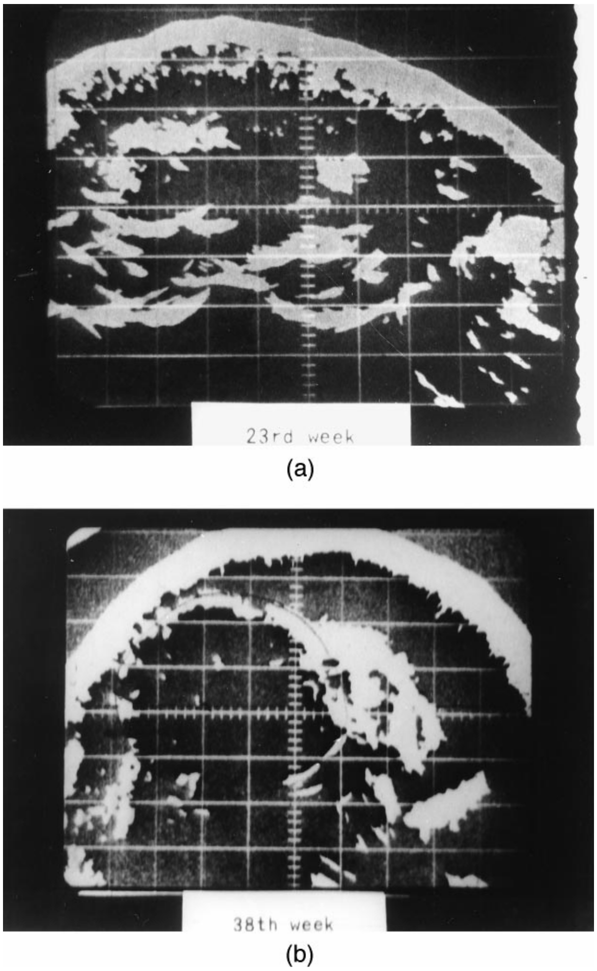

Fig. 30. Growth of fetal thorax at (a) 23 weeks and (b) 38 weeks. Taken in Denver. (From AIUM Archives, courtesy of Professor B. B. Goldberg.)

remain in widespread use (British Medical Ultrasound Society 1990).

Trunk measurements, including thorax and abdomen. In 1965 at the Pittsburgh meeting, Thompson (1966) described the technique for measurement of the fetal thorax (Fig. 30) using the static B-scanner. He recognised that there were difficulties in always obtaining a true cross-section of the chest, but the early results were encouraging. The measurements obtained by scanning before birth and directly from the neonate after birth were compared and shown to agree within ±3 cm in 90% of the infants studied. Estimates of fetal weight also were made based on thorax circumference alone and in combination with the BPD. Using the latter method, estimates of weight were accurate to ±300 g in 66% of the patients.

Garrett and Robinson (1971) reported growth of the fetal trunk area from 30 weeks onward, and Hansmann and Voight (1973) provided data on thorax measurements. Campbell was concerned about the reproducibility of the section of the thorax and considered abdominal circumference measurements (AC) to be preferable. The main clinical application for these was in estimating fetal weight. Campbell and Wilkin (1975) published their results on the accuracy of birth weight prediction and their assessment of its potential role in screening for the small-for-date fetus.

Campbell and Wilkin described their technique as follows. "*Ultrasound compound B-scans are first made at different angles to the midline of the maternal abdomen to identify the position of the long axis of the fetal body; where there is marked flexion of the fetal body, it is helpful to identify a significant length of fetal abdominal aorta, or fetal dorsal spine. Scans are then made orthogonal to the long axis of the fetal body and a section across the upper abdomen selected; this is recognised by the typical appearance of the umbilical vein as it passes under the fetal liver. Usually the umbilical vein can be quickly and easily recognized from 24 weeks onwards except in about 5% of cases when the fetal spine is directly anterior, which means that the walls of the umbilical vein are not orthogonal to the ultrasonic beam. Under these circumstances we have found the fetal stomach to be the most suitable reference point; it is not so precise a location for when distended it extends over a greater length of the fetal abdomen but it does lie in the upper abdomen to the left of the fetal liver and both umbilical vein and stomach can usually be visualized on the same section. Circumference measurements were made to the nearest millimeter on a Polaroid photograph by means of a map measurer with appropriate correction for picture size.... In all cases an ultrasonic frequency of 2.5 MHz was used and the velocity calibration set to 1540 metres per second.*"

The technique of AC measurement described has stood the test of time. Real-time equipment and improved measurement facilities have made the whole process much easier and quicker, but basically the same technique is used. The choice of the particular plane by Campbell was considered very important, as this ensured reproducibility of measurement.

Femur length. O'Brien et al. (1981) were the first to introduce the concept of using limb length, in their case, the femur, to predict gestational age. Jeanty et al. (1984) subsequently provided data on measurement of all the long bones. Femur length (FL) has been used most commonly, because it is the longest and is usually the easiest to visualise and measure, but this does not preclude using the others.

Other dimensions. Mayden et al. (1982) reported their experience of orbital diameter measurement and its value in both dating and prenatal diagnosis. Yarkoni et al. (1985) and Birnholz (1986) published their work on the clavicle and lumbar spine, respectively, suggesting a role for these in dating and growth assessment. Reece et al. (1987a) measured the cerebellum and correlated its growth with gestational age. In practice, these measurements all have proved of limited value for dating purposes, but they do have an important role where abnormality is suspected. The same holds true for measurements of the cerebral ventricle-to-hemisphere ratio, and the chest circumference and renal measurements.

Which measurements and charts should be used? The choice of data varies both from center to center and from country to country. Many workers have produced charts applicable to their own area. In the UK, a working party was established in 1986 by the BMUS to examine the evidence and recommend which charts should be used nationally. In their final report in 1990, a summary of their recommendations was provided. Subsequently, Chitty et al. (1994a, 1994b, 1994c) published statistically superior data, which received the full endorsement of the BMUS.

Assessment of gestational age

First trimester. The first trimester is the period of gestation during which fetal growth is most rapid and biological variation is least marked. It was logical to expect that measurement during this period would provide a good estimate of gestational age, which was demonstrated in the work of Robinson and Fleming (1975), Drumm et al. (1976), and Pedersen (1982). Measurement of the CRL remains the method of choice for estimation of gestational age in the first trimester.

Alternatives to CRL include measurement of the gestation sac, which is known to increase rapidly in the early weeks of pregnancy. This method also was used as a means of assessing continuation of the pregnancy (Kohorn and Kaufman 1974; Levi and Erbsman 1972). The shape of the sac was noted to vary considerably, which led to quite complex formulae being used in conjunction with time-consuming planimetry to obtain an accurate assessment of the volume (Robinson 1975). In general, the relative simplicity of obtaining CRL measurements led to this being the preferred method of assessing gestational age once the fetus could be identified. Measurement of gestation sac size retains its role in the time before the fetus can be identified.

Other parameters, including BPD (Bovicelli et al. 1981; Selbing and Kjessler 1985), AC (Reece et al. 1987b; Selbing 1986), femur length (Selbing 1986), and foot length (Mercer et al. 1987), have been suggested for dating in early pregnancy but are better reserved for the second trimester, because they confer no advantage over measurement of the CRL.

Second trimester. Biological variation remains small before 18 weeks. Campbell et al. (1985) demonstrated the advantages of BPD measurement between 12 and 18 weeks. The BPD remains the most commonly used dimension for determining gestational age in the second trimester, because it is easily obtained and reproducible.

Hadlock et al. (1984) assessed the value of combining the parameters BPD, FL, HC, and AC, using a stepwise regression analysis, and showed that BPD and HC were the best predictors between 12 and 18 weeks' gestation, with HC having an advantage over BPD from 18–24 weeks. This was probably because the HC takes into account changes in shape referred to previously. Using a combination of these dimensions also increased the accuracy of prediction.

Persson and Weldner (1986) published correlation coefficients for gestational age assessment for BPD, FL, abdominal diameter, and occipitofrontal diameter, showing that the BPD had the narrowest confidence intervals and FL the next best when measurements were made between 80 and 180 d. Using multiple regression analysis, a combination of BPD and FL was shown to give an even more accurate prediction, but combining all four variables was of no additional advantage.

BPD and FL, therefore, remained the dimensions of first choice in the assessment of gestational age in the second trimester.

Third trimester. Biological variation increases with advancing gestation, and dating of pregnancy in the third trimester was found to be least accurate. If late dating was required clinically, Hadlock et al. (1983, 1984) advocated a composite age method based on multiple growth parameters. They found that the best overall results were obtained using the four parameters BPD, FL, HC, and AC.

Role of routine scanning for the assessment of gestational age. With regard to routine scanning for dating purposes, Campbell was one of the first and most vocal protagonists. In a review of the rationale for routine dating, Campbell (1993) argued that the overwhelming evidence from clinical studies confirmed the superiority of ultrasound fetometry over other methods, including a certain last menstrual period, in estimating gestational age and predicting an expected date of delivery. As Campbell pointed out, some obstetricians were reluctant to recommend routine dating until proof of benefit was provided by randomised prospective studies, but no such study with sufficiently large numbers was ever performed and so there was no absolute proof of the value of routine dating of all pregnancies. The early studies on smaller numbers of patients showed the benefits of ultrasound dating and led many to accept and implement a policy of routine scanning, making additional studies impossible to undertake.

Progress in genetic technology and in the identification of markers of fetal abnormalities visible on ultrasound in the first trimester has led to the acceptance of the potential value of an early scan by many clinicians and mothers. Some patients have demanded an early scan. In societies where diagnostic imaging was readily available, public pressure has been influential in changing clinical practice. It is not uncommon, in the late 1990s, for patients to request a late first-trimester scan primarily for the purpose of identifying markers for fetal abnormalities as well as for accurate dating.

An additional advantage of offering and carrying out a scan on all mothers in the early stages of their pregnancy is providing them, and their families if so wished, an opportunity to see the fetus on the screen. The reassurance this provided, especially if there had been previous problems, was recognized by the early workers. Obstetric ultrasound examination has proved to be one of the few methods of clinical investigation that offers such immediate benefit to the patient.

