FETAL ECHOCARDIOGRAPHY

By

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Organisation of the Thesis

The first three chapters are introductory. Chapter 4 lays out the overall study design and patient material. Chapters 5-10 deal with various aspects of the echocardiographic study mainly in the normal fetal heart. Chapters 11-13 describe abnormalities seen in the fetal heart during the study. Details of the methodology of the different aspects of echocardiography in the fetus are described in the appropriate chapters. There is a discussion section in each chapter of results. Chapter 14 details the follow-up studies and summarises the results. Chapter 15 is the conclusion chapter with overall discussion of the technique and its potential application.

Note on Terminology

Ultrasound imaging techniques which display the cardiac anatomy as a moving pictorial image are variously designated as two-dimensional, real-time or cross-sectional echocardiography. Most correctly the technique should be called real-time cross-sectional echocardiography but the clumsiness of this term makes it impractical. Cross-sectional echocardiography was the term preferred throughout the text but two-dimensional was occasionally used as an equivalent term, as it is in the literature.

Acknowledgements

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Summary

Congenital heart disease is the commonest form of congenital malformation. Approximately 8/1,000 live born infants are affected in this country. Over half the deaths from congenital heart disease occur in the first year of life. Delay in diagnosis of a defect is an important contributor to morbidity and mortality in early infancy. Prenatal diagnosis of a defect will therefore optimise the chances of survival of an affected infant.

The cross-sectional echocardiogram is becoming an increasingly useful diagnostic tool in the study of congenital heart disease post-natally. Experience of the echocardiographic appearances of cardiac malformation is expanding and becoming increasingly accurate and reliable. This study was undertaken therefore, in order to find out if the fetal heart could be visualised; if visualisation were possible, in how much detail normal characteristics could be identified; at what gestational age this could be done; if structural abnormality could be identified and with what accuracy.

The fetal heart of 647 pregnancies was examined by real-time cross-sectional ultrasound. An initial series of 200 unselected pregnancies was studied and the anatomical

details which could be visualised in the normal heart were described. It was found possible to identify positively the venous, intracardiac and arterial connections of the fetal heart in every case between 16 weeks gestation and term. The gestational age range at which the fetal echocardiographic study was found to be easiest was between 18 and 28 weeks. The echocardiographic interpretation of cardiac sections was validated by indirect anatomical studies which took place during this initial series. Anatomical validation was undertaken because the fetal echocardiogram was not found to be identical with the echocardiographic appearances of the heart in post-natal life.

A series of 28 pregnancies, about to undergo mid-trimester termination, were studied to provide direct anatomical correlation with echocardiographic findings. Five structural abnormalities were detected echocardiographically within this group, and the ultrasound and anatomical findings compared. Three false negative and one false positive diagnosis were made in this early series.

Pregnancies at increased risk for congenital heart disease in the fetus were subsequently selected for study. These "high-risk" groups included those with a family

history of congenital heart disease, cases of maternal diabetes, or pregnancies in which fetal extracardiac abnormality, fetal arrhythmia or fetal ascites had been detected. Thirty-six structural or functional cardiac abnormalities were detected during this part of the study. Each case is described and discussed and the validation of the findings, either anatomically or by postnatal examination detailed. Prenatal diagnosis of cardiac malformation became more reliable and accurate as experience increased.

Once experience with the cross-sectional echocardiographic examination became established it became possible to expand the echocardiographic study to include the M mode echocardiogram and a fetal electrocardiogram.

The M mode echocardiogram provided additional information to the cross-sectional study. Cardiac wall and valve motion could be studied, timing of events within the cardiac cycle could be made more accurately and measurement data for intracardiac chambers acquired. The structures measured were septal and posterior left ventricular wall thickness, aortic root and left atrial internal dimensions, left and right ventricular internal dimensions. Growth charts for these parameters in the normal heart were constructed throughout pregnancy. The availability of normal measurement data was of value in the elucidation of structural cardiac abnormality.

Functional characteristics of the left ventircle were derived using the M mode echocardiographic data and compared with postnatal measurements. The systolic time intervals of the left and right ventricles could be compared using the fetal electrocardiogram.

Examination of the fetal heart is already becoming incorporated into routine obstetric scanning. Thus a screening test can be established for the commonest group of congenital anomalies, congenital heart disease. The technique of fetal heart study can be readily learnt and quickly performed by a experienced ultrasonographer. Differentiation of the normal from the abnormal heart and referral of suspected abnormalities to specialised centres will allow concentration of experience. Antenatal management and delivery within a centre equipped to provide paediatric cardiac investigative and surgical facilities will in the long term contribute to improve the high infant mortality from congenital heart disease.

CHAPTER 1

INTRODUCTION

The importance of congenital heart disease in paediatric practise

During the twentieth century many changes have occurred in the pattern of paediatric practise in the developed countries. The overall mortality rate in childhood has fallen (1). This is shown in Figure 1.1. Using data published by the Registrar General for England and Wales, the fall in death rate per 1,000 living children, in four age groupings between 1900 and 1970, can be seen. In the first half of the century, infections, birth injury and immaturity were the main causes of paediatric mortality and morbidity and this remains true in the third World. This is seen in Figure 1.2. The causes of mortality in childhood are compared in Venezuela and England and Wales in 1967.(2). As Figure 1.2. demonstrates, congenital anomalies in England and Wales are of much greater relative importance throughout childhood, than in a developing country. That this has been a change in relative importance is shown by Figure 1.3. The death rate between 0-14 years from four major causes, infection, immaturity, birth injury and congenital anomalies are shown in 1939-1941 and in 1974-1976 (3). The greatest reduction in mortality in childhood have related to the control of infection and improved obstetric care. Decreasing mortality from infection in childhood has been due to

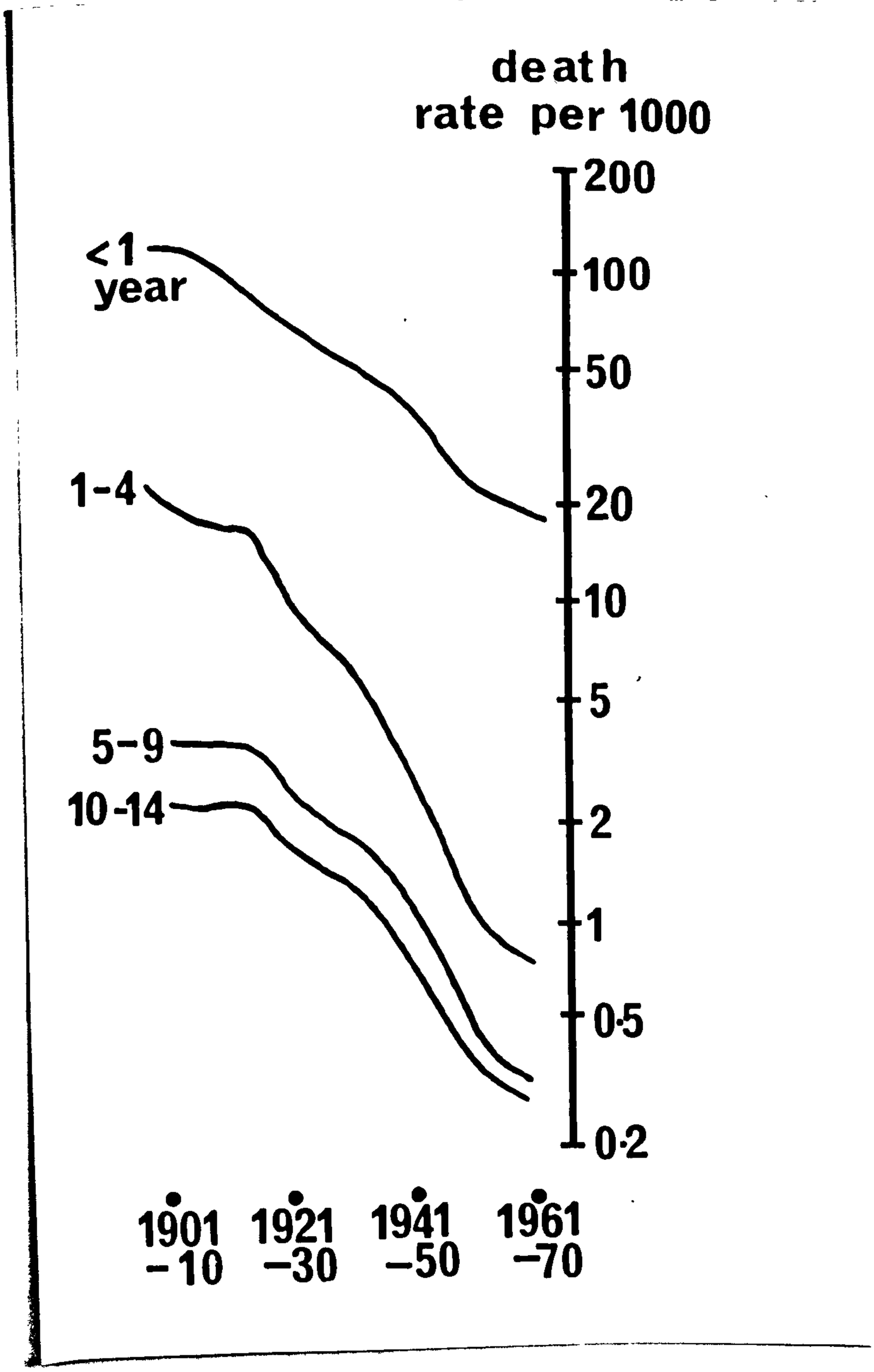


Figure 1.1. The death rate per 1,000 living children in age groupings, less than one year, 1-4 years, 5-9 years, 10-14 years is shown between 1900 and 1970 using statistics published by the Registrar General.

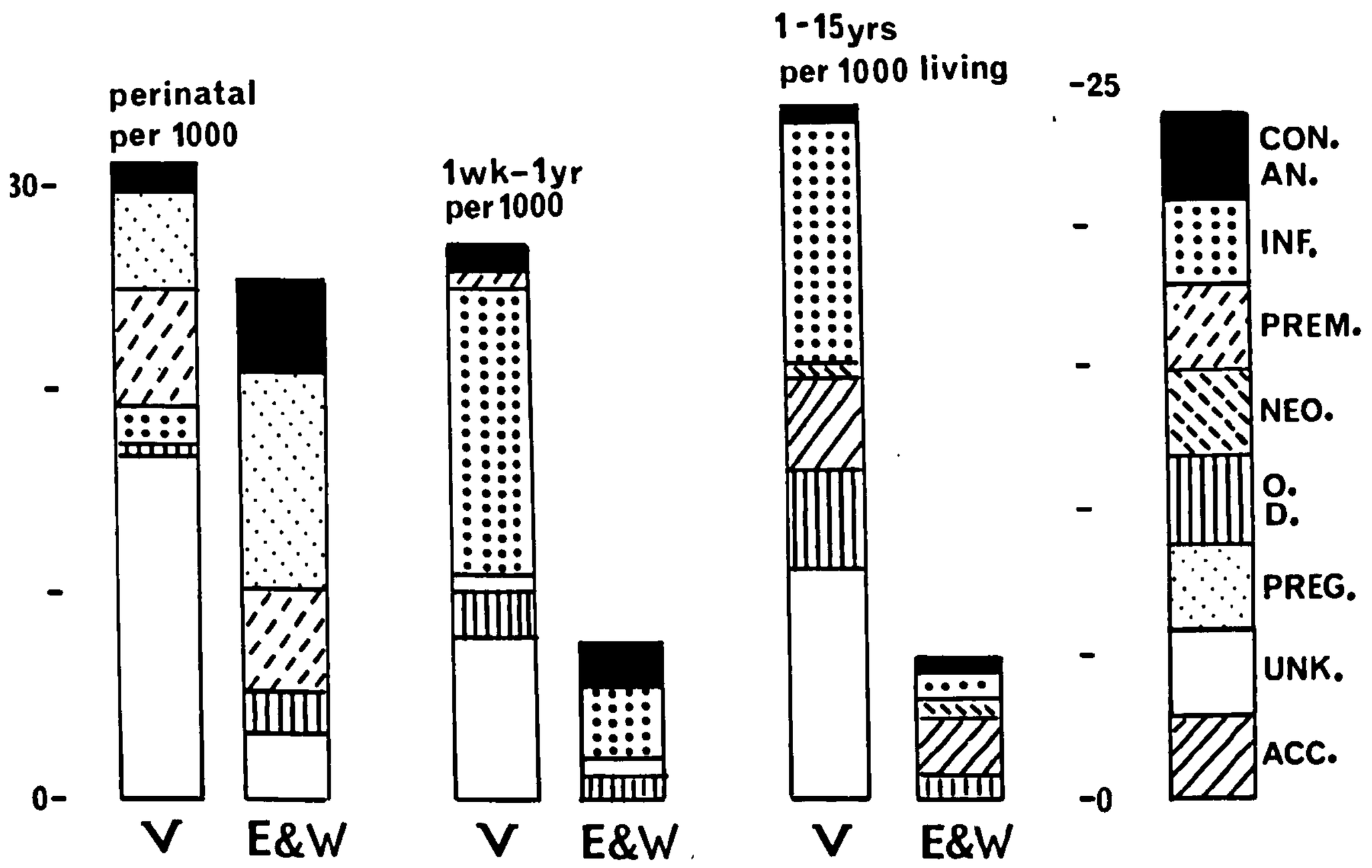


Figure 1.2. The causes of death in 1967 are compared between a developing country, Venezuela, and England and Wales, in three age groupings, perinatal, 1 week to 1 year and 1-15 years. Con. An. is congenital anomalies, Inf. is infection, prem. is prematurity, neo. is neoplasms, O.D. is other defined causes, preg. is complications of pregnancy, UNK. is unknown causes and Acc. is accidental death.

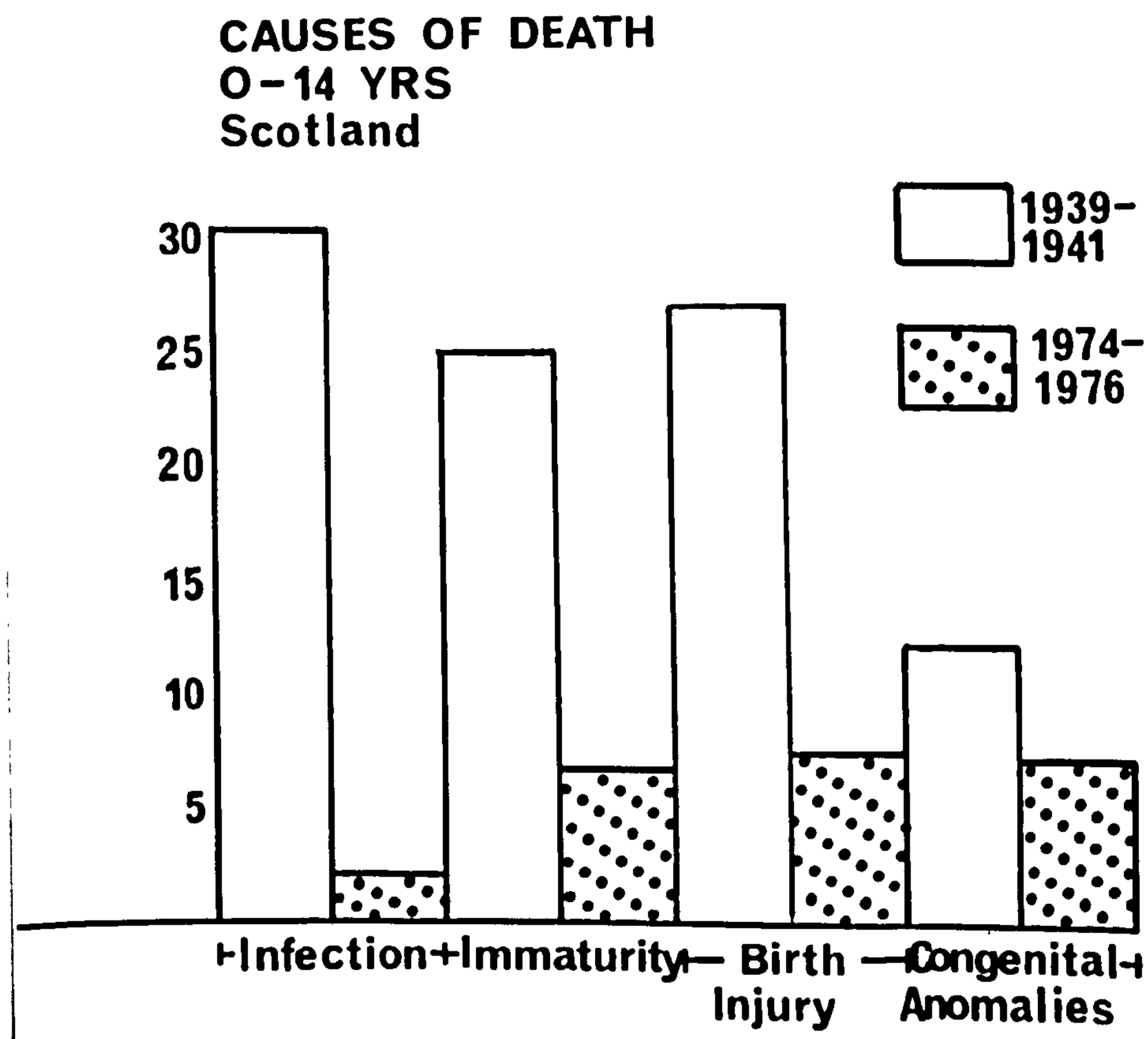


Figure 1.3. The fall in death rate from four causes, infection, immaturity birth injury and congenital anomalies is seen. The years 1939-1941 and 1974-1976 are compared.

improvement in standard of living, diet and public health measures as well as more specific immunisation and anti-biotic therapy (4). Improved obstetric care, coupled with improving standards of living, have reduced the incidence of both immaturity and birth injury (5,6). Although Figure 1.3 shows that the death rate from congenital anomalies has also decreased since 1939-1941 the change is less than for other causes of death. Approximately 25% of deaths in childhood are now due to congenital anomalies (3). Thus congenital anomalies are of increasing importance in paediatric practise.

The overall incidence of congenital anomalies will depend on the definition of terms, the method of ascertainment, the nature and size of the population studied, the length of follow-up and whether still births are included or not (7). Despite these difficulties in ascertainment several studies conclude that the incidence of major congenital defect is at least 2% of newborns with a further 4% showing genetic or developmental abnormalities of some degree (7,8,9). One of the commonest congenital defects is congenital heart disease (8). The factors influencing the recorded incidence of congenital abnormality apply equally to the recorded incidence of congenital heart disease (10). The reported incidence of congenital heart

disease varies widely from 4.23 per 1,000 total births (11) to 8.8 per 1,000 in a more recent publication (12). The accuracy of some of the very low incidences must be questioned. In general the larger the series the more accurate the incidence should be, but in a very large series the use of multiple sources for ascertainment of necessity detracts from the accuracy. Hoffman and Christianson (1978) (12) studied a cohort of 19,502 births, a relatively small series, but because of the nature of the population very few cases of congenital heart disease were thought to have been missed. On the other hand in their series social class V was underrepresented,which might influence the incidence of some congenital heart defects (13). Carlgren (1959) (14) followed up all children born alive in Gothenburg, Sweden, from 1941 to 1950 for a minumum of seven years. He found 369 cases of congenital heart disease in 58,105 children, an incidence of 6.4 per 1,000 live births. Mitchell (1971) (15) in a study of 56,109 total births found an incidence of 8.14/1,000 with an average follow up of 3 years. The importance of the length of follow up was shown by a study from Birmingham, England where the recorded incidence rose from 2.2 per 1,000 at two weeks after birth to 4.2 per 1,000 with a six year follow up (16). This is further shown by Hoffman and Christianson (12) where the diagnosis of congenital heart disease was made in 46% by age 1 week, 88.3% by age 1 year and 98.8% by age 4 years.

Some studies found the inclusion of still births to minimally affect the incidence of congenital heart disease; for example in the Liverpool series (10) the incidence was 6.6 per 1,000 total births and 6.5 per 1,000 live births. However, Hoffman and Christianson critically assessed their autopsy reports in 221 still births and found that only 166 reports included descriptions of the heart. The incidence of congenital heart disease in the more detailed group of still births was 10.2 percent, the incidence of more severe defects being much higher in the still birth than live born series. This would indicate that the inclusion of still births in an estimation of the rate of congenital heart disease would greatly increase the incidence. This confirms the finding of Richards (1955). Their incidence of congenital heart disease rose from 0.7 to 0.83 if still births were included (17). In summary, therefore, the incidence of congenital heart disease lies between 6.4 per 1,000 live births and 8.8 per 1,000 total births if all the series with the least inaccuracies are considered (10,12,14 & 15).

Not only is congenital heart disease the commonest form of congenital anomaly but it also is responsible for nearly half the deaths in childhood due to congenital anomalies. Results published in England and Wales in 1973

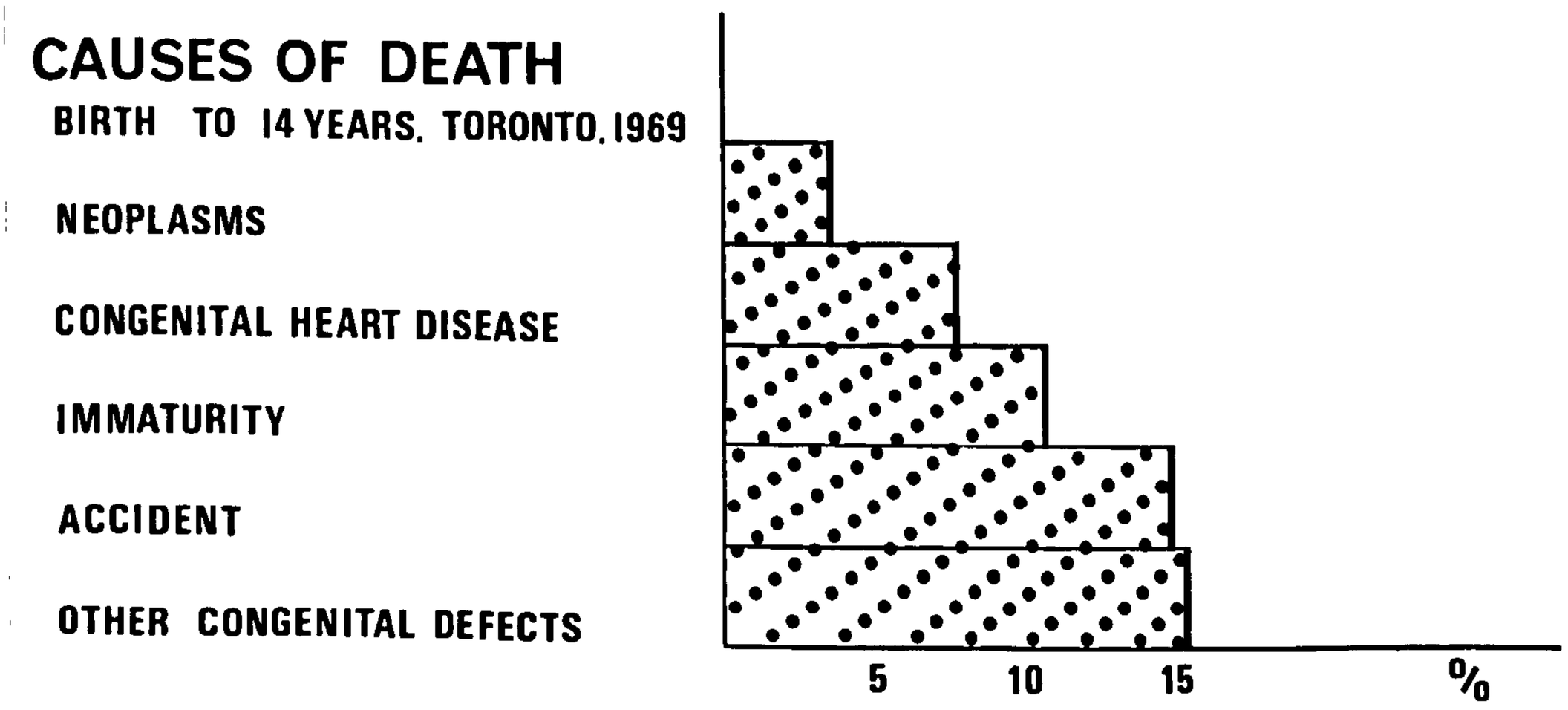


Figure 1.4. The main causes of death between birth and 14 years are seen in a series published from Toronto in 1969. All congenital defects cause nearly a quarter of the deaths in childhood, congenital heart disease causing approximately 8% in this series.

occurred (22) but more specifically the advent of balloon atrial septostomy for transposition of the great arteries (23) and the use of prostaglandins in neonates (24,25) are examples of some advances which have dramatically altered the mortality from congenital heart disease in infancy (26,27,28). Simultaneously the results of surgical palliation or correction of anomalies in infancy have greatly improved (26,29,30,31,32). One of the most important factors influencing survival in infants with congenital heart disease is the clinical state at presentation. The degree of acidosis at presentation in a recent series of infants with total anomalous pulmonary venous drainage, (33) acidosis and hypothermia or severe heart failure in coarctation of the aorta (34) have been shown to influence the surgical mortality. The importance of early diagnosis of a defect is further shown by Leanage et al (35) who found that balloon atrial septostomy in transposition of the great arteries before the age of one week,had a favourable effect on mortality. Appropriate medical management of the infant with congenital heart disease before hypoxia, shock or acidosis can adversely affect surgical results or even be fatal will depend on early diagnosis of a defect. Prenatal prediction of a congenital cardiac malformation will therefore optimise the chances of infant survival.

The place of echocardiography in the diagnosis of congenital heart disease

The early evolution of echocardiography was in the development of the M mode technique which has now been evaluated in clinical use over the last ten years (36,37). However, more recent major changes have been effected by the advent of cross-sectional echocardiography (38). The M mode technique had an established place in the diagnosis of cardiac disease but the addition of the cross-sectional facility has greatly enhanced the application of echocardiography (39). This is particularly true of the study of congenital heart disease (40,41,42).

Congenital heart malformations tend to be gross anatomical abnormalities which can be displayed and delineated by cross-sectional techniques (43,44,45). Elucidation of the precise anatomy of the lesion is essential in the management of a congenital heart defect. The anatomy can be accurately described from the interpretation of the real-time echocardiogram if the heart is logically and carefully studied. It is important to remember that congenital heart defects are commonly multiple. The examination therefore must follow the cardiac connections stepwise from venous drainage, through the intracardiac anatomy to the great arteries. To then direct the M mode beam under two dimensional control greatly enhances the accuracy and capability of the M mode echocardio-

gram (46). For example, measurements can be made on the M mode echocardiogram that can be more precisely timed within the cardiac cycle. Or, as another example, the single beam can be employed to confirm the two dimensional appearance of an absent valve by detailed sweeping of the area of the heart where the valve should be. The two echocardiographic techniques therefore should be considered as one study with each part complementary to the other and providing slightly different and additive information.

In this country, both echocardiographic techniques have only been in use in the field of paediatric cardiology for two to three years. However this time has seen a great change in the course of management of congenital heart disease as a result of increasing confidence and reliance on the echocardiogram. In some cases it has supplanted invasive techniques, in others facilitated them greatly (47,48). Continuing experience can only increase the role of echocardiography. It is equally important however, to recognise and define the limitations of the echocardiogram and to be aware of the confidence limits of the observer and the technique, in the ability to define a particular abnormality accurately. For example, a ventricular septal defect of under 3-4 mm in size is impossible to define

accurately with the resolution limitations of currently available machinery (49,50). Or, as another example, the severity of pulmonary stenosis is difficult to accurately predict by either M mode or two dimensional techniques (51). On the other hand the diagnosis of hypoplastic left heart syndrome is unmistakable and irrefutable on the echocardiogram (52).

In summary, therefore, echocardiography has an ever increasing importance in the diagnosis and management of congenital heart disease. Experience and understanding of the anatomy of the normal and abnormal heart is essential to accurate interpretation, as is an appreciation of the limitations of the technique.

The growing application of ultrasonic imaging to the prenatal diagnosis of fetal abnormality

The development of techniques for prenatal diagnosis has been a major advance in medical genetics over the last ten to fifteen years. The different approaches to prenatal diagnosis include amniocentesis, ultrasonography, fetoscopy and maternal blood sampling. Amniocentesis has specific use for chromosomal abnormalities (53), inherited metabolic

disorders (54,55) and neural tube defects (56,57) but does carry some risk to the fetus (58). Fetoscopy for direct visualisation of the fetus or for fetal blood sampling is finding an increasing role in diagnosis (59). The discovery that a raised maternal serum alpha-fetoprotein can predict certain anomalies (60,61) is important because it involves no risk to the fetus. Screening programmes can therefore be undertaken on a population basis (62).

The use of ultrasonography is finding increasing application to the diagnosis of congenital anomalies during pregnancy. The initial contribution of ultrasound to obstetrics was in the determination of the number of fetuses, fetal position, placental localisation and estimation of fetal age and growth by measurement of the bi-parietal diameter (63). But improved image quality due to increasing resolution in ultrasonography and the additional development of real time cross-sectional display has allowed the fetal anatomy to be visualized in previously unimaginable detail. The recognition of detailed anatomy, within soft tissues in particular,is continually improving with further sophistication of grey scale imaging. The ultrasonic description of structural abnormality in every system in the fetus has now been recorded.

One of the earliest abnormalities to be detected prenatally by ultrasound alone was that of anencephaly (64) where the fetus lacks both cerebral hemispheres. This is readily detectable by ultrasound and has been diagnosed as early as 14 weeks gestation (65). As it is a uniformly fatal anomaly its detection is an indication for termination of pregnancy. The accurate diagnosis of microcephaly, hydrocephaly and spina bifida (66) require greater skill but serial measurements should predict both cranial abnormalities. Even a sacral meningocoele should not be overlooked if the spine is examined carefully by an experienced observer.

Gastrointestinal tract obstruction at varying sites, giving the appearance of excess fluid filled cavities proximal to the obstruction,have all been described pre-natally (67,68). Congenital umbilical hernia, omphalocoele, gastroschisis and prune belly syndrome are all abnormalities of the anterior abdominal wall which have been described in utero (69). Both kidneys and the bladder can readily be visualized on ultrasound so it is not surprising that renal agenesis (70), polycystic kidneys (71) or multicystic kidneys have been described. Obstructive uropathy causing bladder, and ureteric dilatation can be determined (72). Poly-hydramnios tends to be associated with gastrointestinal

abnormalities, oligohydramnios with renal anomalies. Reduction deformities of the limbs are an even more recent addition to the list of deformities which are possible to diagnose accurately prenatally (73).

Ultrasound has now become a reliable predictor of abnormality in fetal life. Decisions concerning termination of pregnancy can be made on the ultrasound diagnosis alone of several severe defects. Until recently no comprehensive attempt to study the fetal heart had been made. This is because of the apparent anatomical complexity of the heart and also because congenital heart malformations are so various. However, as we have shown in the first part of this chapter, congenital heart disease is a numerically important cause of morbidity and mortality in early infancy. Increasing experience of the reliability of echocardiography in postnatal life has led to this technique being applied to the examination of the fetal heart.

CHAPTER 2

THE EVOLUTION OF CLINICAL ULTRASOUND IMAGING:

Physical Properties of Ultrasound

Ultrasound is now utilised to visualize many soft tissue organs of the human body. Some understanding of the physical properties of ultrasound is necessary to appreciate fully the advantages and limitations of this diagnostic procedure.

Sound is transmitted through all media by a series of compressions and rarefractions (Figure 2.1). The combination of one compression and one rarefraction represents one cycle. The distance represented by one cycle is known as the wavelength (λ). The frequency (f) is defined as the number of cycles per given time, usually in terms of cycles per second, commonly known as Hertz or Hz. The velocity (v) represents the speed with which sound waves travel through a particular medium and is equal to frequency times the wave length (74).

$$v = f \times \lambda$$

The velocity at which sound travels through a medium depends on its density and elasticity. Sound travels faster through

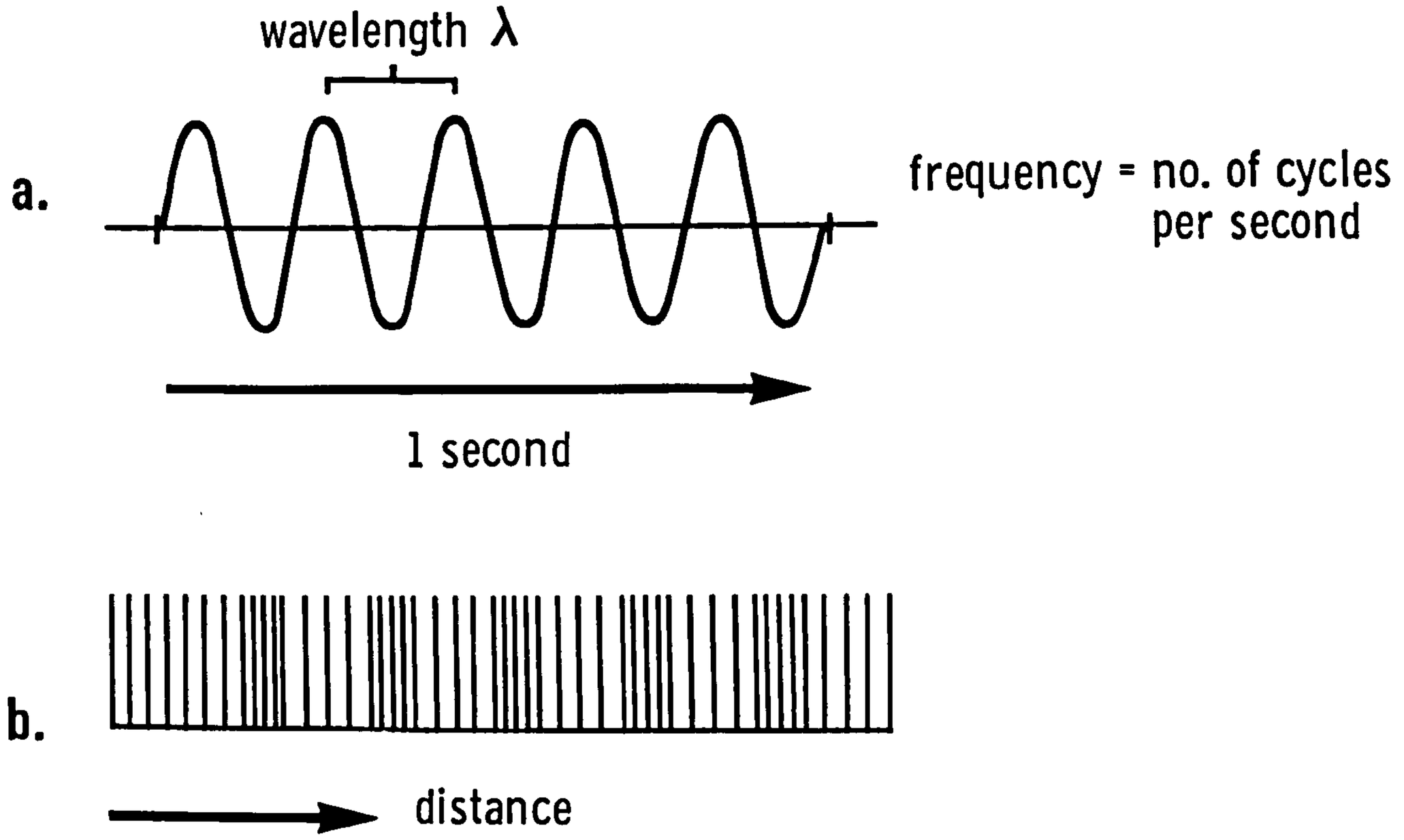


Figure 2.1. Sound is transmitted through media in a series of compressions and rarefractions represented in 2.1.b. The wavelength λ is the distance between each cycle and the frequency of the sound wave is the number of cycles that occur in each unit of time usually expressed in cycles per second. The velocity of sound transmission in a given medium therefore will be the frequency multiplied by the wavelength $v = f \times \lambda$ The time a sound wave takes to travel through a given medium will depend on the frequency of the sound wave and the acoustic impedance of the medium. The distance a sound wave travels will additionally depend on the amplitude of the sound wave.

a dense medium, a solid such as an iron bar or bone, than it does through a less dense medium, for example water.

By definition ultrasound is sound with a frequency above the audible range, greater than 20,000 cycles per second (20 kHz). Generally, frequencies in the range 1-20 MHz are used for medical diagnostic purposes. Ultrasound is particularly useful for diagnostic imaging because, in contrast to audible sound, it can easily be directed in a beam and is also reflected by objects of small size. The principle disadvantage of ultrasound is that it propagates poorly through a gaseous medium. As a result the ultrasound transducer must be in airless contact with the body during the examination of a patient and organs containing air cannot be visualised.

An ultrasonic beam obeys the laws of reflection and refraction when passing between media of different acoustic impedance. Acoustic impedance, Z, is, by definition, the density of the medium, p, times the velocity (v) that ultrasound travels through that medium.

$$Z = p \times v$$

At an interface between two media a portion of the incident wave is reflected and the remainder refracted. For smooth

plane interfaces the angle of incidence equals the angle of reflection, and the angle of refraction is related to the ratio of the velocity of ultrasound in the two media. The amount of ultrasound that is reflected depends on how the beam strikes the interface, the angle of incidence and also the difference in acoustic impedance of the two media. The closer the angle of incidence is to 90° the greater is the amount of sound reflected. The reflected fraction of the incident energy (R) is also determined by the impedance mismatch between the two media. This is approximately 1% for a fat-muscle interface, 40% for a muscle-bone interface and 99.9% for an air soft tissue interface.

In biological tissues ultrasound also interacts with many small structures within the parenchymia. The energy is re-radiated in all directions, and is lost from the propagating beam. In addition ultrasonic energy is absorbed by chemical and molecular mechanisms. The absorption and scattering of the ultrasonic beam result in attenuation of the beam's energy as it propagates through biological media. The extent of the attenuation depends on the frequency of the ultrasonic beam and the scattering and absorption properties of the tissue which are usually expressed in dB/cm/MHz. (75).

The need to balance improved resolution, obtained by using higher frequencies, against reduced penetration of the ultrasonic beam restrict the application of ultrasound to the frequency range 1-20 MHz, usually 3-5 MHz for general abdominal and cardiac imaging purposes.

Imaging Methods

Special devices, called ultrasonic transducers, are required to produce vibrations in the frequency range 1-20 MHz. In their simplest form these are discs of a ceramic material, generally lead zirconium titanate, across which is applied a rapidly varying electrical signal. This ceramic is one of the piezoelectric materials which have the special property of being able to transmit and receive ultrasound waves. An electrical signal across the face of the ceramic crystal will propagate an ultrasound signal; similarly, returning reflected ultrasound signals can be converted to an electrical signal. The same transducer is used therefore for the transmission and reception of ultrasound. The transducer emits short pulses of ultrasound, rather than a continuous signal, so that during the pauses in transmission the weaker returning echoes can be detected. Typically a pulse of ultrasound lasting 1 μsec, containing several cycles of ultrasound is transmitted every second. The transducer therefore transmits for 1 sec and "listens" for 900 μsec.

The ultrasound signal will be reflected at each interface encountered. The amplitude,A-mode,of these echoes can be displayed on an ocilloscope (Figure 2.2.1.) The base line represents the time interval between pulse transmission and detection of the reflected echoes. When the velocity of ultrasound in soft tissues is known the A scan can be used as an anatomical "range finder". Dimensions of organs can be measured by defining the depth of each interface from the transducer. An alternative way of displaying echo amplitude is by the brightness of a spot on a cathode ray tube or television monitor, B mode (Figure 2.2.2.). In a similar way to A mode,the distance between the transducer and each interface is represented by the time taken for the reflected echoes to return. Amplitude is represented by the brightness of each dot on a grey scale display. If B mode is displayed on a screen and light sensitive paper is drawn across the display, the motion of structures within the body can be recorded with time. As, for example, the position of heart valves and cardiac structures is constantly changing with time, by this means the depth of each interface relative to the transducer can be traced. This demonstrates the pattern of movement with time and is M mode echocardiography. Figure 2.3. A further way of using a B mode display is seen in Figure 2.2.3. The transducer is moved across the patient and an image of the shape of interfaces can be built up by

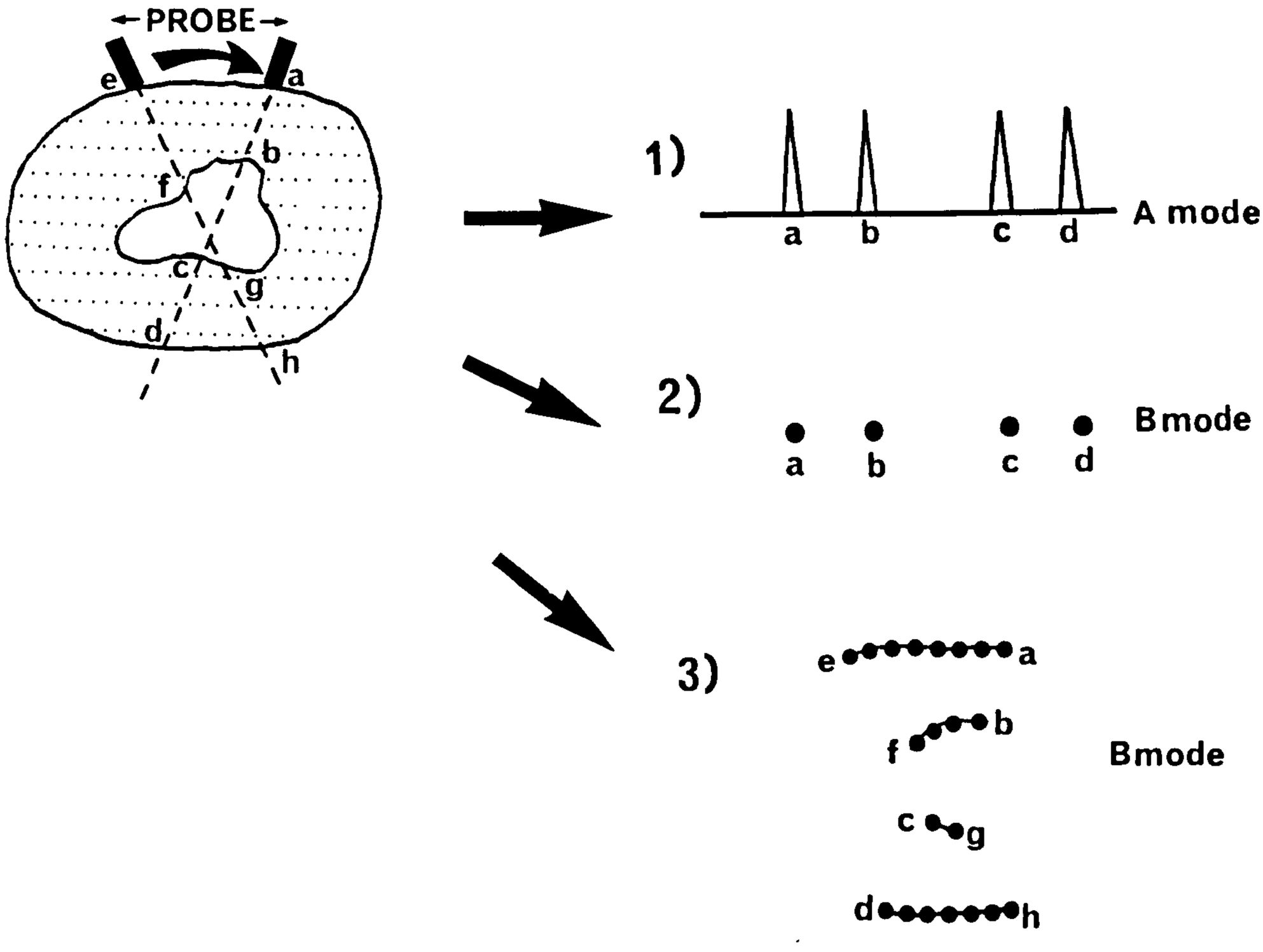


Figure 2.2. The ultrasound probe is held at point a. The reflected echoes from the structure scanned can be represented, as in (1) in A mode. Each spike represents an interface. The amplitude of the spike represents the intensity of the returning echoes from the interface. The distance between interfaces, a, b, c,and d can be measured by the distance between each spike.

In (2) the interfaces are each represented by a dot. This is B mode. The brightness of the dot represents the intensity of the returning echoes. The distance between dots represents the distance between each interface.

In (3) the probe has been swept, manually, between points a and e. This builds up an image which imitates the interfaces of the structure being scanned, by a series of dots. Thus a visual picture of this structure is built up and can be displayed on a screen.