Assessment of fetal growth

Growth, as the dictionary definition reminds us, is not simply an increase in size but has to be considered in the more complex terms of progress, development, and advancement toward maturity. It was not surprising, therefore, that fetal growth could not be assessed simply by measurement of individual dimensions, which provided useful but limited information. It was necessary to look at additional features in order to reflect the more complex nature of growth. Manning et al. (1980) described the fetal biophysical profile as a means of antenatal fetal surveillance, particularly in cases of growth retardation. Deter et al. (1983) described the prenatal growth profile, which included measurement of a number of variables such as head and trunk size, soft tissue mass, weight, length, and body proportionality. Both biophysical assessment and measurement of size provided a more comprehensive assessment of fetal growth. These, together with fetal heart rate (FHR) monitoring and evaluation of fetal blood flow using Doppler, were all to prove of value in the overall assessment of fetal growth and development. We will consider the various methods in turn.

Fetal size and weight estimation. Serial measurements of the head were used initially to detect fetal growth retardation (Campbell and Dewhurst 1971; Willocks et al. 1967), but a single measurement of the head

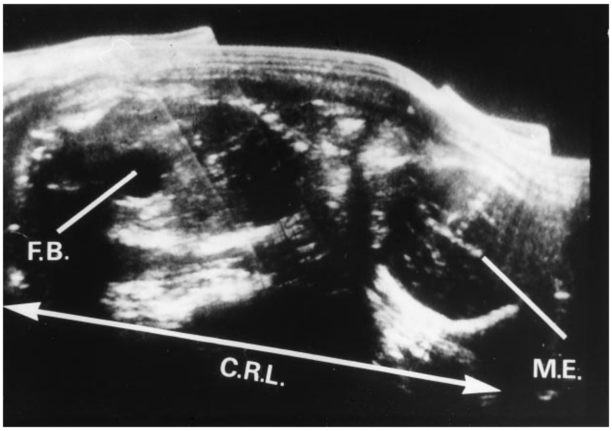

Fig. 31. Static scanner image of the crown–rump length (C.R.L.) in late pregnancy. F.B. = fetal bladder; M.E. = mid-line echo in the head. (Courtesy of Professor J. P. Neilson.)

in late pregnancy was not shown to be clinically useful in predicting birth weight (Campbell 1974). The fetal thorax then was considered for weight estimation (Hansmann and Voight 1973). Campbell and Wilkin (1975) preferred AC measurements, which were related to the birth weight of babies delivered within 48 hours of being scanned. At a predicted weight of l kg, 95% birth weights fell within 160 g, whereas at 2, 3, and 4 kg the corresponding values were 290, 450, and 590 g.

Using this method, estimation of fetal weight proved of some clinical value, but there were still marked limitations because of the imprecision of the technique and the inherent systematic and random errors in any measurement. The cynical clinician who did no scanning would take great delight in announcing in a loud voice in a public place and to the amusement of all except the sonographer just how wrong the scan estimate had been. Even in the 1970s, ultrasound was not fully accepted. Yet in some ways it was the clinicians who were responsible for the situation. They wanted information on fetal size, and an estimation of weight was a figure that was easily understood. There might have been less criticism had the researchers chosen to publish only the actual measurements with their error ranges rather than use the measurements as a means of estimating birth weight.

Neilson et al. (1980, 1984a) reported their experience using the product of the CRL (Fig. 31) and abdominal circumference or area (Fig. 32) in the identification of the small-for-date fetus. The method seemed to have potential for identification of the small-for-date fetus in a high-risk population, but CRL measurement in later pregnancy is impractical with real-time scanners, and the disadvantages of the technique outweighed any possible advantages. Interestingly, Neilson and his colleagues did not attempt to predict an actual fetal weight. They chose

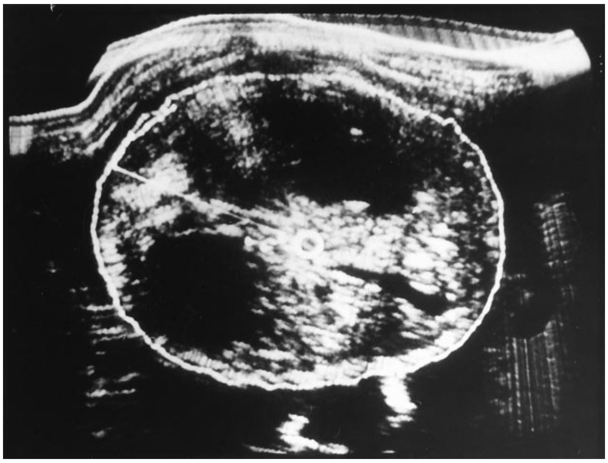

Fig. 32. Cross-section of the fetal abdomen delineated by the device illustrated in Fig. 21, which gave measurements of area and perimeter. (From BMUS Collection.)

to publish graphs of growth curves on which actual measurements could be plotted.

The potential value of using some means of reflecting overall fetal length (or height) in assessing size had been recognized and, if the CRL could not be used, there were alternatives. The femur was included in some formulae for estimating fetal weight (Hadlock et al. 1984; Vintzileos et al. 1987). In an attempt to duplicate postnatal assessment before birth, several investigators reported their experience in measuring the fetal thigh circumference as an indication of the amount of fat deposition (Jeanty et al. 1985; Vintzileos et al. 1985; Warda et al. 1986).

Attempts to estimate fetal weight dominated the literature, some using a single dimension, others two or more parameters (Hadlock et al. 1984; Shepard et al. 1982; Warsof et al. 1977). The use of two dimensions resulted in improvement in the accuracy of prediction of about 5%, but the addition of a third parameter or more resulted in a difference of $<$1%. Opinion continues to vary on the merits of one method compared with another. The authors' group (Smith et al. 1997) described a retrospective study of more than 3500 women in whom estimates of weight were made using both AC and FL (if available) or AC alone. They concluded that the latter should be used. There is still no absolute means for estimating fetal weight, and errors as large as 15% can be expected, but weight estimation continues to have an important role in the assessment of fetal growth and development in later pregnancy. This role is based on the long-term practice of relating neonatal outcome to weight.

Measurement of the head-to-abdomen ratio, HC/AC, was shown to provide information on the relative proportions of the fetus (Campbell and Thoms 1977). This was found useful in the assessment of abnormal growth patterns, such as asymmetrical growth retardation, where the fetal body is very thin whereas the head is relatively normal in size. This is the result of the brain-sparing effect where, in situations of reduced oxygenation, blood flow to the brain is maintained in preference to other organs. In contrast, cases of genetically small fetuses are symmetrically small. The head-to-abdomen ratio also proved of value in the identification of microcephaly. Several workers, including Vintzileos et al. (1985), considered the ratio of various body dimensions in assessing growth.

Screening for intrauterine growth retardation. Campbell and Wilkin (1975) used their data on AC measurements to assess the probable value of these measurements in screening the whole obstetric population. They predicted that 87% of small-for-date fetuses could be identified at 32 weeks, falling to 63% at 38 weeks, with a false-positive rate at just over 1%. They proposed a combination of early determination of gestational age by CRL in the first trimester or BPD in the early second trimester, followed by a late measurement of fetal size using the AC between 32 and 36 weeks to predict growth retardation.

Many other authors (Bakketeig et al. 1984; Ferrazzi et al. 1986; Geirsson et al. 1985; Neilson et al. 1984b; Persson and Kullander 1983; Warsof et al. 1986) reported their results with screening for intrauterine growth retardation. Deter and Harrist (1993) reviewed these results and concluded that the sensitivity, specificity, and predictive value of the methods considered were lower than what was required for acceptable predictability (values over 90%). One of the problems was that there is no generally agreed definition of what constitutes a growth-retarded or small-for-date fetus. Some researchers have used the third and others the fifth or tenth percentile of birth weight as the cutoff. The role of ultrasound in the assessment of fetal growth has been restricted in most centres to use in high-risk cases, because there is no proven benefit in using ultrasound routinely to screen all pregnancies for growth.

Amniotic fluid assessment. Several workers recognised the value of assessment of amniotic fluid volume, which was known to be reduced in growth retardation. The problem was which method to use for assessment. Amniotic fluid surrounds a complex structure and does not lend itself to measurement. Gohari et al. (1977) chose total intrauterine volume (TIUV) and correlated their findings with fetal growth. They used a simple method, assuming the uterine shape to be a prolate ellipsoid. This is not always the case and was partly responsible, at least for the method being shown, for it being inaccurate in the prediction of growth retardation (Chinn et al. 1981; Grossman et al. 1982; Kurtz et al. 1984). Geirsson (1986) favoured the use of the parallel planimetric area method, which he found more reliable. These methods both required the whole length and breadth of the uterus to be measured. As this could only be achieved using a static scanner, these methods fell into disuse with the advent of the real-time scanner, which, although easier to use, had a limited field of view. Although TIUV measurement proved impractical, it was possible to measure the depth of pockets of amniotic fluid. This is another example of the design of equipment influencing the clinical application of imaging, and it demonstrates the need for compromise on the part of both manufacturer and clinician.

A simple subjective assessment of amniotic fluid volume was proposed by Crowley (1980) in pregnancies of 42 weeks or more and by Zamah et al. (1982) in cases of polyhydramnios, but, in general, the climate at that time seemed to favour methods of assessment that included an actual measurement. Manning et al. (1981) showed that the presence of a pocket of fluid of <1 cm either vertically or horizontally was associated with an increased risk of a growth-retarded fetus. Manning et al. (1980) also had included measurement of pockets of amniotic fluid as one of the components of their biophysical profile, which is described in the next section. Chamberlain et al. (1984a, 1984b) confirmed the findings of Manning et al. (1981) but suggested that patients in whom the depth of pocket was between 1 and 2 cm also warranted close attention. In other words, there was a recognition of the importance of a reduction in fluid volume, but that there was a spectrum from normal to abnormal without a clear cutoff between the two. Additional attempts to assess more accurately fluid volume were made by Patterson et al. (1987), who suggested that an average diameter of the largest pocket be taken. Phelan et al. (1987) favored the four-quadrant approach to provide the so-called amniotic fluid index (AFI). This was first reported in pregnancies over 35 weeks and has been used for antepartum fetal monitoring (Phelan 1988).

Smith and Weiner (1993) summed up the work on amniotic fluid volume assessment in the following terms: "*Although the importance of quantitation is unquestioned and several useful techniques have been described, a practical, precise and reproducible technique has not yet been widely accepted.*"

Biophysical assessment. From the preceding paragraphs, it may seem that measurements were the only means of fetal assessment. This was not the case, however, although huge efforts were made to make measurements similar to those made after delivery, when weight, length, and measurements of head and skin thickness are used to provide a basis for ongoing assessment of a child's growth. A role for qualitative assessment of the fetal condition also was recognized. Measurement may have been considered more scientific than subjective assessment, but with the passage of time there seems to have been an acceptance of the merits of both qualitative and quantitative, and subjective and objective, assessment, and this applies to all aspects of scanning. The human being is a complex animal and cannot be reduced to an assessment in simple terms of measurement alone. Various types of biophysical assessment are described.

Fetal heart rate monitoring. During the 1960s, various methods, including direct and indirectly obtained electrocardiograms and phonocardiography, were proposed for continuous FHR monitoring, because it was becoming increasingly recognised that intermittent auscultation was of limited value in high-risk pregnancies. The FHR also could be recorded using the Doppler principle (Callagan et al. 1964; Johnson et al. 1965). Bishop (1966) then suggested a variety of obstetric uses for the ultrasonic motion sensor, including continuous heart rate monitoring. The Doppler principle could be used to display the FHR from movement of the heart itself or from blood flow in the major vessels or in the umbilical cord. Additional developments took place. Serr (1974) reviewed the technique, "*An ultrasound beam of low energy intensity is directed through the abdominal wall to the fetal heart. The frequency of the beam is changed when it strikes a structure moving perpendicularly to its direction (the Doppler effect). Part of the transmitted beam altered in frequency is reflected back to the source, and picked up by a receiver usually housed in the same head as the transmitting crystal. The signal is then processed....The ultrasound technique has its place in most labour room monitoring systems, and its usefulness should not be under-rated. The advantage over phonocardiographic pick-ups is that it is relatively free of extraneous noise produced by sounds in the acoustic range and is quite comfortable for the patient. It requires a coupling medium between the transducer and the skin, but the patient may lie on her side, and it can be applied by nurses and midwives with ease.*"

Various refinements to the technique have taken place, and ultrasound has made a major contribution to FHR recording methods. Interpretation of continuous FHR records and the role of FHR monitoring has been the subject of widespread debate for many years, and the reader is referred to more appropriate texts for further information. This history is concerned primarily with diagnostic ultrasound imaging, but it is right to record the role of ultrasound in other areas particularly when they may be used in combination with imaging.

Fetal movements. Long before ultrasound imaging was introduced, fetal movements were well recognised by mothers and were documented by various observers. Even with the compound static scanner, movements could be monitored on screen (Higginbottom et al. 1976) if the transducer was moved rapidly to and fro. The advent of real-time scanning provided the opportunity to witness and record movements in much greater detail.

Hofmann and Hollander (1968) demonstrated fetal movement at 12 weeks. Eight years later, Jouppila (1976) had recorded movement at 8 weeks. The same year, Reinold (1976) published his classification of fetal motor behavior in early pregnancy. Subsequently, various workers (Birnholz et al. 1978; De Vries et al. 1981; Ianniruberto and Tajani 1981) described the development from simple to more complex movements. Flexion and extension were followed by hand-to-face movements, sucking, swallowing, breathing, hiccups, and eye movements. Gradually, more and more information was being obtained, which could be related to the neurological development of the fetus. De Vries et al. (1981) reported that all the movements seen in the fetus at term were present at 15 weeks, only the percentage of the time during which they were seen altered with increasing gestation. Changes in movement patterns were observed in pathologic pregnancies, including growth retardation (Roberts et al. 1979; Trudinger et al. 1978), preeclampsia, rhesus isoimmunization, and malformations of the central nervous system (Ianniruberto and Tajani 1981).

Recognition of different movements has contributed to some understanding of the neurological development and maturation of the fetus and is an area where additional research is continuing. Nijhuis (1993) has provided a review of the role ultrasound has played in recognising fetal behavioral states, which in turn has led to the realisation that the fetus develops an awareness as it grows. This has been the subject of a recent report from the Royal College of Obstetricians and Gynaecologists (RCOG 1997a), which makes recommendations for those who undertake diagnostic or therapeutic surgical procedures on the fetus from 24 weeks' gestation onward that they consider analgesia and sedation for the fetus and not just the mother.

Fetal breathing. Boddy and Robinson (1971) devised a method for detecting human fetal breathing. Dawes (1974) reviewed the early descriptions as follows. "*From a transducer strapped to the maternal abdomen a narrow ultrasonic beam is directed to the fetal heart, which is readily identified by its characteristic rhythm. The ultrasonic beam must then pass through the fetal thorax, and examination of an A-scan display shows echoes from the wall of the fetal chest as well as from the heart. Observations with this method on the fetal lamb in utero showed that with breathing movements, which were recorded from a catheter previously implanted in the trachea, changes in the echo from the chest wall were readily identified and could be recorded to give a quantitative measure of the rate of breathing and a qualitative indication of its depth. The method has been used successfully to record fetal breathing movements in several hundred women during pregnancy and in labor (Boddy and Mantell 1972).*"

Even in 1972, a great deal was known about fetal breathing. It was episodic, in normal pregnancy occurring about 70% of the time at a frequency of 30–70 times a minute, but it was reduced in high-risk pregnancies such as in diabetes, hypertension, or preeclampsia, and in labour. Breathing had been recorded as early as 13 weeks' gestation.

More detailed studies showed that fetal breathing was affected by a variety of external influences. Giving the mother a glucose load (Lewis et al. 1978) led to an increase in fetal breathing, as did increasing the mother's oxygen levels in cases of preeclampsia or growth retardation, whereas increasing carbon dioxide levels had the opposite effect in normal pregnancies (Ritchie and Lakhani 1980a, 1980b). Maternal alcohol ingestion resulted in a decrease in breathing (Fox et al. 1978), but there were conflicting reports on the influence of cigarette smoking. Marsal (1983) reviewed the effects of these different factors on fetal breathing.

Biophysical profile. When considering the physical state of the child or adult, it was standard practice to consider multiple variables, and this had been extended to the neonate with the introduction of the Apgar score. It seemed reasonable to utilise ultrasound to record similar fetal biophysical activities. Manning and Platt were the key proponents of the use of a fetal biophysical profile (Manning et al. 1980). With some modifications, their "planning score" received widespread acceptance, although its name, combining the two main authors' names, fell into disuse, most sonographers preferring the term BPP for biophysical profile.

Five fetal variables were recorded by Manning et al.: breathing movements, tone, gross body movements, qualitative assessment of amniotic fluid volume, and response of the heart rate to movements. These five parameters were measured during the same observation period in high-risk patients to determine their relationship, singly or in combination, with pregnancy outcome as determined by the incidence of fetal distress in labour, the 5-min Apgar score, and the perinatal mortality rate. By considering all five variables, the sensitivity and specificity of prediction of an adverse outcome was improved. At the same time, the technique was shown to be practical in the clinical situation.

Use of Doppler and assessment of blood flow. In 1842, Christian Doppler (1842) described the effect that would bear his name, but it was 1959 before Satomura (1959) reported on the study of flow patterns in peripheral arteries utilising the Doppler effect. This followed reports from Japan on studies of the adult heart. In 1964, Callagan et al. (1964) reported their observations of the fetal heart. The subsequent role of Doppler ultrasound in FHR monitoring has been described previously. The application of the Doppler principle to the investigation of blood flow itself has enabled the fetal circulation to be studied in some detail. Pourcelot in France contributed to much of the work on blood flow in the 1960s, having chosen this as the subject of his thesis for his doctorate in engineering. His first recordings in humans were made in 1965. His interest continued, and he and his colleagues were involved with the development of the first Doppler equipment for the surveillance of the cardiovascular system of astronauts in space (Pourcelot 1988).

Technological developments with Doppler equipment brought improvements in parallel with those seen in imaging systems. Initially, there was simply continuous wave, and one had to rely on recognizing the pattern of flow in the vessels under investigation rather than actually identifying the vessel by imaging it and then looking at the flow. The concept of the duplex scanner incorporating both imaging and Doppler was a later development. Gill (1979) described such a system using a static scanner, but again it was the advent of real-time scanning that made such a difference to future developments. Eik-Nes et al. (1980) described the first linear array duplex system in which an offset pulsed Doppler was attached to a linear array imaging transducer, so that the Doppler beam intersected the plane of the image at a fixed angle. Teague et al. (1985) refined the system by mechanically connecting the Doppler and the imaging transducer via two arms that were jointed so as to allow free movement only within the plane of the real-time image. An almost unnoticed paper by Namekawa et al. (1982) working at Aloka laid the foundations for colour Doppler. Rapid development and improvement followed, leading to 2D images overlaid with color to indicate blood or tissue velocity. This not only allowed observation and recognition of flow patterns, but also acted as an aid in the recognition of anatomy and pathology. Additional improvements have been the more recent development of power Doppler, which identifies regions of tissue perfusion without being dependent on flow velocity or direction. All these developments have led to increased clinical application.

Some 20 years ago, Fitzgerald and Drumm (1977) reported their early findings using this new method of assessment of the fetal circulation. In the intervening period, there have been a plethora of reports and differences of opinion both for and against the use of Doppler in the assessment of fetal well-being, much in the same way there has been controversy regarding the routine use of ultrasound imaging.

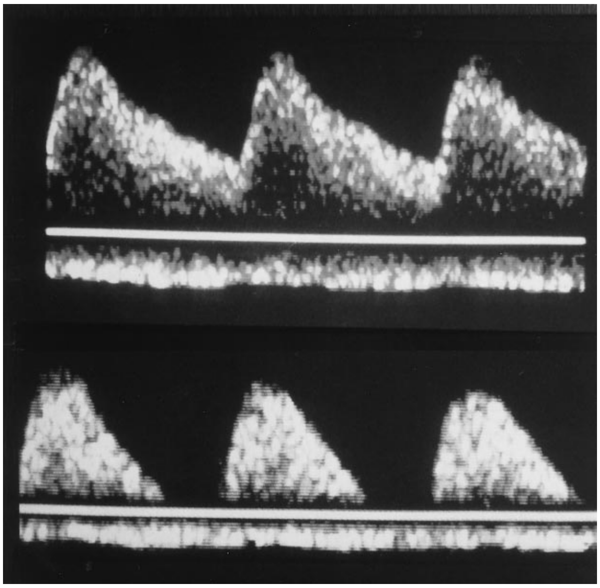

Fig. 33. Doppler spectral waveforms of the umbilical artery. The top panel shows a normal waveform with end-diastolic flow present; the bottom panel shows an abnormal waveform with absent end-diastolic flow.

Initially, there were efforts to assess the Doppler signals both quantitatively and qualitatively. From the former, actual measurements of flow could be obtained but required accurate knowledge of the angle of the Doppler beam to the vessel. Qualitative assessment of the flow velocity waveform (FVW), which shows relative changes in maximum velocity with time independent of the angle of insonation, was a simpler technique with fewer potential errors, but still required great care on the part of the operator in obtaining the waveform (Fig. 33). One problem was that the equipment incorporated a "thump" filter, but too high a setting of the filter, which removes low-frequency, high-intensity signals produced by pulsatile movement of the vessel wall, could lead to spurious waveforms.