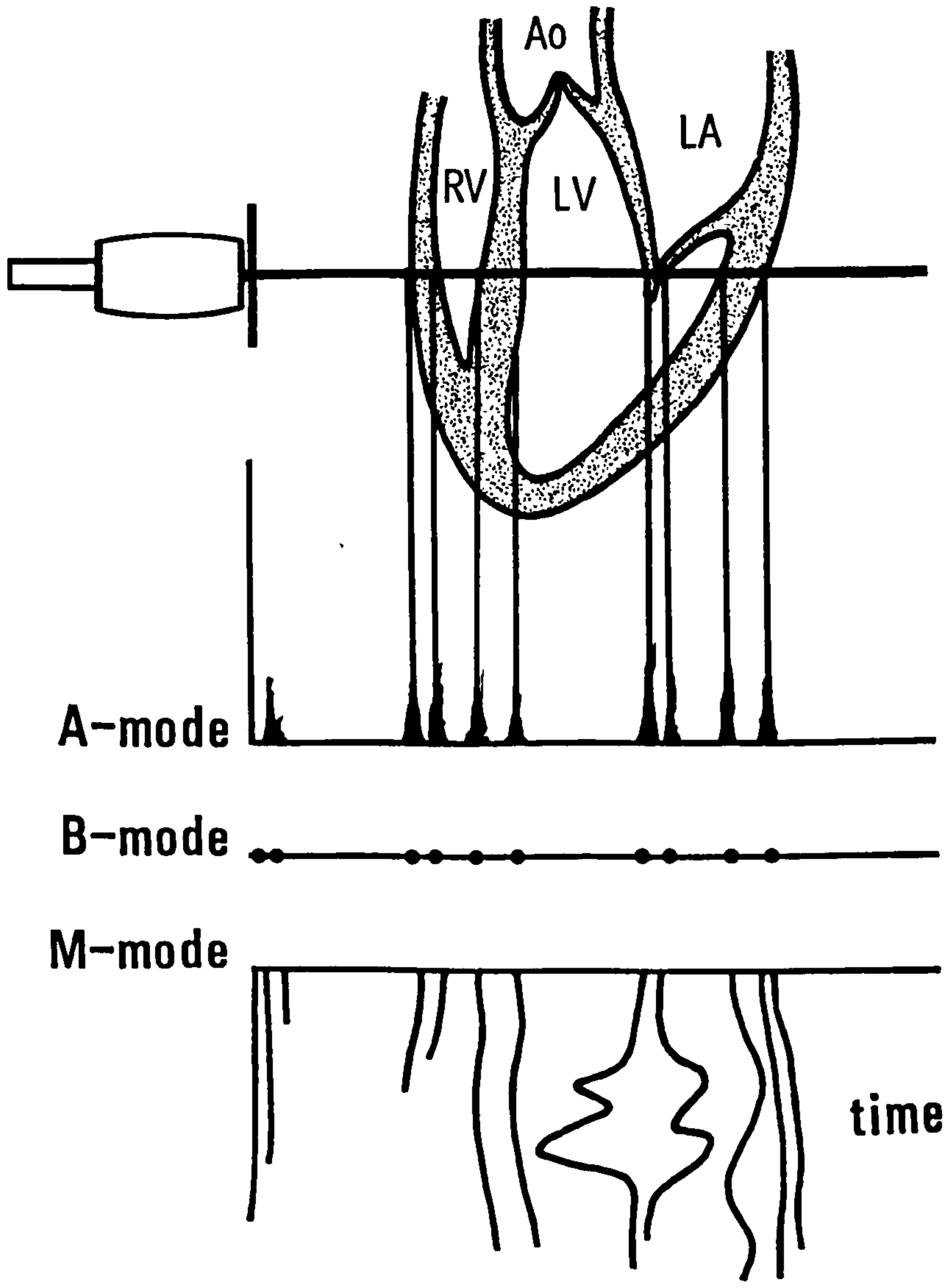


Figure 2.3. A single beam of ultrasound is directed through the chest wall and heart at the level of the mitral valve. The reflected echoes from each interface can be represented in A mode or in B mode as illustrated. As the intracardiac structures are in constant motion, the A mode spikes and the B mode dots would be continually moving and blurred. By displaying B mode however on an oscilloscope and drawing light sensitive paper across the image, the motion of the reflected echoes can be recorded against time. This is M mode echocardiography.

a series of B mode dots. This type of B mode display is suitable for static objects, for example, the kidney. The shape of the organ can be delineated on a screen by repeated sweeping of the ultrasound beam across it. This is a cross-sectional image. However, this method of producing a cross-section is not suitable for cardiac imaging, because a hand manipulated probe could not delineate a section of the heart before movement had occurred. A method of displaying a cross-sectional image in "real time" therefore must be used.

A real time cross-sectional image can be produced in several ways; by using a mechanical sector scanner, a linear array system or a phased array system (76). The imaging technique used in this study was a mechanical sector scanner, an Advanced Technology Laboratories Mark II, in which three standard piezo-electric crystals are mounted within the transducer head and rotated rapidly (Figure 2.4.). Only one crystal is active at any one time. A fan shaped 90° sector is produced with maximal line density at the top of the image. Axial resolution is better than lateral resolution. That is, it is easier to distinguish two interfaces 1 mm apart if they lie on top of each other rather than side by side. Resolution is best at a depth of 2-6 cms. (77). With all equipment a compromise must be reached between the number of lines of information and thus clarity of imaging, the frame rate and

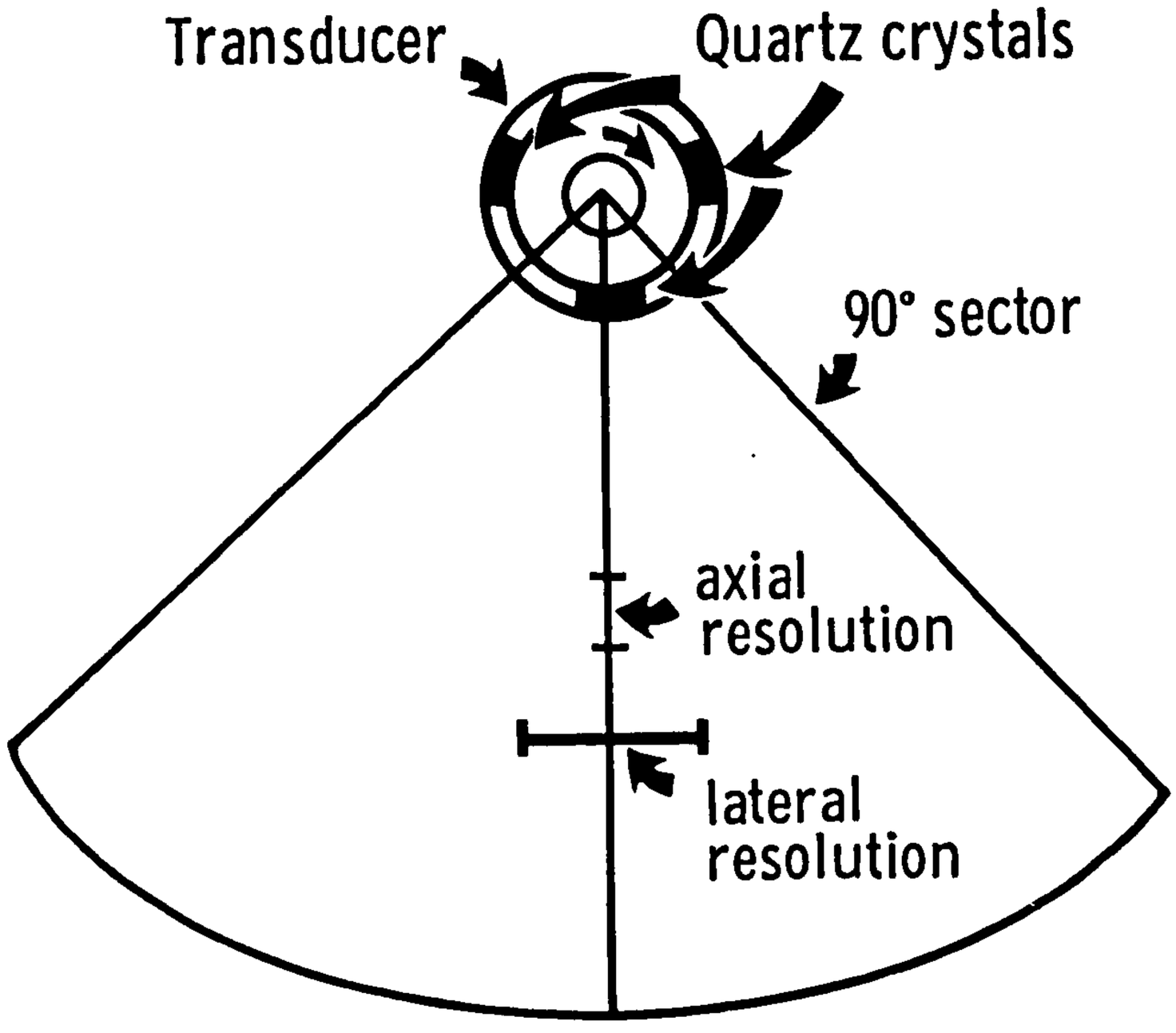


Figure 2.4. The transducer head of a rotating sector scanner is seen diagrammatically. The crystals revolve rapidly displaying a 90° cone shaped image, containing 128 lines of information. Axial resolution, where interfaces are perpendicular to the ultrasound beam, is better than lateral resolution. This type of sector scanner was used in this study.

thus appreciation of motion, and the depth of image penetration. A 3.5 MHz. transducer was found to be most suitable for the majority of antenatal imaging except in a few cases where a 5 MHz transducer gave greater clarity of image when the abdominal wall was thin.

Development of Clinical Applications

The principles of sound propagation, as described in the first section of this chapter, have been known for many years. But the first practical application of an ultrasonic imaging technique was in depth determination and submarine detection during World War I. Improvement and miniaturisation of transducers led Firestone in 1945 to apply pulsed ultrasound to the detection of flaws in metal (78). From this use of ultrasound arose the idea of applying the imaging technique to clinical medicine, specifically to the study of soft tissues, which had always been poorly visualised radiologically.

It was two workers in different centres, namely Donald (79) and Holmes (80) who separately saw the medical potential of ultrasonic imaging and applied it to obstetrics. They both developed and designed equipment which over a period of twenty years has revolutionised the practise of obstetrics. Despite poor image quality in the early 1960s the growth of the fetal head, using the biparietal diameter, was measured and growth

charts constructed for the last two trimesters of pregnancy. Diagnosis of pregnancy,and evaluation of the first trimester by detection and measurement of the volume of the gestational sac or the crown-rump length of the early fetus,was a further development in the study of normal pregnancy (81). Abnormalities of pregnancy have naturally been discovered during the study of normal pregnancy. Similarly fetal abnormalities have been increasingly recognised (82). This has been due to continual improvement in image quality coupled with expanding experience in the field of detection of fetal anomaly. The first fetal anomaly detected by ultrasound and subsequently treated by surgical intervention was only in 1972. (83). The safety of repeated or lengthy observation and examination of the fetus by ultrasound has been a continual source of anxiety and extensive research. However no deleterious effect on the fetus has ever been detected despite large multicentre studies and long term paediatric follow up (84,85).

Simultaneously ultrasonic imaging has been applied to cardiology. The pulsed ultrasound described by Firestone was first used by Hertz in Sweden in 1954 (86). Initially an insensitive recording of posterior left ventricular wall motion was obtained and a more anterior reflection,which was only identified as the mitral valve,some years later in 1960 (87). Collaboration between Hertz and Edler produced a commercial ultrasonoscope by 1960. The only ultrasonic

imaging technique available at this time,suitable for cardiac study,was M mode. Improvement in resolution and printing techniques combined with experience in the interpretation of the M mode echocardiogram,have given this technique an essential place in cardiac investigation. The more recent development of cross sectional techniques have further broadened the horizons for non invasive cardiac study (88). The M mode and cross sectional study are not only complimentary diagnostically but enhance each other. Because endocardial surfaces are more easily defined on the M mode echocardiogram it provides more accurate measurement data and derived functional characteristics can be examined from it. The cross-sectional echocardiogram can more accurately display altered cardiac anatomy and contribute to the M mode study by allowing more precise guidance of the M line to the structure to be studied. Cross-sectional echocardiography lends itself particularly well to the study of congenital heart disease. This is because abnormalities tend to be gross structural defects which can be clearly defined anatomically using two dimensional imaging (89). The appearance on the cross-sectional echocardiogram of nearly every permutation of congenital heart defect has now been described (90) in postnatal life.

Ultrasonic imaging therefore has found an invaluable and ever-increasing application to both obstetrics and cardiology. The more recent addition of two dimensional techniques has allowed more detailed study of both the fetus and congenital heart disease. Thus the study of congenital heart disease in the fetus has become possible.

CHAPTER 3

Literature Review - Approaches to Fetal Echocardiography Published to Date

The first report of visualisation of the fetal heart using ultrasonic imaging was that of Garrett and Robinson in 1970 (91). They identified the fetal cardiac cavity and intraventricular septum using a static B scanner and followed the growth of the cardiac cavity during pregnancy. They found the cardiac cavity to increase proportionately with the fetal thorax during gestation, the heart occupying about one half of the thoracic cavity. They suggested a ratio of 1.23 for the right to left ventricular chamber measurement in 96 patients. In 1972 Winsberg studied the fetal heart in 150 pregnancies using a static scanner to locate an M mode beam (92). He obtained good quality M mode echocardiograms and measured the left ventricular internal dimension and left ventricular wall thickness during pregnancy in 13 patients. He was attempting to estimate fetal cardiac output from the echocardiogram, a technique which is now considered too unreliable in postnatal life when compared to more direct measurements (93,94). Further reports on the identification of fetal cardiac anatomy during pregnancy came from Egeblad et al in 1975 (95) and Lee et al in 1977 (96). The accuracy of identification of moving cardiac structures was limited

in Lee's study by use of a static B scanner. Egeblad made the first attempt to identify cardiac anatomy using real time ultrasound,but the poor resolution of equipment available at that time (1975) did not allow positive identification of such prominent features as the atrio-ventricular valves. Also the study was limited to twenty pregnancies between 36 weeks and term. Baars and Merkus, in 1977,used real time cross-sectional imaging to direct an M mode beam and recorded partial M mode echocardiograms in 43 cases (97). More recently in 1979,Vosters and Wladimiroff (98,99) have described the use of M mode directed by the cross-sectional image, to measure fetal ventricular chamber dimensions and left ventricular function. The change in right and left ventricular dimensions after birth in six pregnancies and the ratio of right and left ventricular chambers in eleven pregnancies are documented by them. Ventricular shortening and velocity of fractional shortening were also estimated in 46 patients between 28 and 42 weeks gestation. In 1979 Iannioroberto used the cross-sectional echocardiogram to direct the M mode beam to study the fetal heart in 90 patients between 34-40 weeks of pregnancy (100). The velocity of mitral valve closure and aortic root dimension was measured in all cases. Pulmonary artery dimension, tricuspid valve closure velocity, right and left ventricular internal dimensions and septal thickness

could be recorded in a proportion of cases. Henrion and Aubry in 1979 (101) published the first case of a cardiac abnormality detected prenatally. They were unable to identify the intraventricular septum and autopsy confirmed a "single ventricle" .

At the beginning of 1980,the study which forms the basis of this thesis, was started. It was undertaken in order to evaluate the application of fetal echocardiography in assessing the normal fetal heart, and in the prediction of congenital cardiac malformations. Since the initiation of the study several publications have appeared in the literature relating to this subject.

Two papers describing normal fetal cardiac anatomy appeared almost simultaneously in 1980. Sahn et al (102) described four chamber, long axis, short axis and inferior and superior vena caval sections in a study of 71 patients between 20 and 41 weeks gestation. He also estimated total cardiac dimension, right and left ventricular chamber dimensions, pulmonary artery and aortic root size using real time frozen frame images for measurement. He derived growth charts for these values against estimated fetal weight. Allan et al (103) described eight echocardiographic sections obtainable of the fetal heart. Two hundred patients between

14 weeks and term were studied echocardiographically and anatomical sectioning of preserved fetal specimens was undertaken to imitate the echocardiographic sections and thereby verify interpretation. (All related papers by the author are bound in the back of the thesis). In 1980 Kleinman et al described a case of pulmonary atresia detected at 34 weeks gestation and a univentricular heart at 28 weeks gestation (104). This was in a study of 180 high risk pregnancies. Two arrhythmias, namely complete heart block and atrial flutter, were also seen within this study. In 1981 Allan et al (105) published the abnormalities seen in a series of 350 pregnancies. There were five structural abnormalities detected prenatally and confirmed, with one false positive diagnosis. The echocardiographic study of a series of twenty-one mid trimester terminations was also published by the same author later the same year (106). Fetal ascites, or non immune hydrops, has a known association with congenital heart disease described at autopsy (107). Allan et al reported a case of isolated congenital heart disease and associated fetal ascites, seen at 34 weeks gestation, in 1981 (108). In 1982 Kleinman et al studied thirteen fetuses presenting with non-immune hydrops (109). All were studied by cross sectional and M mode echocardio-graphy. Ten of the thirteen fetuses were found to have

cardiovascular anomalies which were thought to account for the observed intra-uterine cardiac failure. Three fetuses had arrhythmias, seven structural cardiac anomalies.

In summary, therefore, although the first description of ultrasonic imaging of the fetal heart appeared in 1970 only sporadic reports of fetal echocardiography appeared between 1970-1980. Since then several centres have become actively involved in a structured approach to scanning high risk pregnancies. As a result the normal appearance of the fetal heart has been well described and reports of abnormalities detected prenatally are continually increasing.

CHAPTER 4

STUDY DESIGN AND PATIENT MATERIAL

Study Design

The study was organised in order to assess the feasibility, accuracy and potential value of prenatal echocardiography. The feasibility was assessed by examination of the fetal heart by echocardiography and correlation with indirect anatomical dissections. The accuracy was assessed by a direct echocardiographic and anatomical correlative study and by follow-up examination of the pregnancies studied. The potential value of the technique was assessed by evaluation of the results in terms of prediction of normality and abnormality.

Feasibility. Initially the cross-sectional echocardiogram was used to study unselected pregnancies of varying gestational ages in order to describe the features of the normal fetal heart that could be visualised. The first 100 pregnancies were scanned using a Kretz Combison 100 Sector Scanner but since then subjects have been studied using an Advanced Technical Laboratories Mark III Sector Scanner. In all cases the cross sectional images were recorded on videotape and stored for restudy. The adequacy of visualization of various cardiac structures was assessed

at each gestational age. Once the initial concept of fetal cardiac anatomy, as seen echocardiographically was gained, indirect anatomical studies were performed to confirm the echocardiographic interpretation of the cross sectional images. The indirect anatomical study took the form of dissection of 20 fetal specimens, and sectioning the fetal heart in such a way as to imitate the echocardiographic sections which were most commonly recognised.

After the anatomical studies and after further practise in achieving cross sectional images, it became possible to add an M mode study to the examination. The M mode echocardiogram allows pattern of motion of valves and chamber walls to be studied. This is described in Chapter 7. As endocardial surfaces are more readily defined on the M mode echocardiogram this mode was chosen, in preference to a frozen frame cross sectional images, for the collection of measurement data of intracardiac chambers throughout pregnancy. These are detailed in Chapter 8. The addition of the fetal electrocardiogram gave more precise timing of events within the fetal cardiac cycle as described in Chapter 9. Derived functional measurements could be estimated from the M mode measurements and compared to paediatric values (Chapter 10). As this information,in addition to the cross-sectional examination,became more

readily achievable as the study progressed,the feasibility of prenatal echocardiography in the prediction of normality and abnormality increased during the study.

Accuracy. The accuracy of the echocardiographic prediction of cardiac normality and abnormality was evaluated early in the study by a direct anatomical correlative study. This was achieved by the echocardiographic study of a series of pregnancies about to undergo midtrimester termination. The prediction of normality or the description of abnormality was made before anatomical dissection of the fetal heart was undertaken. The results could thus be directly correlated with each other. The accuracy was further evaluated by long term follow up of the pregnancies after delivery. In the cases of perinatal death the anatomical specimen was studied. The surviving offspring were all evaluated clinically, or clinically and echocardiographically in most of the "high risk" pregnancies studied. The high risk groups are described in the next section of this chapter. Full details, of the method and results of follow up, are given in Chapter 14. The accuracy of echocardiographic prediction of normality or abnormality of the fetal heart increased with experience and "feed back" from anatomical dissections and post natal follow up.

Thus both feasibility and accuracy increased as the study progressed, although this is difficult to substantiate objectively.

The potential value of fetal echocardiography is discussed in Chapter 15 when the results of the complete study have been presented and described.

Patient Material

The first 200 patients studied were randomly selected from the routine antenatal ultrasound clinic. They were all apparently normal pregnancies and were studied initially to establish a basic knowledge of normal fetal cardiac anatomy. The gestational age ranged from 14 weeks to term. It was during this part of the study that the indirect anatomical studies took place. A further series of 54 normal pregnancies were studied when the feasibility of M mode measurement was being assessed. An attempt was made to record the aortic root dimension by M mode in a consistent fashion. This proved possible in all 54 patients and led to the accumulation of further M mode measurement data described in Chapter 8.

None of the pregnancies in these two normal series had any "high risk" factor operating. These factors are described below.

High Risk Groups

Family history of congenital heart disease: The majority of congenital heart disease (90%) follows the pattern of multi-factorial inheritance (110). The incidence of recurrence in a family with one affected child will vary with the defect involved but lies between 1 in 50 (111) for common defects to 1 in 80 for rarer defects. Where a parent is affected the incidence of recurrence is approximately 5% (112). Three percent of congenital heart disease occur as a component in single gene disorders. Marfan's syndrome is a connective tissue disorder transmitted as an autosomal dominant with varying penetrance. There is therefore a 1 in 2 chance of a child being affected if the parent is affected. The most important cardiac manifestation of this syndrome is dilatation of the aortic root (113) which can be readily appreciated echo-cardiographically in post natal life. The Holt-Oram syndrome is a dominant disorder in which a common component of the syndrome is an atrial septal defect (114). Some disorders, such as the asplenia and polysplenia syndromes, have been described in sibships,(115) and may be transmitted in a recessive manner although the commonly quoted incidence of recurrence of these abnormalities is 1 in 20 (116).

Maternal diabetes: The incidence of fetal abnormality in general, including heart disease, is increased by a factor of two in maternal diabetes (117). Transposition of the great arteries is said to be up to 11 times more common (118).

Fetal ascites: Fetal ascites,or non-immune hydrops fetalis,has a known association with cardiac abnormalities (119). In some cases hydrops may be due to cardiac failure which may be functional or structural in origin (120,121).

Fetal arrhythmia: These are of three main types, tachy-arrhythmias, bradycardias and irregularity of rhythm. Although none are strongly associated with structural cardiac abnormality there is an increased risk of congenital heart disease particularly in the bradycardia group (122).

Fetal anomaly: If any extracardiac fetal abnormality was suspected on ultrasound or chromosome analysis, this group of pregnancies was selected for study. This is because there is an increased incidence of congenital heart disease in association with other anomalies, an incidence of approximately 30% (123). Five percent of congenital heart disease occurs in association with chromosomal abnormalities (124). Forty percent of children with Down's syndrome have congenital heart disease and between 90 - 100% of trisomy 13 and 18 are affected (125).

Intrauterine growth retardation: Babies born with isolated congenital heart defects are rarely of low birth weight (126) whereas approximately 10% of fetuses with multiple congenital defects are growth retarded (127). Therefore congenital heart disease as part of multisystem abnormalities was looked for in these cases.

Miscellaneous groups: This group of pregnancies studied included those exposed to infection or drug ingestion during the first trimester,where the infection or drug had a known association with the causation of congenital heart disease. Rubella virus, mumps and cytomegalovirus, are known to affect the fetal heart (128). Steroid, oestrogen, lithium and anticonvulsant ingestion during early pregnancy are all said to increase the incidence of congenital heart malformations (129).

Suspected cardiac anomaly: During the latter part of the study, other centres, aware of our interest in the fetal heart, referred cases where cardiac abnormality had been suspected on a routine antenatal ultrasound scan.

Summary

The aims of the study and an outline of the design of the study have been given in the first part of this chapter. The detailed methodology of each aspect of the fetal echocardiographic study is described in the appropriate subsequent chapters of results. The initial series of normal pregnancies were studied in order to evaluate the feasibility of the study. Subsequently the study has been confined to high risk pregnancies in order to gain the maximum potential experience of abnormality of the fetal heart.

CHAPTER 5

RESULTS

Indirect echocardiographic and anatomical correlative study

When the fetal heart was studied at the start of the project it was found that certain sections were more easily recognised than others. The heart was examined in rather a staccato fashion seeking identifiable planes and describing them. Each plane seen echocardiographically then had to be interpreted in relation to the cardiac structures within each section. At this point,the anatomical studies were carried out mainly in order to confirm the echocardiographic interpretation by imitating each planeof section. The anatomical studies not only verified the echocardiographic interpretation however,but also helped the author's understanding of cardiac anatomy. Since then the method of examining the fetal heart has evolved into a more fluid and continuous procedure, searching initially for a recognisable section of the fetal heart,but then following cardiac connections by transducer angulation. Experience and practice has allowed this to become a simple technique. From any section of the fetal heart a known angulation of the transducer will produce sections containing other structures to be recognised.

The maternal abdomen is scanned and the fetal position identified. The fetal heart is first of all orientated within the context of the whole fetus. The heart is then focused on, looking for particular structures. A number of structures are considered essential to identify fetal cardiac normality. These are listed below.

1. Two atria, and the mechanism of the foramen ovale.
2. Two ventricles, with intact ventricular septum.
3. Two great arteries.
4. Inferior vena cava draining into the anterior atrium.
5. Superior vena cava draining into the anterior atrium.
6. Pulmonary veins draining into the posterior atrium.
7. The foramen ovale flap seen in the posterior atrium.
8. Differential ventricular trabeculation.
9. Differential atrioventricular valve insertion.
10. A complete muscular infundibulum in the anterior ventricle supporting the pulmonary valve.
11. Arterial-atrioventricular valve continuity in the posterior ventricular chamber.
12. The right ventricular outflow connected via the pulmonary artery and ductus arteriosus to the descending aorta.
13. The left ventricular outflow tract connected via the arch of the aorta to the descending aorta.

It was found that between 14 and 18 weeks gestation several of these features were recognisable,but the fetal heart is small and fine detail was impossible to identify. However, it was always possible to detect two atria, two ventricles and the aortic root at this stage.

Between 18 and 28 weeks gestation,it was possible in every case to identify all the normal structures with the exception of the pulmonary veins. Pulmonary veins in the fetus are very small. Even in the last trimester positive identification of the pulmonary veins was only possible in about half the cases studied. It is not advisable to examine the pregnant patient supine for longer than 30 minutes, partly because of discomfort to the patient but also because pressure of the uterine contents on the maternal inferior vena cava can cause hypotension. But during the 18-28 week gestational age range,in the majority of cases, a complete real-time and complete M mode echocardiogram,with a fetal E.C.G.,could be readily achieved within this time. In a few cases maternal obesity, oligohydramnios or unfavourable fetal position made the examination more difficult and therefore repeat examination was necessary. There is a lot of fetal movement during the midtrimester which can make the M mode examination more difficult, but overall, movement is advantageous, as the required real-time sections are "presented" to the examiner as movement of the fetal trunk occurs.

After 28 weeks gestation,the fetus becomes more fixed in position usually with the fetal spine anterior. This means that the fetal heart is some distance away from the transducer so that penetration and therefore resolution of cardiac structures is reduced. Also rib shadowing becomes more marked in later pregnancy (See Figure 5.12) and this again limits the accuracy of detailed examination of, for example, the ventricular septum. In spite of these difficulties,it was still possible to predict confidently normal cardiac connections in the majority of cases seen in the last trimester of pregnancy.

The fetal echocardiogram does not directly compare with postnatal echocardiography. This is because the fetal lungs are airless and fluid-filled allowing unrestricted access to ultrasound imaging of the fetal heart. The fetal heart can be viewed circumferentially and thus seen in unusual projections which are impossible postnatally. Also the extracardiac connections which are difficult to visualise postnatally, for example, the complete course of the inferior vena cava, or the arch of the aorta, are easily seen and their courses followed. Another observation made early in the study was that the fetal heart lies in a more horizontal position than the postnatal heart. This renders the right ventricle anterior to the left. This is because of cranial displacement of the cardiac apex probably by the large fetal liver.

In the midtrimester fetus the liver is the major haemopoeitic organ and it extends to the left side of the abdominal wall.

The postnatal real-time cross-sectional echocardiogram has been evaluated anatomically (130) but because we found the fetal echocardiogram not directly comparable for the reasons described above, we undertook anatomical evaluation in the fetus. This firstly increased anatomical understanding. It also verified echocardiographic interpretation of cardiac structures. Lastly, it allowed accurate identification of the transducer orientation, relative to the fetal trunk, required to produce a recognised cardiac section. In order to perform anatomical evaluation eight echocardiographic sections were chosen for description and anatomical imitation. These sections were named according to the main structures displayed by them and taken together provide all the information necessary for a diagnosis of fetal cardiac normality. This division of fetal echocardiography into "scan planes" is of course artificial. The technique is performed as a continuous process, involving the integrated study of all the scan planes, seeking the specific structures to be identified.

Twenty abortus specimens were used for the anatomical studies. These were fetuses, preserved in formalin, of gestational age range of 12-28 weeks and collected after spontaneous abortion. They were taken from the museum collection in the Institute of Child Health, Liverpool by kind permission of Dr. J.L. Wilkinson and Dr. A. Smith. The first dissection illustrated the echocardiographic impression that the fetal heart lay in a more horizontal position than postnatally (See Figure 5.1). The large fetal liver displaces the cardiac apex cranially. The right ventricle thus lies anterior to the left.

Sectioning of the rest of the abortus material allowed imitation of four longitudinal and four transverse echocardiographic planes. It sometimes required several anatomical sections to reproduce exactly a given echocardiographic section and thus to discover accurately the correct transducer orientation necessary.

Longitudinal Planes

Figure 5.2 illustrates the transducer orientation necessary to visualise the four longitudinal planes. The inset displays the direction of the ultrasound beam relative to the fetal thorax required to produce each described section when the fetus is scanned in the longitudinal or sagittal plane.

In order to illustrate the text, photographs of frozen frame, videotaped images were used. However,not only does videorecording degrade the live image, but also a still image is much less easy to understand and interpret than the real time image.

Figure 5.3 illustrates the tricuspid-pulmonary plane echocardiographically,correlated with the same anatomical section. This was the most readily and consistently obtained echocardiographic section in the early part of the study. It is achieved, as can be seen by reference to Figure 5.2. by scanning obliquely between the two fetal shoulders with the beam angled to pass closer to the right shoulder. This will display the right atrium, tricuspid valve, pulmonary outflow tract and pulmonary valve. The aortic root sweeps out of the centre of this plane from the left ventricle which lies behind this plane of section. Moving the transducer into a more antero-posterior position just to the left of the fetal sternum as indicated diagrammatically in Figure 5.2,will visualise the short axis left ventricular plane. This is seen echocardiographically and anatomically in Figure 5.4. It displays the left ventricle as a concentric structure posteriorly,with the pulmonary outflow tract and muscular infundibulum supporting the pulmonary valve,arching around it. Angling the transducer from this plane so that the ultrasound beam passes from the

right of the sternum towards the left scapula will display the ductus plane illustrated diagrammatically in Figure 5.2, and anatomically and echocardiographically in Figure 5.5. The aorta is seen as a circular structure in the centre of this scan plane with the aortic valve within it. The right atrium, tricuspid valve, pulmonary outflow tract, pulmonary valve, pulmonary artery and its connection to the descending aorta via the ductus arteriosus can be seen. The left atrium can be seen lying posterior to the aorta. The eustachian valve guarding the top of the inferior vena cava and the flap of the widely patent foramen ovale can often be detected in this scan plane. These are both prominent structures which can be identified when sought in the fetal heart. Further transducer angulation from this scan plane will allow visualisation of the aortic arch. This is achieved by scanning in a very oblique plane from just anterior to the right shoulder and towards, but passing behind, the left shoulder as illustrated in Figure 5.2. The anatomical and echocardiographic features of the aortic arch can be seen in Figure 5.6. The head, neck and arm vessels can be seen arising from the arch,and the inferior vena cava is usually visualised in the same section.

Transverse planes

When the fetus is scanned in its transverse axis, the transducer orientation required to visualise all four scan planes, is illustrated diagrammatically in Figure 5.7. The most readily and consistently obtained plane, displays the four cardiac chambers and is achieved in a completely transverse section of the fetal thorax as seen in Figure 5.8. The right ventricle is seen anterior to the left in the fetal thorax, the mitral and tricuspid valves can be seen between the left atrium and ventricle and right atrium and ventricle respectively. The foramen ovale flap can be seen in the left atrium in this section. It is sometimes possible from this echocardiographic section, particularly in the later gestational age fetuses, to detect that the pulmonary veins are inserted in the back of the left atrium. Maintaining a transverse section of the fetal thorax but scanning a little higher, at about the level of the manubrio-sternal junction as illustrated in Figure 5.7, will produce the aortic wedge plane. This is displayed echocardiographically and anatomically in Figure 5.9. The aorta is seen as a circle at the centre of this scan plane wedged down between the two atrioventricular valves. Returning the transducer to the four chamber plane and then angling the transducer cranially will allow the four chamber aortic root plane to be seen. This plane is illustrated anatomically and echocardiograph-

ically in Figure 5.10. The two atrioventricular valves can be seen and the aorta arising from the left (or posterior) ventricle. Aortic-mitral continuity can be observed. Angulation of the transducer from the horizontal plane into a more sagittal plane between the left hip and right fetal shoulder will demonstrate the long axis of the left ventricle. This plane is seen echocardiographically and anatomically in Figure 5.11. The infundibulum of the right ventricle is seen anteriorly. Aortic-septal and aortic mitral continuity are demonstrated by observing the origin of the aorta from the left ventricle. Thus the membranous and infundibular septum are well seen in this scan plane.

By utilising these described sections in a composite fashion the structures to be identified can be recognised and studied. Taking advantage of the unobstructed access to visualising the fetal heart the cardiac connections can be sought and followed from the venous to the arterial side in the right and left heart. It is essential to differentiate left from right atrium, left from right ventricle and aorta from pulmonary artery. Normal relations and connections must be identified before a diagnosis of cardiac normality can be given.

Atrial differentiation

In practical terms the right atrium can be distinguished by noting its venous connections. Just behind the tricupid-pulmonary plane,the inferior vena cava and the superior vena cava can be noted entering the atrium thought to be the right atrium (Figure 5.12). Without losing sight, echo-cardiographically, of this atrium the transducer is turned through 90°. It can then be seen in the normal heart, that this atrium is the anterior one and that it connects to a morphological right ventricle. In the posterior atrium the foramen ovale flap can clearly be seen in the four chamber plane (Figure 5.13). The pulmonary veins can sometimes be detected entering this posterior atrial chamber. These normal atrial features taken together,allow a fairly positive differentiation of the atrial chambers.

Ventricular differentiation

The morphologically right ventricle can be distinguished from the morphologically left by observing differential trabeculation between the two ventricles and differential septal insertion of their atrioventricular valves. The right ventricle is more trabeculated than the left and this is manifested by additional echoes seen in its apex. The septal insertion of the tricuspid valve is more apical than the

mitral insertion and can be detected by a difference in angulation of the two atrioventricular valves. Both these ventricular differentiating features are best noted in the four chamber projection of the fetal heart. But it is more easily appreciated in an "apical-type" four chamber projection than in a "subxiphoid-type" four chamber. These four chamber projections are illustrated in Figure 5.14 (a) and (b). Figure 5.14 (a) is a four chamber projection of the fetal heart but the ultrasound beam is at right angles to the ventricular septum. In this projection it is much more difficult, if not impossible, to be sure of the difference in septal insertion of the atrioventricular valves and trabecular pattern. This section corresponds to the subxiphoid four chamber echocardiographic section seen in postnatal life. In Figure 5.14 (b) the ultrasound beam is parallel to the ventricular septum. The extra apical echoes in the anterior ventricle and the difference in angulation of the two atrioventricular valves can be seen. This corresponds to the apical four chamber plane seen in postnatal echocardiography. It is usually possible in any single fetus to achieve both four chamber projections by moving "round" the fetal thorax by moving across the maternal abdomen. If not, fetal movement during the period of scanning will often display both projections.

Differentiation of the great arteries

Cranial angulation of the transducer from the four chamber projection of the fetal heart will demonstrate a great artery arising from the posterior ventricle (Figure 5.10). There is continuity between this arterial valve and the atrioventricular valve in the posterior ventricle. But unless this artery is followed to its connection to the descending aorta, it could be either the pulmonary artery, as in transposition of the great arteries, or the aorta. Normally this artery will lead to the ascending aorta, the arch of the aorta with the head vessels arising from it, and the descending aorta (Figure 5.6). The pulmonary artery can be seen arising from the anterior ventricular chamber seen in the short axis left ventricular plane (Figure 5.4). Following this artery,in a similar way to following the aorta,will show this artery connecting via the ductus arteriosus to the descending aorta (see Figure 5.5). Not until both great arteries have been followed to their connections have they been differentiated.

Discussion

In the original paper describing echocardiographic and anatomical correlates in the fetus (131) we enumerated the frequency of identification of each section in two series of 100 patients each. The first hundred patients were examined

before the anatomical studies were made, the second hundred after. As we have indicated in the introduction to this chapter our method of examining the fetal heart has progressed from this approach, so that now, instead, a "check-list" of structures to be identified is considered at every examination of every patient. Any structure not seen at the first examination can be specially sought if a second examination is performed.

It is possible to identify normal cardiac connections in every case between 16 weeks gestation and term. The identification of normal cardiac connections excludes many major congenital defects. It is easiest to be confident of fine detail in the optimum scanning time between 18 and 28 weeks gestation. Optimum image quality is obtained in over 95% of patients within this gestational age range. However even when this is achieved it is likely that minor valvular anomalies, small atrial or ventricular septal defects will be overlooked. In postnatal life clinical signs may suggest a diagnosis of mild aortic or pulmonary stenosis or a small ventricular septal defect. Despite the prejudice these clinical signs produce in the observer it is often impossible to either identify or exclude such minor defects with absolute confidence in the postnatal echocardiogram.

The prenatal echocardiogram must always be considered in isolation or "blind", unlike the postnatal study. Therefore it is essential to identify each normal structure, chamber or connection in a logical and thorough fashion. Only if the method of study we have described is carefully followed will errors be minimised. But despite this, as we have indicated, minor anomalies will be overlooked.

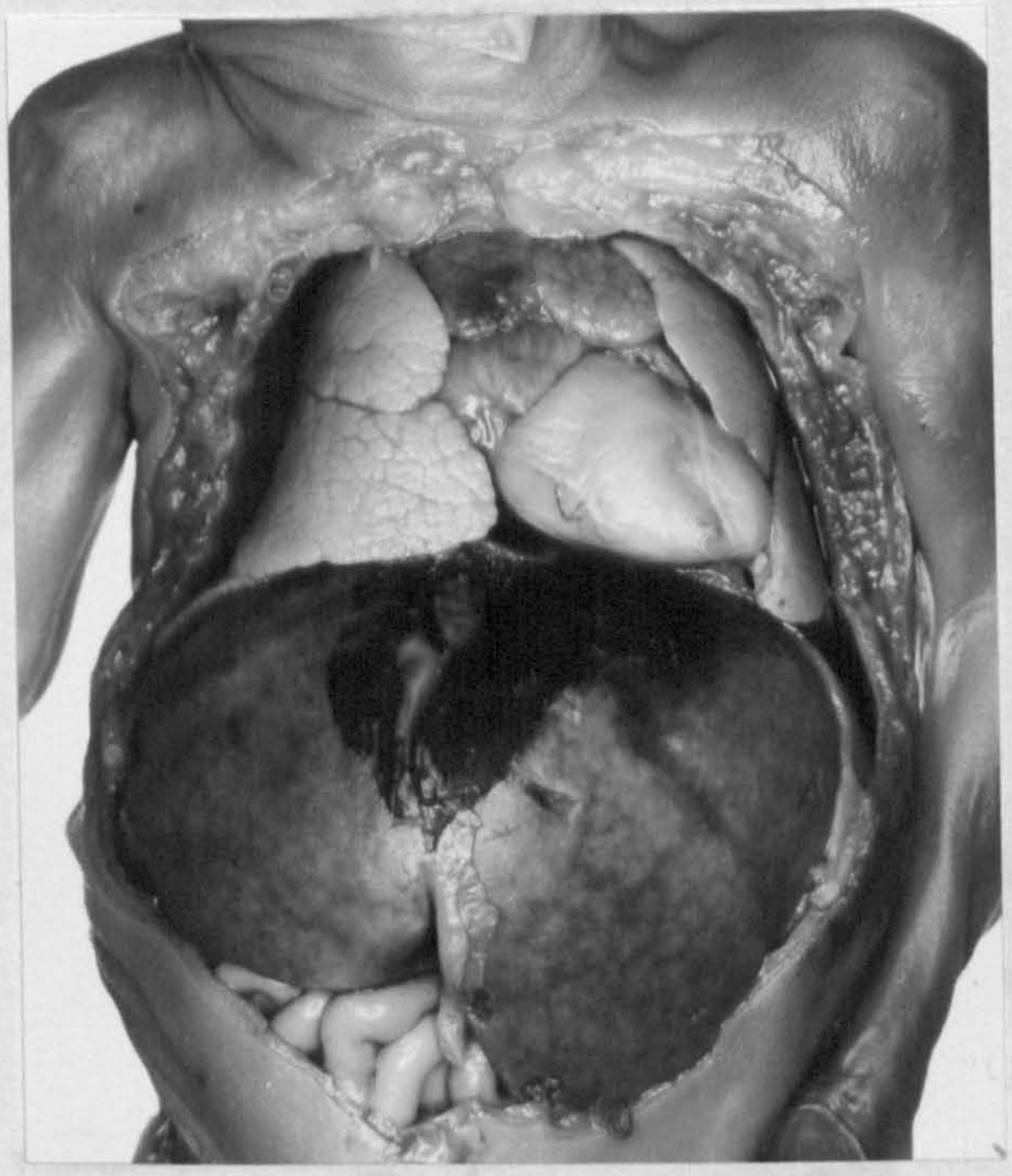


Figure 5.1. Anterior dissection of an 18 week fetal thorax. Note airless lungs, large fetal liver, cranially displaced apex of the fetal heart.

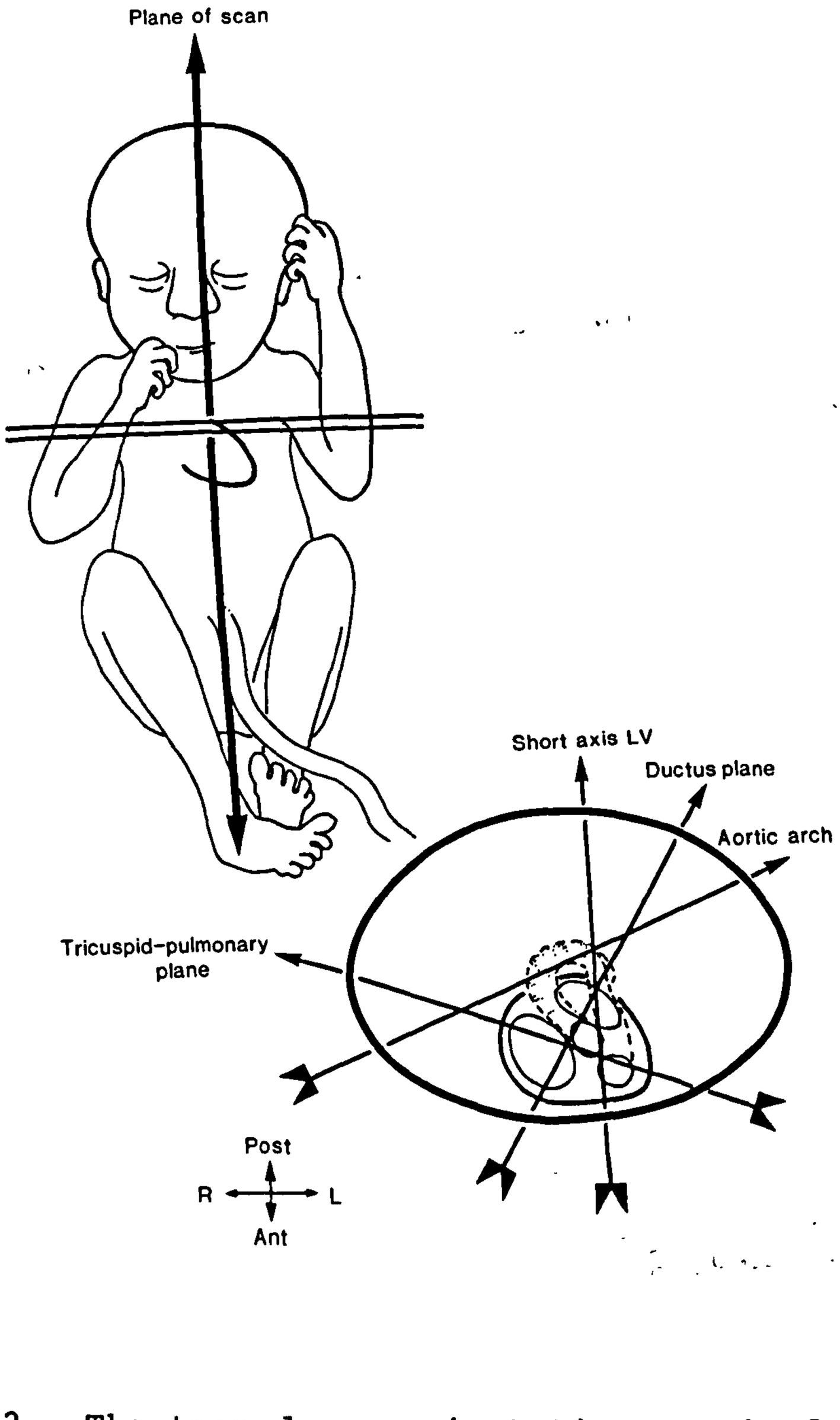


Figure 5.2. The transducer orientation required to visualise the four longitudinal planes. The inset represents a section removed from the fetal thorax to display diagrammatically the direction of the beam, relative to the heart and thorax, required to produce each plane, while scanning up and down the fetal trunk.

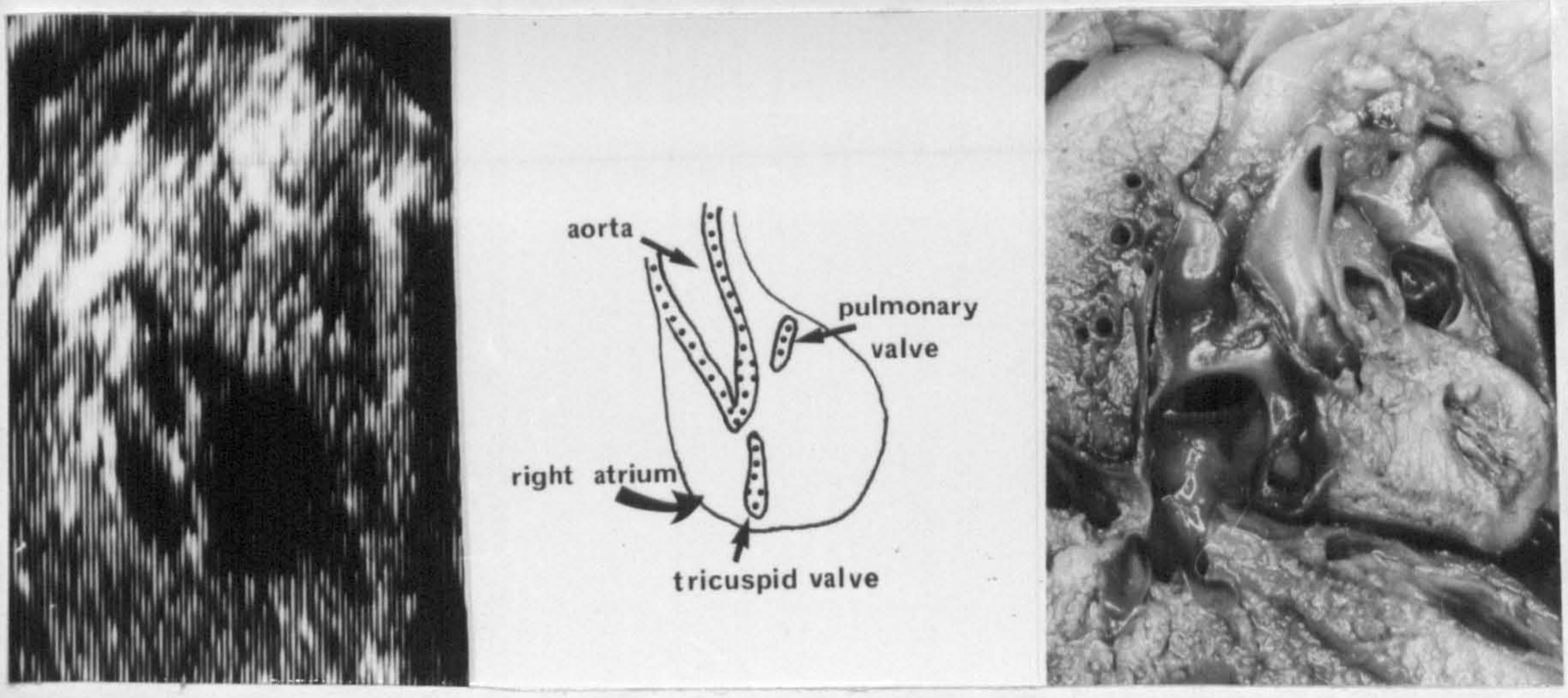


Figure 5.3. The tricuspid pulmonary plane displayed echocardiographically and anatomically. The right atrium, tricuspid valve, pulmonary outflow tract and pulmonary valve can be seen. The aorta sweeps out of the centre of this section from the left ventricle which lies posteriorly.

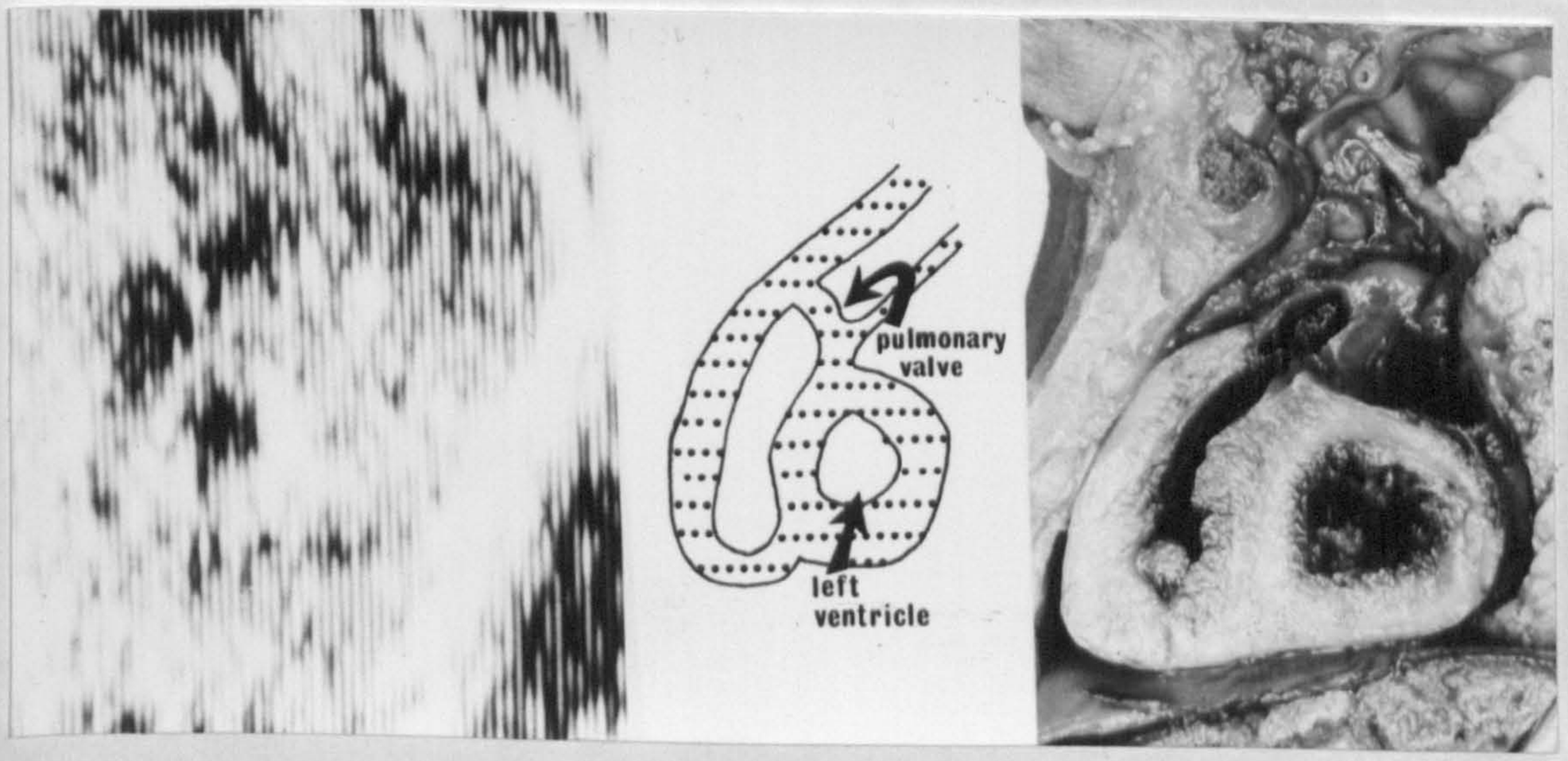


Figure 5.4. Short axis left ventricular plane displayed echocardiographically and anatomically. The left ventricle is seen as a concentric structure with the pulmonary outflow tract and complete muscular infundibulum which supports the pulmonary valve, arching over it.

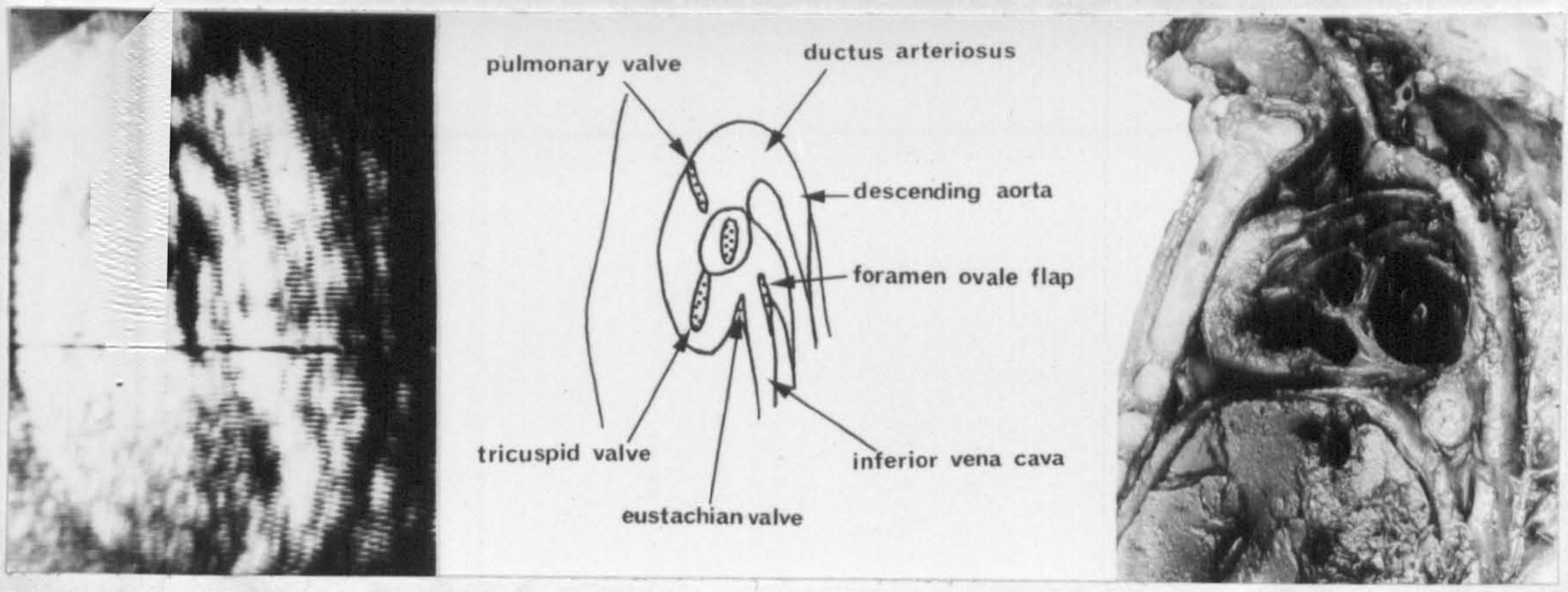


Figure 5.5. Ductal plane displayed echocardiographically and anatomically. The aorta and valve closure line is seen as a circle in the centre. The inferior vena cava can be seen entering the right atrium. The tricuspid valve, pulmonary outflow tract, pulmonary valve, pulmonary artery and ductus arteriosus connecting to the descending aorta are also seen in this plane.

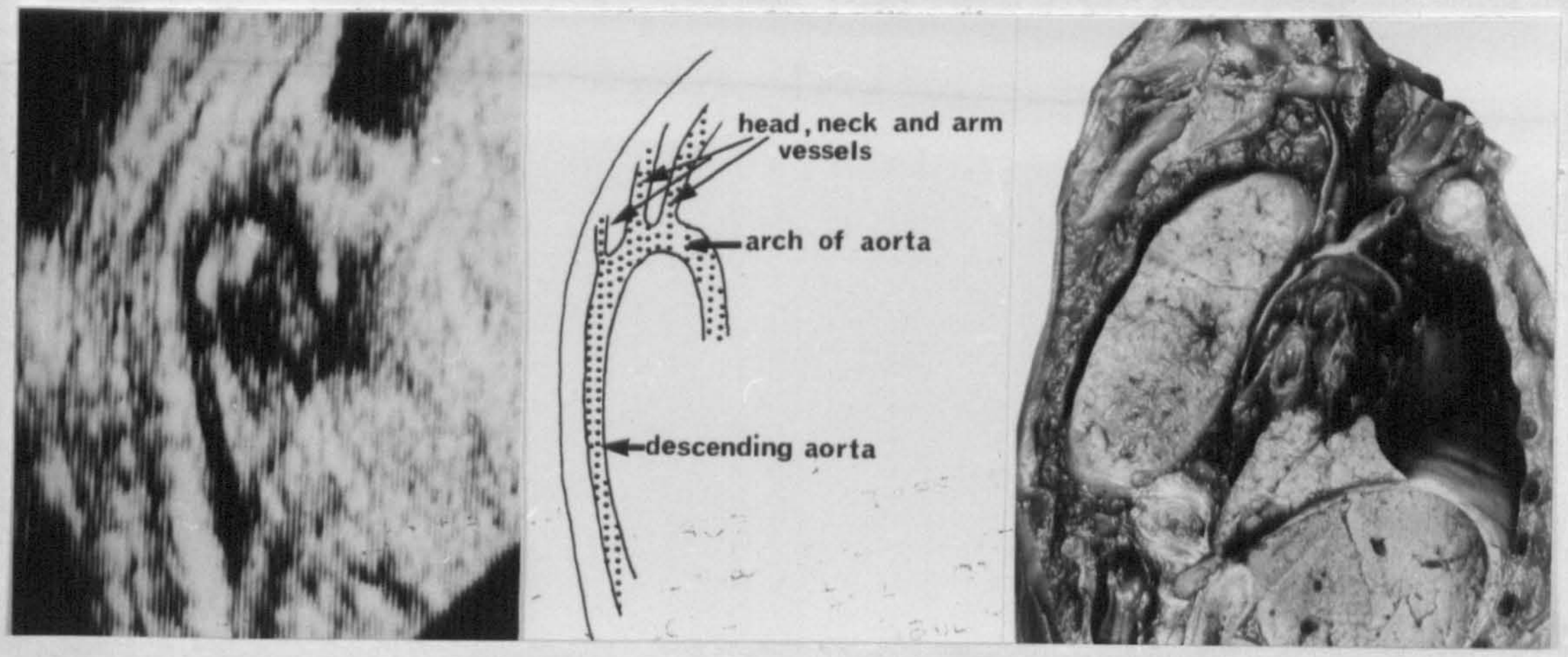


Figure 5.6. Aortic arch plane displayed echocardiographically and anatomically. The ascending, descending and arch of the aorta can be seen with head, neck and arm vessels arising from the arch.

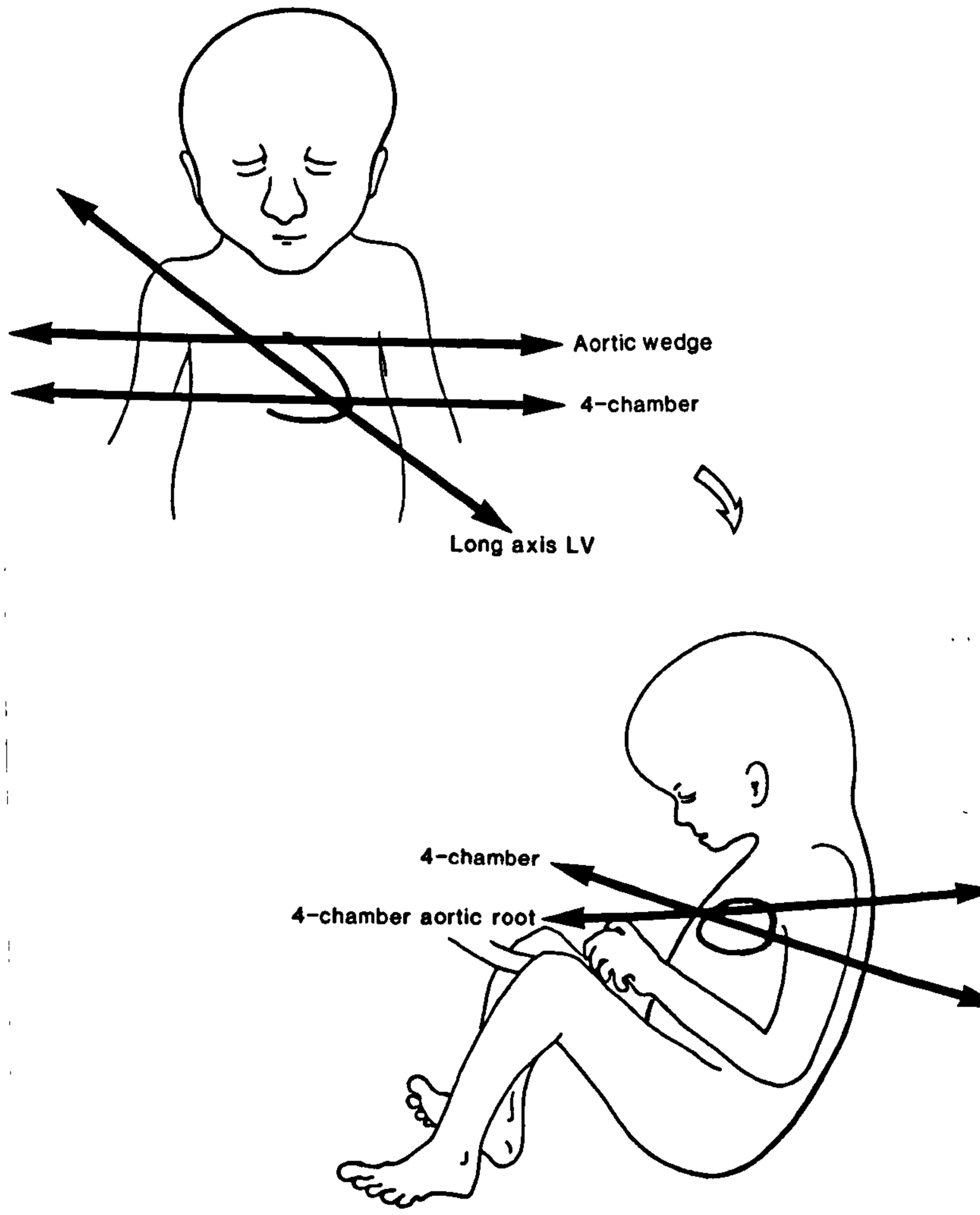


Figure 5.7. Transducer orientation required to visualise the described horizontal scan planes of the fetal heart. The four chamber and aortic wedge planes are truly horizontal, cranial angulation visualises the four chamber aortic root plane, angulation towards the right shoulder displays the long axis of the left ventricle.

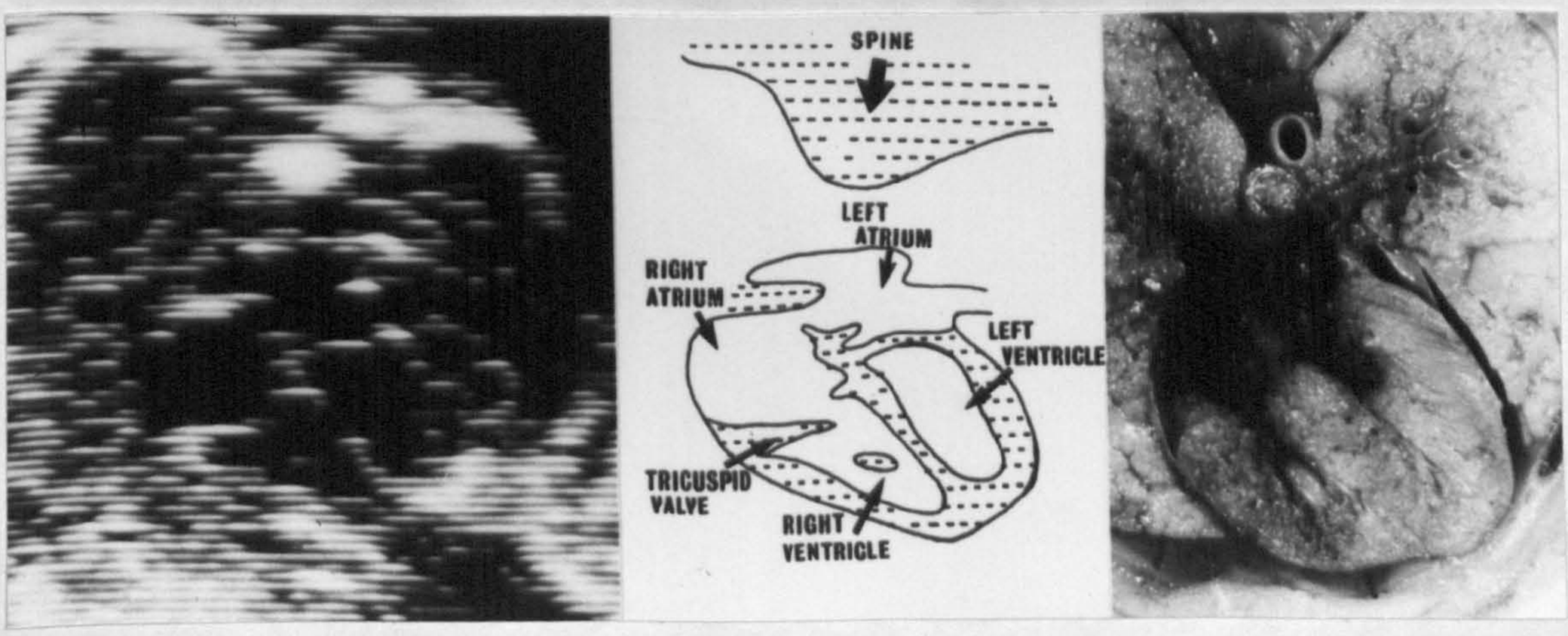


Figure 5.8. The fetal heart is seen echocardiographically and anatomically in the four chamber projection. The two atria and intra-atrial septum are seen. The right and left ventricle and intra-ventricular septum are seen. The mitral and tricuspid valves are seen.

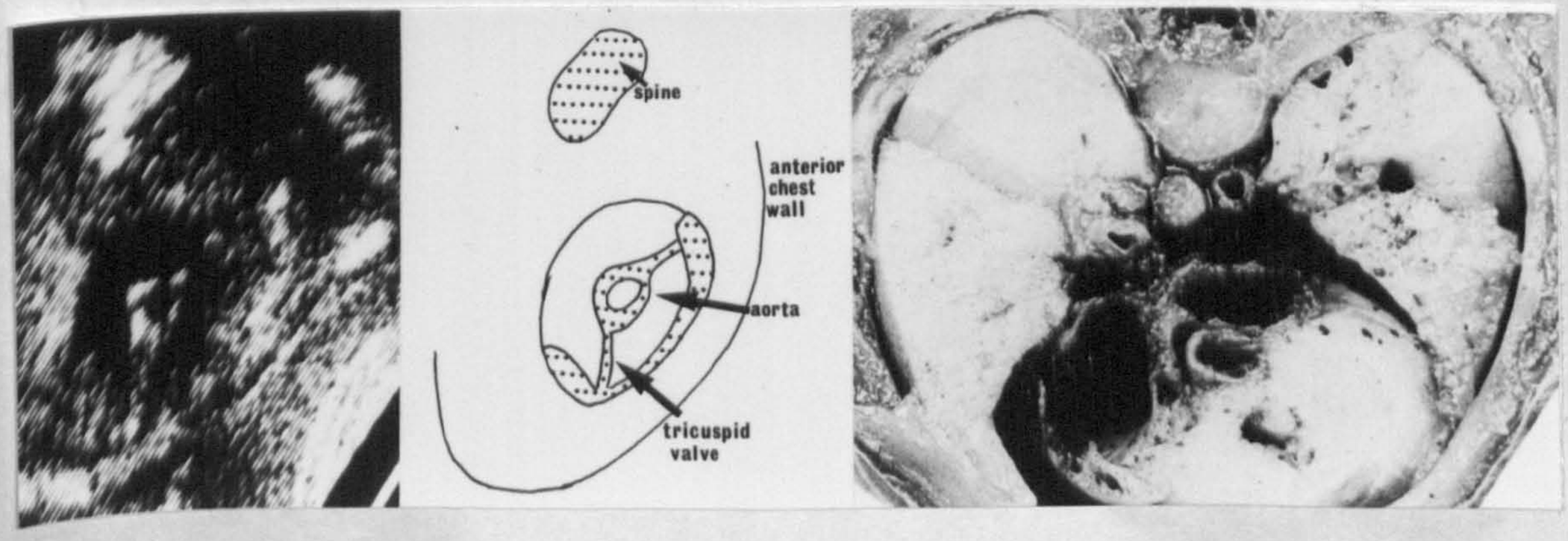


Figure 5.9. The aortic wedge plane is seen echocardiographically and anatomically. The aorta is wedged down between the two atrioventricular valves in the centre of the heart.

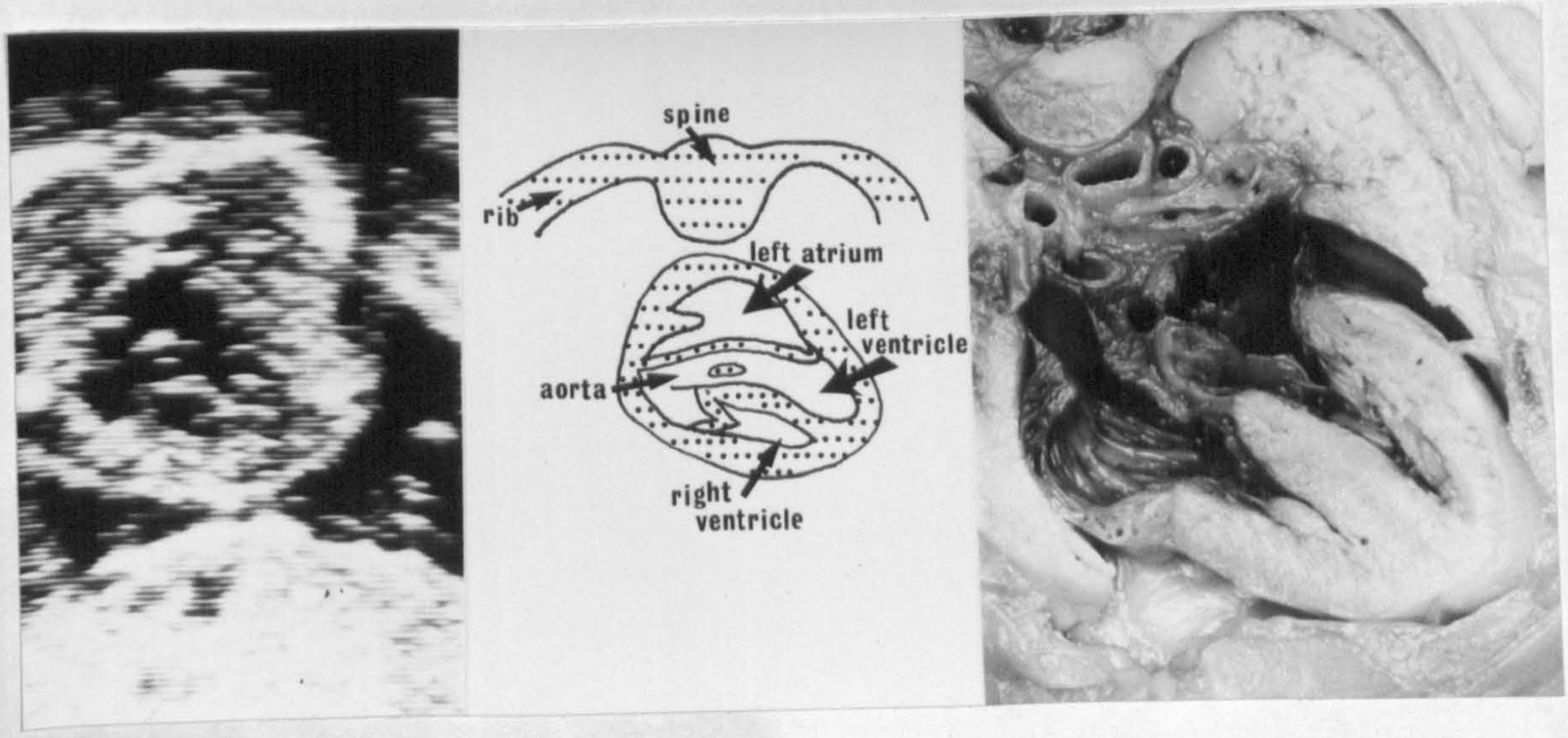


Figure 5.10. Four chamber aortic root plane. The aortic root is seen arising from the left ventricle; aortic septal and aortic-mitral continuity can be observed.

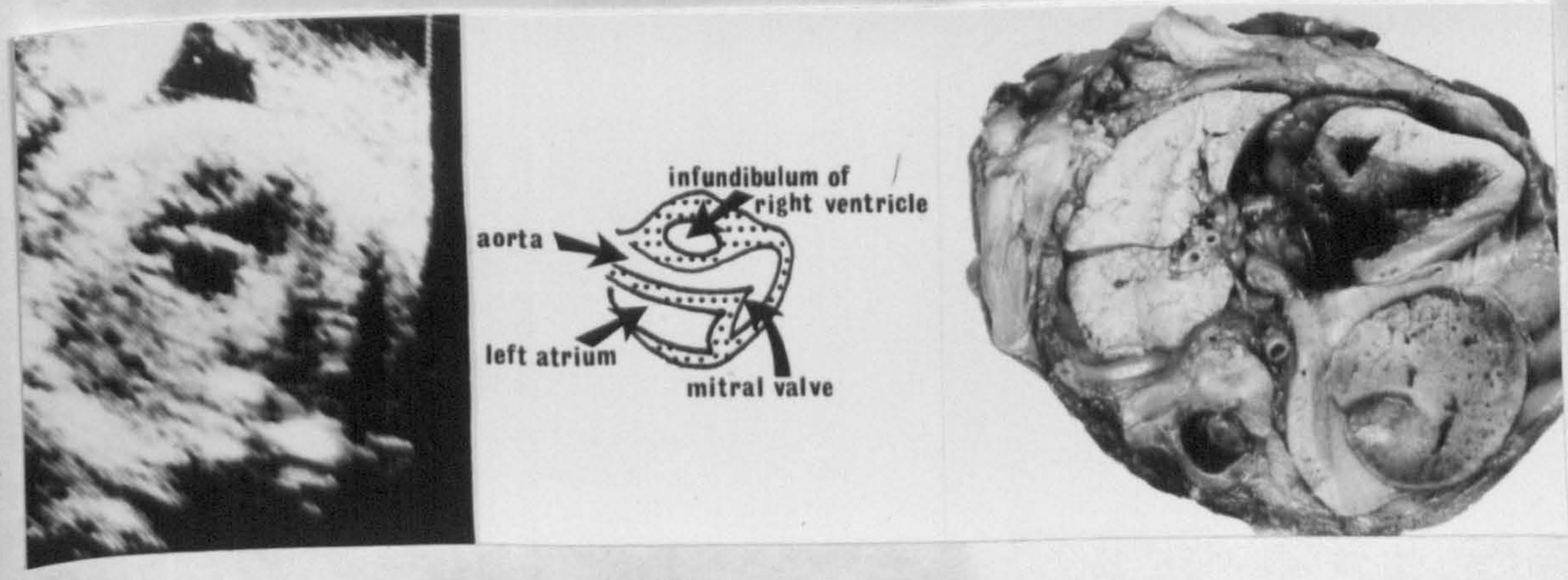


Figure 5.11. Long axis of left ventricle plane. The infundibulum of right ventricle can be seen anterior to the left ventricle. The aorta, mitral valve, left atrium and left ventricle can all be seen.

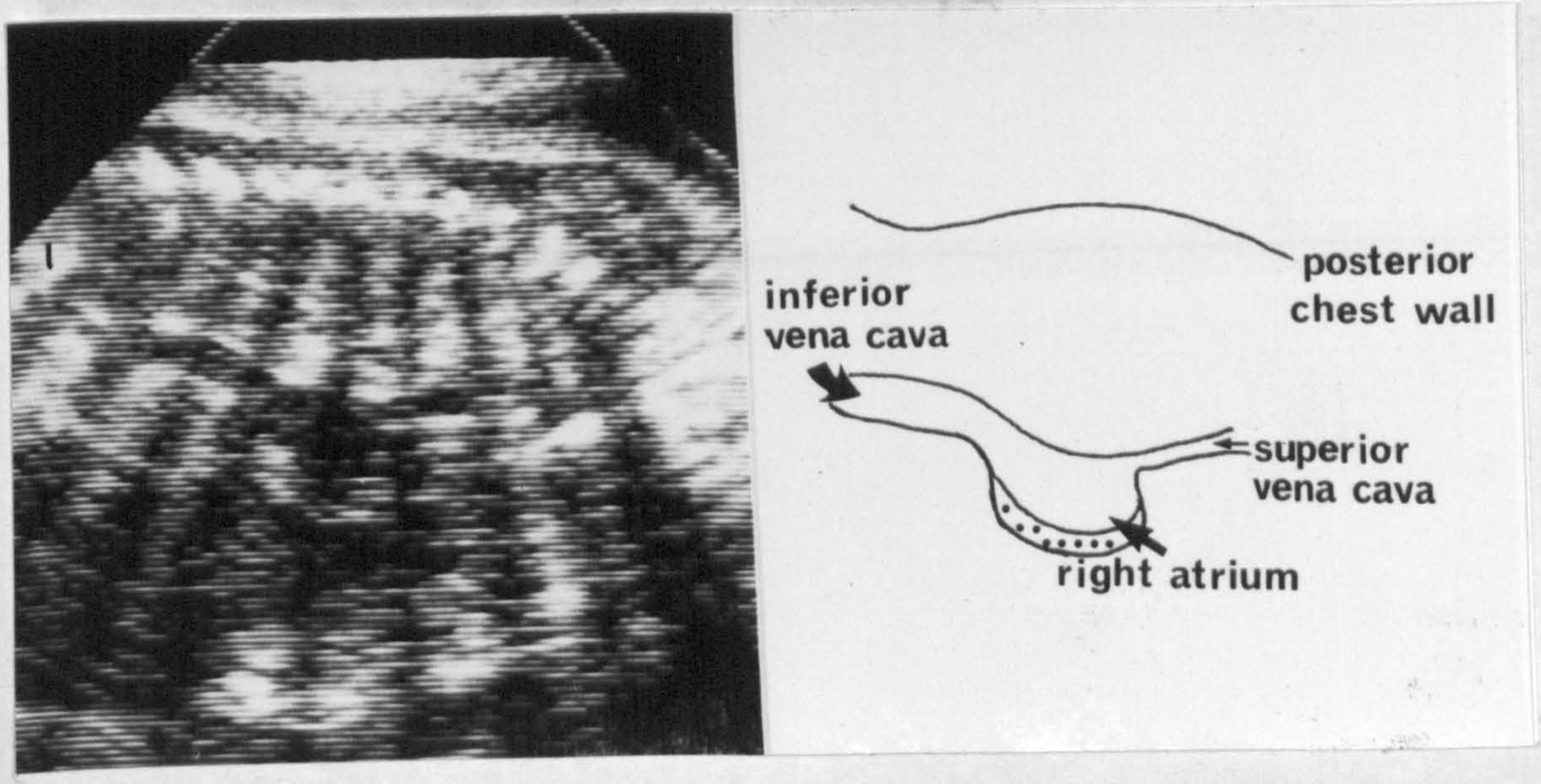


Figure 5.12. The superior and inferior vena cavae can be identified entering the anterior atrium.

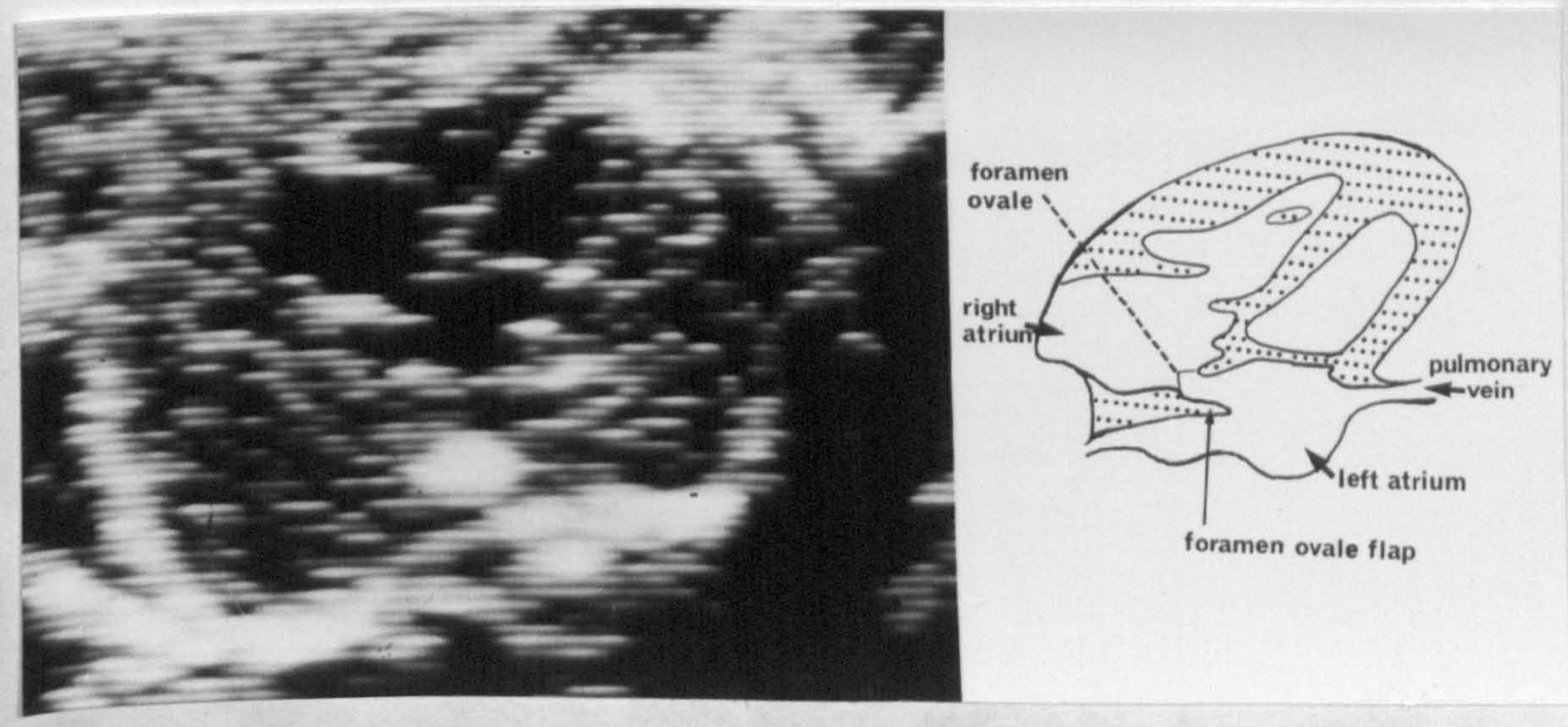


Figure 5.13. Four chamber projection showing the foramen ovale between the two atria and the foramen ovale flap in the posterior atrium.

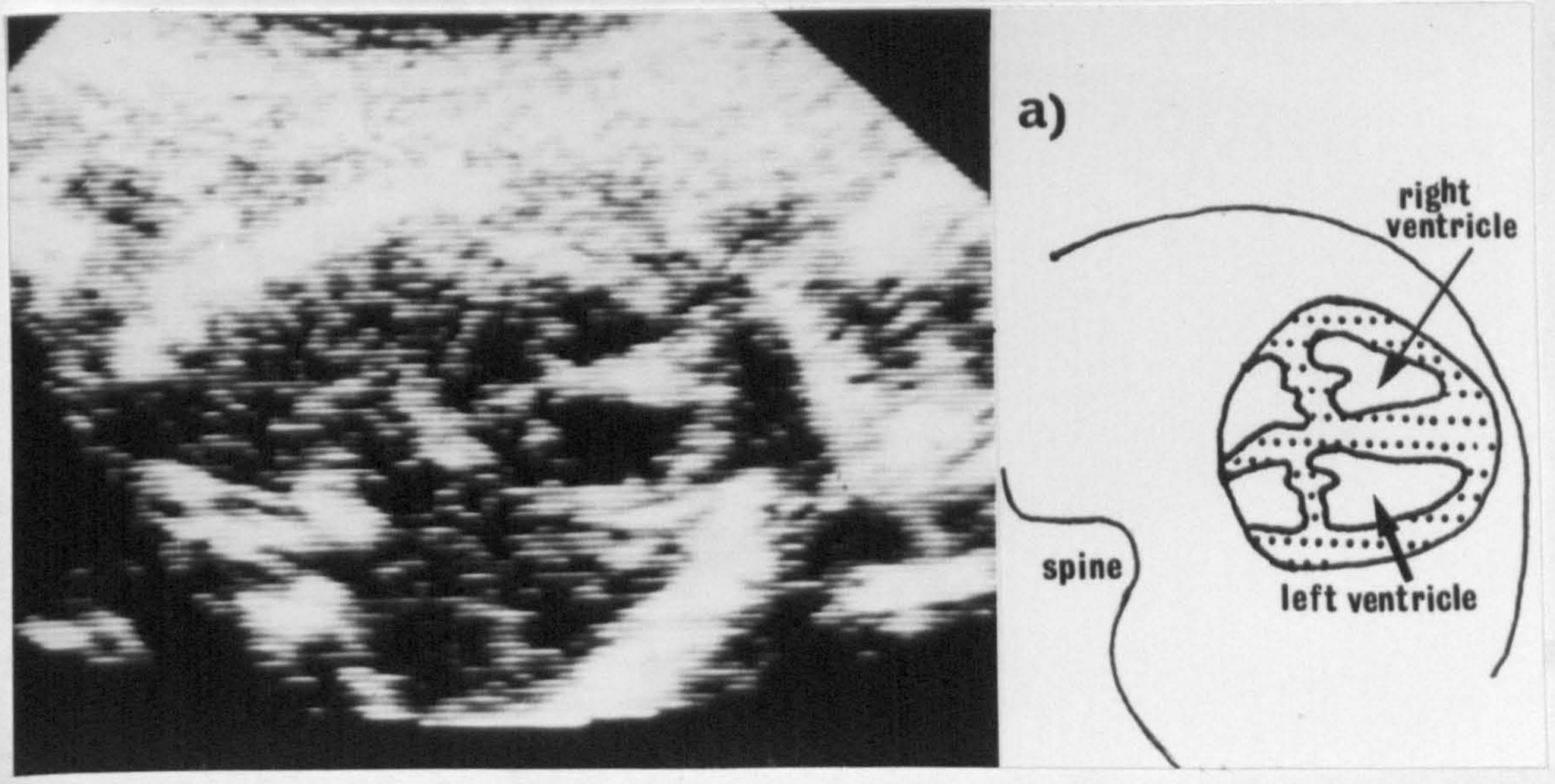


Figure 5.14a. "Subxyphoid type" four chamber projection of the fetal heart showing both atrio-ventricular valves. Differential insertion can in fact be appreciated but differential trabeculation can not.

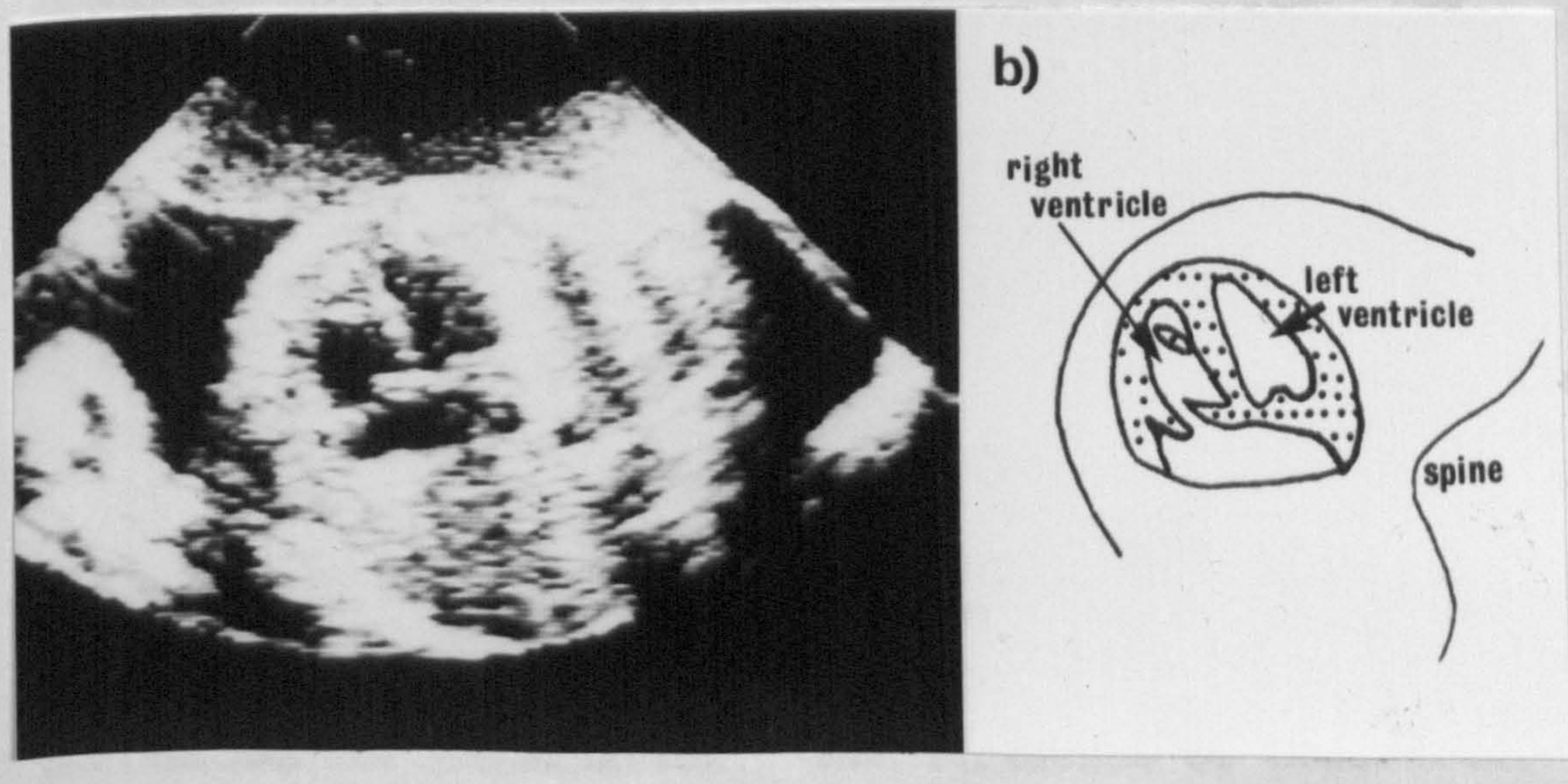


Figure 5.14b. "Apical type" four chamber projection of the fetal heart. The difference in insertion can be detected by the difference in angulation of the two atrioventricular valves. Differential trabeculation can be seen.