The interpretation of FVW became the most accepted method of assessment of Doppler flow. Arterial flow was seen to be typically biphasic, with a systolic peak and continuing forward velocities through diastole. Waveforms could be quantified in different ways. Stuart et al. (1980) described the A/B ratio, which is the ratio of peak systolic (A) to end-diastolic (B) velocities. Pourcelot (1974) described the resistance index (RI), which is the ratio of the difference between peak systole and end-diastole to peak systole, $(A - B)/A$. Gosling and King (1975) had introduced, for general angiology, the pulsatility index (PI), which is the ratio of the difference between peak systole and end-diastole to the mean deviation from the baseline, (A − B)/mean. All three methods had their advocates.

The larger the vessel, the easier it was both to image and to obtain a Doppler signal. The earliest reports, therefore, tended to be from the umbilical artery. Fitzgerald and Drumm (1977), Stuart et al. (1980), and Trudinger et al. (1985) all studied umbilical artery FVW using continuous-wave Doppler alone, directing the beam at pools of amniotic fluid and searching for the typical signal from the cord. A progressive decrease in pulsatility with an increase in diastolic flow was noted with increasing gestational age. End-diastolic flow was accepted as an indicator of peripheral resistance, and so the findings were indicative of a reduction in peripheral resistance with advancing gestation. As a corollary, the evidence suggested that reduced end-diastolic flow was associated with increased peripheral resistance and could be associated with increased perinatal morbidity and mortality.

Changes in umbilical artery flow were thought to be secondary to alterations in uteroplacental flow, which was, therefore, also the subject of investigation. Knowledge of the complex branching system of the uterine arteries led Campbell et al. (1983) to record the FVW of the arcuate arteries, but it became clear that assessment of the uterine arteries themselves provided the most useful and reproducible information. Early studies, such as those of Fleischer et al. (1986) and Trudinger et al. (1985), showed much promise for the clinical application of the technique of Doppler flow assessment, particularly in high-risk pregnancies. Neilson (1987) reviewed the situation at that time and concluded that "*There is nothing in the published literature to indicate that the impact of Doppler ultrasound will be of such overwhelming value that it should be rushed into clinical practice without proper assessment.*" Gradually, however, the use of Doppler ultrasound became more widespread, but its value remains the subject of much debate. The potential for its use as a screening tool was advocated by Bower et al. (1993), but this has not yet been established.

The fetal descending aorta and cerebral vessels also have been studied in some detail (Eik-Nes et al. 1982; Stuart et al. 1980; Wladimiroff et al. 1986). In his review of normal flow in these vessels, Wladimiroff (1993) noted that changes in cerebral flow during the last few weeks of pregnancy suggested a haemodynamic redistribution favouring the blood supply to the brain. He also highlighted the importance of taking into account the FHR, breathing movements, and behavior when studying fetal blood flow. Vyas and Campbell (1993) described several studies demonstrating the association of hypoxaemia with centralisation of blood flow to the brain at the expense of organs such as the kidneys.

Doppler studies of the fetal heart have provided additional information to that obtained by imaging alone in the evaluation of normal and abnormal cardiac function. Reed et al. (1986) and Allan et al. (1987) were among those who contributed to the early data in this field. Identification of the vessels and areas under study has been made much easier since the introduction of colour flow imaging (Fig. 34).

Summary of the role of ultrasound in fetal assessment

The role of ultrasound in determining gestational age has been well established and now is used routinely for this purpose in many countries. Its role in the assessment of fetal growth and well-being in high-risk pregnancies also has been established. To date, there is insufficient evidence for it to be accepted widely for screening all pregnancies for this purpose.

The following paragraph was quoted by Holmes in 1981. The words are those of Gottesfeld and provide a most appropriate summary of the general view of ultrasound at that time. The sentiments remain, and the research in the intervening years has borne out many of the hopes and aspirations of the early investigators.

"*I think we are progressing further and further into the field of fetal evaluation to make the nine months which the fetus spends in utero a much safer, healthier time and to aid in the recognition of fetal anomalies. By the use of this instrumentation we have brought the fetus from a point where it hides beneath our fingertips and the necessity for the obstetrician to spend a lot of time guessing what is going on to a point where we actually feel the fetus is an active part in the management of pregnancy. We can observe it. We can visualise motion, breathing, activity, and bring reassurance to the mother.*"

MULTIPLE PREGNANCY

Multiple pregnancy has long been recognized as a contributor to perinatal mortality and morbidity (Donald 1966). One of the main difficulties in the management of twins was that the diagnosis often was missed, the patient and her attendants being quite unaware of the presence of more than one fetus until delivery. This may seem difficult to comprehend in the late 1990s in developed countries, but one has to remember that conditions were very different in the 1950s and 1960s. In the Glasgow Royal Maternity Hospital, 1960–1962, the perinatal mortality rate was more than 50 per thousand, worse than the national average. There were several contributing factors, including the preponderance of poor people in the city and a shortage of hospital beds; as a result, only 64% of obstetric patients received hospital care. The diagnosis of multiple pregnancy depended on clinical suspicion with confirmation on x-ray examination.

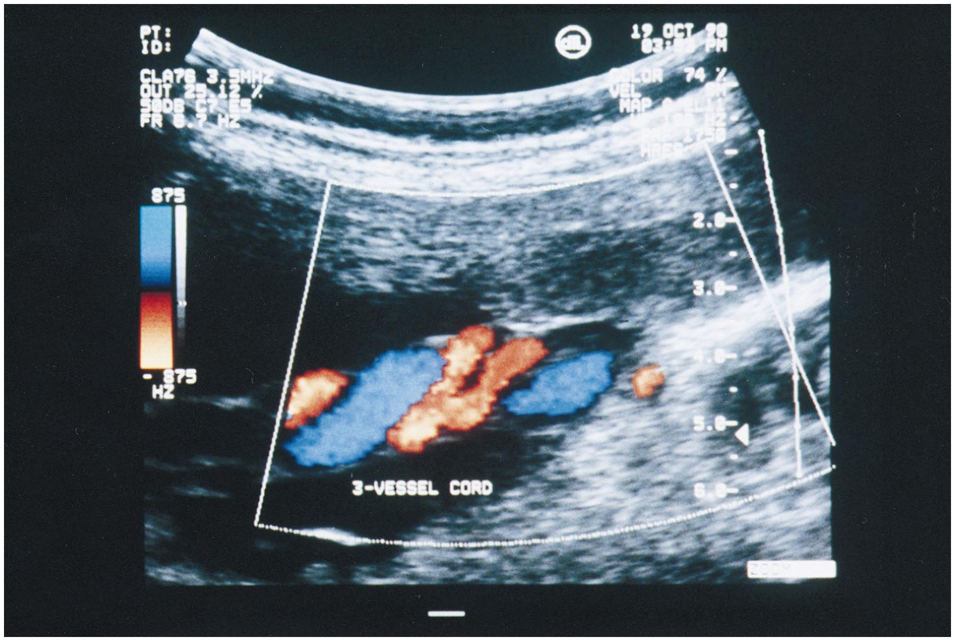

Fig. 34. Color Doppler image of a three-vessel cord. (Courtesy of Advanced Technology Laboratories UK, Ltd.)

The introduction of ultrasound made a huge impact on the recognition of multiple pregnancy. This, together with improvements in health, social conditions, and obstetric care, has contributed to the reduction in perinatal mortality and morbidity from all causes. The single most important contribution of ultrasound to the management of multiple pregnancy remains its recognition. This enables the mother's care to be adjusted accordingly and appropriate monitoring introduced as necessary. The role of ultrasound that has been described for singletons applies also to multiples. In addition, it was recognized that the zygosity of twins might be established. This would be of clinical importance, because more complications were known to arise in uniovular cases. Attempts at establishing zygosity on ultrasound were made by looking at several features, including the sex of each fetus, the placentae, the thickness of the membranes, and their insertion into the placental tissue (Barss et al. 1985).

Ultrasound has an important role in the recognition of fetal abnormalities in multiple pregnancy and their investigation by diagnostic tests such as amniocentesis and chorion villous sampling. It was realized from an early stage that it was essential to identify clearly each sac before sampling and that there would be problems arising as a result of diagnosing abnormality in multiple pregnancy. If one fetus was found to have an anomaly while the other was normal, the parents would be faced with a very difficult decision. There was a need for appropriate counselling and information to be made available to parents. Inevitably, situations arose where a request was made for selective termination of one fetus. The term selective feticide was introduced, and the technique was described by Aberg et al. (1978) and Kerenyi and Chitkara (1981) using ultrasound-guided cardiac puncture, and by Rodeck et al. (1982b) using air embolism delivered via a fetoscope. Since then, the technique of needle placement has been refined. In countries where selective feticide is legal, most workers now use ultrasound-guided intracardiac injection of potassium chloride.

Following the increased availability of assisted conception, greater numbers of higher order multiple pregnancies were seen. These numbers have decreased again in countries, such as Great Britain, when legal restraints were introduced on the number of embryos that could be implanted. The presence of several embryos and the expected later loss of these because of the large number led several workers and patients to request selective feticide in these cases. There was considerable resistance among those skilled in needle placement that their expertise should be required in these situations. Fortunately, changes in assisted conception treatment should reduce the number of higher order multiples, limiting the need for feticide.

A particular problem that was known to occur in uniovular twins was the potential for twin-to-twin transfusion syndrome, which is the result of imbalance in blood flow between the placenta and each twin. One twin is the donor whereas the other is the recipient, so that the former becomes anemic and the latter hypervolemic.

Perinatal loss is markedly increased in this condition. Prior to ultrasound imaging, the condition remained undiagnosed *in utero,* and no treatment was available. With ultrasound, the disparity in fetal size and amniotic fluid volume can be recognized and, in the most severe cases, the smaller twin gives the appearance of being "stuck" to the wall of the uterus because there is no amniotic fluid around it. The other twin may be huge in comparison, hydropic and surrounded by an increased volume of amniotic fluid. Nicolaides et al. (1997) reviewed the treatment options, including serial amniocentesis to relieve the polyhydramnios, and they described their experience with laser coagulation of the communicating placental vessels. This technique is one of the latest developments in the use of ultrasound as a guide for invasive procedures, which are described in a later section.