CHAPTER 6

RESULTS

Direct anatomical and echocardiographic correlative study

During the early part of the study, fetal echocardiograms were performed in 28 pregnancies prior to midtrimester termination. This provided direct correlation between the echocardiographic findings and the structural anatomy. It allowed validation of the technique at an early stage in the study. It also demonstrated some of the possible limitations of fetal echocardiography in the early gestation fetal heart. This chapter introduces the topic of prenatal detection of congenital heart disease which is more fully dealt with in Chapters 11,12 and 13. However, as the abnormalities detailed here were detected in this early validatory part of the study, it is relevant to describe them here.

A series of 28 patients about to undergo midtrimester termination of pregnancy were studied. The indications for termination are detailed in Table I. It can be seen that the majority (19) had an extracardiac fetal anomaly as the indication for termination. The incidence of congenital heart disease is increased in fetuses with extracardiac anomalies, particularly so in those fetuses with a chromosomal

abnormality (8 cases) (132). The anatomical specimens are collected and dissected between one day and three weeks after the echocardiographic study. All the anatomical dissections were undertaken by one morphologist (Professor R.H. Anderson) with the author. This enabled direct correlation of the echocardiographic findings with anatomical findings and thus evaluation of echocardiographic prediction at an early stage in the study.

In all 28 cases only one opportunity for echocardiographic study of the fetus was possible. In one case fetal size and picture quality was considered inadequate for any prediction to be made. In one case picture quality was poor and no prediction would have been made had there been an opportunity for restudy. In 26 pregnancies adequate image quality was achieved to allow prediction of the findings.

Prediction of normality

Twenty fetal hearts were judged as normal echocardiographically. That is, they were seen to have two atria and two ventricles normally connected with normal venous and arterial connections. The mechanism of the foramen ovale within the atrial septum was noted and the ventricular septum thought to be intact. The gestational age range of this group was between 16 and 27 weeks gestation. All twenty fetal hearts were confirmed to be normal anatomically.

Predicted malformations

In five of the cases seen in this series fetal echocardiography detected abnormalities which were confirmed anatomically.

Case 6.1. was a Down's fetus of 16 weeks gestational age. On the echocardiogram no atrial septum could be visualised. The two atrioventricular valves inserted equally at the top of the ventricular septum suggesting an ostium primum atrial septal defect. A diagnosis of common atrium was suggested. Anatomical dissection showed an ostium primum and an ostium secundum atrial defect. There was only a thin band of atrial septum between the two defects. Figures 6.1 and 6.2 illustrate this case. Figure 6.1 shows the echocardiogram and the anatomical section cut in the same plane. Figure 6.2 shows the anatomy of the atrial septum in greater detail.

Case 6.2. This was a fetus with fetal ascites and cystic hygromata diagnosed at 18 weeks gestation. The diagnosis of Turner's syndrome was suspected and amniocentesis performed for chromosome analysis. The fetal heart was examined at this time and several observations were made. Firstly the right ventricle was larger than the left. Measurement data

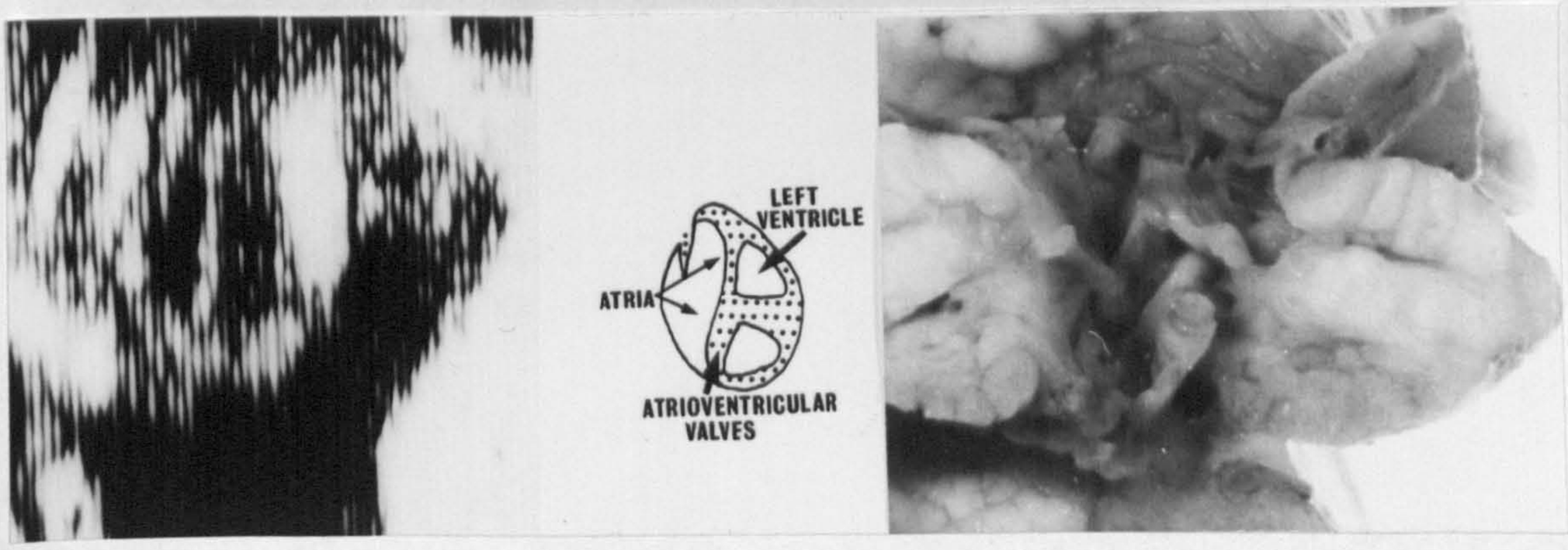


Figure 6.1. Case 1. The heart is seen echocardiographically and anatomically in the four chamber projection. The two atioventricular valves are inserted equally on the septum. There was no atrial septum seen in the echocardiogram.

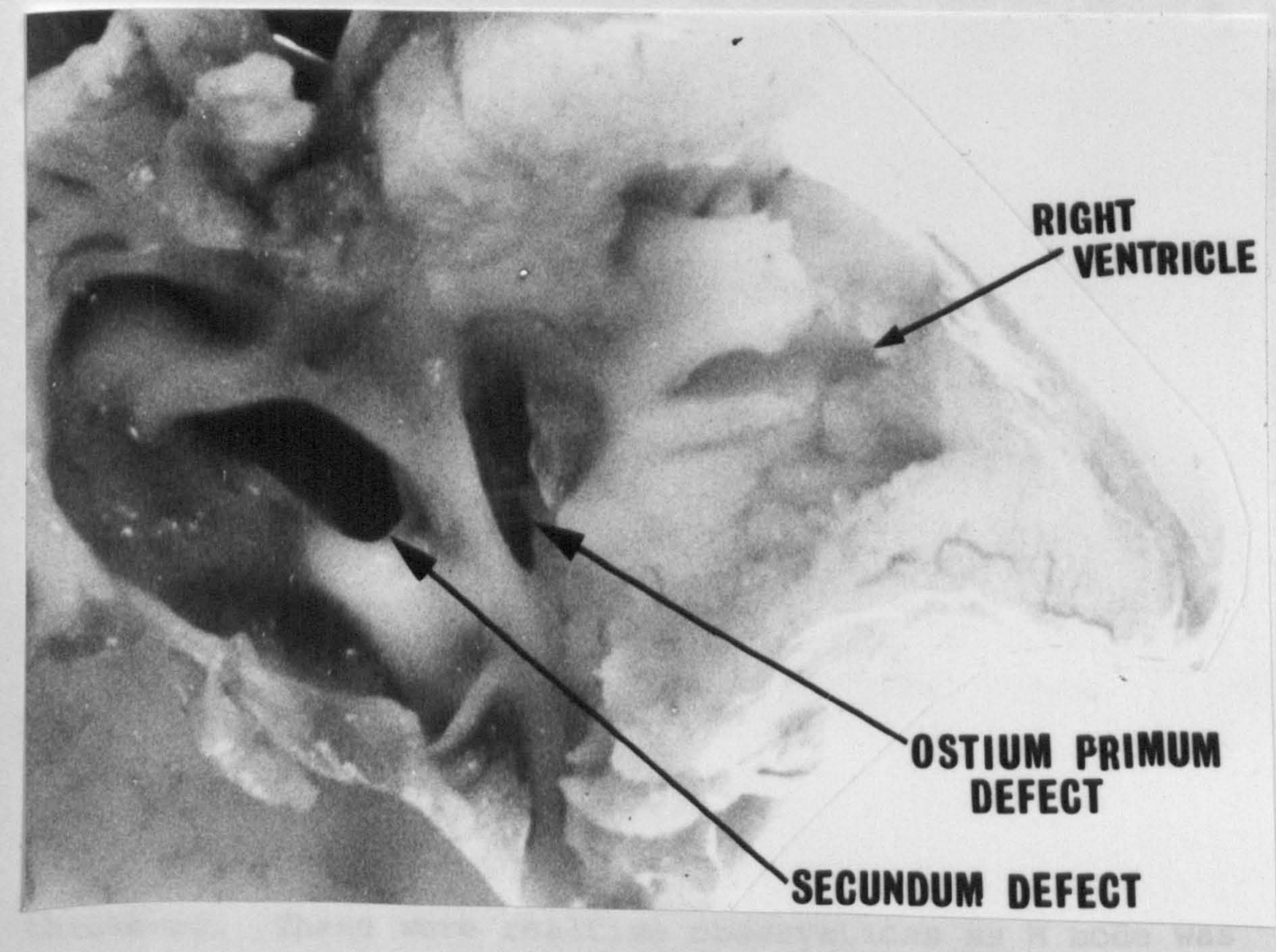


Figure 6.2. Case 1. The atrial defects can be seen in greater detail. The heart is viewed from the right after opening the right atrium and ventricle. The primum and secundum defects can be seen and the narrow intervening band of intact atrial septum.

was not available at this time so it was not known whether the left ventricle was small for the gestational age or the right ventricle enlarged. However there appeared to be a normal mitral valve in the left ventricle so it was suspected that the right ventricle was dilated. Retrospective comparison with M mode measurement data, described in Chapter 8, confirms this. Pulmonary valve motion also seemed flatter than usual suggesting increased pulmonary artery pressure. These findings are illustrated in Figure 6.3. The intracardiac connections appeared normal. The ascending aorta and the descending aorta could be visualised but no connection between the two could be seen. A diagnosis of coarctation or interruption of the aortic arch was suspected. Anatomically a grossly hypoplastic section of the aortic arch was found between the left carotid and left subclavian arteries. This is illustrated anatomically in Figure 6.4.

There were three fetal heartswhich showed similar abnormalities.

The first, Case 6.3., was a case of Meckel's syndrome, polycystic kidneys and encephalocoele (133) seen at 24 weeks pregnancy. The left ventricle was seen to be very thick-walled and very little intraventricular cavity could be seen on systole, Figure 6.5. The intraventricular septum was also thickened. These were realtime observations as M mode was

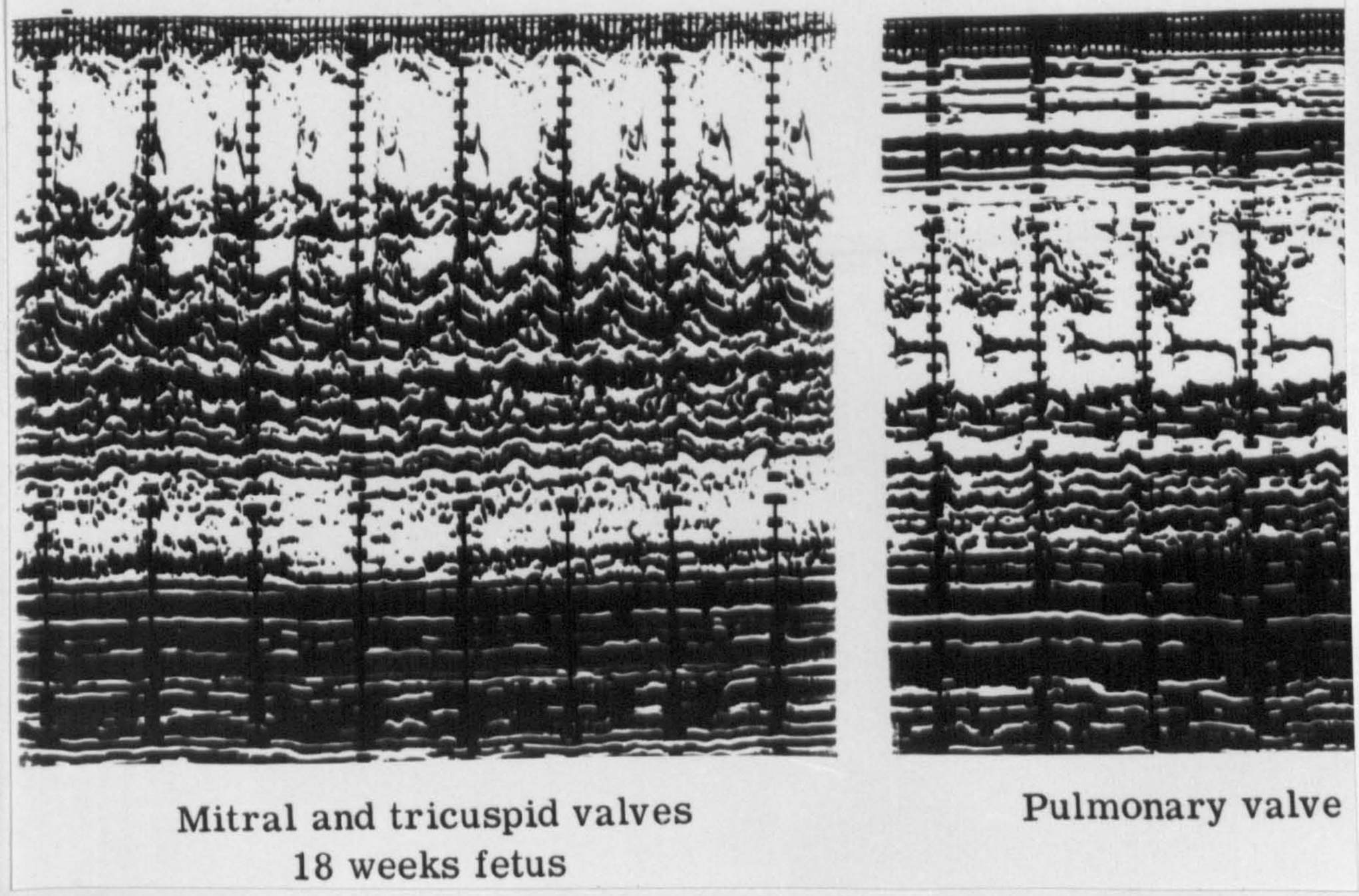


Figure 6.3. Case 2. The M mode echocardiogram through both ventricular chambers. The right ventricle is superior to the left and can be seen to be dilated, measuring more than twice the size of the left ventricle. The pulmonary valve motion is very flat with no "a" dip suggesting raised pulmonary artery pressure.

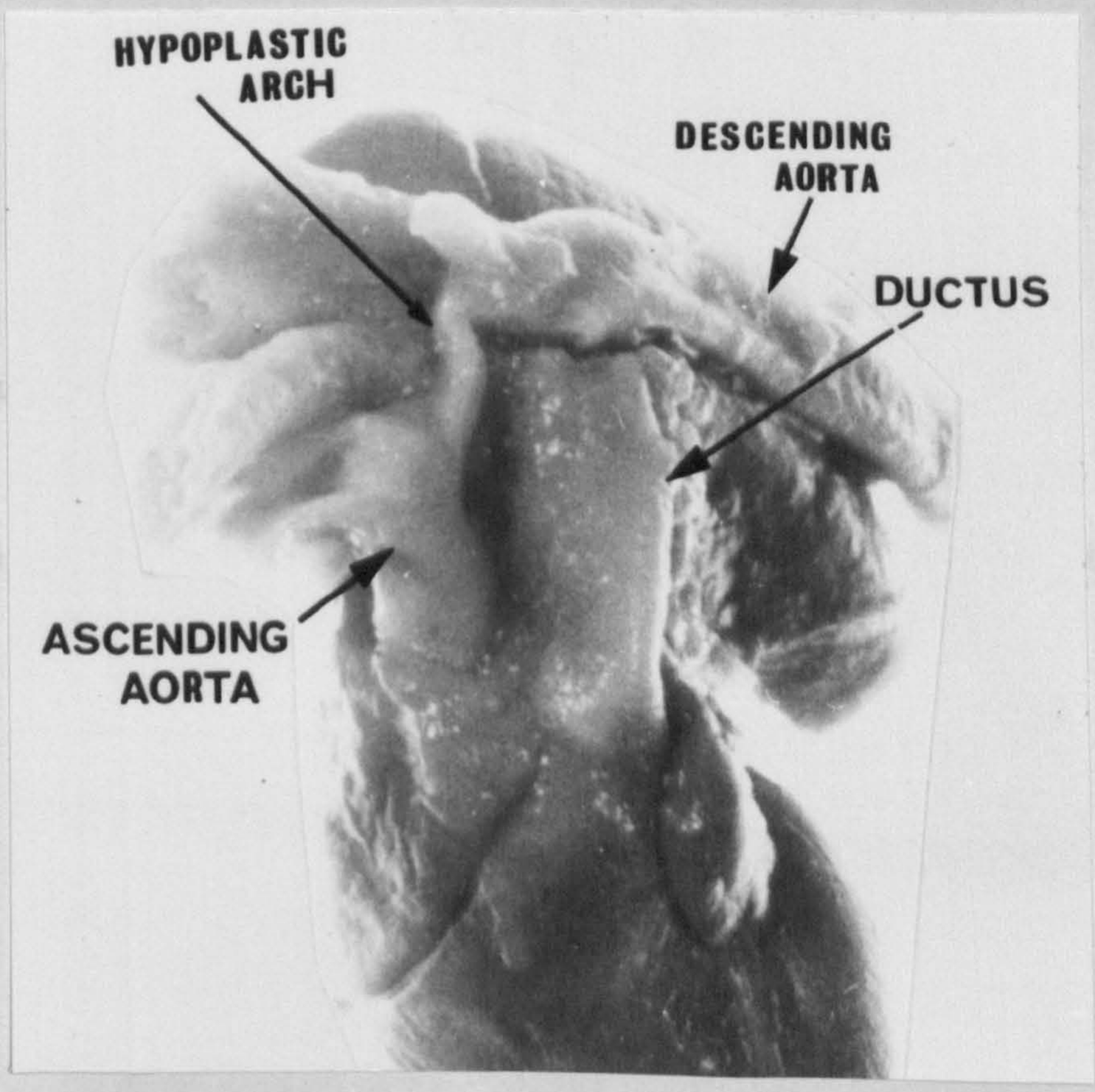


Figure 6.4. Case 2. The anatomical specimen shows hypoplasia of the aortic arch between left carotid and left subclavian arteries.

not available at that time. Anatomical dissection confirmed concentric left ventricular hypertrophy, Figure 6.6., but histological examination of the specimen showed the disorganisation of muscle fibre orientation that is strongly suggestive of a diagnosis of hypertrophic obstructive cardiomyopathy.

Case 6.4. presented at 25 weeks gestation with oligohydramnios. No renal tissue could be detected. The heart was found to show gross concentric hypertrophy, Figure 6.7, but the additional features of systolic anterior motion of the mitral valve and midsystolic closure of the aortic valve were seen on M mode examination. Figure 6.8 shows the M mode recording demonstrating the septal and left ventricular posterior wall thickening that was present. Autopsy confirmed renal agenesis and left ventricular hypertrophy.

Case 6.5. was seen at 24 weeks gestation. Severe obstructive uropathy was noted with small kidneys. The heart showed concentric left ventricular hypertrophy and cavity obliteration during systole, Figure 6.9. Termination of pregnancy confirmed the renal lesion and the cardiac findings.

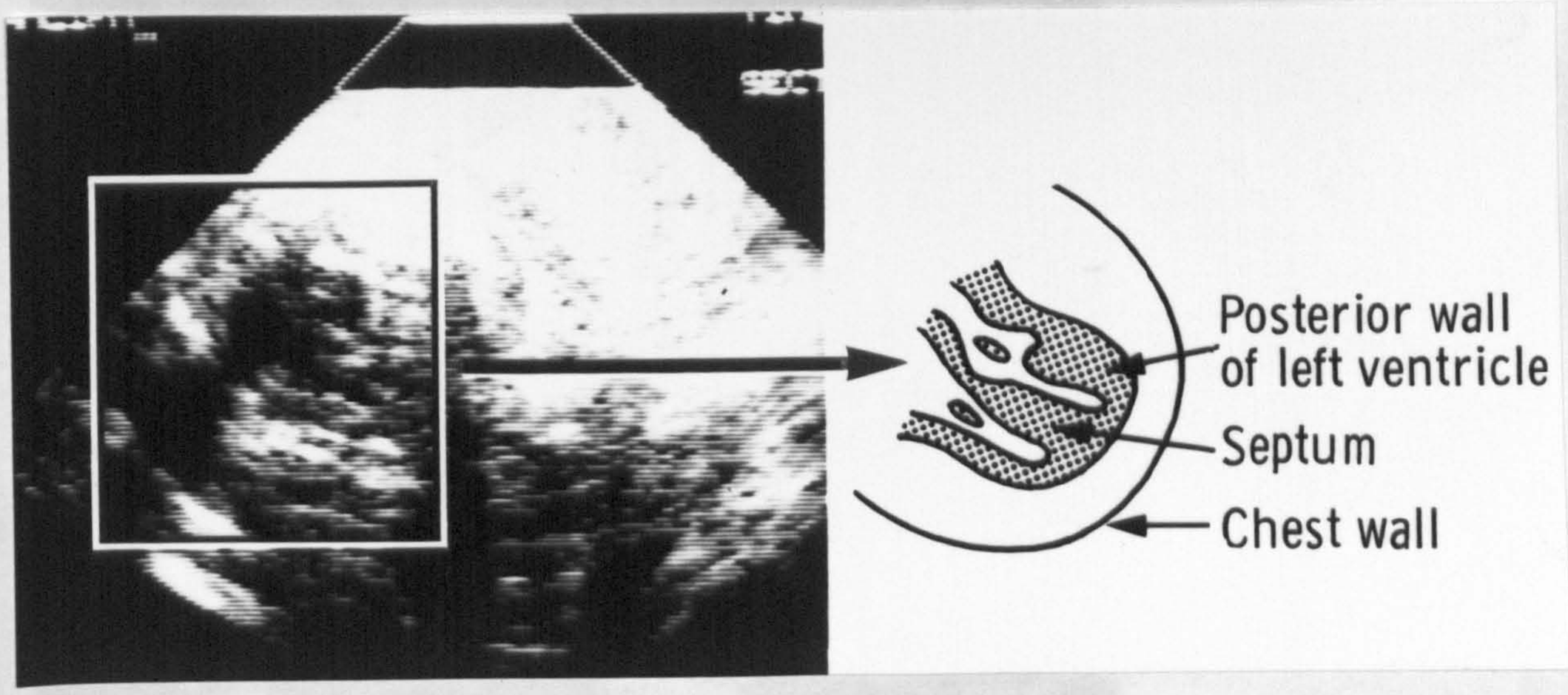


Figure 6.5. Case 3. The heart is seen in a four chamber projection. The left ventricular wall and septum are thickened.

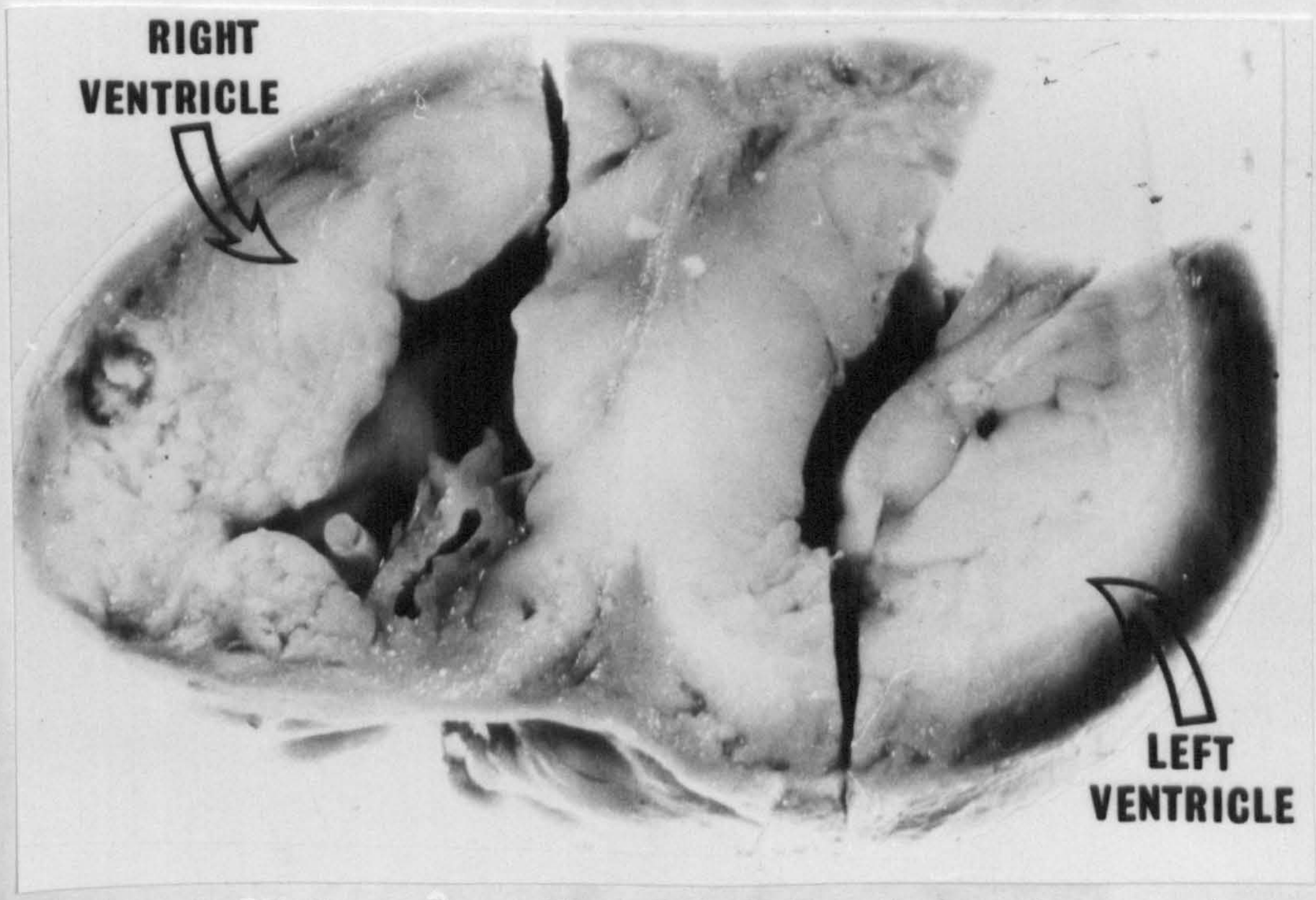


Figure 6.6. Case 3. The fetal heart has been cut in short axis through the body both ventricular chambers. The thickening of the septum and left ventricular wall can be seen. The left ventricular cavity is slit-like as it appeared on the echocardiogram.

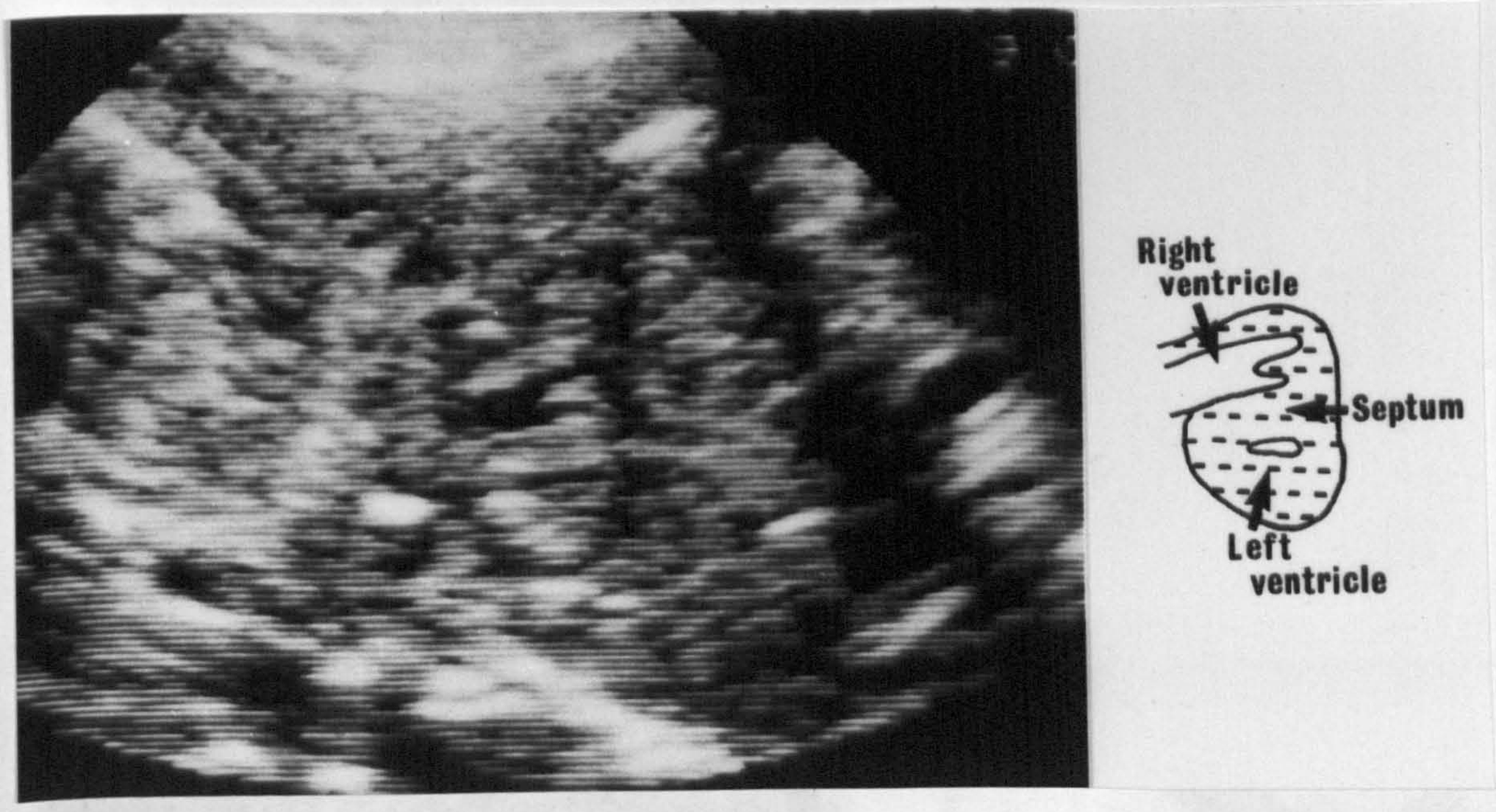


Figure 6.7. Case 4. The fetal heart is seen in the short axis left ventricular plane. The septal and left ventricular walls are hypertrophied.

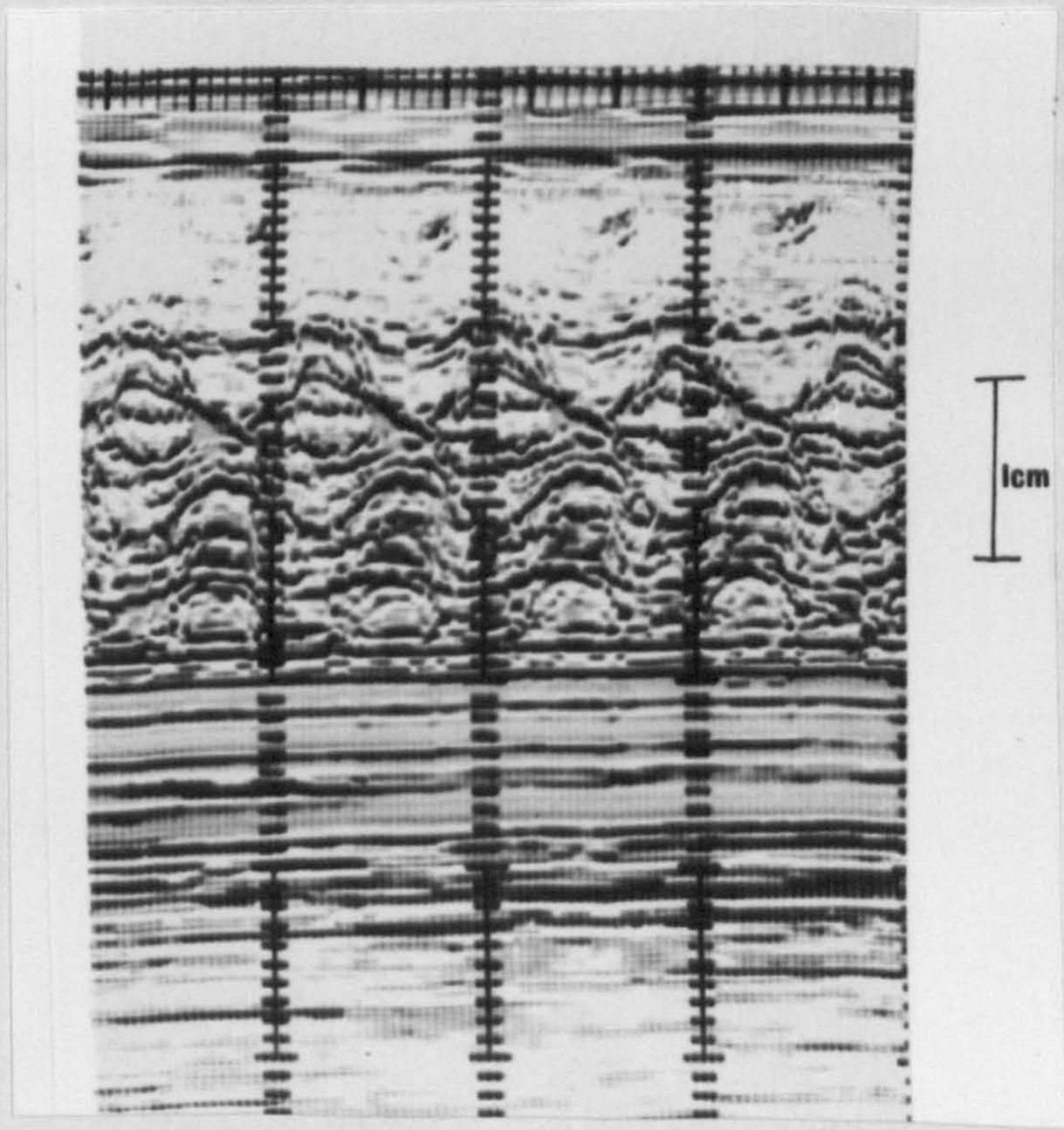
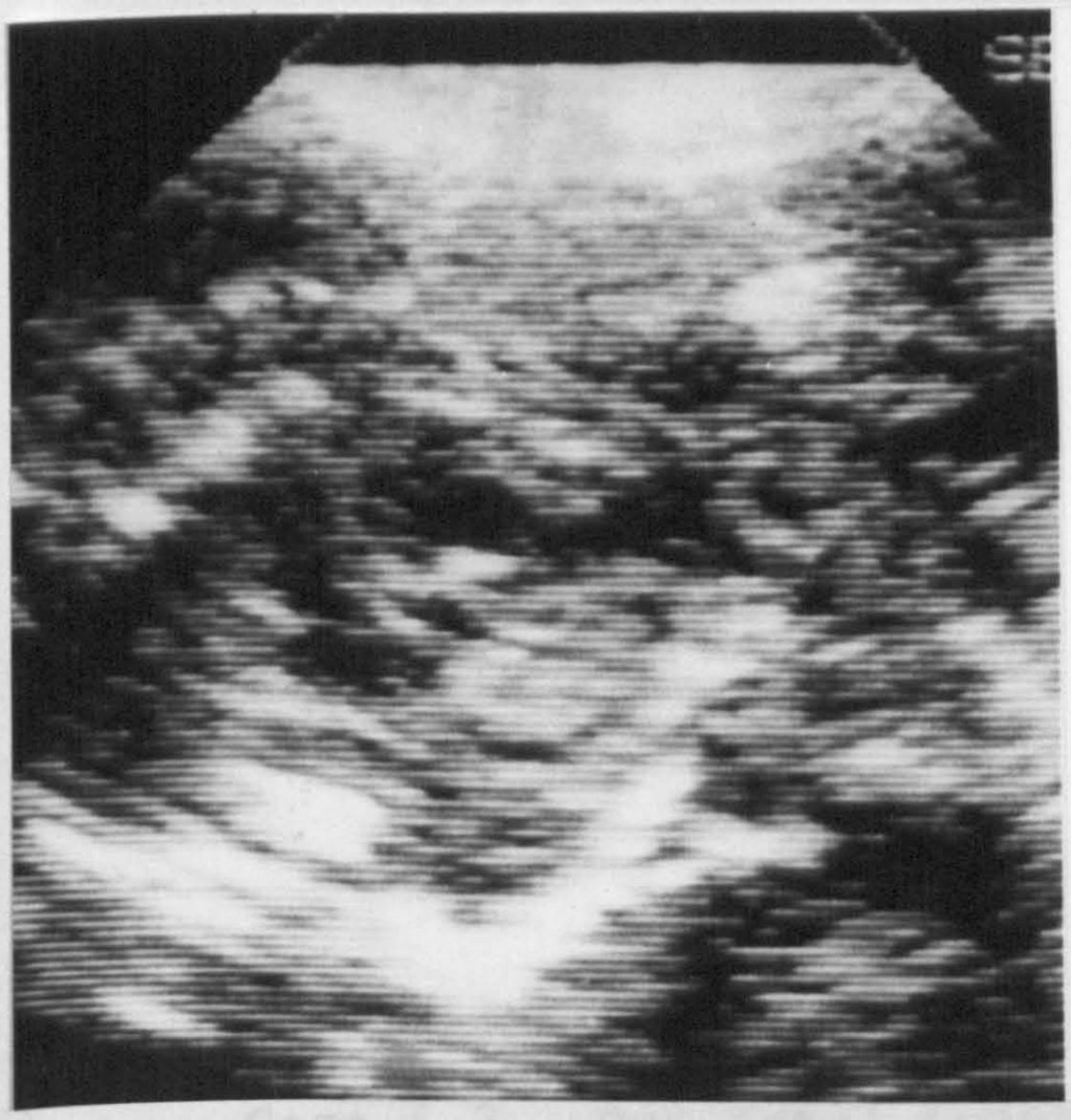


Figure 6.8. Case 4. M mode echocardiogram in the same case as the above figure. Measurement of the septum and left ventricular wall lay outside the 95th percentile for these measurements at this gestational age.



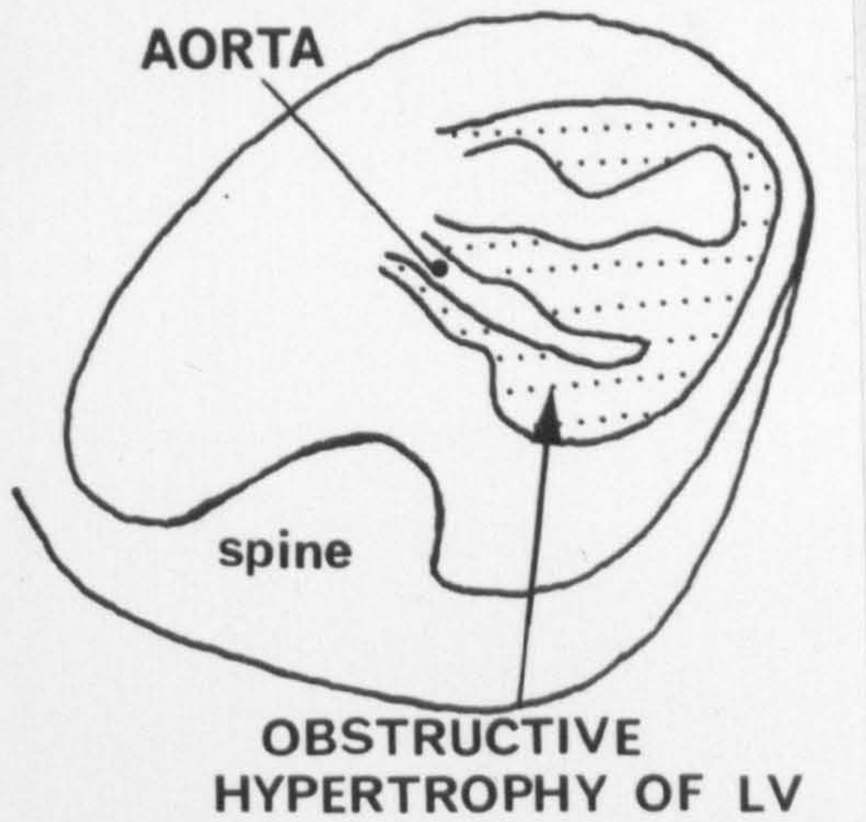


Figure 6.9. Case 5. The left ventricle is seen in long axis showing origin of the aorta. There is left ventricular posterior wall and septal thickening. There is very small intra ventricular cavity on the left side.

False negative predictions

Case 6.6. One fetal heart considered normal echocardiographically was found to show an ostium primum atrial septal defect anatomically, Case 6.6. This was a Down's fetus of 19 weeks gestation where the picture quality was considered good. Unfortunately the recording from this fetus was lost. The pictures therefore,could not be reviewed after the anatomical finding was made, but at the time of the study no defect was noted. Anatomically the defect was between 2 and 3 mm in size. The dissected specimen is illustrated anatomically in Figure 6.10.

Case 6.7. One fetal heart was examined at 23 weeks gestation, Case 6.7. The fetus was a known chromosomal abnormality, trisomy 18. There was maternal obesity, oligohydramnios, a small fetus for the gestational age and a limited opportunity for scanning the patient. The picture quality was very poor but two ventricles, two atrioventricular valves and the aorta were identified. The fetal heart was considered therefore to be probably normal. Anatomical dissection of this fetal heart demonstrated Tetralogy of Fallot (Figure 6.11a and b). Reviewing the echocardiographic recordings the image quality could not allow either identification or exclusion of this diagnosis.

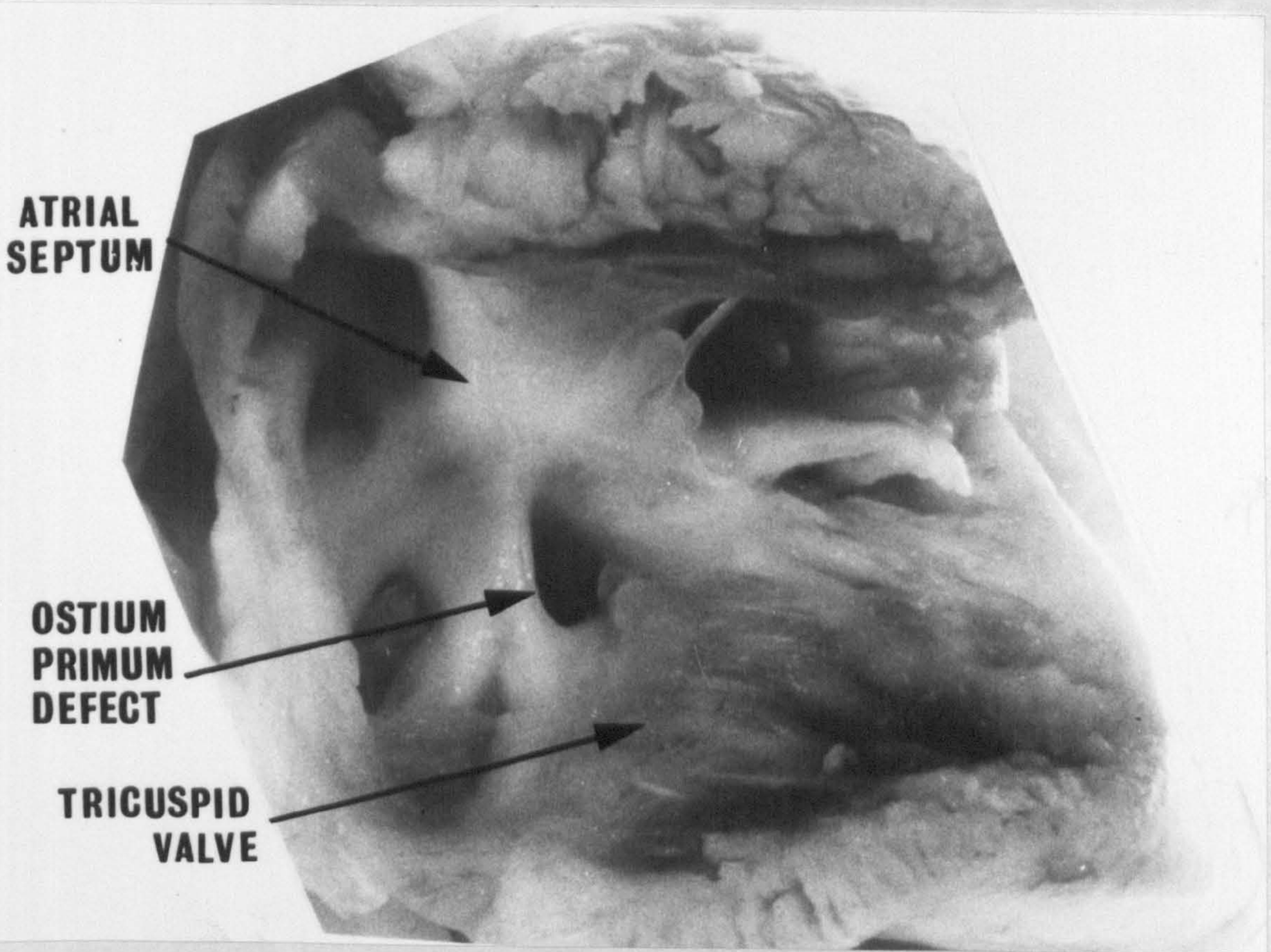
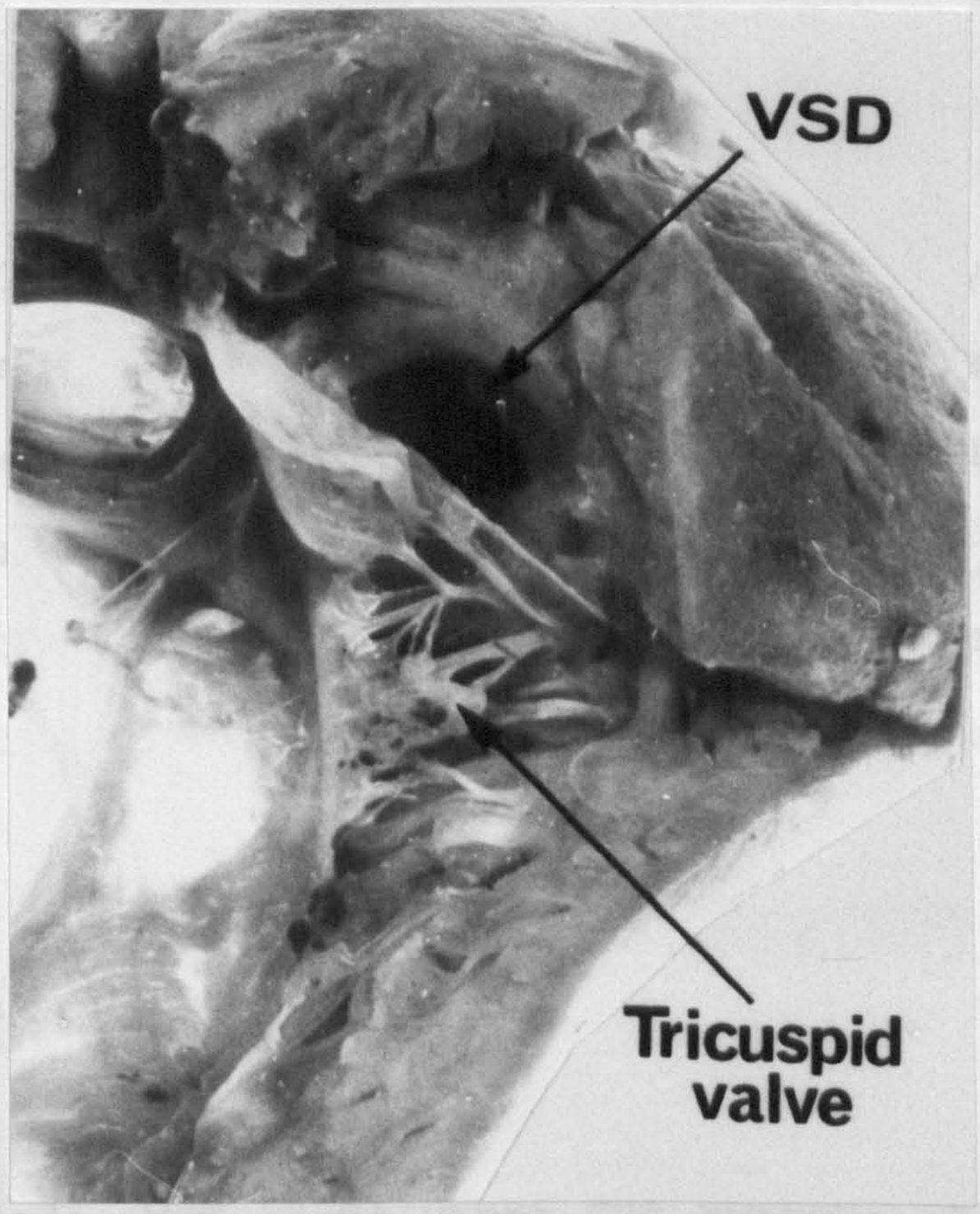


Figure 6.10. The anatomical specimen in Case 6. The heart is viewed from the right side after opening the right ventricle and right atrium. The ostium primum defect can be seen.



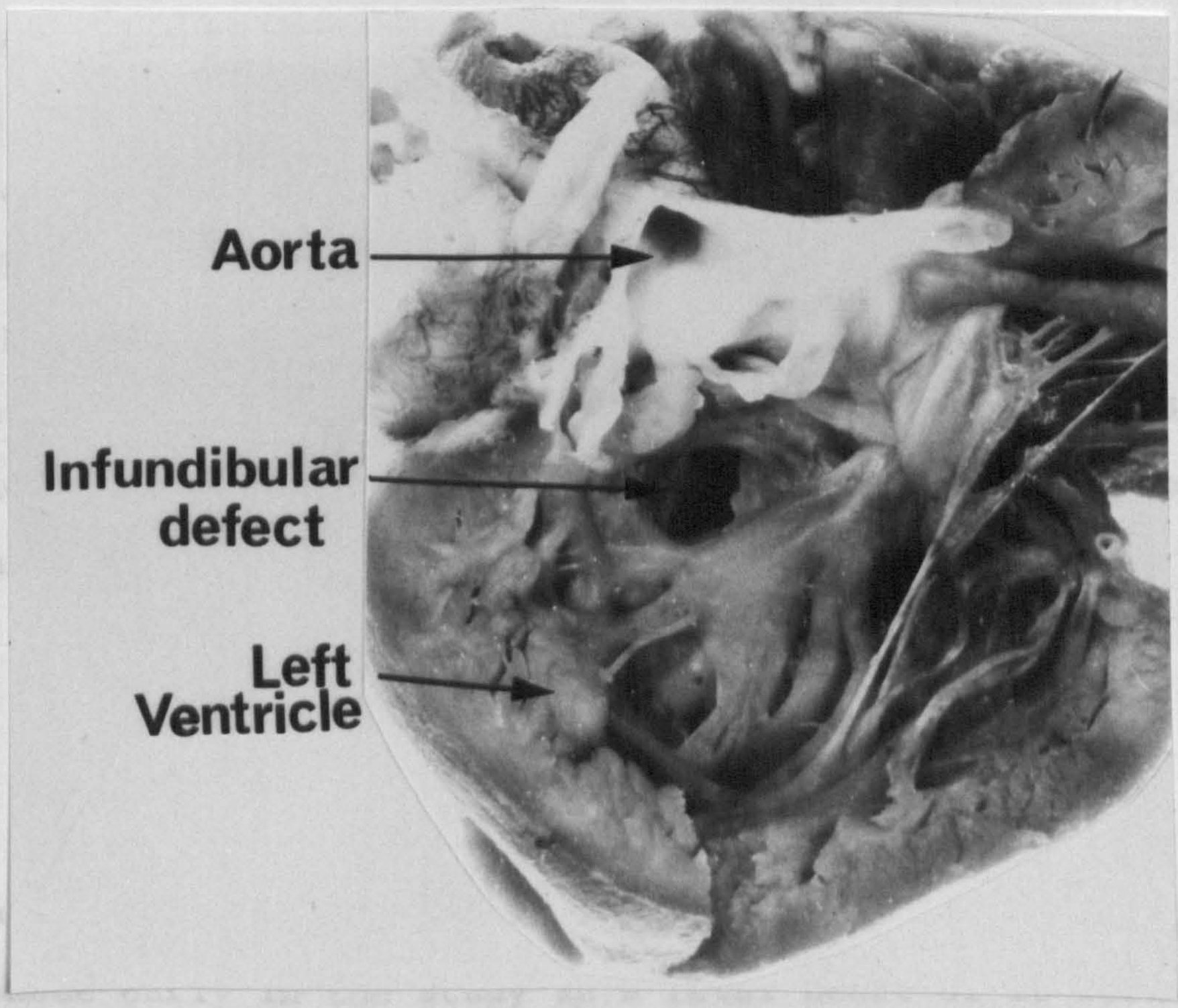


Figure 6.11. (a) and (b). Case 7.

(a) The anatomical specimen is viewed from the right ventricle. The infundibular ventricular septal defect can be seen.

(b) The anatomical specimen is viewed from the left ventricle. The aorta is seen overriding the ventricular septal defect.

Case 6.8. In one case Case 6.8 the fetal heart was too poorly visualised for any judgement of normality or abnormality to be made. This was a case of Meckel's syndrome seen at 15 weeks gestation. There was severe oligohydramnios which greatly influences picture quality. Anatomical dissection of this heart showed dextrocardia, left atrial isomerism, tricuspid and pulmonary atresia. The anatomical specimen is seen in Figure 6.12.

False positive prediction

Case 6.9. One fetal heart was thought to show an inlet septal ventricular defect echocardiographically, Case 6.9. This was a Down's fetus of 18 weeks gestation. The echocardiogram is illustrated in Figure 6.13. The "end" of the ventricular septum was thought to be represented by the bright dot and that there was a defect between this point and the two atrioventricular valves. Anatomical dissection, however, did not confirm this suspicion, the ventricular septum being intact.

Discussion

Thus, in summary, echocardiography predicted a normal fetal heart in 20 subjects. The one false positive diagnosis, was made early in the study in a fetal heart of 18 weeks gestation where a ventricular septal defect was thought to

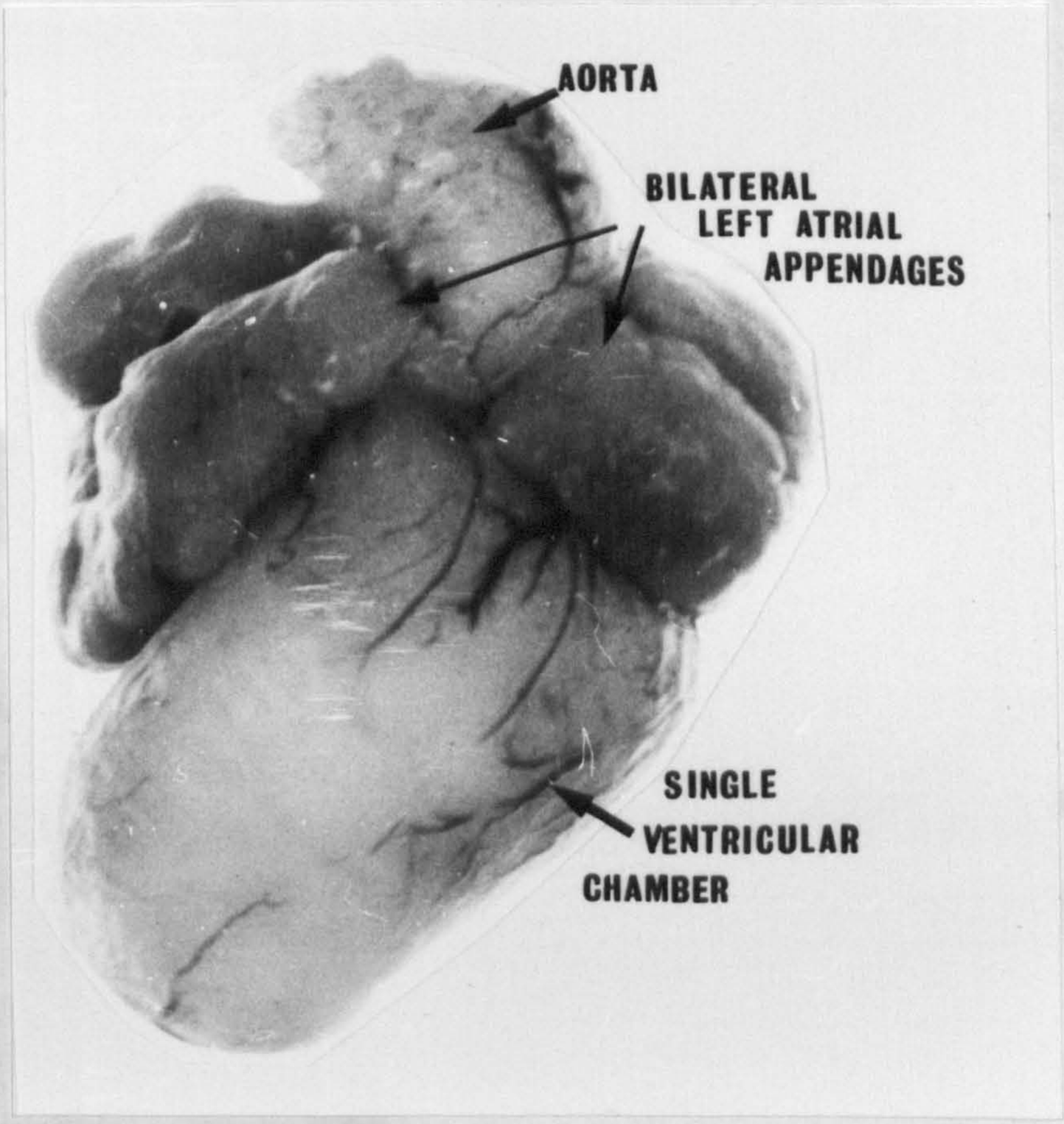


Figure 6.12 The anatomical specimen in Case 8. The heart lay in the right chest. It shows bilateral left atrial appendages. There was absent right atrioventricular connection and pulmonary atresia.

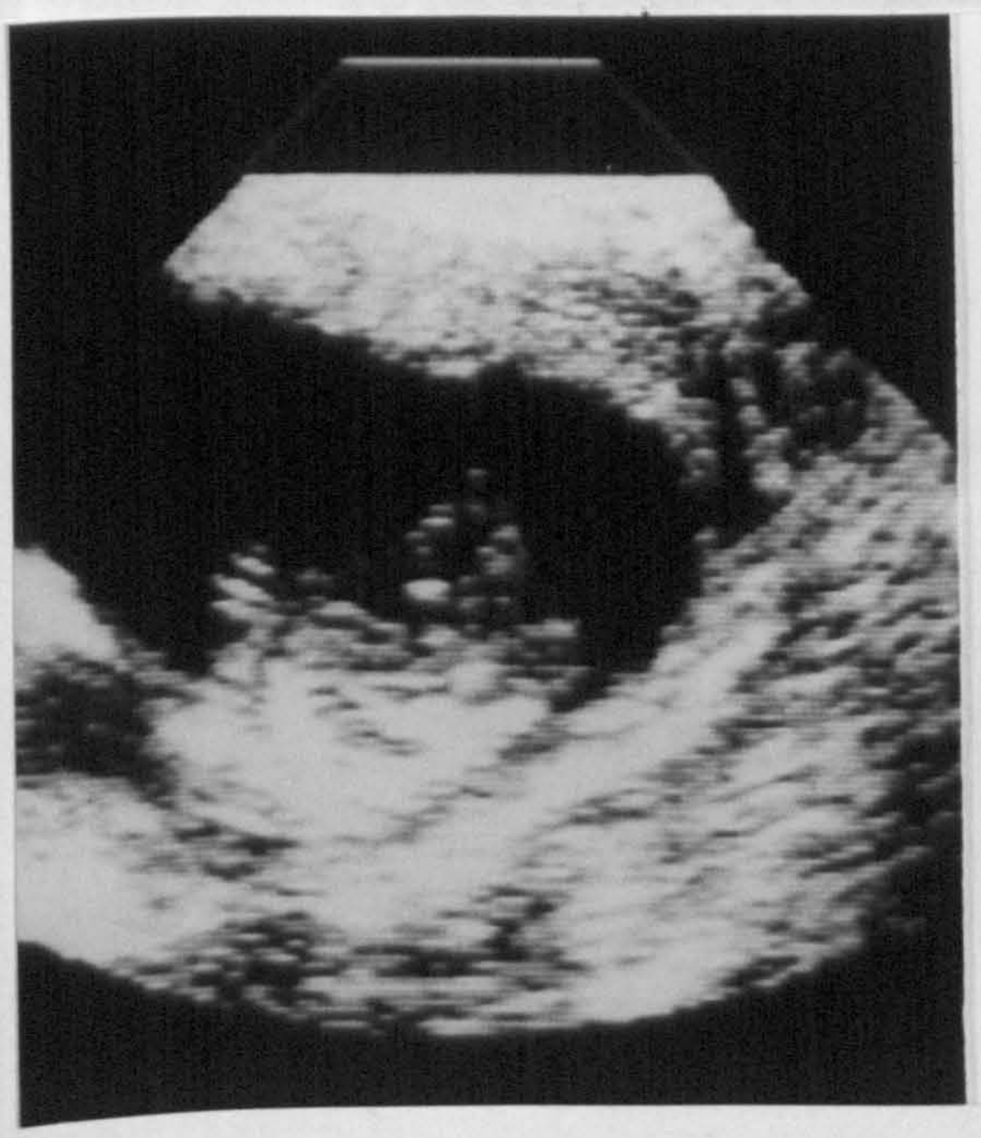


Figure 6.13. Case 9. False positive diagnosis of inlet ventricular septal defect. It was thought that the bright dot was at the top of the ventricular septum and that this was separated from the atrio-ventricular valves.

be present. There were three false negative diagnoses. The first, a primum atrial septal defect demonstrates the limitations of the technique in displaying small defects in these small hearts. Although this defect measured only 0.3 mm at 19 weeks it could have become a functionally significant defect at birth. This case illustrates that the integrity of the atrial or ventricular septum cannot be guaranteed in utero. Indeed this is also true in post-natal life. However, in the postnatal heart, defects that are not visible are rarely functionally significant, as those not visualised are small. This is probably not true prenatally as small echocardiographically invisible defects may be present early in pregnancy but not become visible until the heart grows and the defect enlarges towards birth. Potentially functionally important defects may therefore be overlooked, particularly early in pregnancy. The second diagnosis overlooked was that of tetralogy of Fallot. This case illustrates some of the difficulties encountered in fetal echocardiography, namely maternal obesity, oligohydramnios and a small-for-dates fetus, which all limit picture quality. Also, tetralogy of Fallot can be difficult to detect prenatally. The reasons for this include the fact that normally, the right ventricle is the same size as the left in prenatal life, so this does not provide a clue. The pulmonary outflow tract narrowing does not always develop even in the first year of life and is rarely obvious at birth.

The only features that may be seen are the ventricular septal defect and aortic override. However, the degree of aortic override may be minimal and the same reservations concerning the visualisation of ventricular septal defects hold as have been described in Case 6.6. Had this pregnancy not been proceeding to termination the picture quality would not have been accepted and it is hoped that restudy would have detected abnormality. Case 6.8. demonstrates the size limitation of the technique. A major congenital cardiac lesion cannot be definitely excluded much before 18 weeks gestation. In five cases the cardiac malformations were identified echocardiographically and confirmed anatomically. None of them were gross abnormalities of connection but quite subtle. They suggest therefore that even in the midtrimester of pregnancy minor abnormalities can be accurately detected and that more major defects should not be overlooked.

TABLE 1

REASON FOR MIDTRIMESTER TERMINATION OF PREGNANCY

	NUMBER
Social	8
Neural tube anomalies	4
Meckel's syndrome	2
Down's syndrome	6
Turner's syndrome	1
Trisomy 18	1
Rh-isoimmunisation (intrauterine death)	1
Other non-cardiac congenital abnormalities	5
Total	28

CHAPTER 7

RESULTS

Description of the normal M mode echocardiogram of the fetus

Once the realtime cross-sectional images of the fetal heart,as described in Chapter 5,were thoroughly understood and easily obtained,it was also found possible to record an M mode echocardiogram. With the M mode echocardiogram the pattern of motion of various structures could be studied, for example, the ventricular walls, the mitral, aortic, tricuspid and pulmonary valves and the foramen ovale flap. Actual cusp separation of each valve could be documented,which could not be reliably seen in realtime,particularly in the arterial valves. The M mode echocardiogram adds to the two dimensional study therefore in a descriptive way but as we shall see in subsequent chapters it is of value also for the accumulation of measurement data and derived functional characteristics.

With experience and practice it became easy to locate the M line through the structure to be studied and obtain a good quality M mode recording of all four valves in every case. However, if errors in interpretation are to be avoided it is essential to precede the M mode recording with a complete and thorough two dimensional examination. This is because the

cardiac structures can only be identified accurately from the cross-sectional study. The M mode echocardiogram alone cannot distinguish between pulmonary and aortic valve motion, or between the two atrioventricular valves. The M line must be located,through the appropriate valve or chamber which has been identified on cross-sectional grounds,and will depend on the fetal lie. For example, the right ventricle may be superior,on the M mode echocardiogram,to the left but this will only be the case if the fetus lies with the anterior chest closer to the transducer. As the wall motion of the right ventricle is very similar to that of the left, the ventricular relations must be established using the cross-sectional mode and noted on the M mode paper. Movement of the fetus during the M mode study can alter the location of the M line so that the position of the M line must be constantly checked by referral to the cross-sectional image. Particularly in the midtrimester of pregnancy,the fetus is very active and truncal movements frequent,even in a study lasting less than 10 minutes.

The descriptive M mode material was derived from normal pregnancies in which normal cardiac anatomy had been demonstrated by cross-sectional echocardiography.

Aortic Valve. Any cardiac section which visualises the aortic valve can be used to perform the M mode study (see Figures 5.5,6,9,10,11) but the most commonly used section and

that which gave the best result was the ductal plane. This ensured the M line was at right angles to the aortic walls and usually a valid left atrial recording was simultaneously obtained,although the left atrium did not always lie deep to the aorta on the M mode trace. If the fetus lies with the back closest to the maternal abdomen the M line will cross the left atrium before the aorta. Figure 7.1. shows the M line through the aortic valve and left atrium. The aortic root is then displayed on the M mode recording with the "box" shape characteristic of the aortic valve in systole displayed within it (Figure 7.2. a and b). The closure line in diastole can also be seen.

Left atrium and foramen ovale. When the left atrium is displayed simultaneously left atrial wall movement can be observed. The foramen ovale flap is a prominent structure seen on the cross-sectional image to lie in the centre of the left atrium and constantly flicker. M mode recording of the flap motion however shows it to move in a organised manner. When the fetal electrocardiogram is also recorded it can be seen to move biphasically within each cardiac cycle. The flap closes during atrial contraction, opens again and then closes during ventricular contraction. Atrial contraction causes a sharper closure of the foramen ovale flap than ventricular systole. This is illustrated in Figure 7.3a and

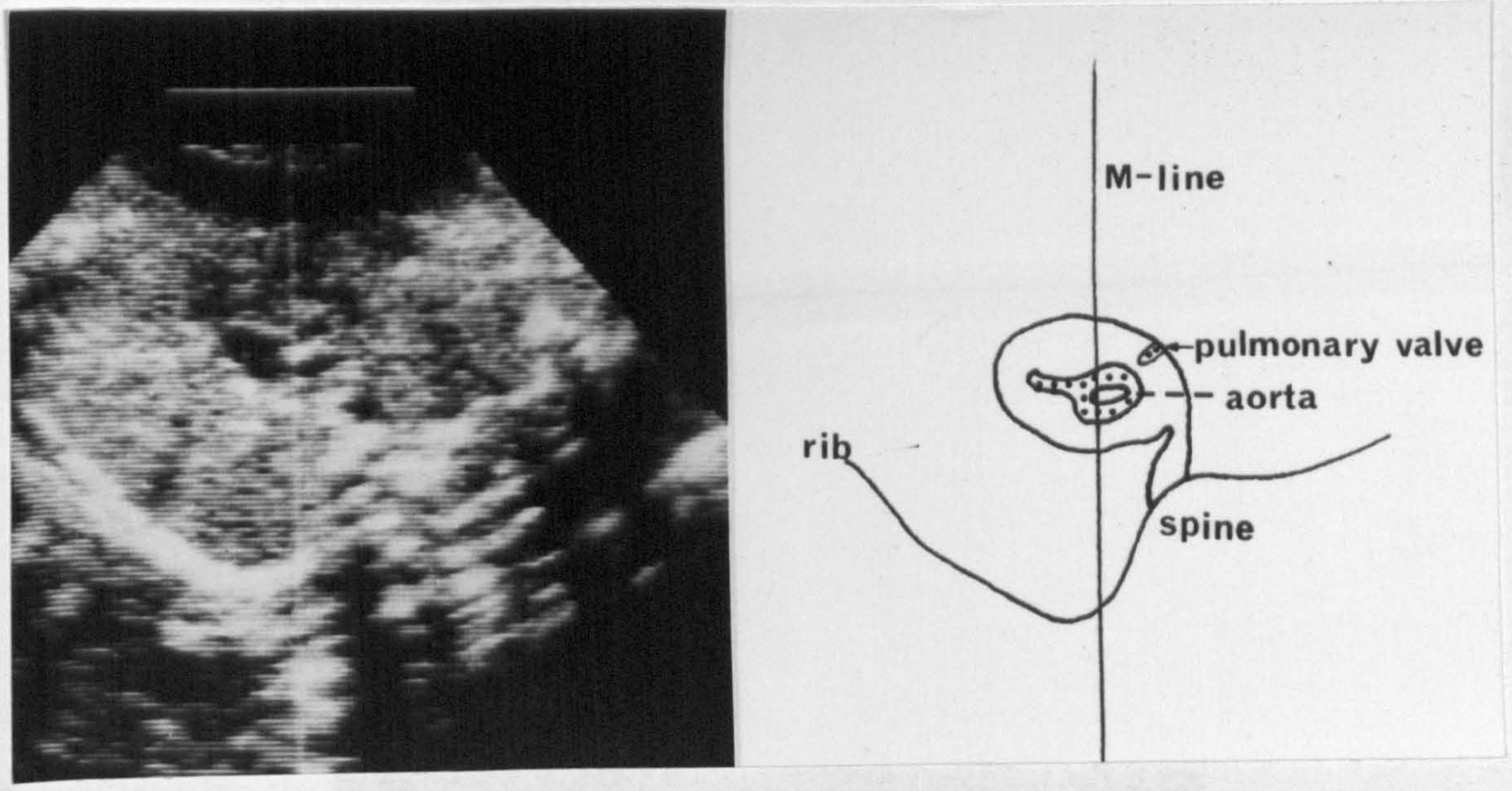


Figure 7.1. The M line passes through the aortic valve which is sectioned in the ductal plane.

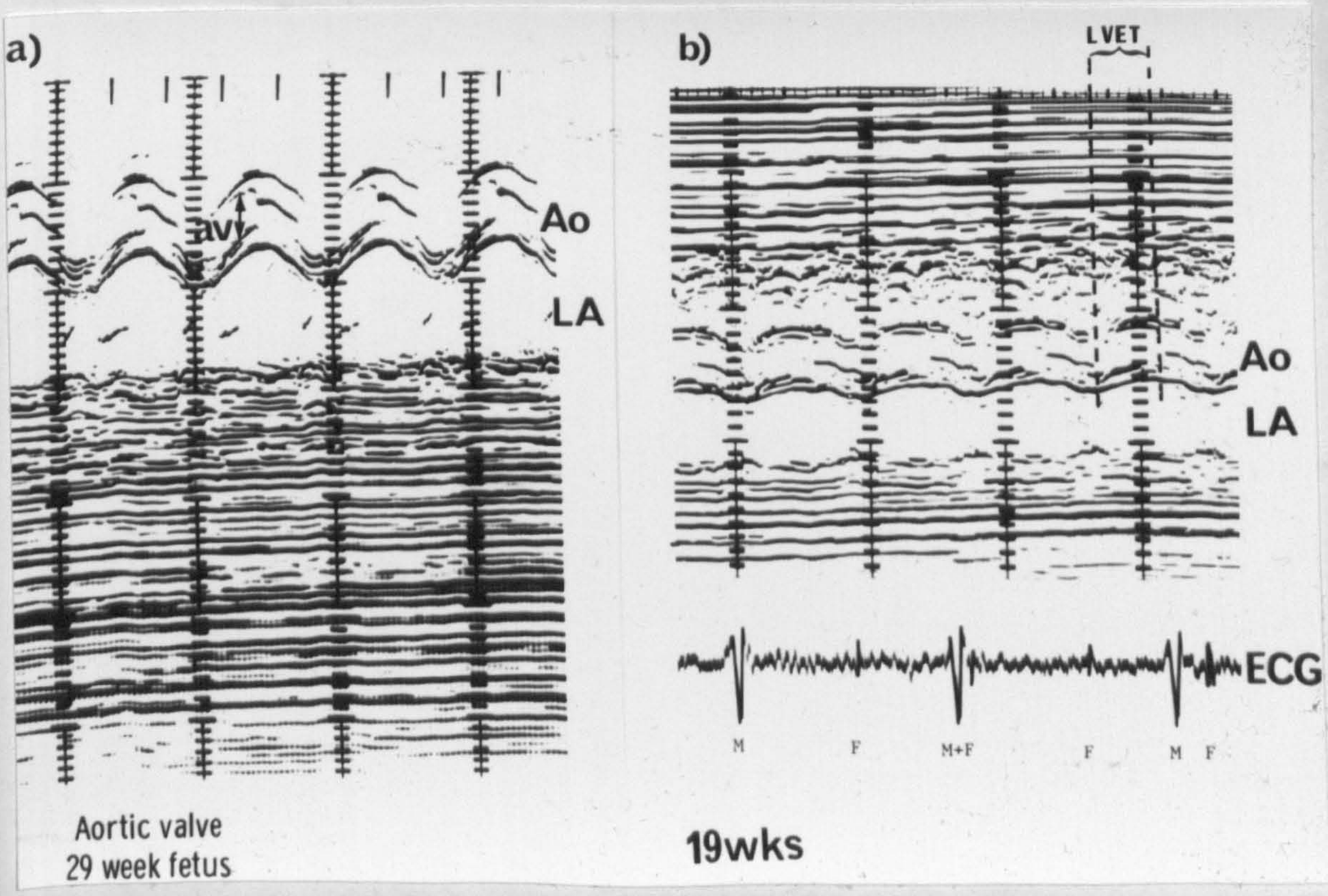


Figure 7.2. (a) M mode echocardiogram of the aortic valve with the left atrium posterior.

Figure 7.2. (b) The fetal E.C.G. allows left ventricular ejection time to be measured accurately. Fetal complexes are marked 'f', maternal 'm'.

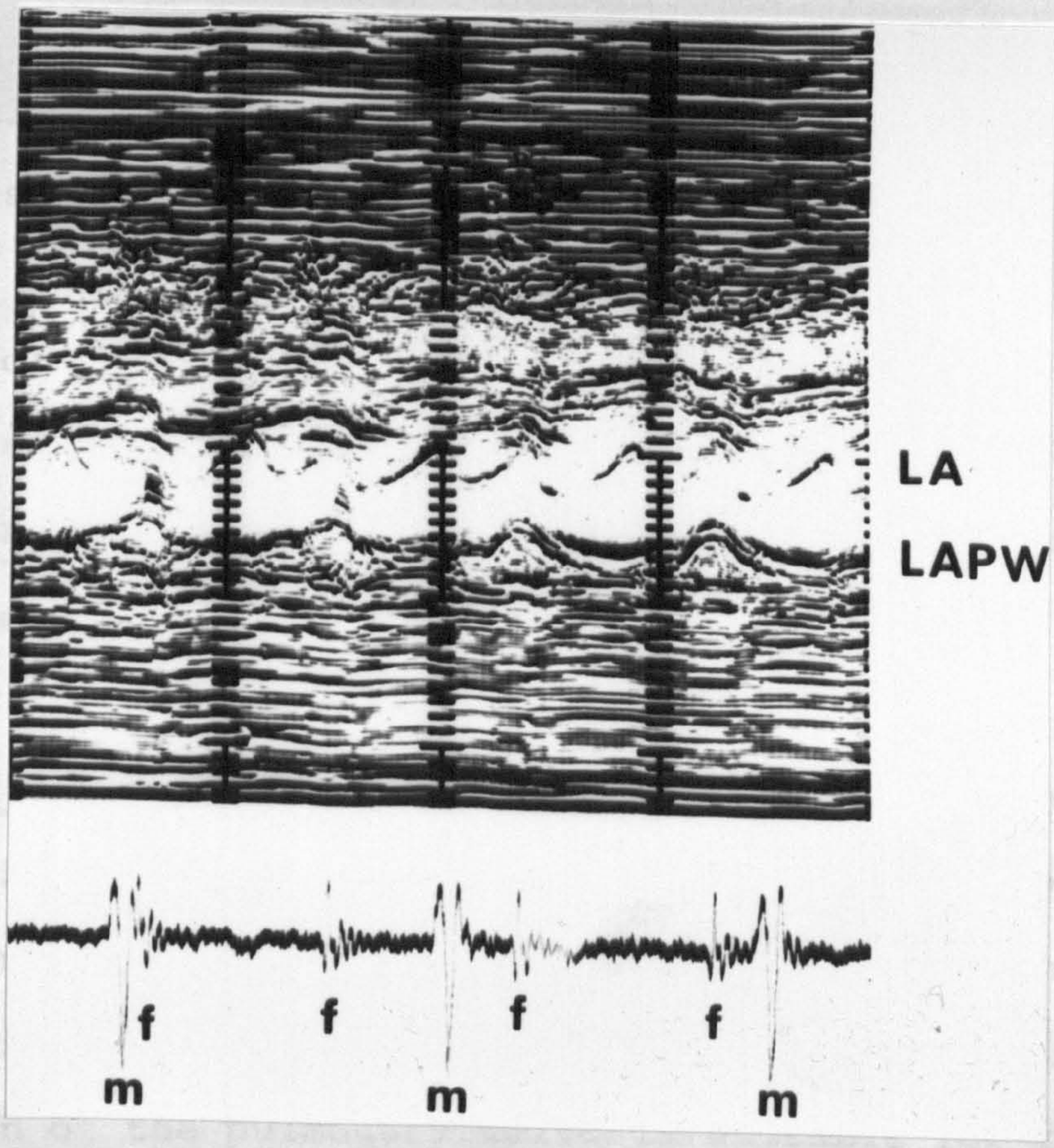


Figure 7.3. (a) The foramen ovale flap is seen moving within the left atrium.

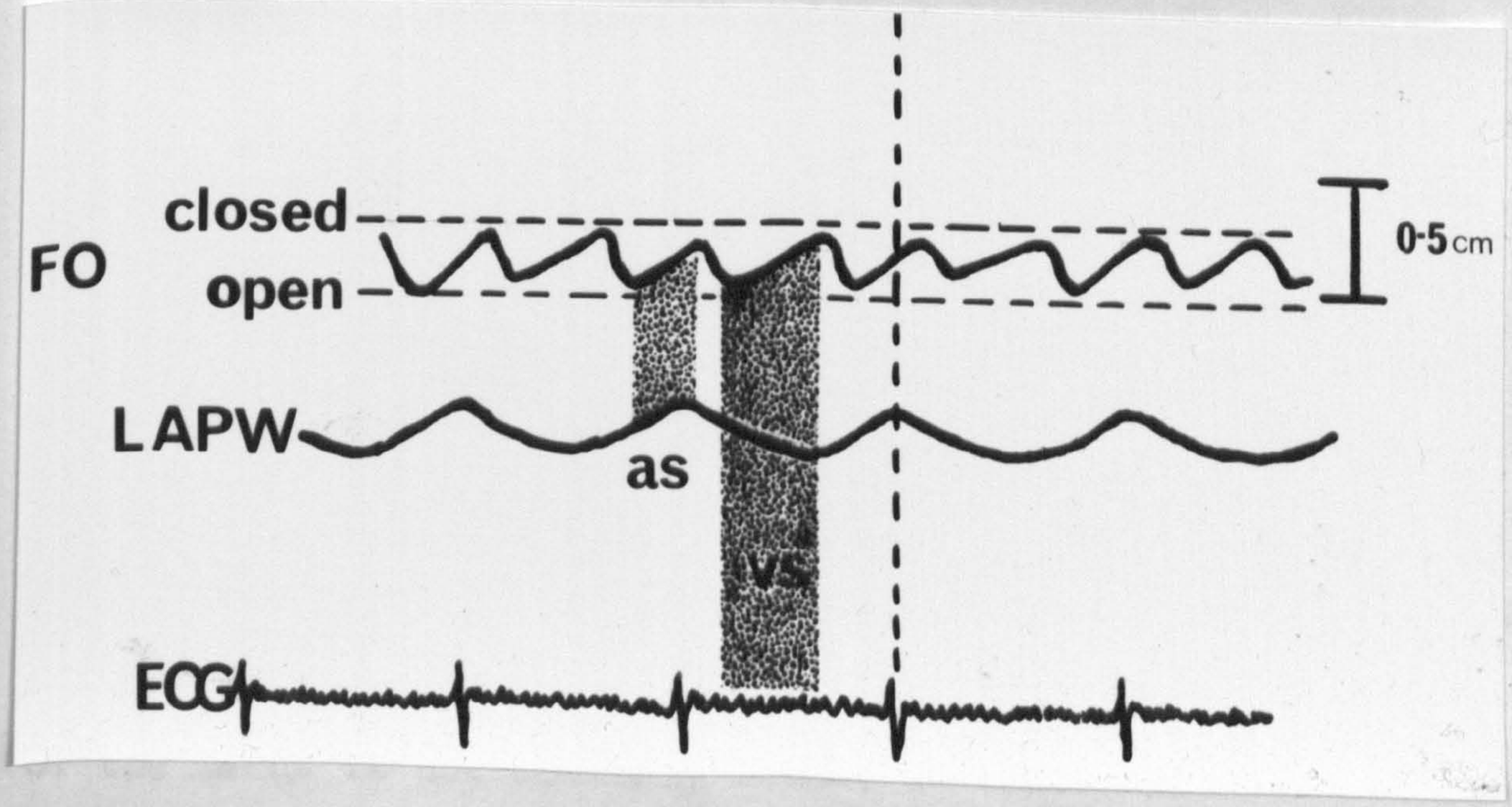


Figure 7.3. (b) Diagrammatic representation of foramen ovale flap motion to illustrate the relationship of movement to the phases of the cardiac cycle.

diagrammatically represented in Figure 7.3b. The excursion of the flap is of the order of 3 mms in the fetal heart illustrated. The actual measurement of the atrium is about 7 mms; therefore the foramen ovale flap moves to almost half-way out into the body of the left atrium during this cycle. This was a consistent finding when the M mode of the foramen ovale flap was recorded.

The pulmonary valve. The pulmonary valve can be seen in three of the sections described in Chapter 5, namely the tricuspid-pulmonary, ductal or short axis left ventricular plane. Any projection or orientation which allows positive identification of the pulmonary valve is suitable for recording pulmonary valve motion (Figure 7.4). The pulmonary valve shows a sloping closure line and it is often possible to record the opened cusps also,as can be seen in Figure 7.5.

The atrioventricular valves, ventricular chambers and septum. The atrioventricular valves can best be studied in one of two cardiac projections. If the fetus lies in such a position that on obtaining the four chamber view of the fetal heart the intraventricular septum lies at right angles to the plane of the M line, the atrioventricular valves and ventricular chambers can be recorded from this position. This is the case in Figure 7.6. However, this fortuitous position of the fetus is not commonly found, in which case a short axis

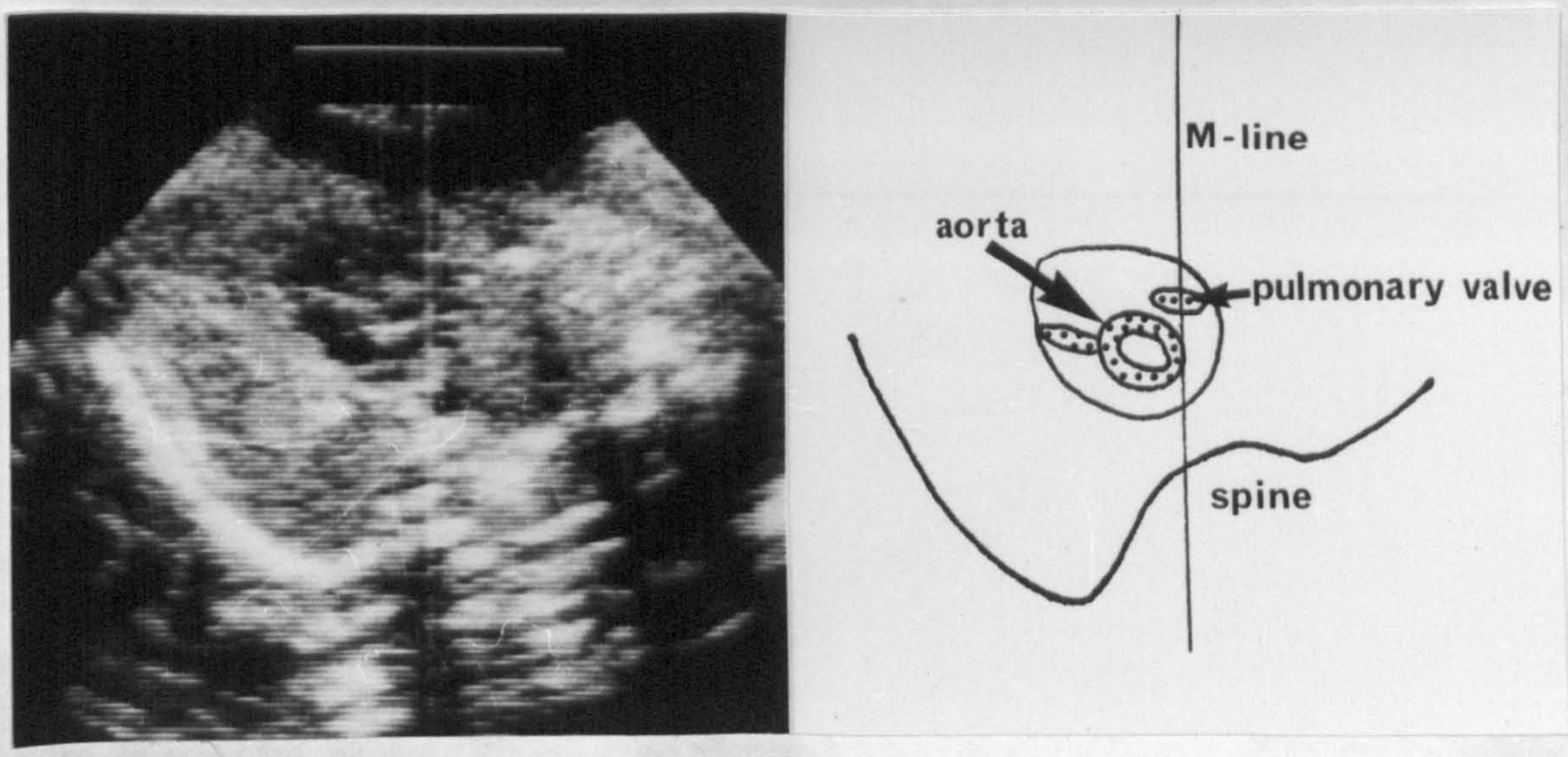


Figure 7.4. The M line passes through the pulmonary valve seen in the ductal plane.

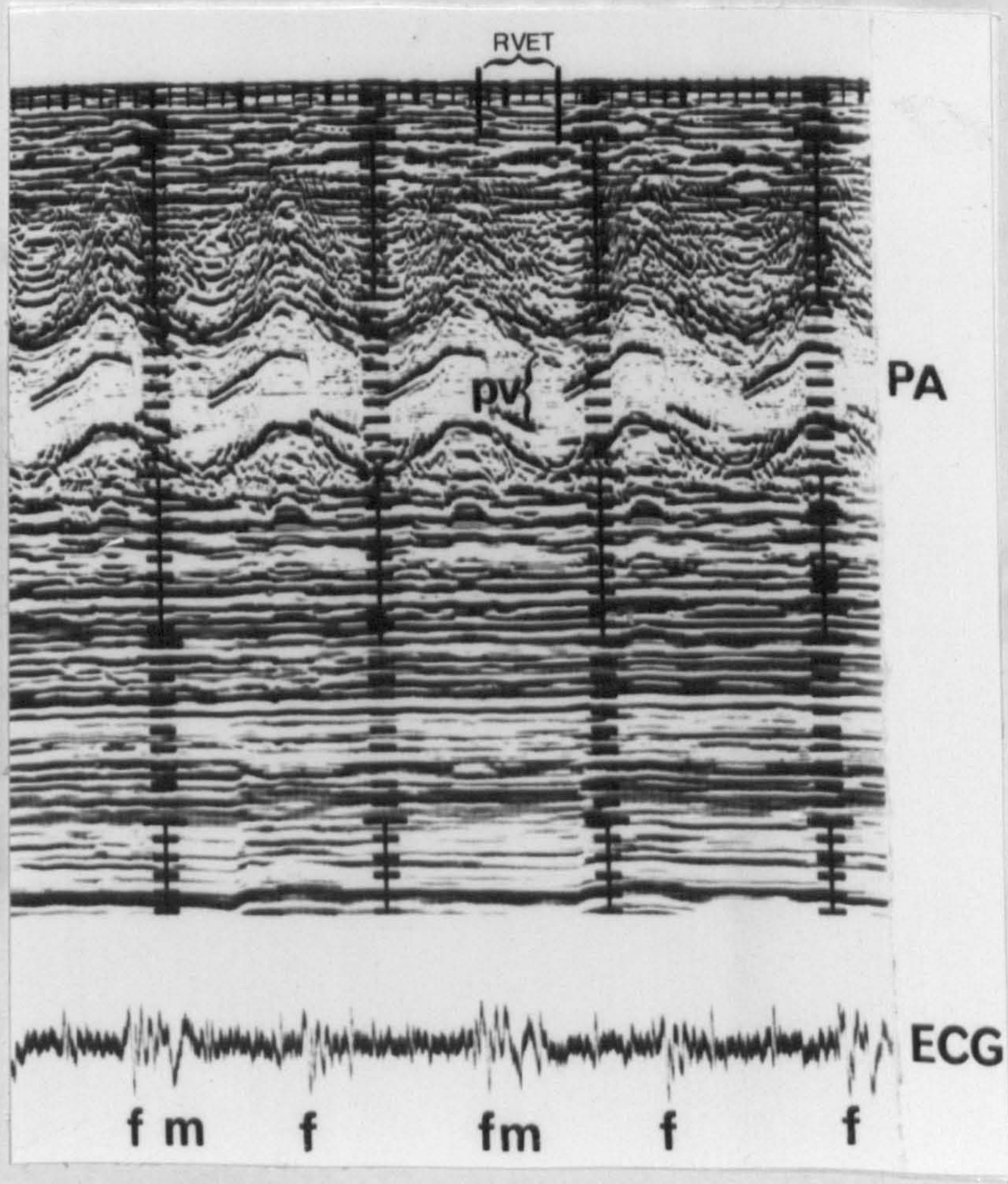


Figure 7.5. The pulmonary valve can be seen open and closed. Right ventricular ejection time can be measured when the fetal E.C.G. is also obtained.