PLACENTOGRAPHY

The site, structure, thickness, and appearance of the placenta have all been studied. The umbilical cord also is included in this section.

Placental localization

It was realized from an early stage by Donald and other pioneers that the placenta could be distinguished on ultrasound examination (Fig. 35). Indeed, reference already has been made to the need for a safe method of placental localization being the stimulus to introducing ultrasound in various centers. Mizuno et al. (1965) published the first article specifically on the diagnosis of placenta previa. The article was written in Japanese and not easily accessible to English readers. The following year, Gottesfeld et al. (1966) published in the *American Journal of Obstetrics and Gynecology* their article entitled "Ultrasonic placentography: a new method for placental localization." Donald and Abdulla (1968) published the first article in the UK on placentography by sonar. These reports were to be followed by many others in many languages. They led to ultrasound becoming an established technique for localization of the placenta.

Problems were recognized from the start, including the difficulty in visualizing the posterior placenta due to fetal shadowing and the apparent "migration" of the placenta due to development of the lower uterine segment in later pregnancy. Some of the difficulties encountered in the early days have persisted, even with the advent of grey-scale, real-time scanning and with the more recent improvements in image quality and use of the vaginal approach (Fig. 36). Timor-Tritsch et al. (1988) were among the first to recognize the advantages of the vaginal probe, which avoided many, but not all, of the problems associated with abdominal scanning.

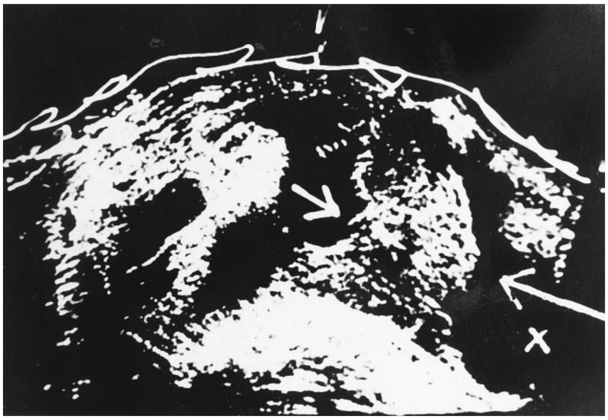

Fig. 35. Placenta praevia at 36 weeks' gestation, shown between the arrows. X = bladder. This grey-scale image from a Diasonograph, at The Queen Mother's Hospital, 1964, looks bi-stable because of the poor quality of reproduction of the photograph. (From BMUS Collection.)

Placental localization is one of the areas where ultrasound has made a particular impact on clinical practice. As a junior in the 1970s, one of the authors (M.B.M.), was taught in a unit where ultrasound was viewed with scepticism and any patient presenting with vaginal bleeding after 28 weeks' gestation was admitted to hospital and remained as an inpatient until bleeding necessitated delivery or, if the bleeding subsided, until 38 weeks when an examination under anesthesia was carried out to determine if the placenta was low-lying. This was standard practice. Women, often with young families at home, sometimes had to spend up to 10 weeks in the hospital—a huge expense for both the patient and the health service. All that is a thing of the past, thanks

Fig. 36. Vaginal scan showing placenta previa, indicated by the lower arrow. The edge of the placenta is covering the cervix, indicated by the upper arrow. (Courtesy of Dr. A. P. M. Smith.)

to ultrasound. The placenta now can be localized and the vast majority of women treated as outpatients.

The introduction of placental localization was of great value as an aid to amniocentesis, and this will be discussed in more detail in the section on invasive procedures. Suffice it to say at this point that M.B.M. well remembers carrying out both early and late amniocenteses without the benefit of ultrasound and being frustrated by getting a dry or bloody tap, a situation virtually unknown today.

Diagnosis of placental abruption

Attempts were made to diagnose placental abruption with ultrasound in the early days by recognizing the presence of a retroplacental or an extramembranous clot, but it was realised that this diagnosis was best made clinically. Where most of the placenta had separated, the diagnosis was easy on ultrasound, but then it was also very obvious clinically and so ultrasound was unnecessary. In cases of a minor abruption, the diagnosis was difficult both clinically and on ultrasound, where the appearances were variable (Nyberg et al. 1987). The availability of color flow Doppler has been of some use in differentiating the appearance of a small clot from that of normal vasculature. Ultrasound has proved of limited value in the diagnosis of placental abruption.

Structure of the placenta

Fisher et al. (1976) reported their observations on placental aging using grey scale echography. They were probably the first to evaluate changes in placental structure by correlating them with placental function and fetal growth. They recognized that this was a potentially valuable method for assessing fetal well-being.

Grannum et al. (1979) in Yale proposed their detailed classification of placental grading. One of their main aims was to relate the appearances of the placenta to fetal lung maturity, thus removing the need for the current, at that time, practice of amniocentesis to establish lung maturity by measuring the lecithin/sphingomyelin ratio. They graded the placenta according to the appearances of the chorionic plate, the placental substance, and the basal layer. They described four grades, from 0–III, the most immature to the most mature, and correlated these with gestational age. Premature maturation of the placenta was associated with conditions such as preeclampsia. Recognition of these changes in placental appearance has been of value and has been included as part of the overall assessment of fetal growth and development.

An increase in placental thickness was noted in association with rhesus isoimmunization and diabetes and a decrease with preeclampsia and growth retardation (Grannum and Hobbins 1982). Tumours of the placenta, fortunately rare, have been recognized on ultrasound from an early stage (Asokan et al. 1978).

Umbilical cord

Abnormalities of the umbilical cord were known to be associated with congenital anomalies, and visualization of the cord and its three vessels was recognized as an important part of any fetal survey. Romero et al. (1988) reviewed the appearances of the cord in various pathologic conditions.

PRENATAL DIAGNOSIS

Diagnosis of structural abnormalities

The recognition of fetal abnormalities was the inevitable result of progress and improvement in image quality. The Australian group, Garrett, Kossoff and Robinson, in their approach to the development of scanning, had concentrated on constructing equipment specifically to provide as good an image as possible. This group was the first to produce really clear details of fetal anatomy, one of their early publications was entitled “Fetal anatomy displayed by ultrasound” (Robinson et al. 1968). A sound knowledge of normal features soon led to the recognition of abnormalities. Garrett et al. (1970) reported on “Prenatal diagnosis of fetal polycystic kidney by ultrasound.”

Ultrasound screening for fetal abnormalities now is offered routinely to many pregnant women, but can the reader imagine how it must have felt to diagnose an anomaly in the early days when there were few, if any, articles, textbooks, or videotapes available to allow comparison of the images? To recognize an abnormality on ultrasound has always required considerable expertise on the part of the person scanning and the total trust of the patient in that person. It is an unenviable task now. It was much more difficult then.

Campbell et al. (1972) published in the *Lancet* their article on “Anencephaly: early ultrasonic diagnosis and active management.” This was the first report of termination of pregnancy being carried out following the ultrasonic diagnosis of anencephaly (Fig. 37). In certain respects, making the diagnosis of anencephaly and proceeding with active management was relatively easy, because the condition is not compatible with independent existence; nevertheless, it was a landmark publication in terms of prenatal diagnosis.

The very term “prenatal diagnosis,” now fully accepted in the vocabulary of obstetricians, was not one that was used regularly in the early 1970s. With the advances in ultrasound together with the more widespread use of amniocentesis for chromosome analysis and the introduction of alpha-fetoprotein (AFP) screening, prenatal diagnosis of fetal abnormalities was established.

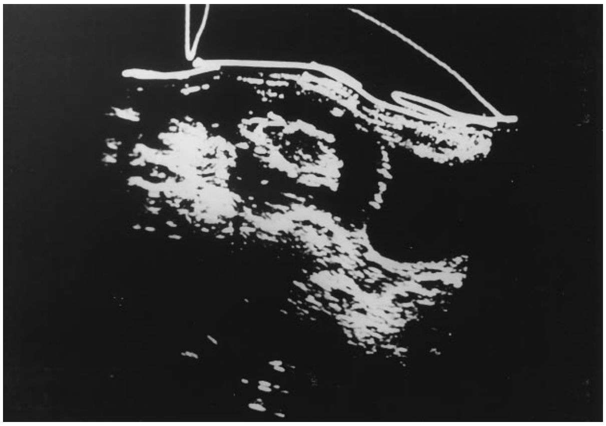

Fig. 37. Static B-scan image of an anencephalic fetus, 1972. (Courtesy of Professor Stuart Campbell.)

Fig. 39. Hydrocephalus seen in a longitudinal static scan of the fetus, head to the right, in late pregnancy, 1979.

Neural tube defects (Figs. 38 and 39) have lent themselves to detection prenatally. As a group, they were the first to be described in detail. Remember that these early diagnoses were made using static B-scanners, without the resolution we have come to expect today nor the flexibility and advantages of real-time transducers. Despite these limitations, Campbell accumulated a considerable experience using ultrasound for the prenatal diagnosis of neural tube defects, including anencephaly, spina bifida, encephalocele, and hydrocephalus. It must be noted that, in his early series, Campbell (1977) reported three cases of false-positive diagnosis using amniotic fluid AFP levels, resulting in the termination of four fetuses (including one set of twins). No anomaly had been seen on ultrasound in any of these cases, but at that time the amniotic fluid AFP level was considered to be a more reliable method of diagnosis than ultrasound, and action had been taken on the AFP alone. With hindsight, we know how wrong this was, but at the time it seemed the correct management. It was only following reports such as this that practice changed, until ultrasound gradually became accepted as the best means of diagnosis. Acceptance was accelerated by the introduction of real-time scanning. This, more than any other development, was the key to the mushrooming and burgeoning use of ultrasound imaging in obstetrics. Prophetically, Campbell (1977) wrote, "*Ultrasound examination of the head and spine by the method described in this paper (using the static B-scan) would be too time consuming for use as a method of routinely screening the obstetric population (but)....the linear array real-time machine, with the improvements in resolution that are likely to occur....may rival maternal serum alphafetoprotein estimation as a screening test for neural tube defects.*"

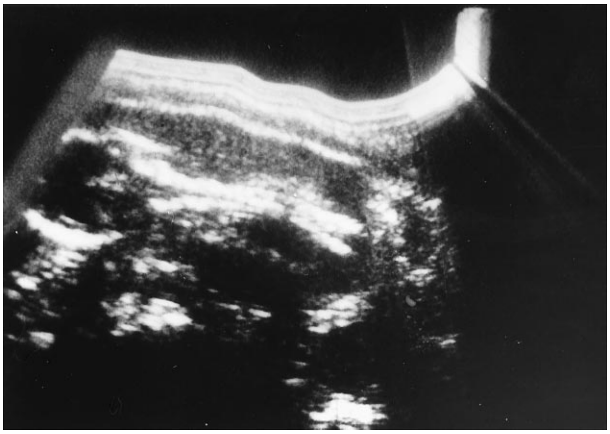

Fig. 38. Longitudinal static scan of the fetus, head to the left, showing spina bifida, 1979.