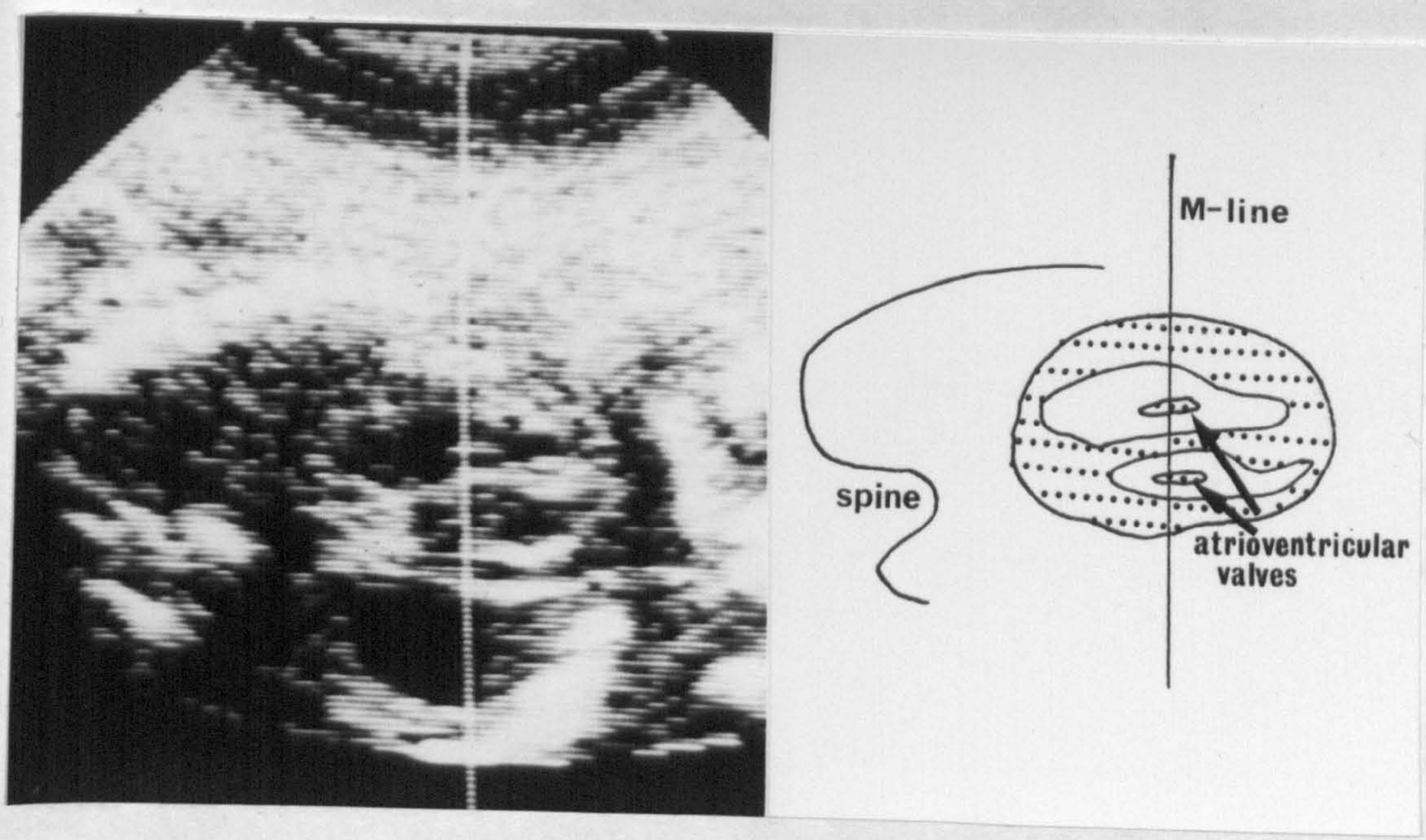


Figure 7.6. The M line passes through both atrioventricular valves perpendicular to the septum. The heart is seen in a four chamber projection.

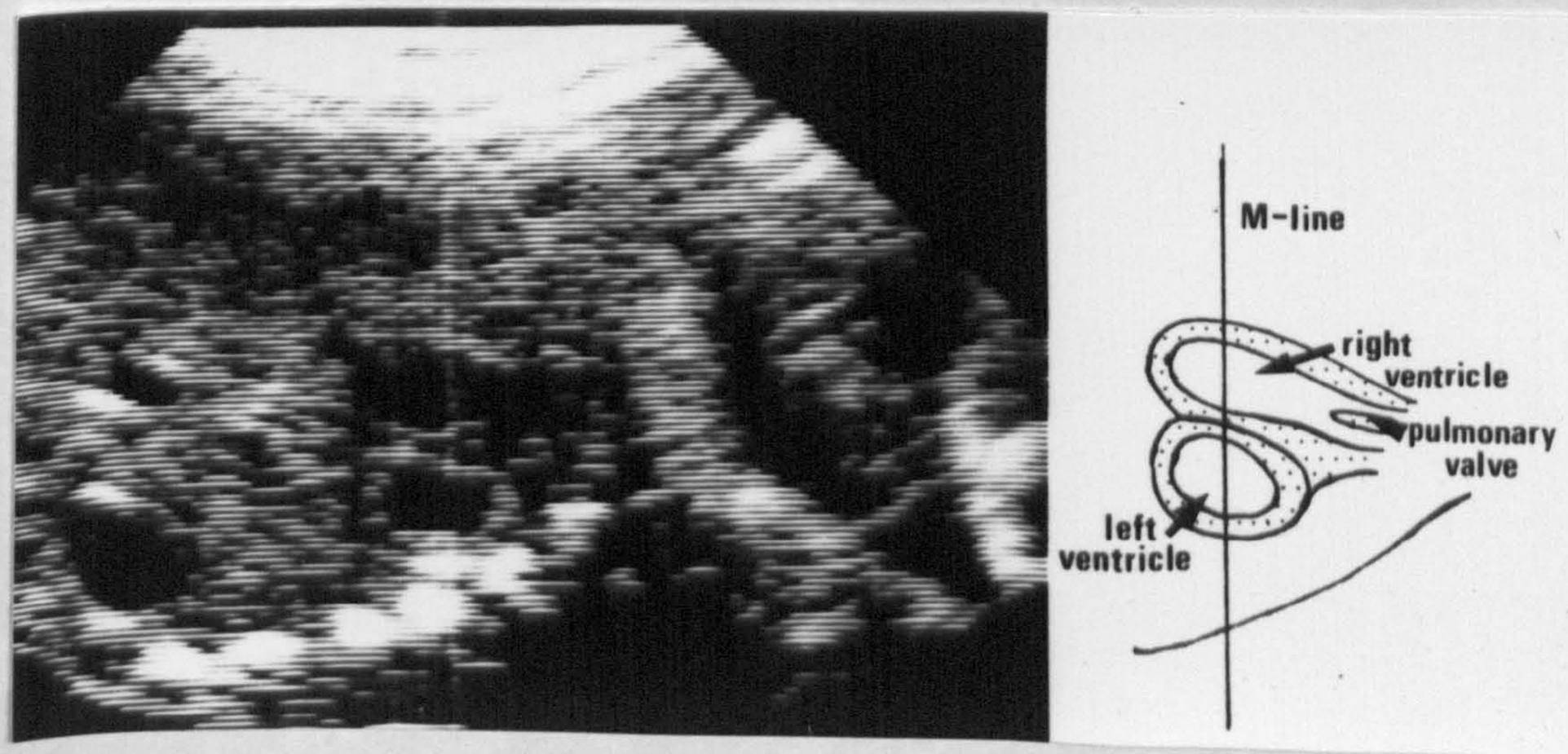


Figure 7.7. The M line is again perpendicular to the ventricular septum but the fetal heart is seen in the short axis left ventricular plane.

projection of both ventricles should be sought. This displays the short axis left ventricular plane, as seen in Figure 7.7. The M line can in both positions be "swept" between the body of the ventricles, and the atrioventricular valves. The M mode echocardiogram obtained across the body of both ventricles can be seen in Figure 7.8. and this is a suitable tracing for making some of the measurements described in the following two chapters. Figures 7.9 and 7.10 show the recordings obtained when the transducer is swept up from the body of the ventricles to the atrioventricular valves. The separation of the valve cusps can be seen,and the pattern of motion is similar in both the tricuspid and mitral valves. Also the "M" shape of motion familiar in the mitral valve in postnatal life is found in fetal life.

Mitral-aortic continuity. The final M mode recording important to make in fetal life is a mitral-aortic sweep. This can only be recorded in the long axis of the left ventricular plane. This can be seen in Figure 7.11 and the corresponding M mode recording in Figure 7.12. This will display the important normal finding of septal-aortic and mitral aortic continuity. It is important however that the position of the M line is exactly correct for this recording to be made as spurious aortic override can be recorded if the M line is not precisely positioned, sweeping up the long axis of the left ventricle.

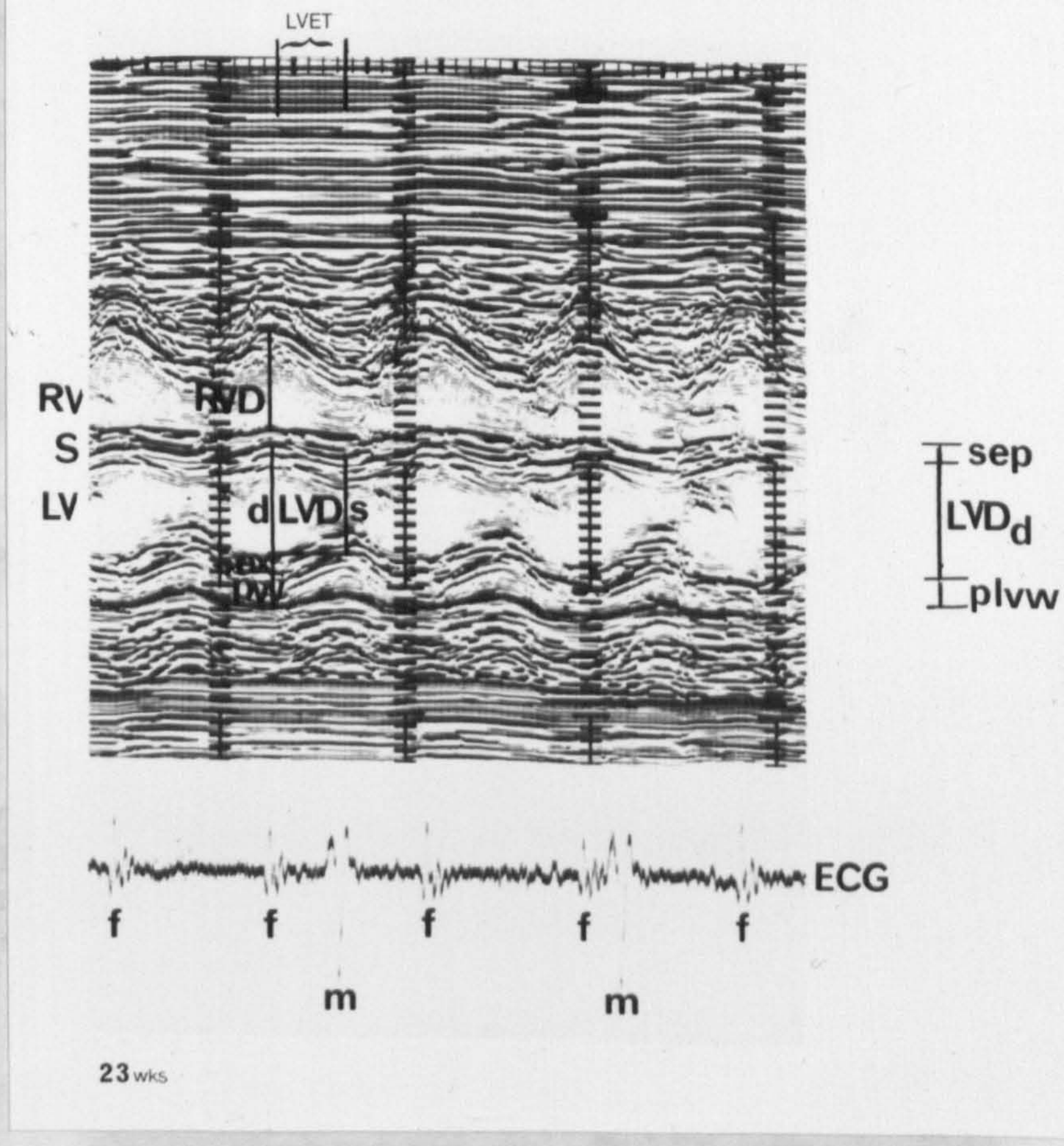


Figure 7.8. The method of obtaining M mode measurements is illustrated. The right ventricular internal dimension, septal thickness, left ventricular internal dimension in systole and diastole, posterior left ventricular wall thickness and excursion can be estimated. In the presence of a simultaneous fetal E.C.G. the left ventricular ejection time can also be measured.

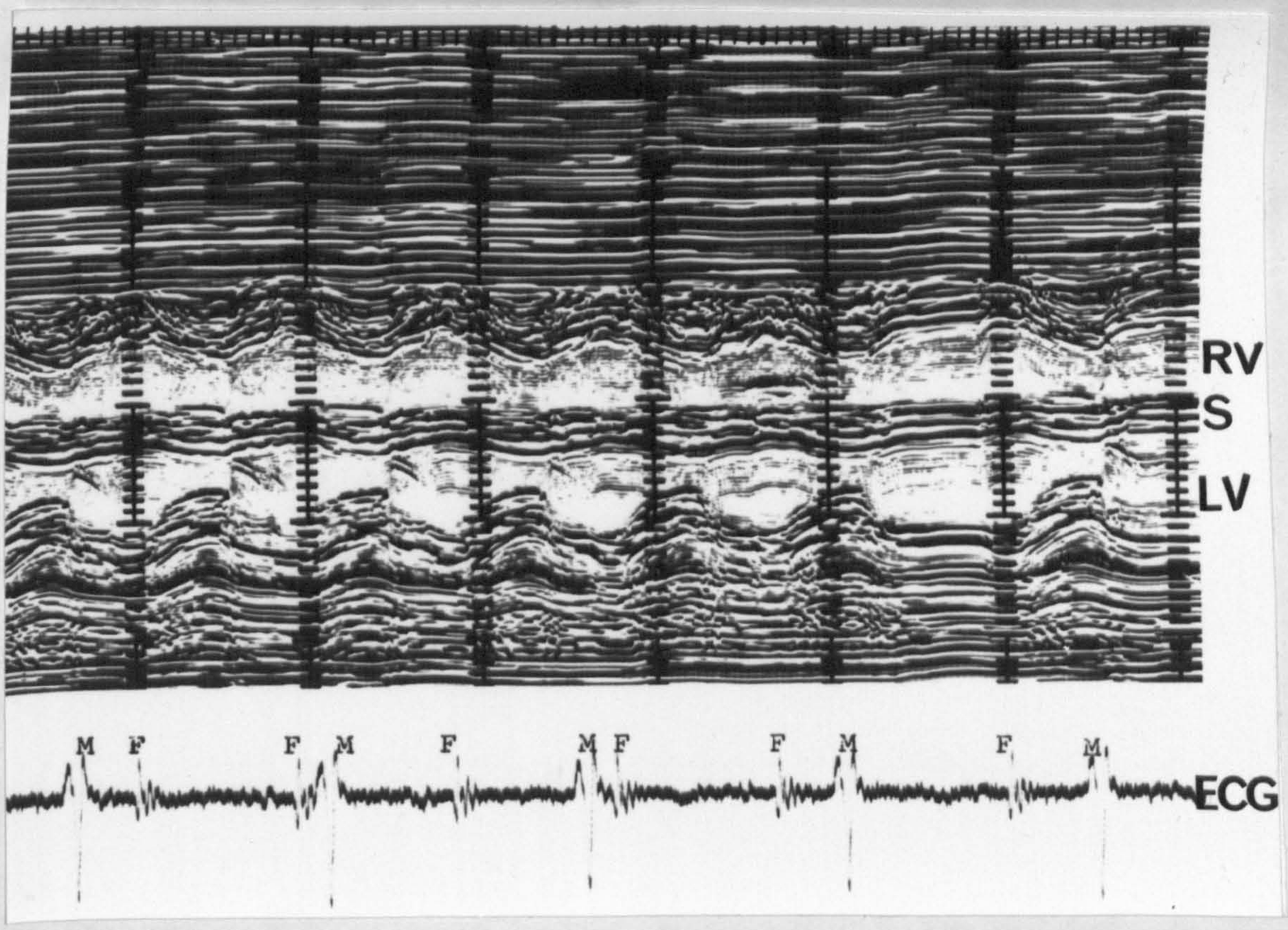


Figure 7.9. The M mode echocardiogram is taken across both ventricular chambers just below the mitral valve. The right ventricle is superior to the left.

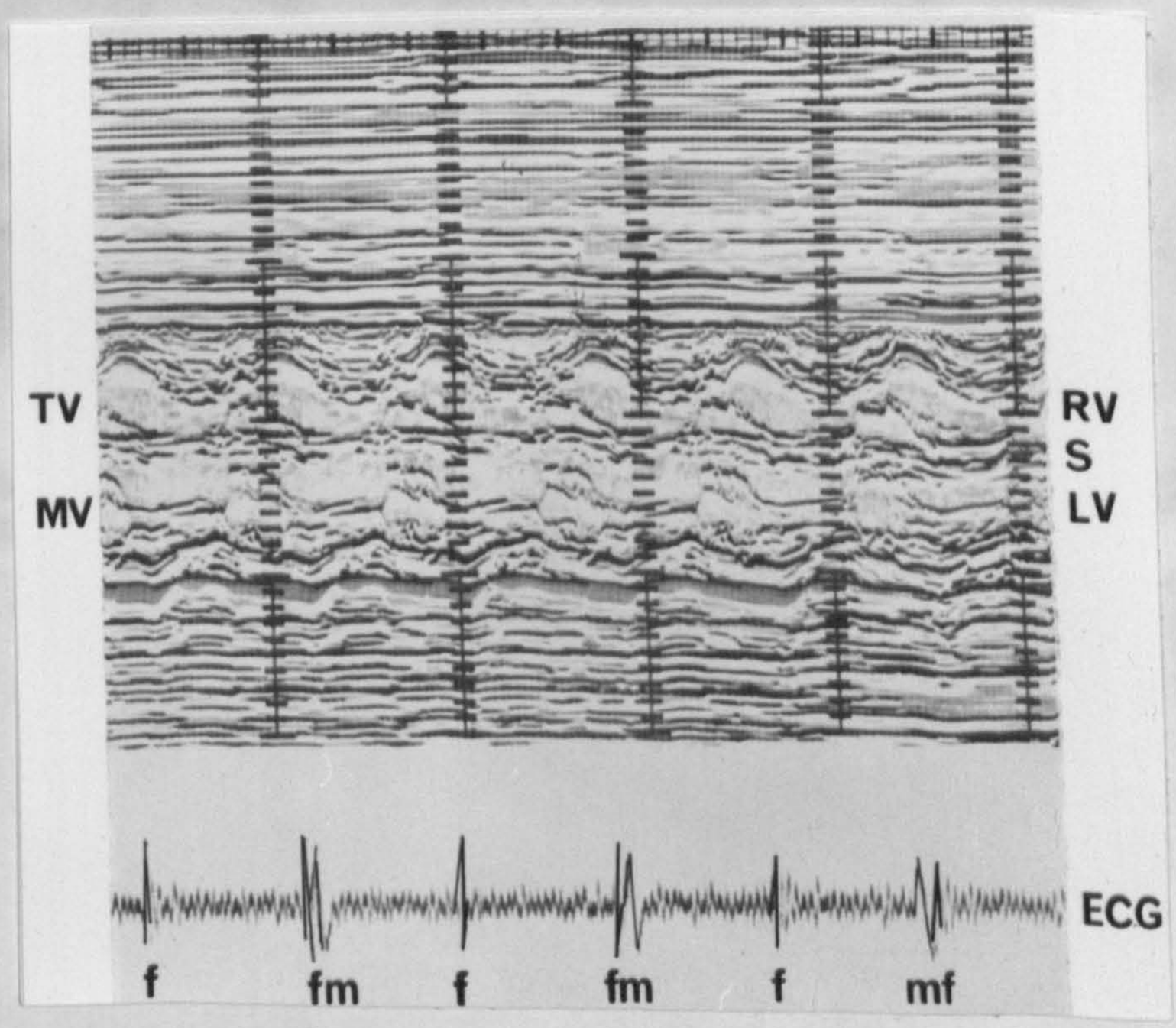


Figure 7.10. Both atrioventricular valves are recorded by M mode within their respective ventricular chambers.

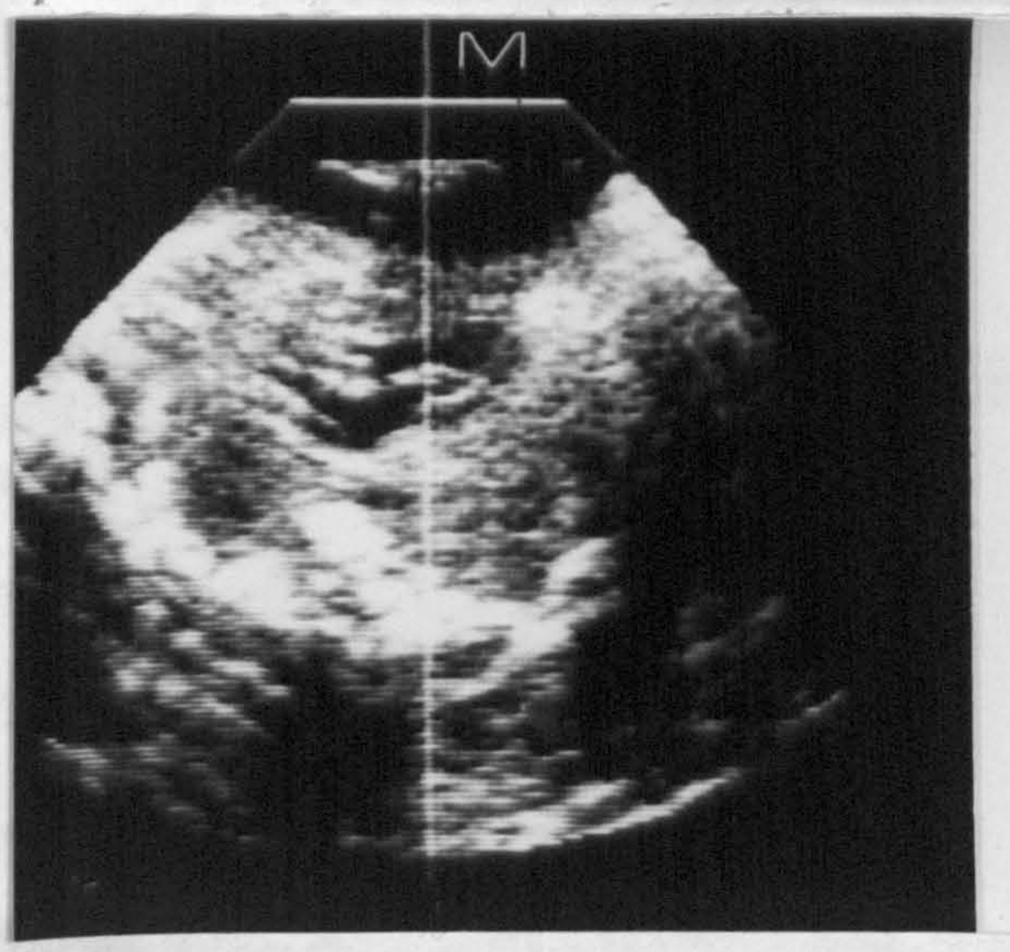


Figure 7.11. The M line passes through the mitral valve which is seen in the long axis of the left ventricle. The M line can then be swept up to the aortic root to record the aortic valve.

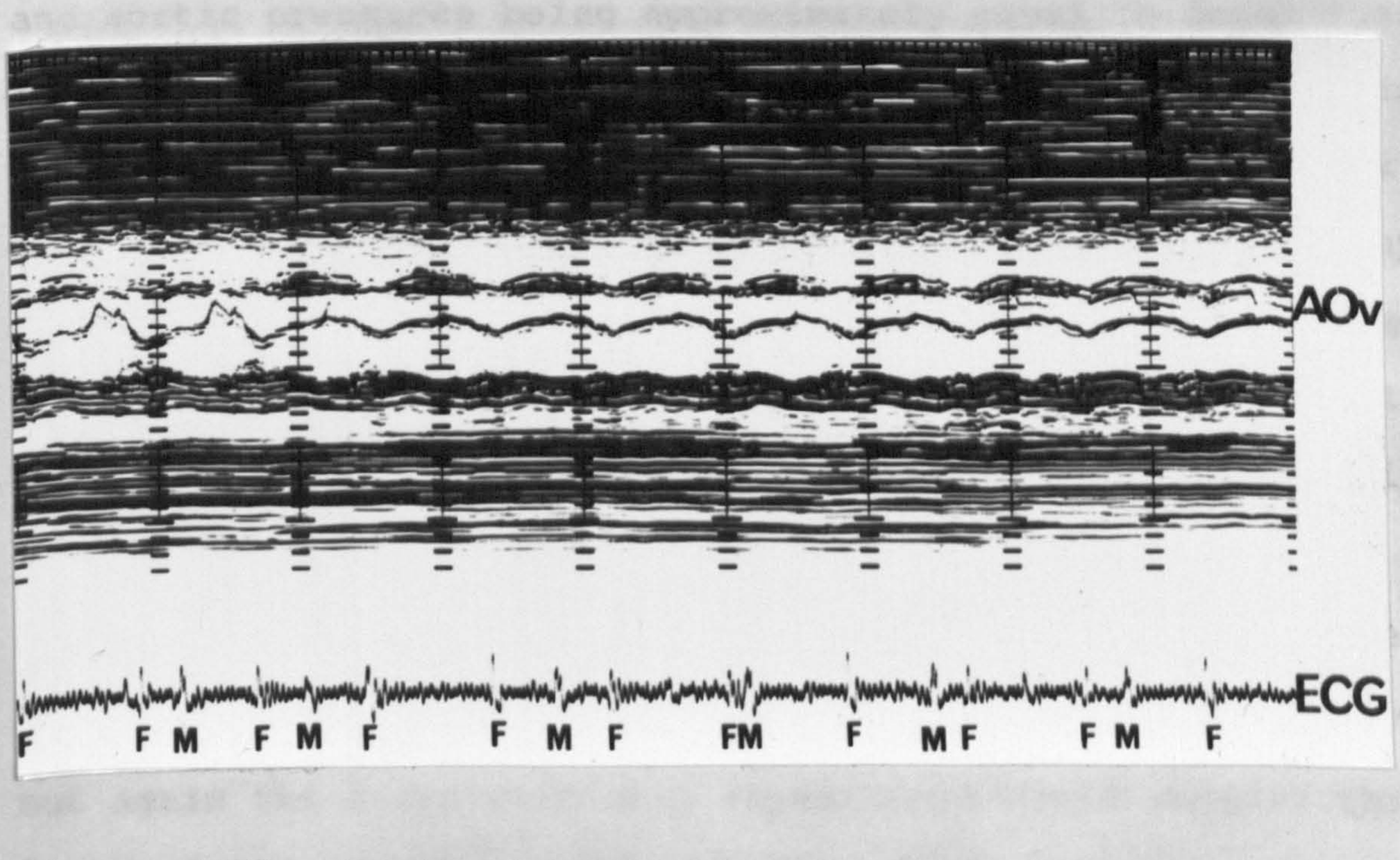


Figure 7.12. A mitral-aortic M mode sweep demonstrating mitral-aortic and aortic-septal continuity.

Discussion

If the pattern of motion of the aortic and pulmonary valves are compared in Figures 7.2 and 7.5. it can be seen that there are no distinguishing features between the two. Both valves are contained within a vessel of approximately equal size and the shape of the closure line is sloping in both valves. The pulmonary valve closure line is flatter than is normally seen in childhood, there is no "a dip",or opening of the pulmonary valve prior to ventricular systole. This reflects the higher pulmonary artery pressure in the fetus associated with the fact that right ventricular ejection is against systemic vascular resistance, the pulmonary artery and aortic pressures being approximately equal in fetal life (134). It is important to display the actual cusp separation of the arterial valves. An atretic arterial valve may look similar to a normal valve on a two dimensional study and may move during the cardiac cycle,but fail to open. There should be other clues on the cross-sectional study, such as the size of the appropriate arterial root, which should be very small if the valve is atretic, but demonstration of actual valve opening is reassuring evidence of a normal valve. This does not absolutely exclude a degree of valvular stenosis, however, but again the cross-sectional appearances would suggest this diagnosis if stenosis were present. (135).

The organised pattern of foramen ovale flap motion is interesting to observe, as it has not yet been previously documented. In fetal life, much of the inferior vena caval flow is directed by the eustachian valve across the atrial septum (136). Flow in the inferior vena cava and higher right than left atrial pressure must maintain the foramen ovale flap open except when atrial or ventricular contraction raises left atrial pressure. Figure 7.13. illustrates the eustachian valve and foramen ovale flap. The eustachian valve can be seen to "guard" the top of the inferior vena cava and direct the flow away from the tricuspid valve towards the left atrium. Thus oxygenated blood from the placenta enters the fetus via the umbilical vein, joins the inferior vena cava via the ductus venosus, then passes directly through the left heart to the head and neck vessels.

The pattern of motion of the two atrioventricular valves is identical. They are contained within chambers of equal size and open simultaneously, because both ventricles have similar pressures. They therefore must be identified by the morphology of the ventricle in which they lie. The morphological differences which distinguish between the ventricular chambers are discussed in Chapter 5.

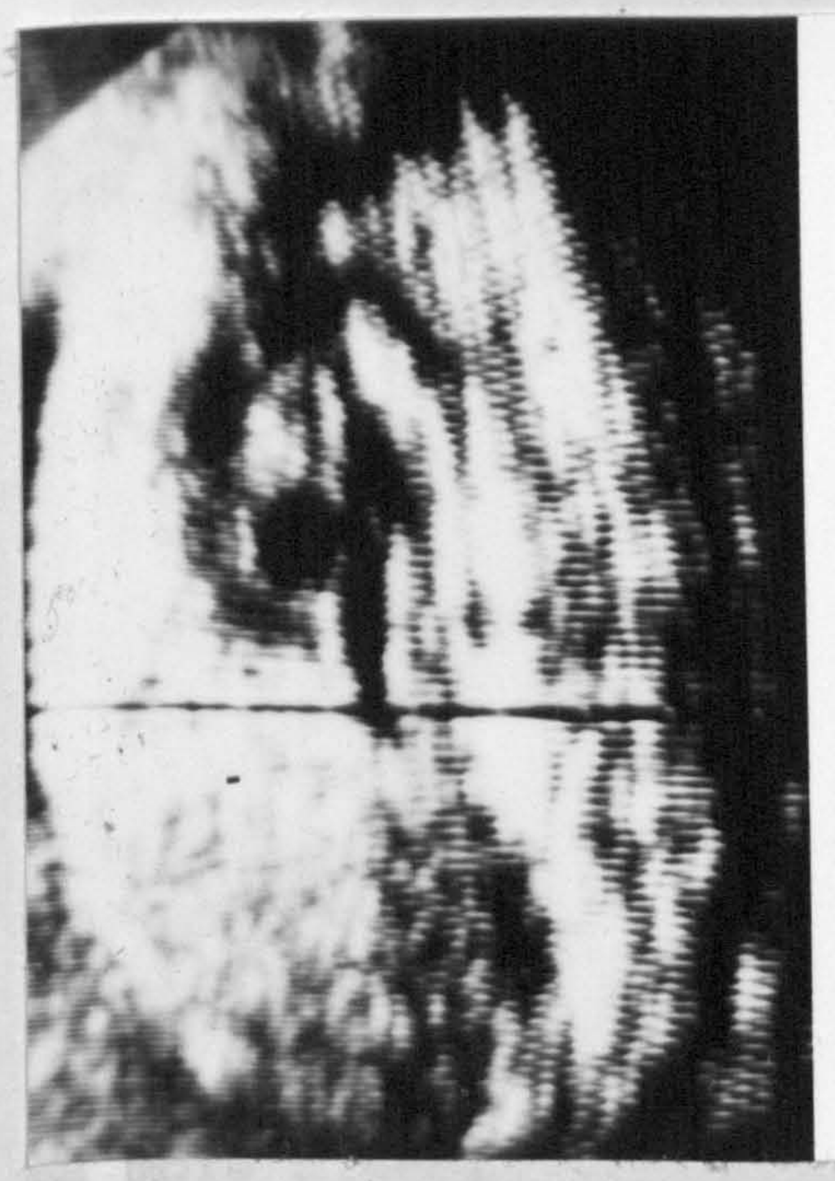


Figure 7.13. The fetal heart is seen in the ductal plane. The eustachian valve is a prominent structure redirecting flow from the inferior vena cava across the atrial septum via the foramen ovale. It obstructs flow from the inferior vena cava to the tricuspid valve. Both the eustachian valve and the foramen ovale flap are readily seen on the real time image.

Right ventricular wall motion appears more undulatory than left ventricular wall motion. The left ventricular wall seems to thicken on contraction. This is illustrated in Figure 7.8. The septal motion is rather flat early in pregnancy but by about 20 weeks gestation it always appears to move towards the left ventricular wall in systole. This is directly opposite to the findings of Kleinman et al who suggest that paradoxical septal motion is a frequent finding (56%) (137). We have never seen paradoxical septal motion in a normal heart. As the two ventricles have an approximately equal output (138) paradoxical septal motion seems to be an unlikely finding.

In summary therefore the M mode echocardiogram allows the pattern of motion of structures within the fetal heart to be more closely observed. Observation of pattern of motion leads to greater understanding of normal function of the heart during prenatal life.

CHAPTER 8

RESULTS:

Measurement Data

The M mode echocardiogram was selected for the collection of measurement data for three main reasons. Firstly, the endocardial surfaces can be more clearly defined on the M mode echocardiogram as compared to a cross-sectional frozen frame image. Secondly, measurements could be made more precisely within the cardiac cycle in relation to systole or diastole. Thirdly, standard orientations for obtaining the tracing can be used so that measurements can be directly compared with already accumulated postnatal data. Also functional values can be derived which can be correlated directly with postnatal values.

As there was no fetal electrocardiogram on the majority of traces,the intraventricular measurements were always made at the maximum diastolic volume of the right and left ventricles. This is fractionally after the R wave of the E.C.G. The systolic dimension of the left ventricle was the minimum dimension. The measurements of septal and posterior left ventricular wall thickness were made at the same place as the intraventricular diastolic measurements as illustrated in Figure 8.1. The aortic root measurement was made at the level of the aortic valve just prior to valve opening at the end of

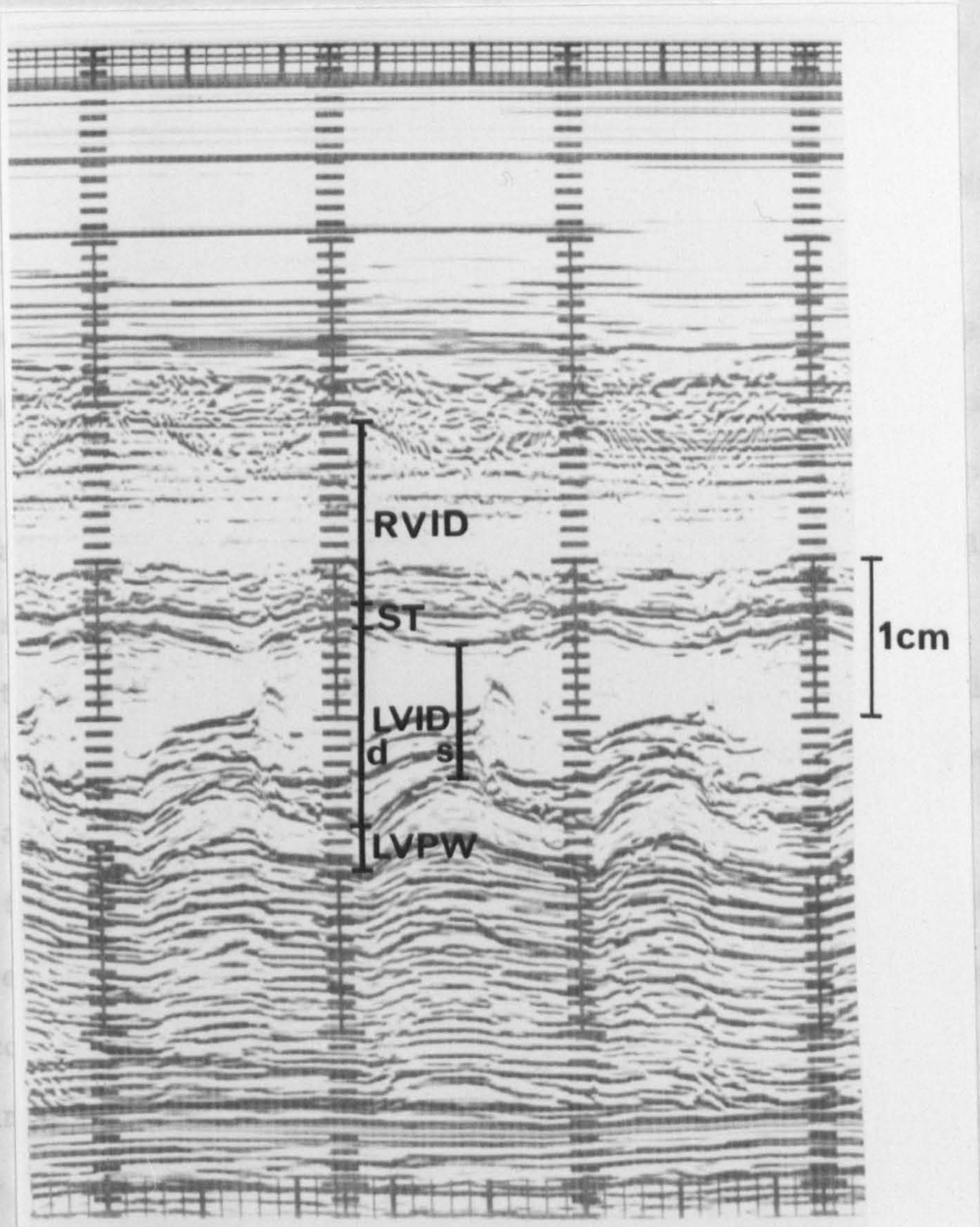


Figure 8.1. The M line is directed across both ventricular chambers perpendicular to the septum. Measurements of septal (ST) and posterior wall thickness (LVPW) right and left internal dimensions in diastole (RVID, LVID) and left ventricular dimension in systole (LVIDs) are made as illustrated.

diastole. Only those tracings in which the aortic valve closure line could be seen clearly were used for measurement. The end systolic, that is the maximum left atrial dimension was measured as is customary in postnatal life (Figure 8.2).

The measurement data was all derived from pregnancies in which fetal age was determined by biparietal diameter measurements made early in pregnancy, that is before 20 weeks gestation. They were all obtained in normal pregnancies and no structural abnormality of any of the fetal hearts was apparent. The relationship between each measurement and gestational age was assessed by linear regression analysis. With some measurements there was an indication of a deviation from linearity in the latter weeks of pregnancy but this was small, inconsistent and bases on fewer data points than were available for the midtrimester. It was therefore, considered that the assumption of any relationship other than a straight line, of the form $y = mx + b$, could not be justified. The "flared" 95% confidence limits for individual measurements (Table II) were only slightly wider at the extremes of the range than at the mean gestation; this again is against a significant deviation from linearity. Straight 95% confidence limits defined by twice the standard error of the estimate of y (SEEY x 2) were in close agreement with the "flared" limits.

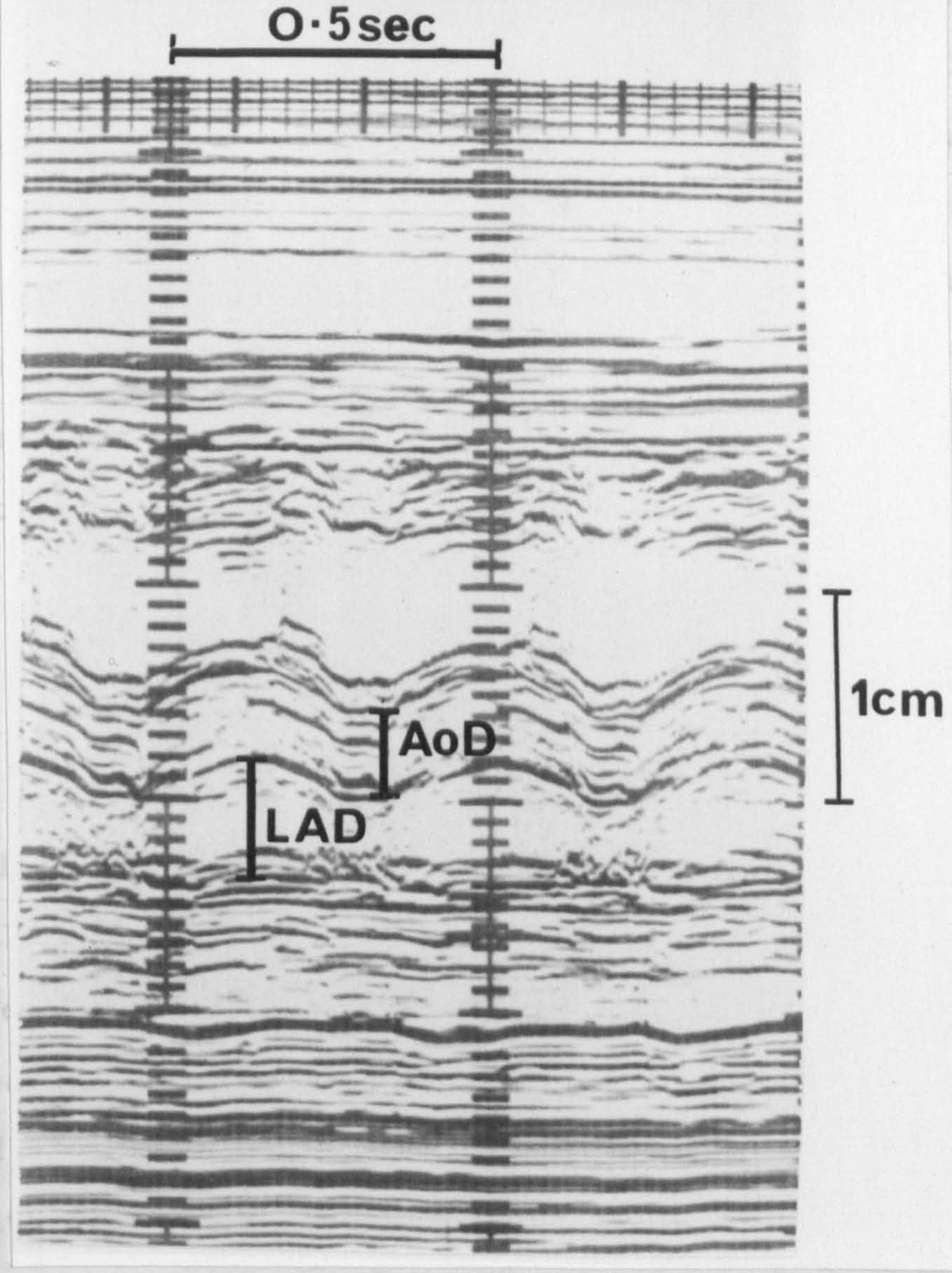


Figure 8.2. The aortic root is seen with the valve closure line within it. The left atrium lies behind the aorta in this projection. The aortic root is measured at end-diastole, the left atrium at end systole, its maximum dimension, as illustrated.

Figures 3,4,5,6,7,8 show respectively the relationship of septal thickness, posterior left ventricular wall thickness, the internal dimension of the aortic root, right ventricular internal dimension, left ventricular internal dimension and left atrial internal dimension to gestational age. The correlation coefficients (r) ranged from 0.836 to 0.895 and these were statistically highly significant ($t>14.968$; $p<0.001$). Statistical data for the relationship of each measurement to gestational age are given in Table III; the equations for the lines are given with the appropriate figure.

Discussion

From the growth charts it can be seen that septal and left ventricular wall thickness grow in a parallel fashion throughout pregnancy, the smallest measurement made being 0.1 cm. increasing to 0.4 or 0.5 cms. by birth. This thickness of septal and left ventricular wall thickness at birth is compatible with values recorded in neonates (139). The left and right ventricular dimensions again parallel each other until term bearing approximately a one to one relationship to each other during gestation. The equal right:left ventricular internal dimension ratio is in agreement with the measurements of Vosters and Wladimiroff made during the last weeks of pregnancy (140). The growth of the cavity of the ventricles

TABLE II 95% confidence limits for measurements at 16,39 weeks and at the mean gestational age.

	SEE y x 2	16 wks	Mean gestation	39 wks
Septal thickness	0.088	0.0873	0.0867	0.089
Posterior left ventricular wall thickness	0.066	0.067	0.066	0.067
Aortic root	0.138	0.138	0.137	0.139 (38)
Right ventricular internal dimension	0.306	0.306	0.304	0.311
Left ventricular internal dimension	0.300	0.300	0.298	0.304
Left atrial internal dimension	0.2995	0.2929 (17)	0.297	0.307

LEGEND

Confidence limits were not found to "flare" significantly at the extremes of gestational age.