In a few short years, the breadth and scope of prenatal diagnosis expanded dramatically (Figs. 40–42). By 1982, "*The Radiologic Clinics of North America*" series devoted a volume to ultrasonography in obstetrics and gynecology (Callen 1982), which contained an article on normal fetal anatomy and three on abnormalities, including anomalies of the head, spine, thorax, abdomen, and skeleton. In 1983, the same publishers, W.B. Saunders Company, devoted a volume to ultrasound and its recent advances in the series, "*Clinics in Obstetrics and Gynecology*" (Campbell 1983). In the space of a year, the additions included articles on the prenatal diagnosis of congenital heart disease, invasive procedures, fetal activity, and fetal and uteroplacental blood flow. These latter developments will be described in more detail. There was also a rapid increase in the numbers of case reports of increasingly varied pathologic diagnoses made using ultrasound.

From the early days when only the crude outline of organs and structures could be identified, increasingly

Fig. 40. Longitudinal static scan of the fetus in late pregnancy, head to the right, showing fluid in the fetal chest, 1979.

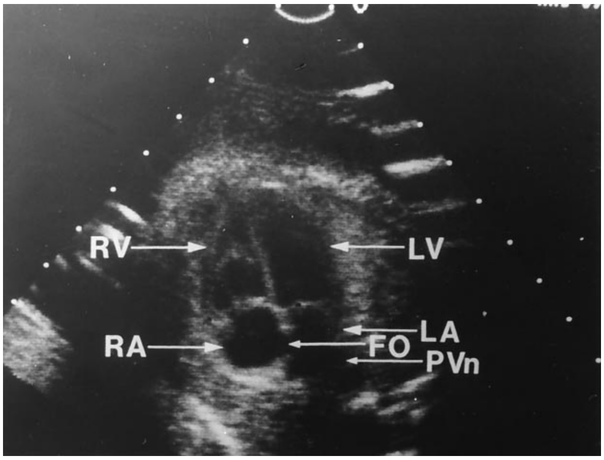

Fig. 42. Real-time scan showing a four-chamber view of the fetal heart, 1980. FO = foramen ovale; LA = left atrium; LV = left ventricle; PVn = pulmonary vein; RA = right atrium; RV = right ventricle.

finer detail became apparent—all due to technological developments. The clarity of detail continues to amaze both parents and sonographers. A careful scan has become an anatomy lesson in itself. More recently, the availability of the vaginal probe has facilitated the recognition of anomalies in the first trimester, and the introduction of 3D scanning has contributed to refinements in diagnostic capabilities. Such technology is becoming more widely available, easier and quicker to use, and no doubt will continue to facilitate the diagnosis of fetal abnormalities.

In parallel with the technical developments came the more complex diagnostic challenges, leading in some instances to confusion and concern both for the patient and the sonographer. Questions arose, such as "what is the significance of the presence of the isolated choroid plexus cyst at 18 weeks or nuchal thickening in the first trimester?" Opinions varied. Should patients be offered screening and, if so, when? What action should be taken if soft tissue markers are identified? Should we be concerned about maternal anxiety resulting from the availability of screening? Are we trying to achieve the perfect child? Ultrasound alone is not the reason for these questions. They are the result of the complex interaction of social and technological changes, not least of which is the development of the "new genetics." All those who scan in obstetrics are now in the position of having to face such questions and consider their response. Medical technology has not developed without attendant difficulties. There are many mothers today who would say of their own mothers, "Ignorance must have been bliss. It would be easier if I didn't know." On the other hand, there are many others who see prenatal diagnosis as a godsend. It is doubtful if the early workers ever considered the potentially far-reaching effects of their pioneering work.

Fig. 41. Oblique static scan showing ascites in the fetal abdomen, 1979.

Routine screening for fetal abnormalities

Reference already has been made to the role of ultrasound in dating pregnancies and screening for growth retardation. Another contentious area has been the question of routine screening for fetal abnormalities. Five major studies in Europe (Chitty et al. 1991; Levi et al. 1991; Luck 1992; Rosendahl and Kivinen 1989; Shirley et al. 1992) addressed the issue, and all provided evidence of the benefits to be gained from routine scanning. In the US, the RADIUS (routine antenatal diagnostic imaging ultrasound) study (Ewigman et al. 1993; LeFevre et al. 1993) showed an increase in the detection of fetal anomalies prior to 24 weeks' gestation. Criticism has been made of this study (Romero 1993). The con-

Table 4. Approaches to pregnancy screening in different countries

Year	Event
1974	Malmo, Sweden, two-stage scanning introduced, dating and 32 wk (Grennert et al. 1978).
1980	The Federal Republic of Germany introduced a similar two-stage programme (Mutterschaftsrichtlinien 1980).
1984	The RCOG, Great Britain, recommended a single routine scan (RCOG 1984).
1984	National Institutes of Health, USA, published a list of clinical situations in which the use of ultrasound would be supported (NIH 1984).
1986	Norway introduced a policy of a minimum of one scan at 17 wk (Konsensuskonferansen 1986).
1987	Iceland introduced a similar policy to Norway (Geirsson 1987).

troversy continues, but the trend has been toward implementation of routine scanning.

A recent report (RCOG 1997b) includes the following recommendations for screening for fetal abnormalities in Great Britain. Screening should be undertaken only after the objectives have been clearly identified for the woman prior to the scan. A two-scan regime is considered to be the ideal, the first primarily for dating in the first trimester and the second between 18 and 20 weeks, which is considered the most effective available method to detect a wide range of abnormalities.

We have made reference a number of times to screening all pregnancies with ultrasound. One of the difficulties in considering screening is that not all studies have addressed the same issue, such as dating, or used the same endpoint, such as a reduction in perinatal mortality. Therefore, comparisons are difficult to make, but it is interesting to note the approaches to screening in different countries (Eik-Nes 1993), as listed in Table 4.

Ultrasound-guided invasive procedures

Kratochwil recognized in the 1960s that ultrasound might prove very useful in selecting the best site for introducing a needle into the uterus. He was using an A-scope and developed a transducer with an axial hole through which a needle could be inserted. As one can imagine, this provided only limited information. It was the introduction of B-scanning into more general use that led to greater realisation of the potential for ultrasound for needle guidance. At that time, the clinical investigation requiring the insertion of a needle into the uterus was amniocentesis. The use of amniocentesis was becoming more widespread but, in the majority of cases, it was carried out "blind," not knowing the route the needle was taking and whether it was avoiding the fetus and placenta. It took some time for the role of ultrasound to be accepted. However, once the technique of ultrasound-guided needle puncture was established, it was clear that the method could be used for various purposes, including aspiration of fluid or tissue fragments, injection of drugs, and transfusion of blood.

Amniocentesis. The increasing use of amniocentesis for prenatal diagnosis occurred in parallel with the more widespread use of diagnostic ultrasound in the 1970s. Amniocentesis in the early second trimester provided fluid for cytogenetic studies, diagnosis of the inborn errors of metabolism, and measurement of AFP levels. In later pregnancy, it was valuable in the assessment of the severity of rhesus isoimmunization and in the prediction of fetal lung maturity by measurement of the lecithin/sphingomyelin ratio. Amniocentesis was utilized therapeutically in some cases to provide temporary relief from polyhydramnios.

Interestingly, it was estimated by Adams et al. (1982) that more than one million pregnant women aged over 35 years in the US would request antenatal karyotyping in the 1980s. This figure provides some guide to the increasing use of prenatal diagnosis and the corresponding increase in the role of ultrasound in obstetric care.

At first, ultrasound was used as an adjunct to amniocentesis. The technique using B-scan was as follows. The pregnant uterus was scanned and a mark made on the maternal abdomen over a pool of fluid that could be accessed, avoiding both fetus and placenta. The operator then washed his or her hands, cleansed the abdomen, and inserted the needle. By that time, the fetal position could have changed, and failure to obtain fluid could be the result. Not surprisingly, there was some scepticism as to the value of ultrasound prior to amniocentesis. There were conflicting reports from different workers on the incidence of dry or bloodstained taps and the need for multiple needle insertions. Evidence in favor of scanning came from Miskin et al. (1974), Nelson et al. (1977), and Crandon and Peel (1979). Those not convinced included Karp et al. (1977) and Hohler et al. (1978).

The need for scanning during the actual needle insertion became apparent, and the technique of ultrasound-guided needle puncture evolved. This was carried out either "freehand," where the needle was moved independently from the transducer, or using a needle guide attached to the transducer, allowing the needle to be inserted, and remain in, a chosen plane. The choice depended on the preference of the operator and the availability of equipment. The widespread use of the technique developed in conjunction with the increasing availability of real-time equipment, with continuing improvements in image quality and eventually Doppler and colour flow imaging. At one stage, attempts were made to improve the identification of the needle tip (McDicken et al. 1984), but the need for this was less important when resolution, in general, was so much better.

The benefits of simultaneous ultrasound in reducing the complications of amniocentesis (Romero et al. 1985; Williamson et al. 1985) were accepted, and now failure to use ultrasound at the time of the procedure could be a subject for litigation.

Amniocentesis was carried out primarily during the second and, to a lesser extent, the third trimester, although theoretically it could be performed from a much earlier stage. The limiting factors were unrelated to ultrasound but to the small number of cells available for culture and the complications resulting from the removal of a relatively large proportion of the fluid.

Fetoscopy. Ultrasound played no part in the first attempts to introduce endoscopes into the pregnant uterus. Mandelbaum et al. (1967) described their unsuccessful efforts at amnioscopy for prenatal transfusion—a concept that was to be developed further, as we shall see later. Valenti (1972, 1973) was able to obtain fetal blood and skin biopsies. Scrimgeour (1973) described an open technique requiring laparotomy and uterine incision under general anaesthesia, almost a precursor of the open fetal surgery, which will be described. The major advance in fetoscopy was the development of a fine 1.7-mm endoscope, which could be inserted transabdominally through a 2-mm cannula, with a side channel for needle insertion. This led to an increase in the use of the technique for clinical purposes. It was clear to the operators that the field of vision through the fetoscope was quite restricted, and it was best to scan the patient first and determine what would be the best direction in which to insert the endoscope so that the point of interest, whether the cord root or a particular aspect of the fetal anatomy, would be in the field of view.

Two groups published their results, showing that fetal blood could be obtained successfully by the fetoscopic method (Hobbins and Mahoney 1977; Patrick et al. 1974). The technique became established, not only for blood sampling but also for skin and liver biopsies, and for examination of the fetus where an abnormality was suspected but could not be seen in sufficient detail on ultrasound alone. The initial reports described the method of obtaining blood from a vessel on the surface of the placenta. Complications of this approach included contamination with maternal blood and/or amniotic fluid and difficulty in sampling from an anterior placenta. Rodeck and Campbell (1978) described an alternative approach, sampling the umbilical vein, which proved more accessible and less liable to prolonged bleeding after needling.

Fetal blood sampling. Fetoscopy was restricted in its use to a few specialized centers. As ultrasound technology continued to develop, it became possible to visualise a needle more easily and, therefore, place it more accurately within the amniotic sac. This enabled more centres to attempt fetal blood sampling. The French group Daffos et al. (1983) reported their success in obtaining pure fetal blood by direct aspiration from the umbilical cord under ultrasound guidance, performed as an outpatient procedure. These results were considered encouraging, but the method needed to be evaluated in a larger number of patients. Evaluted it was, and the technique quickly became accepted as the method of fetal blood sampling. Either the umbilical vein or an artery could be punctured, with the vein being easier because it has a larger diameter. Various names have been used to describe the technique, including cordocentesis and PUBS (per umbilical blood sampling). Improved resolution and colour flow, together with well-developed operator skills, have led to great precision in the placement of needles, reduction in complications, and more widespread use of the technique.

The larger the target area, the easier needling will be. This was probably the reasoning behind the use of cardiac puncture as a means of obtaining fetal blood. Bang (1983) in Denmark first reported its use, and he is the best known proponent of this method, which has been shown to be remarkably free of complications. Perhaps because of the nature of the target, it has found less favor with many workers who prefer the umbilical cord approach.

The availability of fetal blood made possible a wide range of prenatal diagnoses requiring biochemical, hematologic, or genetic analyses and could be used to identify fetal infection. Concern about fetal distress in the severely growth-retarded fetus led some investigators to carry out fetal blood sampling for blood gas analyses (Soothill et al. 1987). This failed to find universal favor as other methods, such as Doppler assessment of blood flow, became more widespread, providing useful information and making blood sampling, an invasive technique with potential complications, less attractive.

Chorionic villous sampling. Chorionic villous sampling (CVS) was developed in China in the 1970s for fetal sex determination. Thereafter, it was realized that it could be developed as a method of first-trimester diagnosis of all the conditions that were, at that time, restricted to detection following second-trimester amniocentesis. The prospect of early diagnosis enabling surgical termination of pregnancy under general anesthesia had much to recommend it. Termination at any stage is traumatic for the mother, but first-trimester diagnosis and management was considered preferable to later intervention.

The initial description of the technique of CVS utilised the transvaginal approach, with the introduction of a cannula through the internal cervical os and placement at the lower edge of the implantation site from where chorionic villi could be aspirated. At first, sampling was carried out blind, with the introduction of ultrasound for more accurate placement of the cannula at a later date (Brambati et al. 1985; Hogge et al. 1985).

As abdominal needling became easier and more acceptable, there was a move toward this approach for CVS (Gilmore and Aitken 1989). In most cases, the patients found the abdominal route preferable to the less dignified vaginal approach, and many workers found that all methods of abdominal needling were basically very similar, requiring the same manual dexterity and skill, making the vaginal route less attractive. As in so many instances, there were proponents of both approaches. In the best hands the techniques had similarly low complication rates (Jackson 1987).

Other fluid and tissue sampling. It became possible to aspirate any fluid collection such as ascites, fluid in the chest, a dilated bladder or renal pelvis, or any cyst for diagnostic purposes. Fetal skin and liver biopsies also were described (Anton-Lamprecht 1981; Elias et al. 1980; Golbus et al. 1980; Rodeck et al. 1982a). These were used initially for the diagnosis of rare congenital abnormalities. As technology progressed and the genetic basis for some of these conditions became known, the need for the biopsy technique was reduced because diagnosis then could be made by DNA analysis. This is an additional example of the complex interactions between developing technology and its practical applications.

Implications of prenatal diagnosis

The rapid expansion of diagnostic capabilities using ultrasound was followed by the first faltering steps toward fetal therapy. The path was fraught with difficulties, and there was a very frustrating time when many anomalies could be recognized on scanning but nothing could be offered to parents to treat the condition. This led to ultrasound being considered as being of use only to identify problems that were dealt with by termination of the pregnancy. Hence, the "search and destroy" analogy that was heard in the early days of prenatal diagnosis and still lingers on today.

Termination of a pregnancy because of the presence of fetal abnormality should be considered in conjunction with the development of prenatal diagnosis and should be set against the background of the social changes of the late 1960s and 1970s. There was a move away from the traditional, paternalistic, imposed behavior patterns toward freedom of choice and individual autonomy. Changes in the law relating to abortion were introduced in many countries. It is unlikely that prenatal diagnosis would have developed as it did if the facilities for termination had not been available.

There is a certain irony in this, in that we know that Ian Donald was opposed to abortion—indeed, it is very probable that he was not offered a knighthood in recognition of his contribution to the development of ultrasound because of his stance on the abortion issue. The issues surrounding abortion were the subject of much public debate prior to its legalization in Great Britain in 1967. One can only wonder what would be the reaction now of Donald and the other early pioneers to some of the clinical applications of ultrasound.

An interesting dilemma for many was the question of the use of ultrasound or ultrasound-guided procedures for fetal sexing, with a view to termination of the pregnancy if the sex was not the desired one. In cases of X-linked inherited disease, fetal sexing was used so that potentially affected males could be aborted. Subsequent developments in genetic technology have meant that a more precise risk for a male being affected can be given on DNA testing and, therefore, fewer parents are in the position of choosing to have all males aborted. The more contentious issue is the termination of female fetuses (Marfatia 1980), mainly in cultures in which the female is regarded as having a secondary role to the male.

Intrauterine therapy

Ultrasound was crucial in the development of prenatal diagnosis, and it has played an equally important role in the development of fetal therapy.

The diagnosis and management of different fetal conditions is outside the scope of this article. Indeed, it would take several textbooks to convey the intricacies of the subject. The purpose of including examples of different diagnostic and therapeutic procedures is to put them into the historical context of the development of ultrasound and its clinical applications.

Rhesus isoimmunization. The *in utero* treatment of rhesus isoimmunization by intraperitoneal transfusion was first described by Liley (1963) using x-rays and contrast media to facilitate accurate placement of a needle in the peritoneal cavity. With the advent of ultrasound allowing first fetoscopy and subsequently direct needling of umbilical vessels, the potential for transfusion under ultrasound guidance quickly was realized (Bang et al. 1982). Once more, the hazards of radiation could be avoided by the use of ultrasound. Direct intravascular transfusion of the fetus became standard practice for the treatment of rhesus isoimmunization. The umbilical vessels, either at the fixed placental end of the cord or the intrahepatic portion of the umbilical vein, were the sites of choice for transfusion. In certain cases, intraperitoneal transfusion was carried out either as an alternative to the intravascular route if this had proved difficult for technical reasons, or as an adjunct to the intravascular route to allow for a longer time interval between transfusions. A major advantage of direct intravascular transfusion was that the fetal haematocrit could be measured at the start of the procedure, enabling the volume of blood required to be calculated, and the haematocrit was checked again at the end of the procedure to ensure that the appropriate amount of blood had been given or more was given if required. In some severely affected cases transfusion commenced as early as 18 weeks' gestation and was repeated every 2–3 weeks until delivery.

Any condition in which anaemia is a feature, such as fetal parvovirus infection, potentially became amenable to treatment by intravascular transfusion.

Hydrocephalus. In the early days of prenatal diagnosis of fetal abnormalities using ultrasound, one of the more easily recognized anomalies was hydrocephalus. It seemed logical to suppose that if ventricular decompression was the treatment of choice after delivery, then this should be considered *in utero* to prevent further ventricular dilatation, increase in intracerebral pressure, and resulting damage to cerebral tissue. Clewell et al. (1982) reported the first surgical approach to the treatment of hydrocephalus *in utero*, and other cases followed. Treatment was either by single or repeat ventriculocentesis or by the insertion of a ventriculo-amniotic shunt (Vintzileos et al. 1983).

Patient selection was of great importance (Chervenak et al. 1985). With the benefit of hindsight, it was recognized that intervention had been inappropriate in some cases because of the presence of other anomalies. This serves as a good example of the learning process, which had to be experienced before it became obvious that, on recognizing one fetal abnormality, there was a need to search for others that might influence management of the first, particularly if an invasive procedure was being considered as a therapeutic option. This search would involve a careful detailed ultrasound inspection of the fetal anatomy and would include discussion of the role of karyotyping. This is now well-recognized good practice, but in those early days it had to be learned.

Initial experience in animal models in the treatment of antenatally diagnosed hydrocephalus was encouraging (Michejda and Hodgen 1981), but sadly this was not borne out in the human situation. One very useful outcome of the early attempts at various interventional procedures was realization of the need for international cooperation in the collection of data and sharing of information when such small numbers of patients were involved. This resulted in the formation of an international fetal surgery register.

By reporting individual experiences, the accumulated data showed, earlier than might otherwise have been possible, the overall poor results obtained following intrauterine treatment of hydrocephalus (Manning et al. 1986). The varied aetiology of hydrocephalus and its association with other abnormalities now is better recognized. In retrospect, it was rather optimistic to expect that a simple shunt would be of benefit in many cases.

Obstructive uropathy. Another area where invasive therapy was the subject of much debate was the management of obstructive uropathy by insertion of a vesico-amniotic shunt (Berkowitz et al. 1982; Glick et al. 1984). The condition lent itself to ultrasound diagnosis, and it seemed logical to suppose that, by relieving the obstruction, one would improve the outcome for the affected fetus. Results were highly variable (Manning et al. 1986), and the key to a successful outcome was seen to lie in the selection of the patient most likely to benefit. Clearly, there was a spectrum of involvement of the renal tract. In the mild case where there was a unilateral obstruction and a normal amniotic fluid volume, intervention was not indicated. Similarly, at the other end of the spectrum where there was bilateral obstruction, profound oligohydramnios, and evidence of abnormal renal function, it was highly unlikely that any improvement could be anticipated no matter what treatment was given. Indeed, to intervene may have caused more harm than good. It was recognized that, in order to benefit from the placement of a vesico-amniotic shunt, the fetus was most likely to have bilateral obstruction and a reduction in amniotic fluid, but evidence of continuing renal function without any other abnormalities being present. Ultrasound was shown to be essential for diagnosis and appropriate management.