TABLE III Summary of statistical data

Y	n	r	t	p	SEE yx2
Septal thickness	178	0.836	20.k83	<0.001	0.088
Posterior left ventricular wall thickness	175	0.884	24.929	<0.001	0.066
Aortic root dimension	254	0.895	31.925	<0.001	0.138
Right ventricular internal dimension	167	0.844	20.183	<0.001	0.306
Left ventricular internal dimension	175	0.876	23.944	<0.001	0.300
Left atrial internal dimension	107	0.823	14.968	<0.001	0.296

LEGEND

This shows the number of determinations (n) correlation coefficient (r) student's t for the significance of the correlation coefficient (t) significance (p) and twice the standard error of y (SEEy x 2) for each parameter.

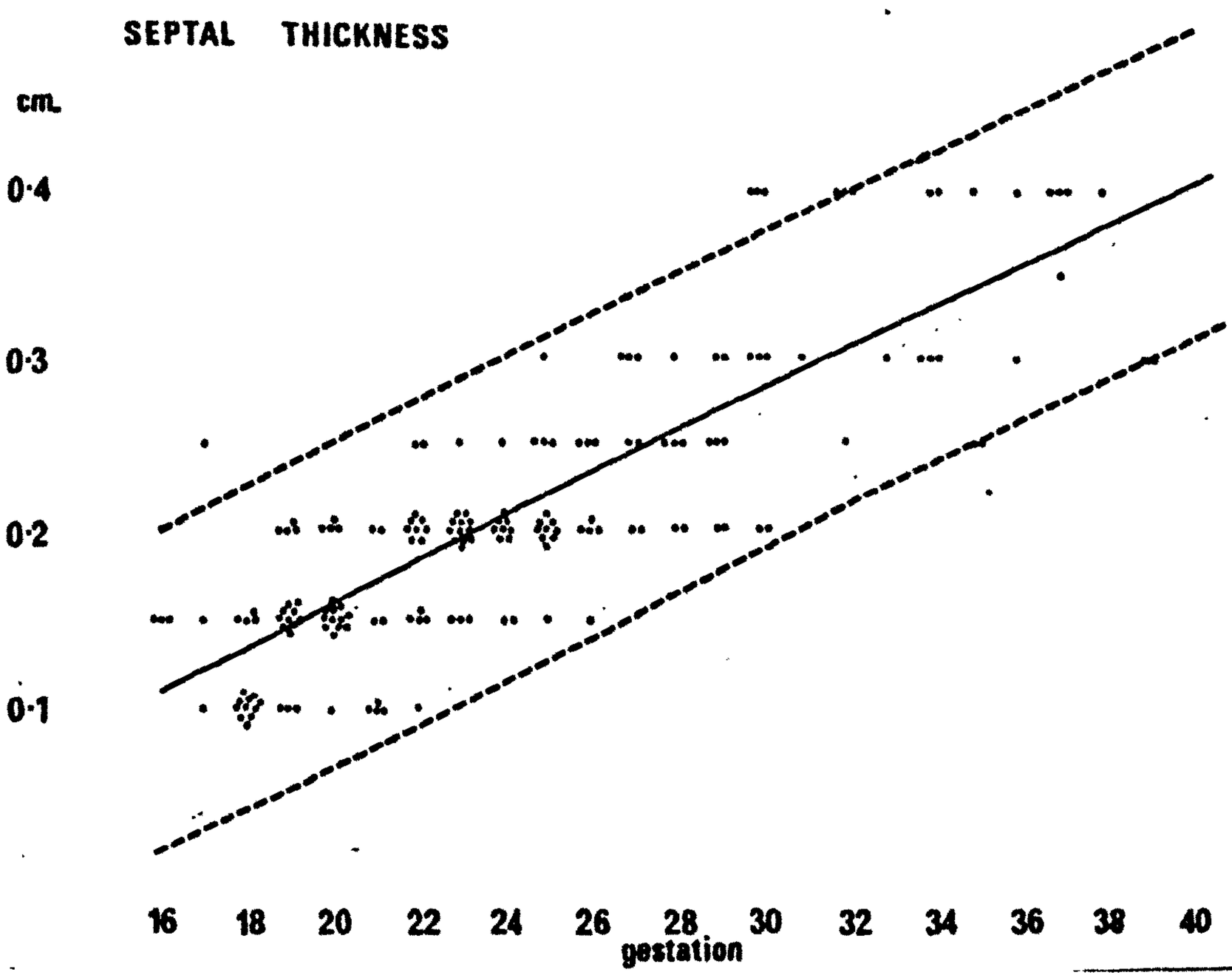


Figure 8.3. Septal thickness plotted against gestational age (n = 178). The 95% confidence limits represent twice the standard error of the mean in each graph. Y = 0.0122 x -0.881.

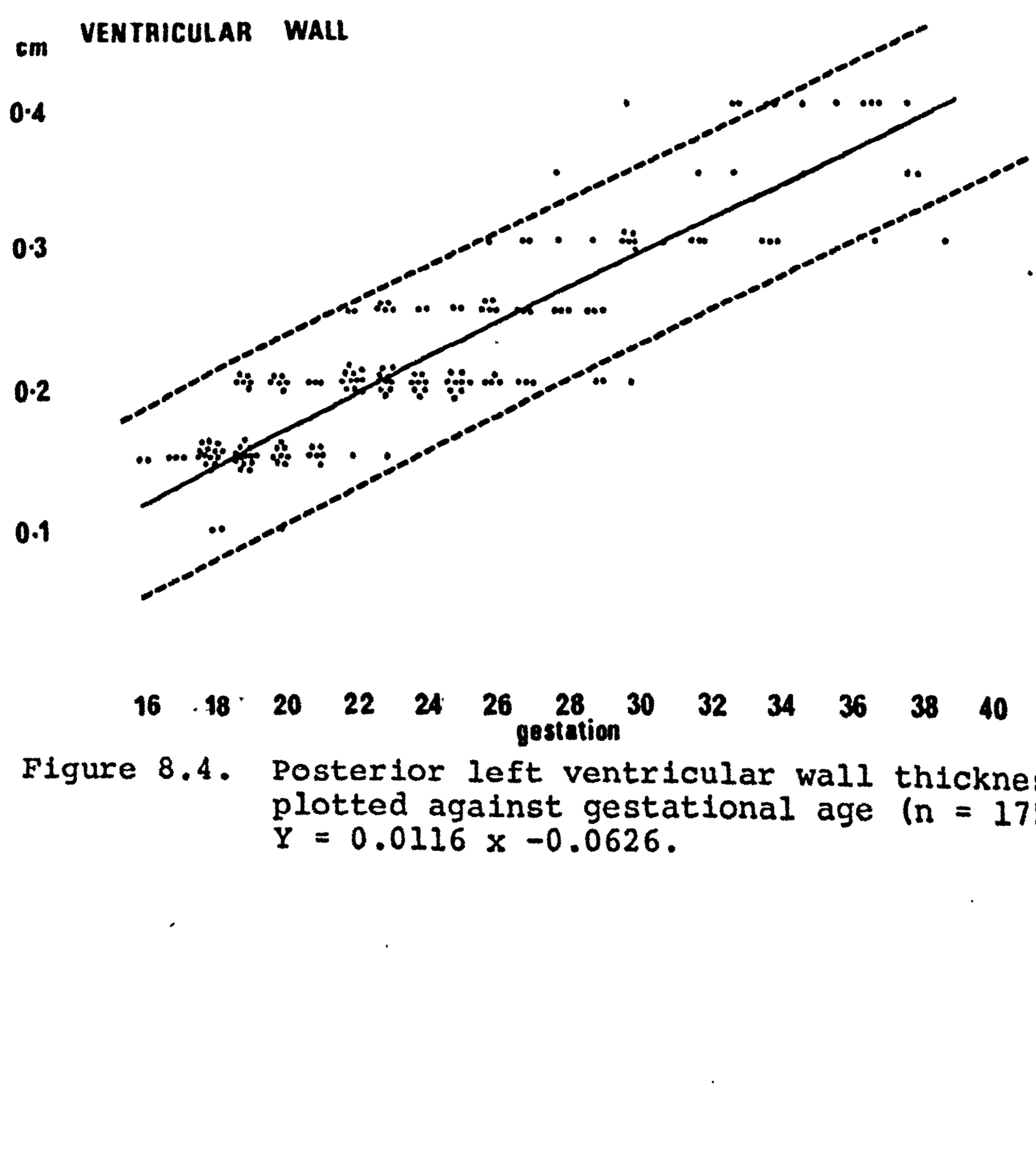


Figure 8.4. Posterior left ventricular wall thickness plotted against gestational age (n = 175). Y = 0.0116 x -0.0626.

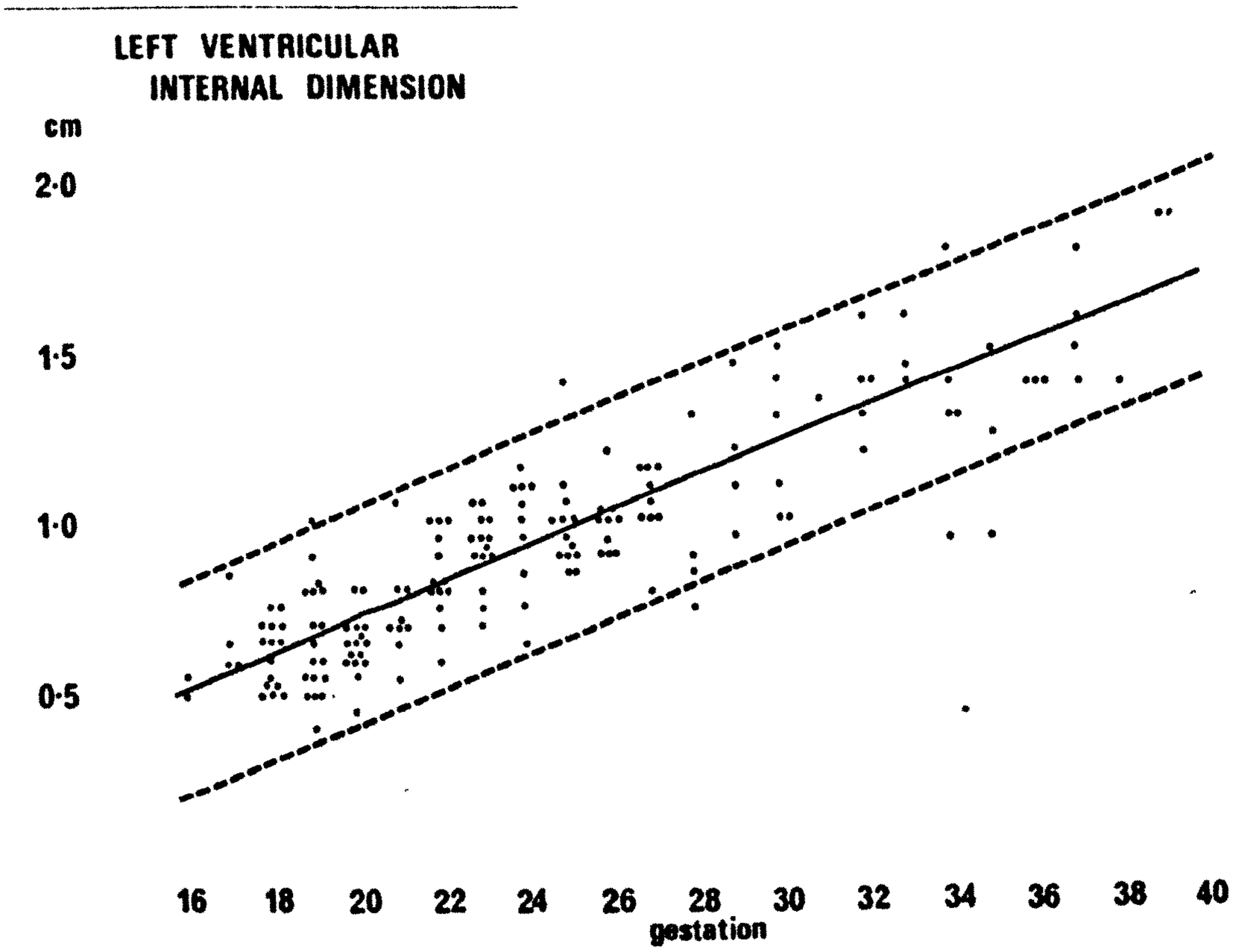


Figure 8.7. Left ventricular internal dimension plotted against gestational age (n = 175). Y = 0.0489 x -0.2621.

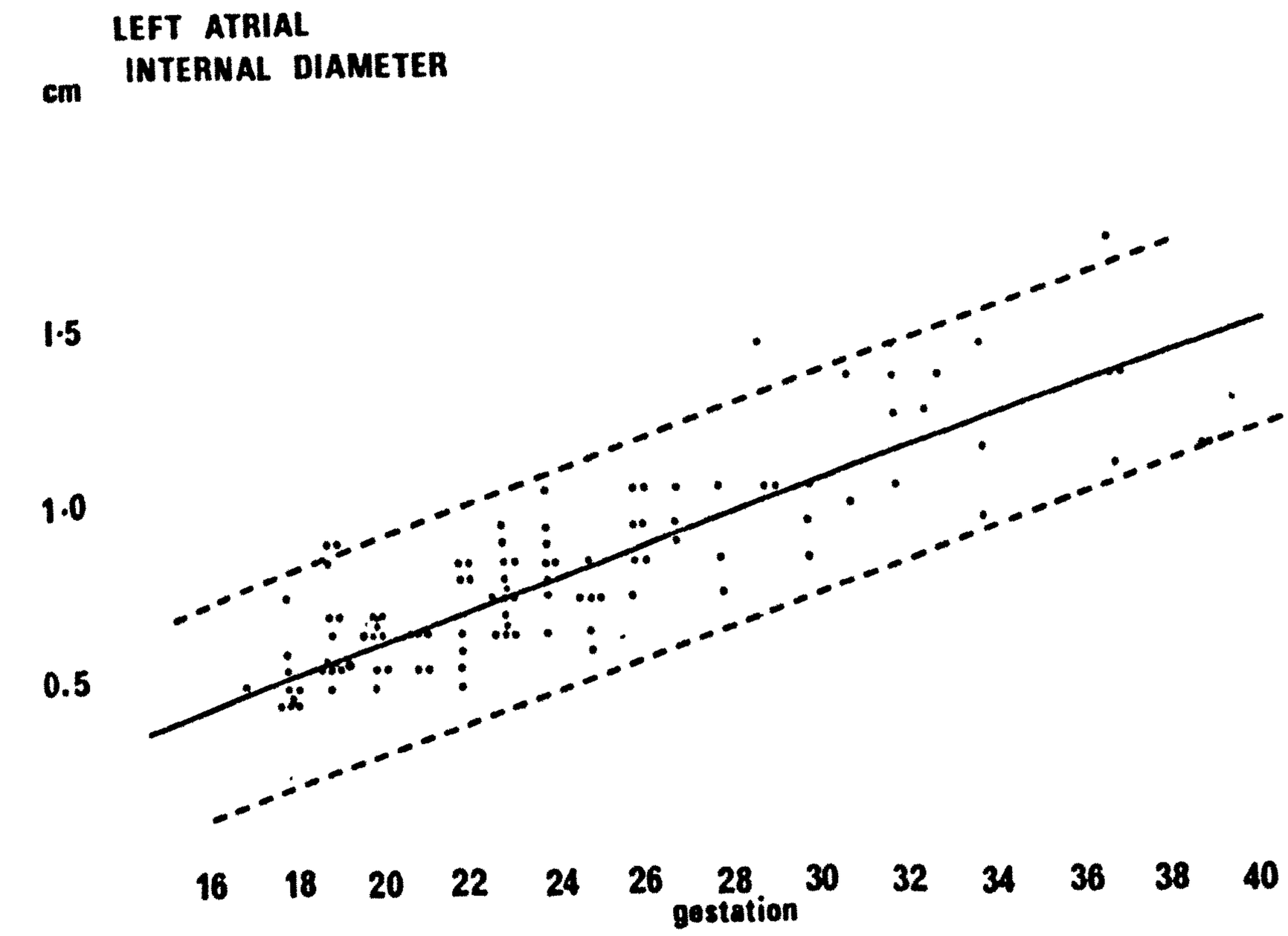


Figure 8.8. Left atrial internal dimension plotted against gestational age (n = 107). Y = 0.0402 x -0.2137.

is from about 0.4 cms. at 16 weeks gestation to over 1.5 cms at birth. The equality in size of the two ventricles in prenatal life, probably represents the fact that both ventricles have approximately equal outputs and are contracting against approximately equal vascular resistances. Dawes found the cardiac output to be slightly greater from the left ventricle than from the right, when estimated directly in the fetal lamb, but the difference was small, the left ventricle contributing 55%, the right ventricle 45%, of cardiac output (141). Other authors have found equal cardiac output using an indicator dilution technique (142). The pressure in the pulmonary artery may even be slightly higher than that in the aorta as the shunt in the ductus arteriosus in fetal life is always from the pulmonary artery to the descending aorta, that is right to left shunting (143).

The aortic root dimension increases from 0.2 cms at 16 weeks to 1.0 cms. at term, this measurement at term being consistent with published neonatal measurements (144). The left atrial dimension was consistently found to be greater than that of the aorta throughout fetal life. This presumably reflects the volume of right to left atrial shunting through the patent foramen ovale. The organised mechanism of this shunt has been described in the previous chapter. The left atrial size is unrelated to the presence of the ductus arteriosus in fetal life as the shunt through this structure is always right to left in the fetus.

The measurement data documented here has several practical and potential uses. Firstly, the measurable range of growth of intracardiac structures during pregnancy is important to document. It has been seen that relative chamber sizes are different from that found in postnatal life and this gives some clues to the differences between prenatal and post-natal cardiac function. An abnormality of chamber size may be suspected on the realtime image but actual measurement of the chamber in question and comparison with the expected chamber size for that gestation will lead to more accurate diagnosis of structural cardiac abnormality. For example, the right ventricle may appear larger than the left on realtime examination. This may be because the right ventricle is large and the left ventricle normal in size for the gestational age; or conversely, the left ventricle may be structurally small and this gives a false impression of an enlarged right ventricle. This is a practical situation which not uncommonly occurs. Reference to the measurement charts should answer these questions.

It should be stressed that the cardiac growth charts should not be used for gestational age dating as this can be more accurately determined by other means (145). Nor should an individual cardiac measurement be considered in isolation from other cardiac measurements. Growth retardation will shift the intracardiac measurements to the left but all the

measurements will be similarly affected. Conversely, a small aortic root measurement for the estimated gestational age, in the presence of other cardiac measurements in the normal range should arouse suspicion of structural abnormality.

In summary, therefore, the measurement data is important in the understanding of cardiac growth during pregnancy and helps to increase knowledge about fetal cardiac function. It is also important in the elucidation of structural cardiac abnormality.

CHAPTER 9

RESULTS:

The fetal electrocardiogram: The method of obtaining it and its use within the echocardiographic study.

External techniques for recording the fetal electrocardiogram have been described in recent years (146). We have used the techniques of Wheeler and Murrills (147) and imitated their adaptation of a general purpose "in house" design of preamplifier. The addition of the fetal electrocardiogram to the M mode echocardiogram allows more accurate timing of events within the cardiac cycle. The opening of the two atrioventricular valves can be seen to have the same time relationship to the Q wave on the electrocardiogram signifying simultaneous opening (Figure 7.10). Similarly, systolic time intervals can be measured by study of the arterial valves. The relationship of foramen ovale flap motion, described in Chapter 7, could be timed according to atrial and ventricular systole with the help of the fetal electrocardiogram together with left atrial wall motion.

Methods

Three standard disposable silver nitrate gel electrodes were applied to the maternal abdomen in the midline. One was placed on the symphysis pubis, one above the umbilicus and the

third between these two. The electrodes were connected to the isolation preamplifier then further processed through a filter unit. Full details of the circuitory and modifications which were used are given in Appendix I. The outgoing signal was then fed into the 800 module of the ATL Mark III in use. The fetal electrocardiogram could then be displayed on the M mode paper chart recorder simultaneously with the M mode echocardiogram. The paper speed was 50 mm/sec. In adequate tracings were obtained when faster paper speeds were used.

The systolic time intervals were measured as illustrated in Figures 9.1 and 9.2. The pre-ejection period (P.E.P.) of each ventricle is the time between the electrical signal and the onset of ventricular contraction. The onset of ventricular coincides with the opening of the arterial valve and ejection time (E.T.) is the length of time the valve remains open.

Results

Recording of the fetal electrocardiogram was attempted in a series of 103 patients. It was obtained in 85 cases. Table IV shows the successes and failures, related to gestational age. The systolic time intervals were only measured when opening and closure of the arterial valve was clearly

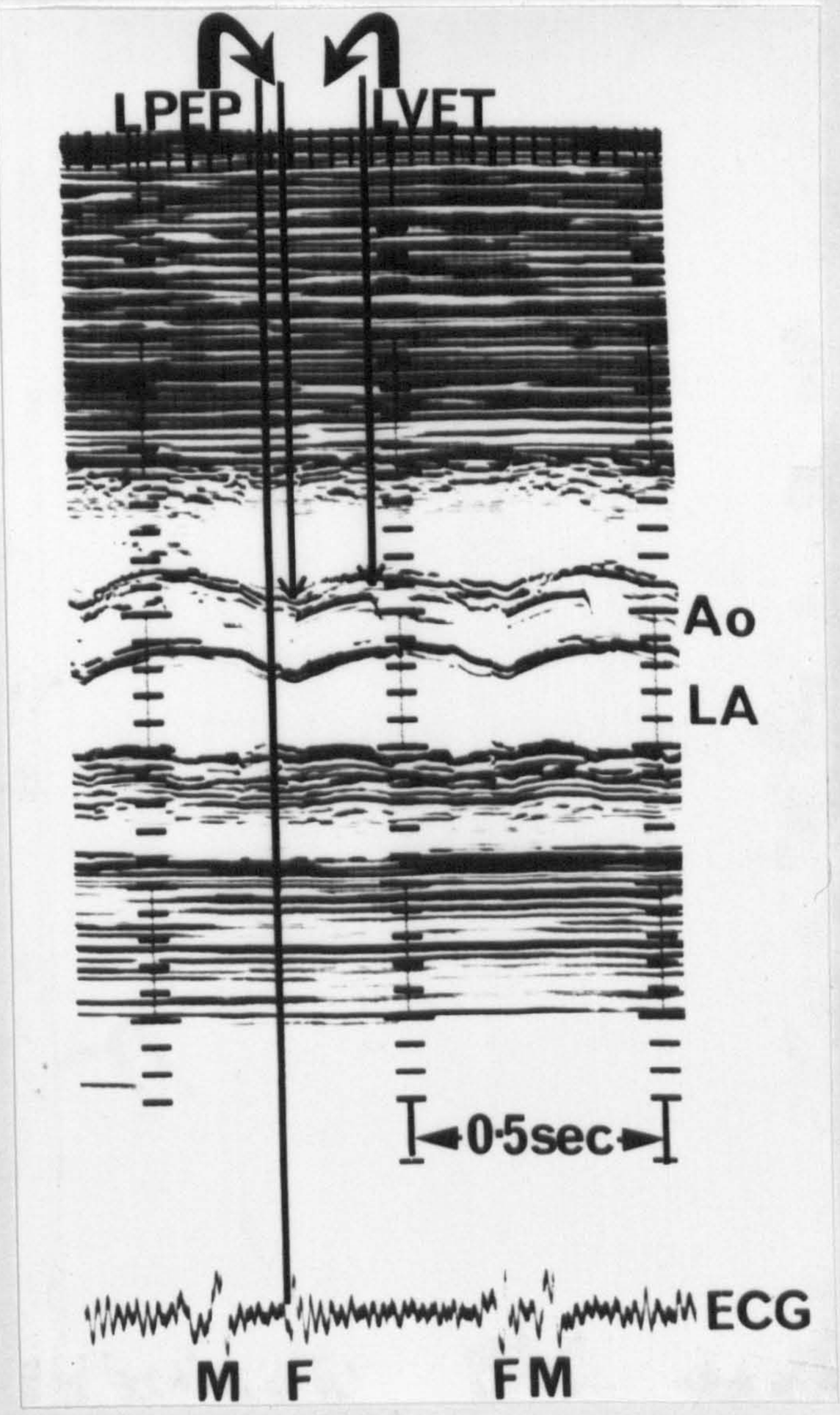


Figure 9.1. The aortic valve is seen within the aortic walls. The left ventricular systolic time intervals are measured. LPEP from the Q wave of the E.C.G. to the opening of the aortic valve, LVET, from the opening to the closure of the aortic valve.

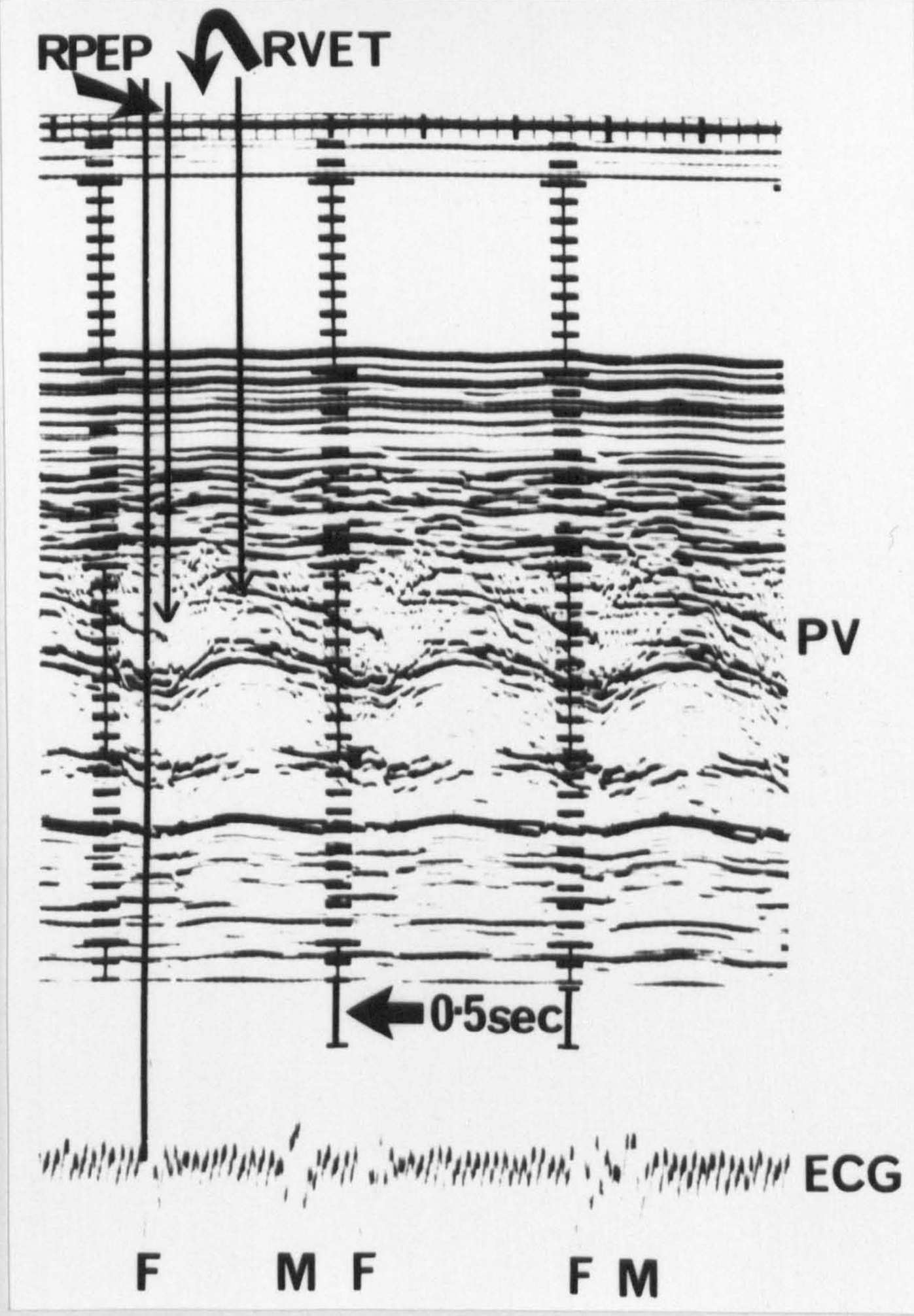


Figure 9.2. The pulmonary valve is seen. RPEP is the time between the Q wave of the electrocardiogram to the opening of the pulmonary valve, RVET, from the opening to the closure of the pulmonary valve.

TABLE IV

Gestational age (weeks)	Successful	Failed
18-28	77	9
18 or under	7	6
Over 28	1	3
	82.5%	17.5%

defined. The left ventricular systolic time intervals could be measured in 55 cases,the right ventricular intervals in 25 cases. The ratio of PEP/VET was calculated for both ventricles. For LPEP/LVET the mean was 0.26±0.04, RPEP/RVET the mean was 0.27±0.04. (Figures 9.3,9.4.) The difference between the means for right and left ventricles was not significant ($p > 0.001$).The systolic time intervals were measured while the heart rate was stable.

The heart rate varied between 130-144 beats/min, the slightly slower rates being obtained later in pregnancy. In midtrimester pregnancy a sudden drop in heart rate is a frequent finding, observed in 70 of the 85 cases recorded. The fetal heart rate may suddenly drop to half the normal rate and very slowly, that is over a minute or two, return to normal.

Discussion

The fetal electrocardiogram is difficult to obtain before 18 weeks gestation because the amplitude of the fetal electrical signal is so small. It cannot be obtained between 28 and 34 weeks gestation. This is thought to be due to insulation of the electrical signal by the vernix caseosa which is present during pregnancy at this time. In our series of

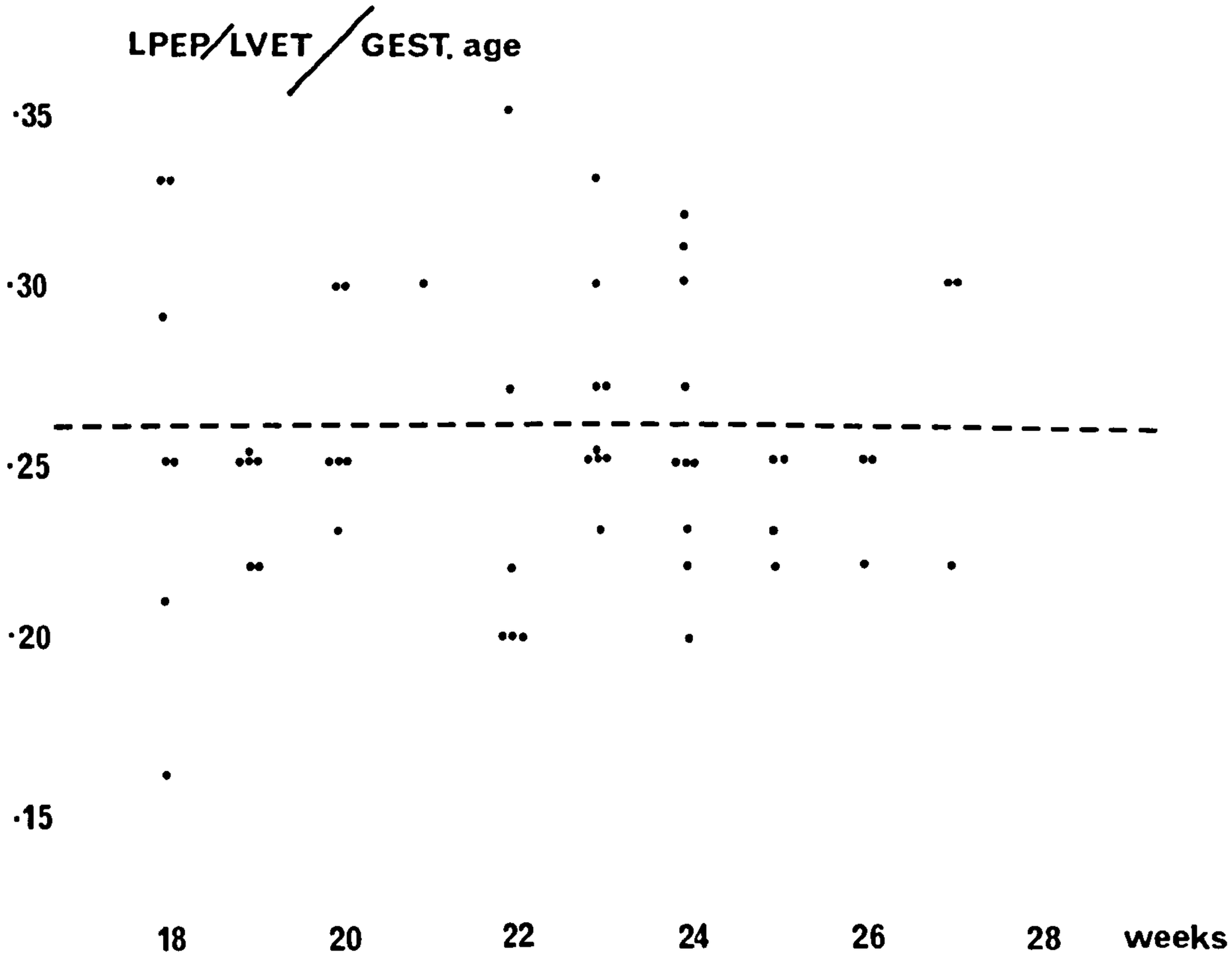


Figure 9.3. The ratio of left ventricular pre-ejection period to left ventricular ejection time is related to gestational age in weeks. There is much the same scatter throughout gestation. The mean is 0.26 ± 0.04 secs. The mean is drawn on the graph. This is slightly below the paediatric mean of 0.3 ± 0.04 secs. Number of estimates is 55.

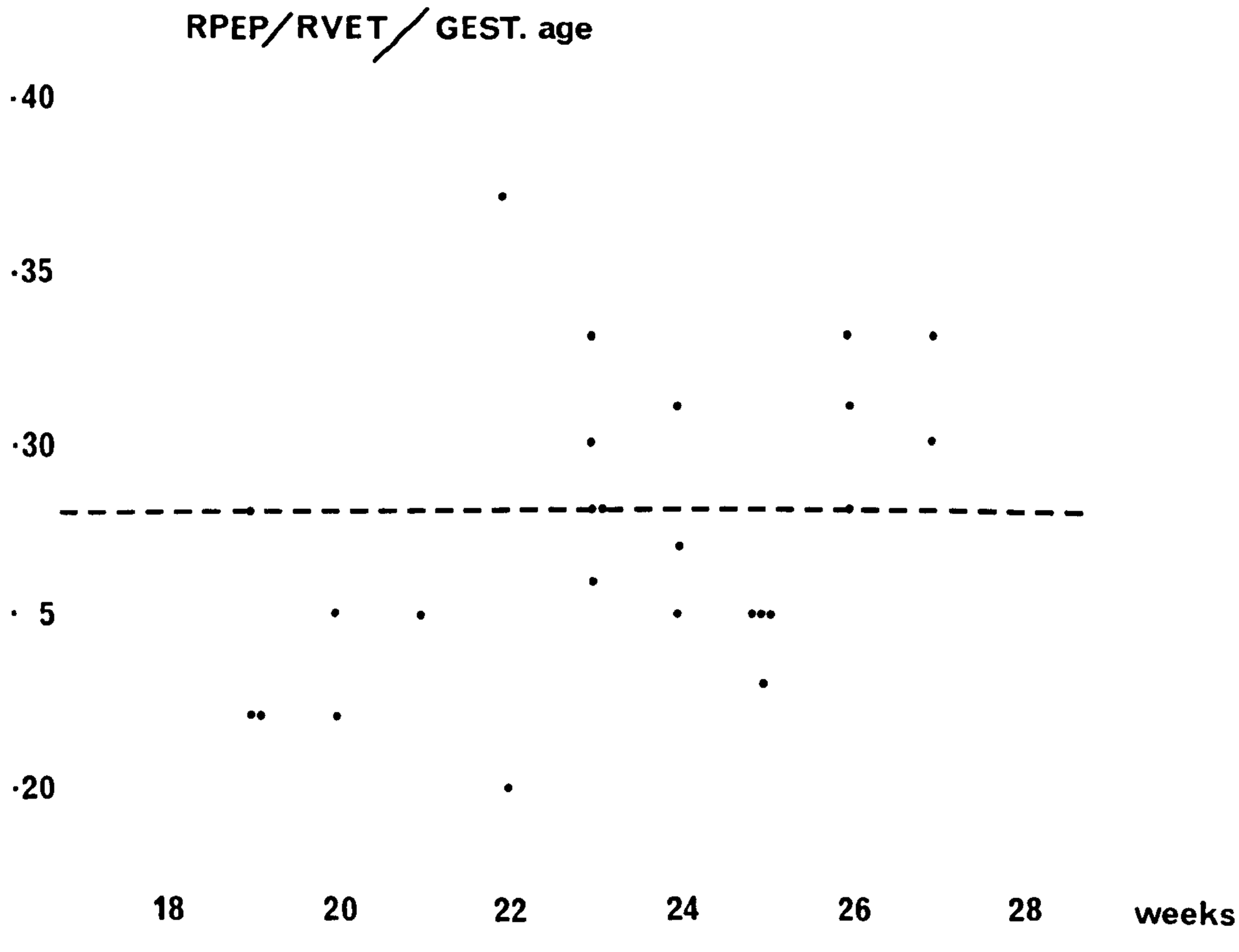


Figure 9.4. The ratio of right ventricular pre-ejection period to right ventricular ejection time is related to gestational age in weeks. The mean is 0.27 ± 0.04 secs. The mean is drawn on the graph. The number of estimates is 25. The difference between the mean for right and left systolic time intervals is not significant.

99 consecutive cases before 28 weeks gestation we were successful in 84 cases. Forty percent of our failures (6/15) were 18 weeks gestation or less. We only attempted a fetal electrocardiogram in 4 cases after 28 weeks gestation, the only successful case being 37 weeks gestation when the signal is known to become more readily obtainable.

The results of fetal heart rate are similar to the findings of other workers (148). During a 15 minute fetal echocardiogram bradycardia was commonly observed and taken to be a normal finding. Wheeler et al recorded up to 49 such drops in heart rate in a hour's recording during the midtrimester. This becomes less frequent in the last trimester of pregnancy.

The LPEP/LVET has been shown to be a reliable indicator of left ventricular function (149). It is relatively independent of age and heart rate (150). Our recordings may have been more accurate had we been able to use a paper speed of 100 mm/sec, but we failed to achieve adequate tracings at this speed and thus only 50 mm/sec was used. However, it can be seen that RPEP/RVET is similar to LPEP/LVET, and the values obtained for each were consistent in the gestational age range studied.

The systolic time interval ratios are determined by preload, afterload, myocardial contractility and electrical conduction (151). Assuming normal myocardial function and electrical

conduction, the time intervals can be considered to reflect preload and afterload. These recordings were all made in normal fetuses with structurally normal hearts. Since delivery there has been no reason to suspect abnormality in any case and therefore the assumption of normality of conduction and contraction is not unreasonable. The correlation between RPEP/RVET and LPEP/LVET, therefore, reflects that in fetal life both ventricles eject a similar volume against a similar arterial pressure. This is consistent with fetal lamb studies (152). The mean value for LPEP/LVET of 0.26±0.04 is slightly below the paediatric normal range of 0.3±0.04. This would be expected as aortic pressure and systemic vascular resistance in the midtrimester fetus is less than in neonatal life. The mean value of RPEP/RVET in the fetus 0.27±0.04 is similar to the normal infant. Although the right ventricular pressure in fetal life is the same as left ventricular pressure both ventricles probably have a systolic pressure of about 30 mmHg. (153). At the present time, however, there is no way of accurately validating these estimates in the human fetus.

CHAPTER 10

RESULTS:

Evaluation of left ventricular function in the fetus

Estimation of left ventricular function from M mode echocardiography has been documented in children. Several functional characteristics have been devised and some correlate well with angiographic techniques (154). The most useful functional measurements are shortening fraction (SF), rate of circumferential shortening, Vcf, and posterior left ventricular wall velocity (PLVWV) (155). Normal ranges in children have been estimated (156). We have therefore studied these functional parameters in the fetus and compared them with estimates in children. We have not derived estimates of left ventricular volume or cardiac output, as has been done by Vosters et al. in the fetus, as these require assumptions of left ventricular geometry that are suspect (159). These values have proved unreliable estimates, when compared to angiographic estimates of left ventricular volume or output (158,159) in children.

Method

The M mode echocardiogram of the left ventricle was obtained as described in Chapter 8. The M line was directed by the two dimensional image and the tracing

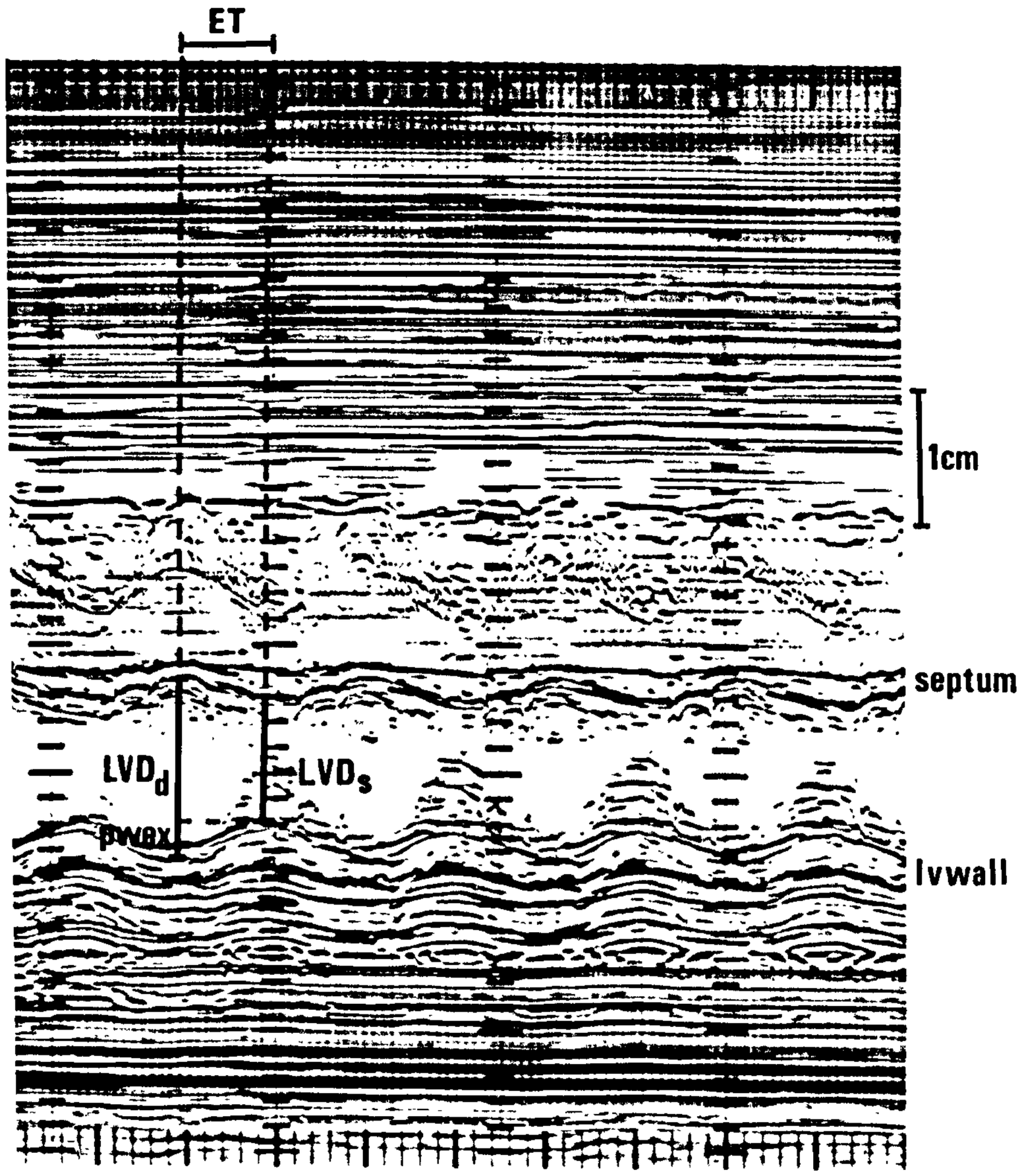


Figure 10.1. The measurements used to derive functional data are made as illustrated. LVD_d is left ventricular internal dimension in diastole, LVD_s the dimension in systole, ET is the ejection time or the time between the maximum and minimum left ventricular dimensions, PWex is the posterior left ventricular wall excursion or the distance the posterior left ventricular wall moves on ventricular contraction.

achieved each time in a standard fashion. That is, the M line was positioned perpendicular to the ventricular septum, either in the four chamber view, or more commonly in the short axis of the left ventricle. The M line was swept up from the body of the left ventricle to the mitral valve leaflets and the ventricular dimensions measured just apical to the mitral valve, as is customary in postnatal practise. The measurements made are illustrated in Figure 10.1. As the fetal electrocardiogram was not available in every trace the maximum left ventricular internal dimension was measured. This is fractionally greater than the end-diastolic dimension which may slightly alter functional measurements. The difference in the fetal heart was so small however, that this was thought acceptable. Measurements were made in 100 fetal M mode tracings. No functional or structural abnormality was suspected in any case from the cross-sectional echocardiogram. All the pregnancies involved in this study have since delivered and there is no apparent structural or functional cardiac anomaly suspected in the baby.

The formulae used were:

$$\text{Shortening fraction (SF)} = \frac{LVD_d - LVD_s}{LVD_d} \times 100$$

$$\text{Velocity of circumferential shortening (Vcf)} = \frac{LVD_d - LVD_s}{LVD_d \times LVET}$$

$$\text{Posterior left ventricular wall velocity (PLVWV)} = \frac{Ex}{LVET}$$

$$\text{and normalised left ventricular wall velocity (NPLVWV)} = \frac{Ex}{LVD_d \times LVET}$$

Where LVD_d is the left ventricular dimension at end-diastole, LVD_s at end systole, LVET is left ventricular ejection time and Ex is the excursion of the posterior left ventricular wall.