Open fetal surgery. Garrett and Kossoff (1976) were the first to publish their views on the selection of patients for fetal surgery. Harrison, a paediatric surgeon, and his colleagues made open fetal surgery a reality (Harrison et al. 1984). They had been frustrated in cases of congenital diaphragmatic hernia (CDH), where the diagnosis had been made on ultrasound at about 20 weeks' gestation. At that time, they knew that there was nothing that could be done until after delivery to help the fetus and allow normal lung development to take place. If only the hernia could be repaired when it was first recognised—basically a simple surgical procedure—but the fetus was not accessible....or could it be? Harrison recognized the need for as great an understanding of the pathophysiology of the development of CDH as possible and began his careful research in the animal model before embarking on any attempt at treatment of the human fetus.

The culmination of the early work by Harrison and his colleagues at the University of California was the establishment there of "The Fetal Treatment Program," with its co-directors Harrison, Golbus, and Filly—a paediatric surgeon, an obstetrician, and a radiologist—a good example of the multidisciplinary approach to which we made reference before. This time the collaboration of clinical colleagues from different specialties illustrates the benefits to be gained compared with the earlier association of clinician, engineer, and physicist.

The California group first reported their research on lambs in whom CDH had been created and subsequently corrected at open operation. The fetus was exteriorized for the procedure and replaced in the uterus thereafter. There were many difficulties to overcome, particularly in preventing or delaying the onset of premature labor, before it was felt reasonable to attempt repair in a human fetus (Harrison et al. 1990). A number of cases have been treated since then, but the results overall have been somewhat disappointing (Flake and Harrison 1995; Sullivan and Adzick 1994). The disadvantages in terms of complications and poor outcomes (Bealer et al. 1995) seem to outweigh any advantages, and the technique has not found universal approval.

Minimally invasive surgery. The move from the open approach to minimally invasive surgery in children and adults found application in the fetus. Endoscopic access avoids the problems of fetal exposure, hypothermia, and loss of amniotic fluid, and it may reduce the risk of preterm labor. MacMahon et al. (1992) reported the first endoscopic vesicostomy, Estes et al. (1992) proposed the endoscopic route for the treatment of various anomalies, and Quintero et al. (1995) described percutaneous cystoscopy and fulguration of posterior urethral valves. Deprest et al. (1997) reviewed the current situation, highlighting the need for the development of animal models as a very necessary step in the evolution of endoscopic surgery for the human fetus. Conditions that particularly lend themselves to correction *in utero* include diaphragmatic hernia, in which tracheal occlusion may prove the treatment of choice and obstructive uropathy. This is an area where research is ongoing, and ultrasound has a continuing role in the insertion and placement of the endoscopes through which surgery can be attempted. Not only will ultrasound be important in the diagnosis of fetal abnormalities, but it should make a major contribution to the development of techniques for their correction.

The fetus as a patient

The ability to visualise the fetus and directly access any area, particularly its vascular system, opened the floodgates for both diagnostic and therapeutic possibilities. Thereafter came the development of surgical techniques both *in utero* and on the exteriorised fetus. From an early stage, it became clear that one could no longer consider the care of the pregnant patient only in maternal terms, but the fetus was coming to be considered as a patient in its own right. But what were these rights? When, if ever, should fetal rights take precedence over maternal rights? The stage was set for much debate over the legal issues relating to potential conflict between mother and fetus. This debate has continued over the last decade or more, and evidence is seen in the various textbooks dedicated to ethical dilemmas in obstetric practice (Bewley and Ward 1994; Goldworth et al. 1995). In most instances, there is no need for conflict, because the facts are quite clear and the wishes of the mother are in the best interests of the fetus and there is no disagreement. Difficulties arise when the potential benefits and the disadvantages of certain interventions are not clear-cut, and there is room for considerable difference of opinion not just between the mother and her obstetrician but among the medical professionals themselves. The rights of the father, if any, depending on the law of the country, also may contribute to additional confusion and debate. Sadly, it has been necessary to resort to the legal process in order to resolve conflicts in deciding upon the management in certain cases.

OTHER USES OF ULTRASOUND IN OBSTETRICS

The cervix

Sarti et al. (1979) described the ultrasound appearance of the dilated cervix during pregnancy, and Brook et al. (1981) reported their experience using ultrasound in the diagnosis of cervical incompetence in pregnancy. Many other publications followed. Wheelock et al. (1984) were among those who suggested that ultrasound would be of assistance in cervical cerclage. Anderson and Rayburn (1993) reviewed the role of ultrasound in cervical incompetence, and Quinn (1993) detailed the role of vaginal scanning in this field.

Postpartum

The potential value of ultrasound in scanning the postpartum uterus was reported by several of the early investigators, including Robinson (1972) and Malvern and Campbell (1973). Since then, ultrasound has had a role in the management of the postnatal patient, as reviewed by Lavery and Shaw (1993).

SUMMARY

It has been estimated that, as the twentieth century draws to a close, there are some 250,000 ultrasound machines worldwide and some 250 million scans carried out each year (Blackwell 1995). A large proportion of

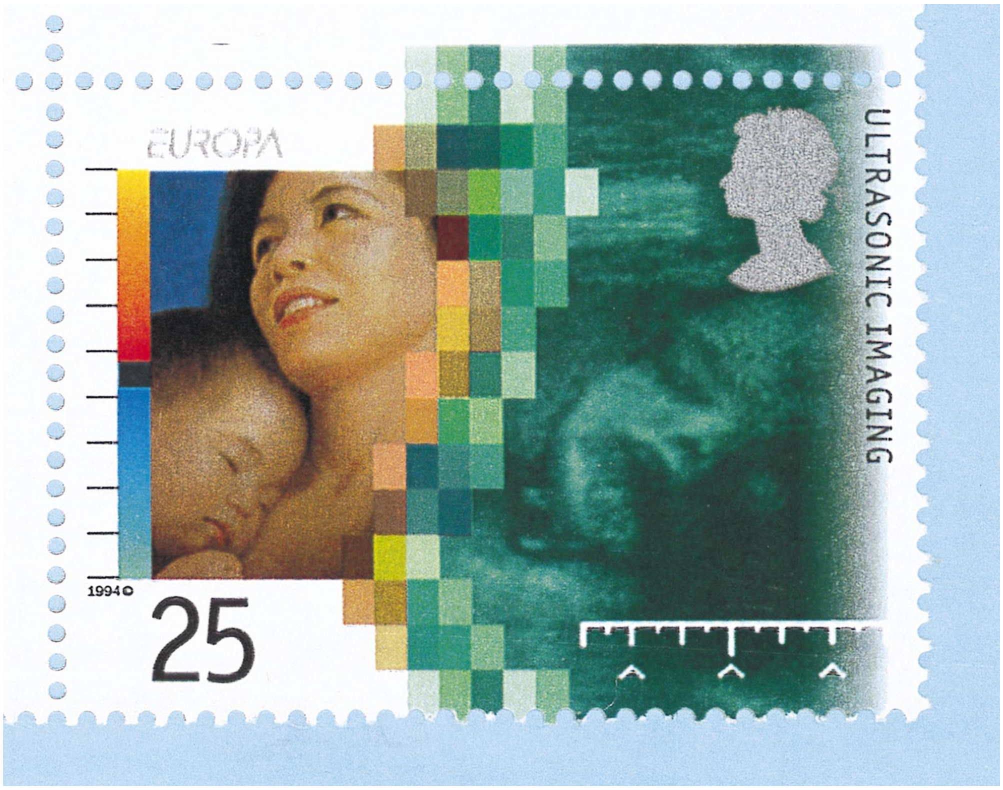

Fig. 43. British 25p stamp "Ultrasonic Imaging" in the Medical Discoveries Series, issued in 1994. (Left-hand illustration attributed to Jean-Paul Tibbles; right hand image courtesy of Acuson Corp. © The Post Office 1998. Reproduced by kind permission of the Post Office. All rights reserved.)

these scans will be on obstetric patients. This is testimony to the pioneers of diagnostic imaging and those who pursued its clinical applications. The impact of ultrasonic development was recognised in Britain by the commemorative issue in 1994 of the Royal Mail Medical Discoveries Series. The 25p stamp (Fig. 43) showed a mother and child and the ultrasound image of a fetal face.

We set out to record the major developments in ultrasound imaging in obstetrics since Donald first used the technique to visualize the fetus in 1957. From Donald, MacVicar. and Brown's first paper in 1958, the number of publications escalated to 298 in 1978 (Fig. 44), a total of 2009 over the 20-year period (White et al. 1982). We have tried to provide a glimpse into the circumstances surrounding the work of the early pioneers that led to the many and various clinical applications. Omissions undoubtedly will have occurred, and for these we apologise. No offence is intended. Further details may be obtained by reading the original article, listed in the references, and our sources of information, which are noted in the acknowledgements. This article is best read in conjunction with the others who have contributed to this series on the history of the development of ultrasound imaging as a diagnostic tool.

The authors have tried to ensure that the contents of this article are factually correct. They would appreciate it if errors or omissions are brought to their attention so that they may be corrected in time to be incorporated into

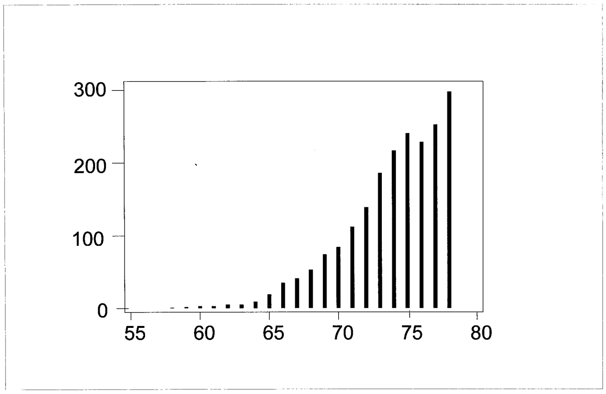

Fig. 44. Histogram of the number of articles published on ultrasound in obstetrics and gynaecology in the period 1958–1978. (From White et al. 1982.)

the book on "The History of Ultrasound," in which the contents of the individual articles on developments in each specialty will be brought together. Publication is planned for early in the new millenium.

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