Results

Figure 10.2 shows the shortening fraction plotted against gestational age in 100 patients. The paediatric range commonly quoted for normality is drawn for comparison (160). It can be seen that 30% of the fetuses showed a shortening fraction below the normal paediatric values. This did not appear to vary with gestational age. Only two values were above the normal range. If a slightly lower "normal" range for fetuses, say between 20 and 40% was accepted, only 8% of the results would be outside this range.

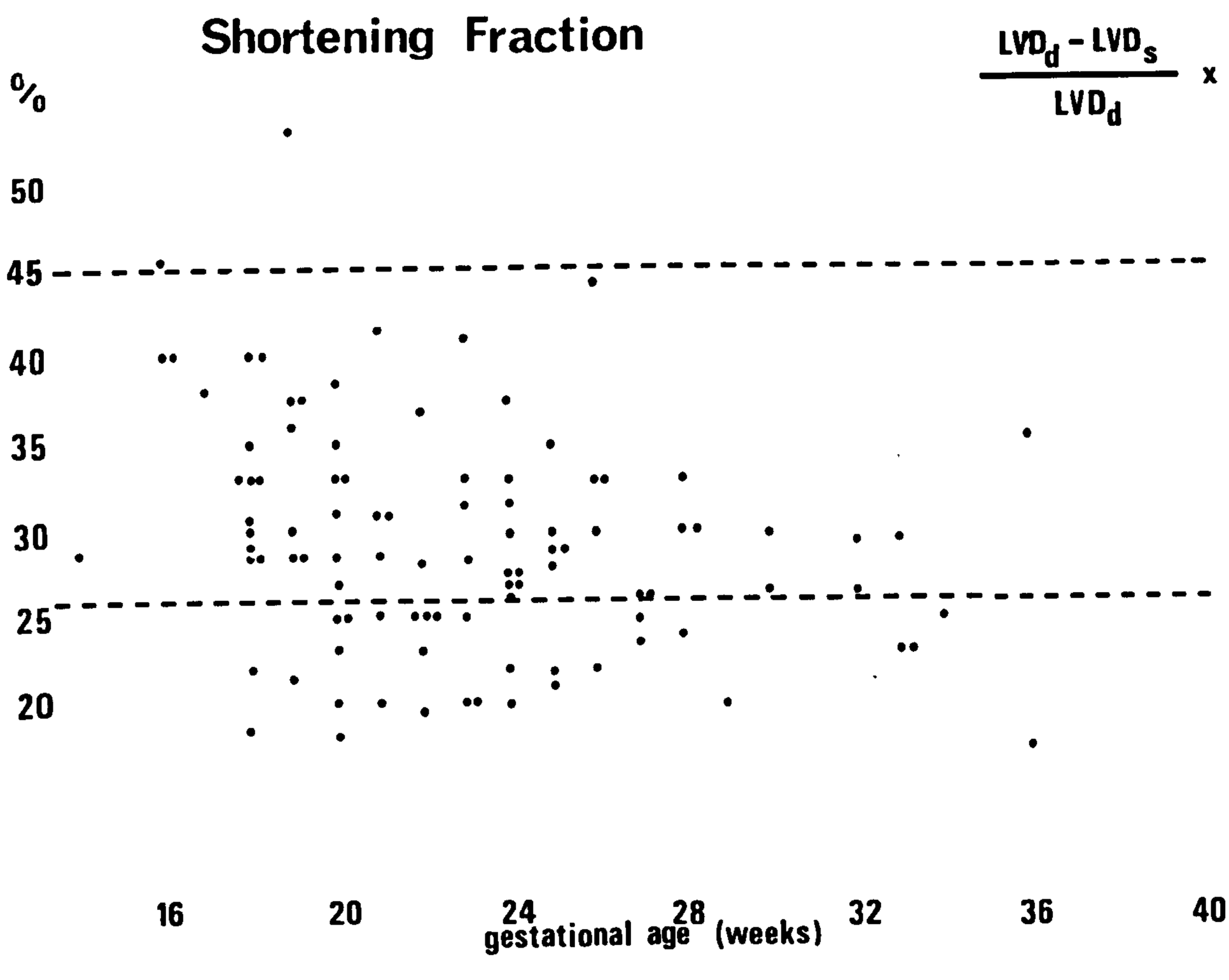


Figure 10.2. Shortening fraction is plotted against gestational age in weeks. The normal paediatric range for shortening fraction (26-45%) is indicated on the figure. LVD_d is left ventricular internal dimension in diastole, LVD_s the dimension in systole in cms.

Figure 10.3 shows the velocity of circumferential shortening plotted against gestational age. This measurement is commonly quoted in cycles per second but it is more accurately termed circumferences per sec. The standard paediatric normal range is drawn on the graph for comparison (161). It can be seen that the fetal heart has a wider scatter for normality, with 38% of the values lying above the paediatric range and 7% below. The scatter does not appear to vary with gestational age, but there were only 9% of the values obtained in fetuses over 28 weeks gestation. As velocity of circumferential shortening is known to vary with heart rate, Figure 10.4 shows Vcf plotted against heart rate. The heart rate in 96% of the fetuses lay between 132 and 156 beats per minute and the rate did not seem to influence the values recorded for Vcf. Good correlation was achieved when Vcf was plotted against S.F. Figure 10.5. There was a straight line correlation with $p = <0.001$, $r = 0.88$, $y = 0.04 + 0.05x$. This correlation of functional measurements would be expected in the normal heart.

The next functional measurement to be derived was posterior left ventricular wall velocity which is seen in Figure 10.6 plotted against gestational age. The normal range for this measurement is 4.44 ± 1.15 cms/sec (161).

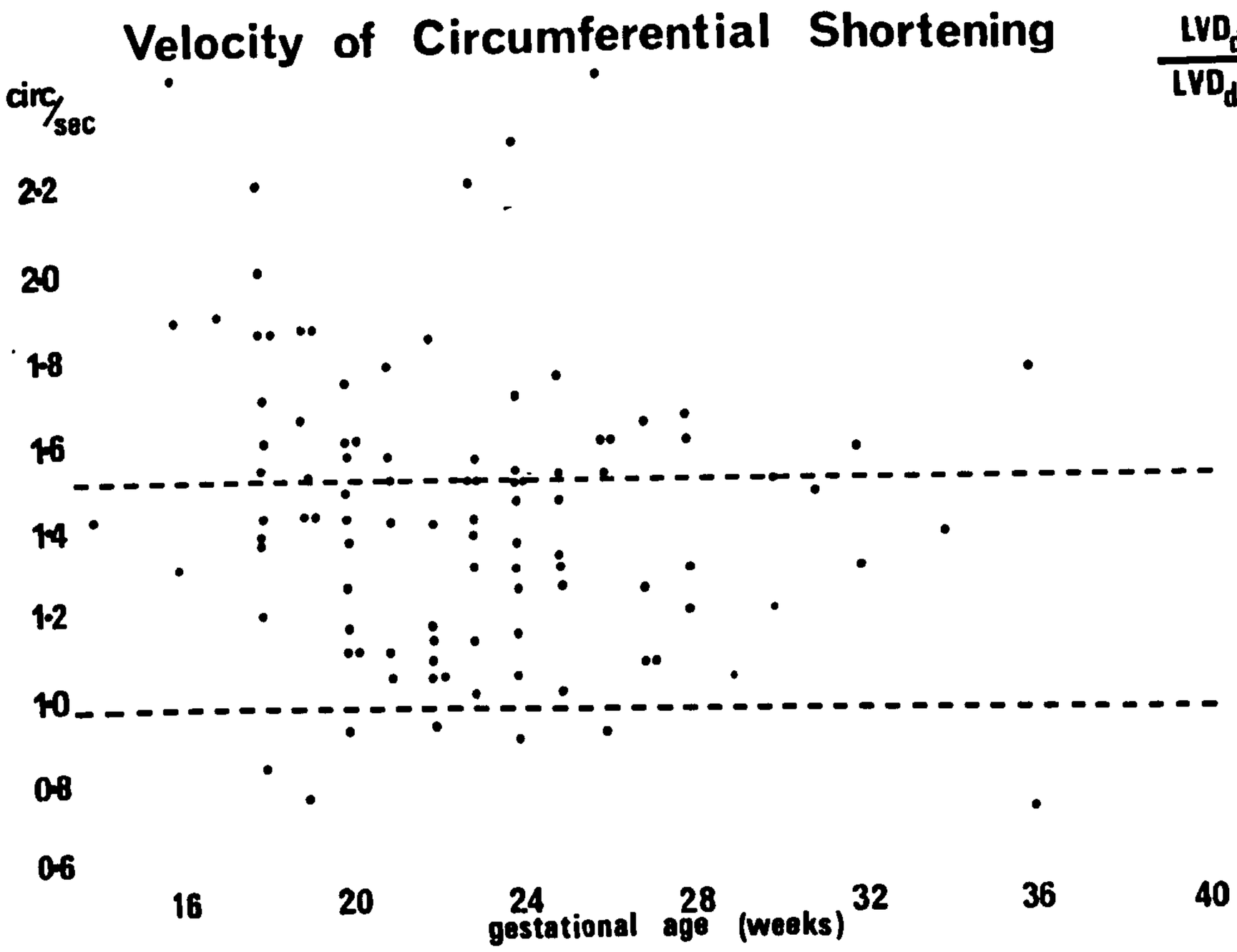


Figure 10.3. Velocity of circumferential shortening in cycles per sec. is plotted against gestational age in weeks. LVD_d is left ventricular internal dimension in diastole, LVD_s the dimension in systole in cms. LVET is left ventricular ejection time in seconds. The normal range of 0.97-1.5 cycles/sec. is indicated on the figure.

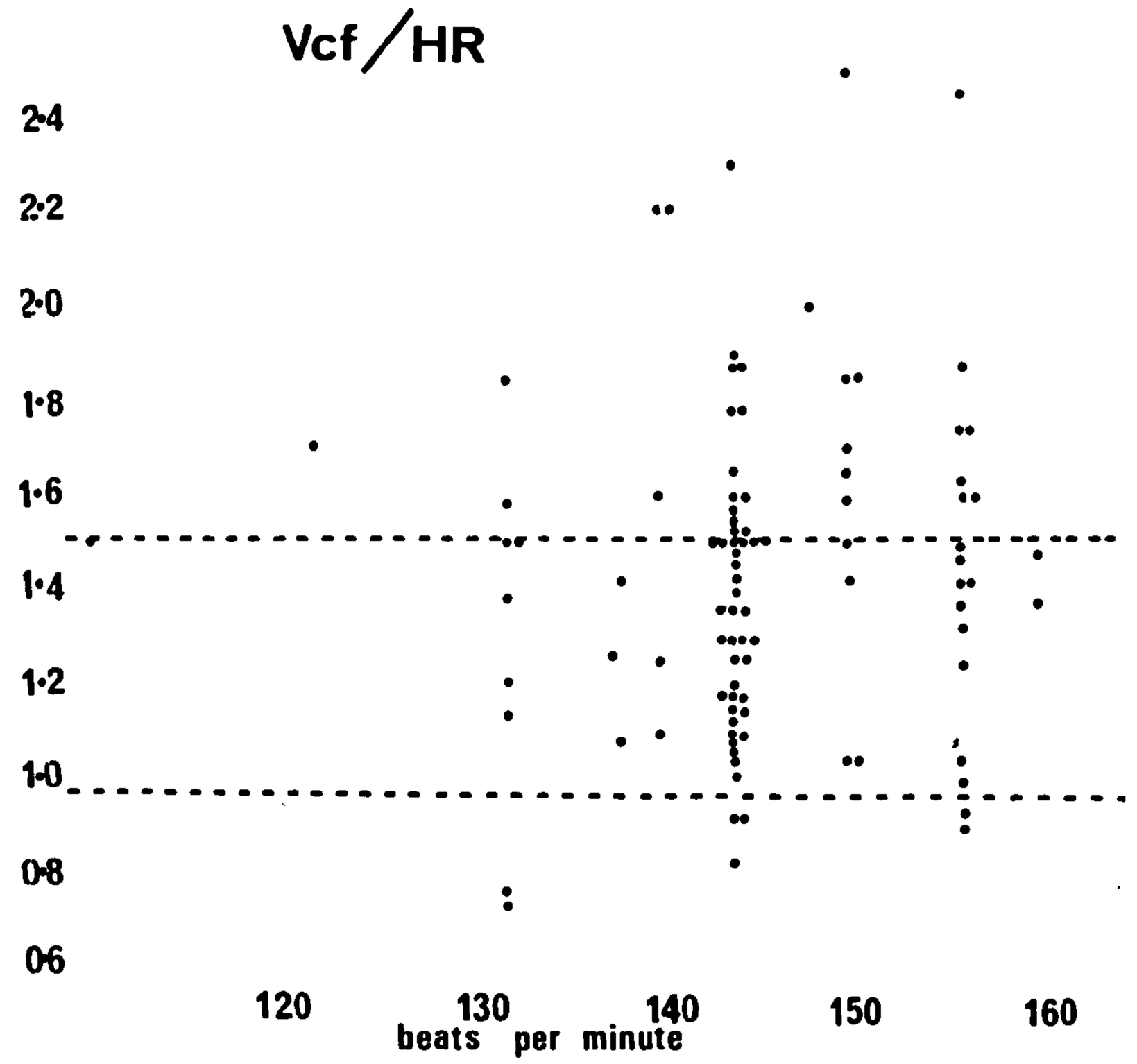


Figure 10.4. The velocity of circumferential shortening in cycles per second is plotted against heart rate in beats per minute. The normal paediatric range for Vef is indicated.

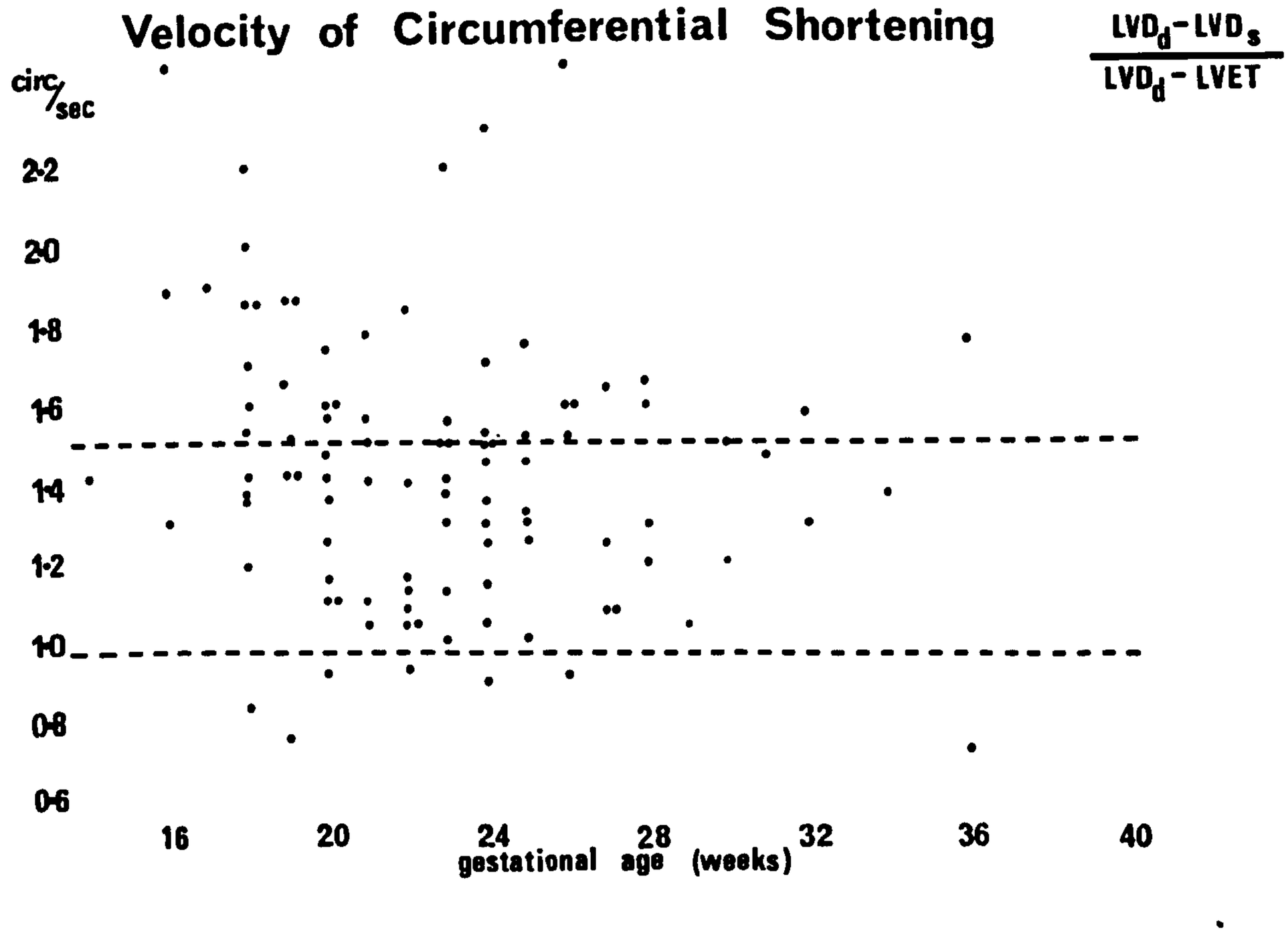


Figure 10.5. The velocity of circumferential shortening is plotted against shortening fraction. A straight line correlation is achieved, $p=<0.001$ $r=0.88$ $y=0.04+0.05x$

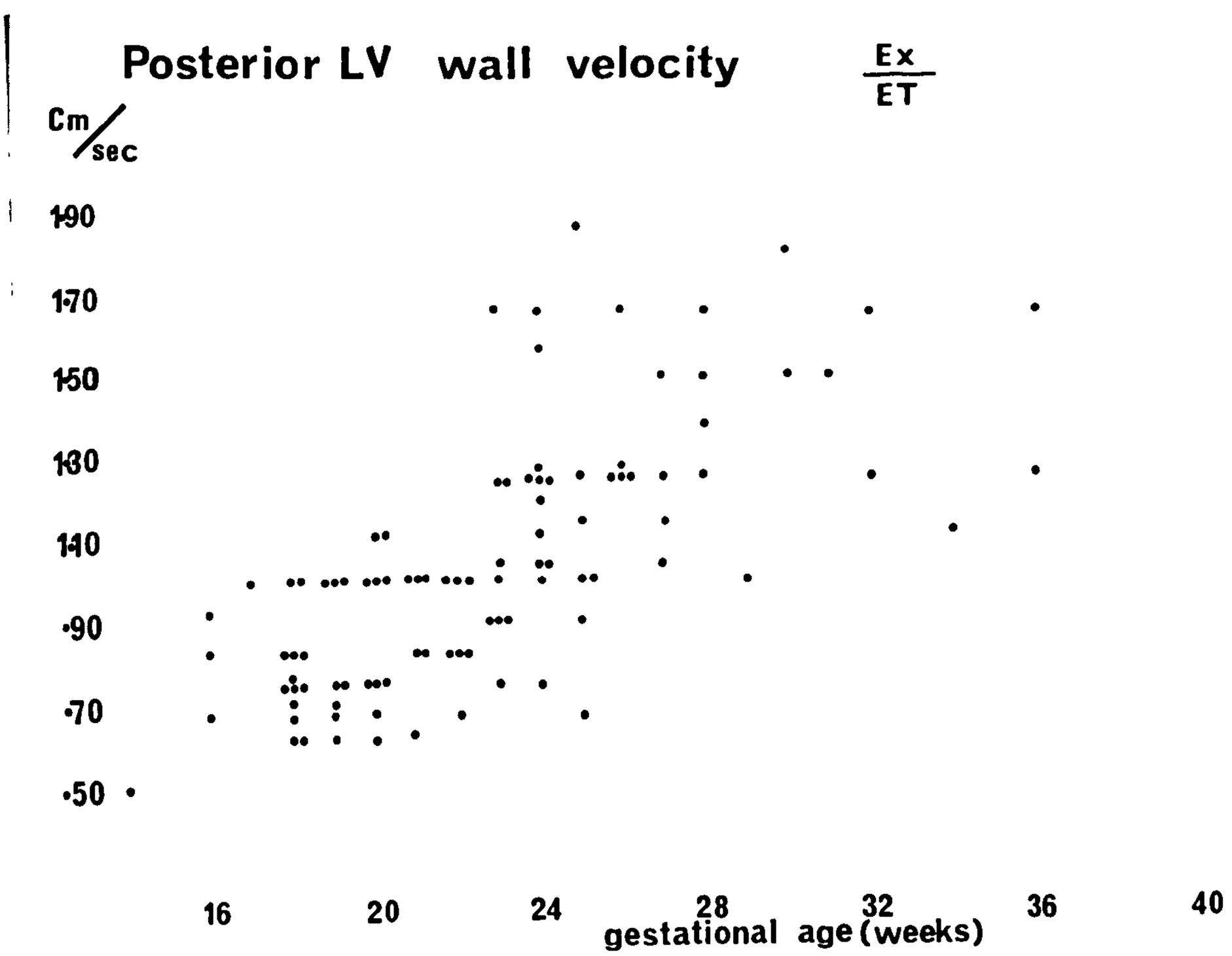


Figure 10.6. Posterior wall velocity in cms. per sec. is plotted against gestational age in weeks.

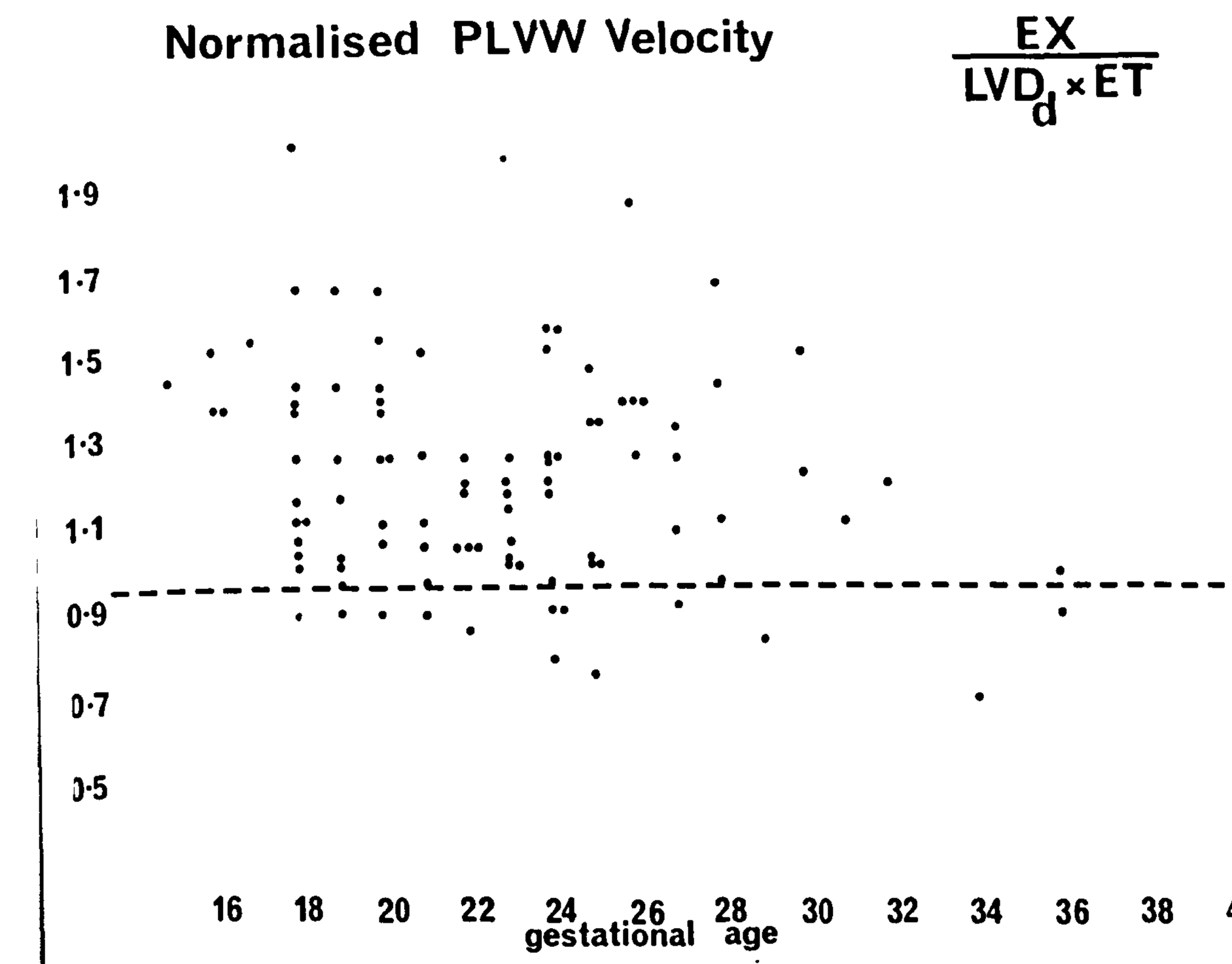


Figure 10.7. "Normalised" posterior left ventricular wall velocity in cms. per sec. is plotted against gestational age in weeks. In both the above figures Ex is posterior left ventricular wall excursion, ET, left ventricular ejection time. LVD_d is left ventricular internal dimension in diastole. The mean paediatric value for normalised left ventricular wall velocity is indicated.

It can be seen that this is well above the fetal range, although posterior wall velocity increases steadily towards term. This is not surprising as ejection time is approximately the same throughout pregnancy at 200 ± 40 msec., whereas the posterior wall excursion increases throughout pregnancy. Posterior wall excursion was found to be the same as left ventricular wall thickness throughout pregnancy and therefore increase as wall thickness increased. Chapter 8, Figure 8, shows the growth of left ventricular posterior wall thickness throughout pregnancy. "Normalising" this derived functional measurement is illustrated in Figure 10.7. It can be seen that when "normalised" for the size of the left ventricle, 87% of fetal values lie above the mean paediatric value. The percentage of values above the paediatric range does not vary with gestational age.

Discussion

It can be seen that shortening fraction of the left ventricle is slightly below that of the left ventricle in childhood, whereas velocity of circumferential shortening is slightly higher than paediatric values. Vcf has a known association with heart rate, values increasing with increasing

heart rate (162). This may explain the higher Vcf found in the fetus. Shortening fraction, however is independent of heart rate (163) and body surface area (164). It was noted that the amplitude of posterior left ventricular wall motion was the same as left ventricular wall thickness throughout pregnancy. Although values for posterior wall excursion relative to wall thickness are lacking in children, the expected mean amplitude of motion in early adult life is 1.2 cms. compared to an expected mean left ventricular wall thickness of 0.9 cms. (165). Therefore amplitude of motion is one third as much again as posterior left ventricular wall thickness. It may be that the measurements in the fetus are so small, that this difference in excursion is undetectable. Or it may be that left ventricular contraction in the fetus is less powerful than in postnatal life. This may account for the slightly lower values of shortening fraction, found in the fetus, in comparison to the normal paediatric range. There is some evidence in the animal model that muscle structure matures during prenatal and immediate postnatal life, and this is very likely to be true also of the human fetus (166). It is possible that muscle immaturity is compensated for by the faster heart rate found in fetal life (See Chapter 9). The fetus also uses both ventricles, working in parallel, Figure 10.8, to drive the circulation, unlike postnatal life where the two ventricles are in series.

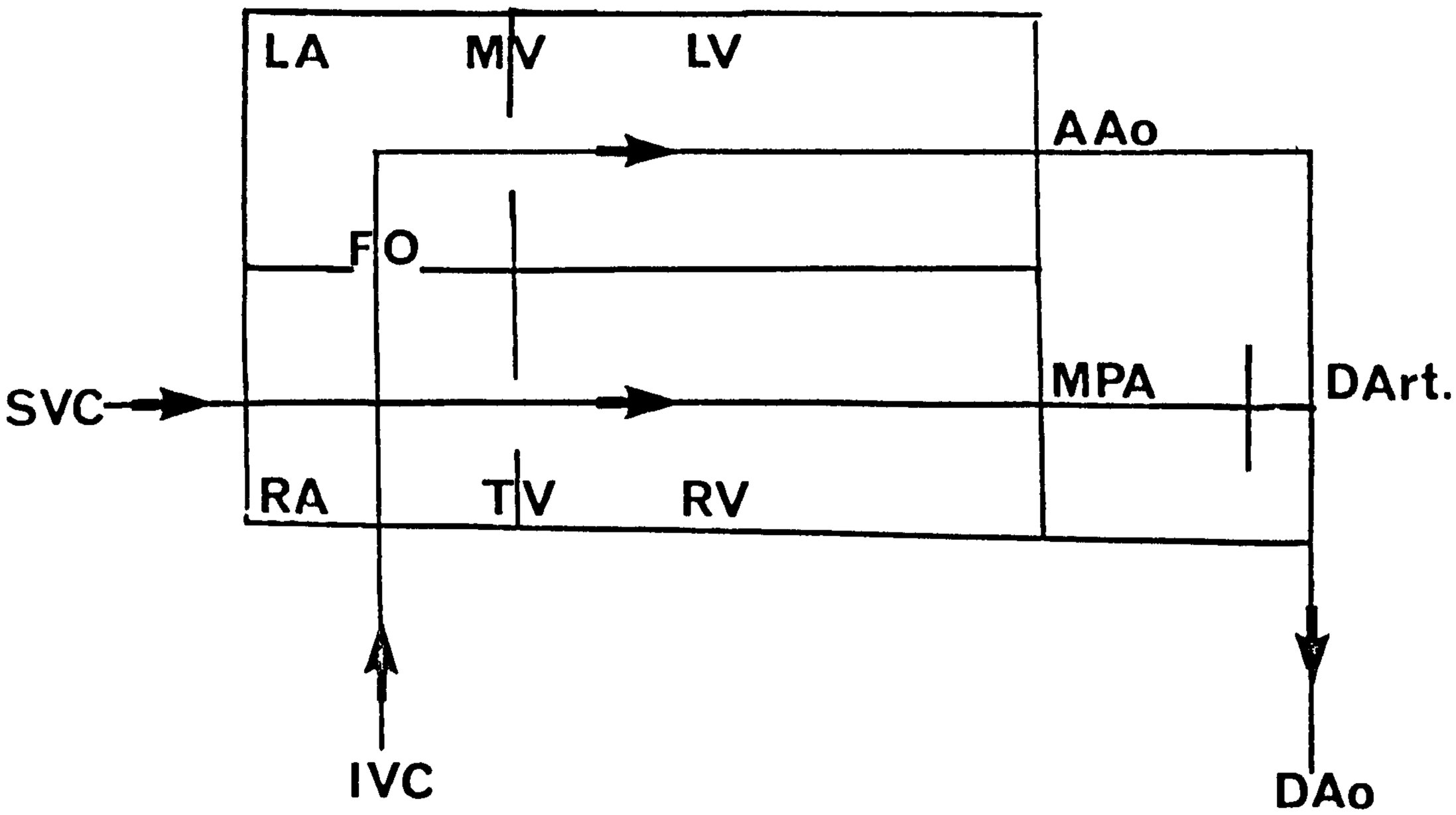


Figure 10.8. The fetal heart is represented in diagramatic form. Most of the blood in the superior vena cava (SVC) enters the right atrium (RA) and hence to the right ventricle (RV). The outlet from the right ventricle is to the main pulmonary artery (MPA) and via the ductus arteriosus (D.Art) to the descending aorta (D.Ao.). Most of the blood entering the right atrium from the inferior vena cava (IVC) passes across the foramen ovale (Fo) into the left atrium (LA) and hence to the left ventricle (LV) and ascending aorta. The output of the two ventricles join at the end of the aortic arch at the ductus arteriosus. MV and TV represent the mitral and tricuspid valves respectively. Thus the two ventricles working in parallel maintain the fetal cardiac output, unlike postnatal life where each pumping chamber acts in series and there is no mixing of the right and left sided blood flows.

Further study of left ventricular function, in situations where the heart rate is substantially increased, as in the tachycardias, or substantially decreased, as in heart block, would be of interest. Antihypertensive drugs, given to the mother, might also be expected to affect fetal cardiac function. Further research in these areas are indicated now that normal baseline measurements of left ventricular function have been documented.

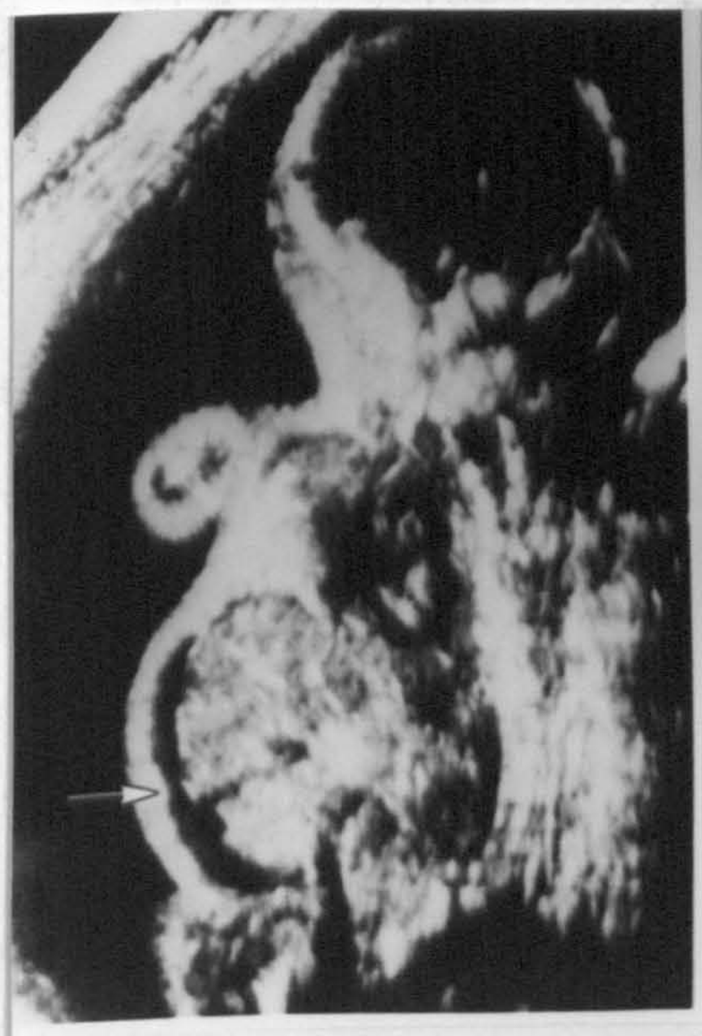
CHAPTER 11

RESULTS:

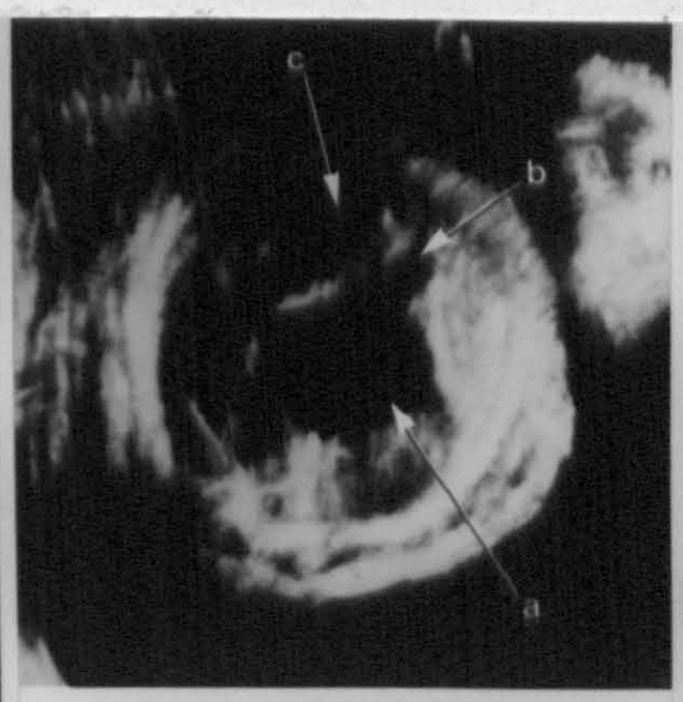
Structural heart disease detected during the study.

In Chapter 6, some fetal cardiac abnormalities, which had been detected echocardiographically, were described. As these were found within the study of the midtrimester pretermination group, it was thought more appropriate to discuss them at that point. Some structural anomalies presented with fetal arrhythmias and these are discussed in Chapter 13. The remaining cardiac anomalies detected during the study are described here. The cases are summarised in Table V .

Case 11.1. Case 11.1 presented very early in the study, before the structured approach to cardiac anatomy now employed and described in Chapter 5, had evolved. The case presented at 34 weeks gestation with gross fetal ascites. The left atrium was enlarged, the left ventricle thickwalled with a small intraventricular cavity,Figure 11.1 a.b.c. The aortic root was small for the gestational age although only a real time measurement was available at the time, 0.16 cms. (normal range at this gestational age on real-time is 0.5-0.6 cms.). The full significance of the findings were only understood retrospectively, although cardiac abnormality



(1a) Fetal ascities (arrow)



(1b) Arrow a Left Atrium
b left Ventricle
c Right Ventricle

(1c) Aortic Root (arrow)

Figure 11.1. Case 1.

(a) shows fetal ascites.

(b) shows marked left atrial dilatation seen in a four chamber projection.

(c) the aortic root is seen beside a centimeter marker. This structure was much smaller than it should have been at this gestational age.

was predicted. Following delivery at 37 weeks gestation the baby was found to be in severe cardiac failure. The diagnosis of critical aortic stenosis was made at cardiac catheterization. Death occurred at two days of age and autopsy demonstrated the small aortic root, with associated extensive endocardial fibroelastosis of the thick walled left ventricular type. The left ventricular cavity was small and the left atrium dilated.

Case 11.2. Case 11.2 presented at 32 weeks gestation with a possible diagnosis of hydrocephaly. This was confirmed on ultrasonography. Examination of the fetal heart showed a dilated aortic root overriding the ventricular septum. The aortic valve appeared thickened. The pulmonary outflow tract was very narrow and no pulmonary valve could be definitely distinguished on two-dimensional or M mode scanning. Figures 11,2,3,4. No main pulmonary artery or ductus arteriosus could be detected. The diagnosis of pulmonary atresia with a ventricular septal defect was suspected. Truncus arteriosus was considered but no main pulmonary artery could be seen arising from the aorta, which was well visualized. The fetus delivered at 34 weeks gestation and was found to have multiple congenital anomalies. He died at 2 days of age. This was one of the few pathological specimens which we failed to obtain but the heart

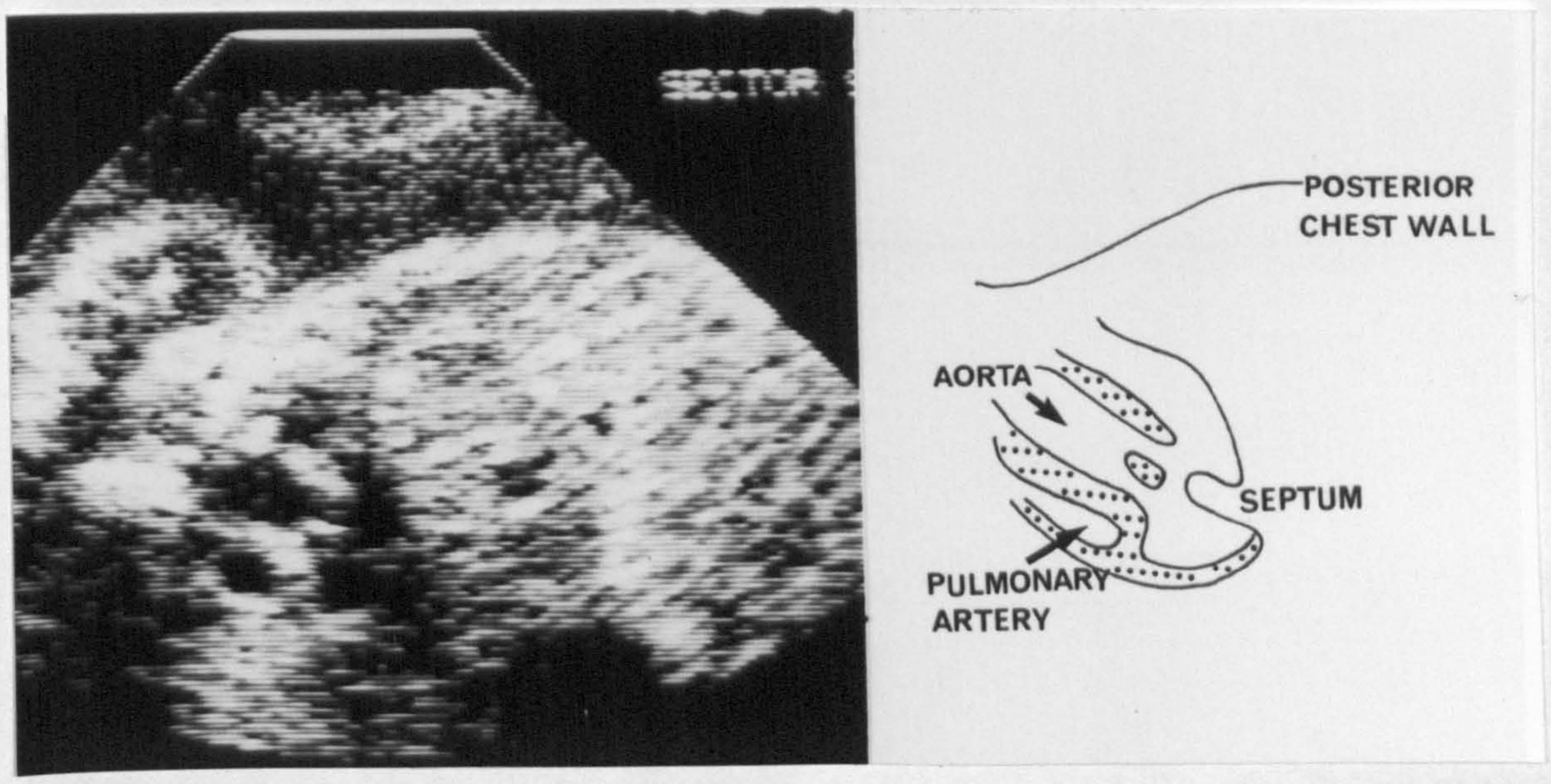


Figure 11.2. Case 2. Dilated aortic root overriding the ventricular septum.

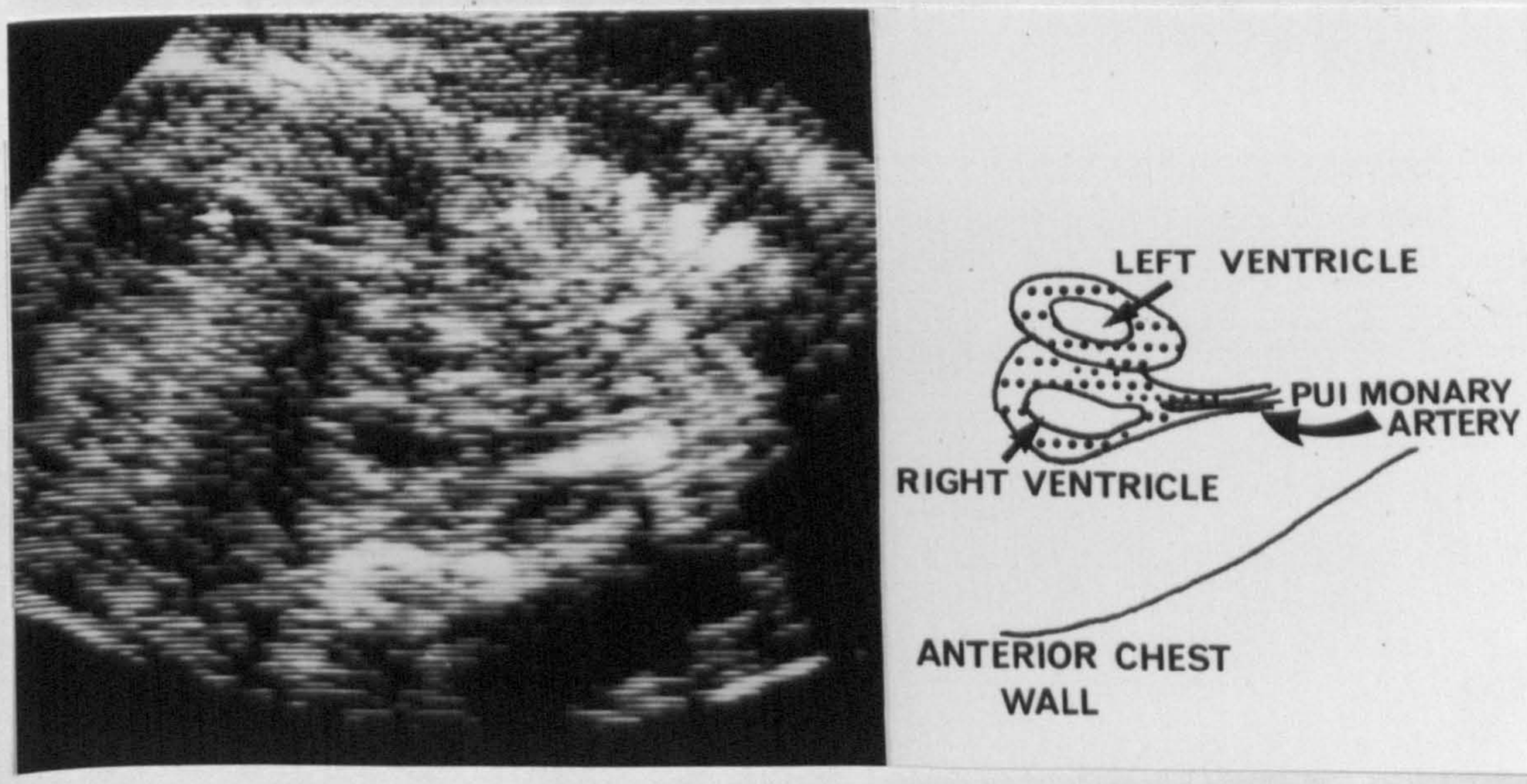


Figure 11.3. Case 2. Short axis left ventricular plane showing narrow right ventricular outflow tract.

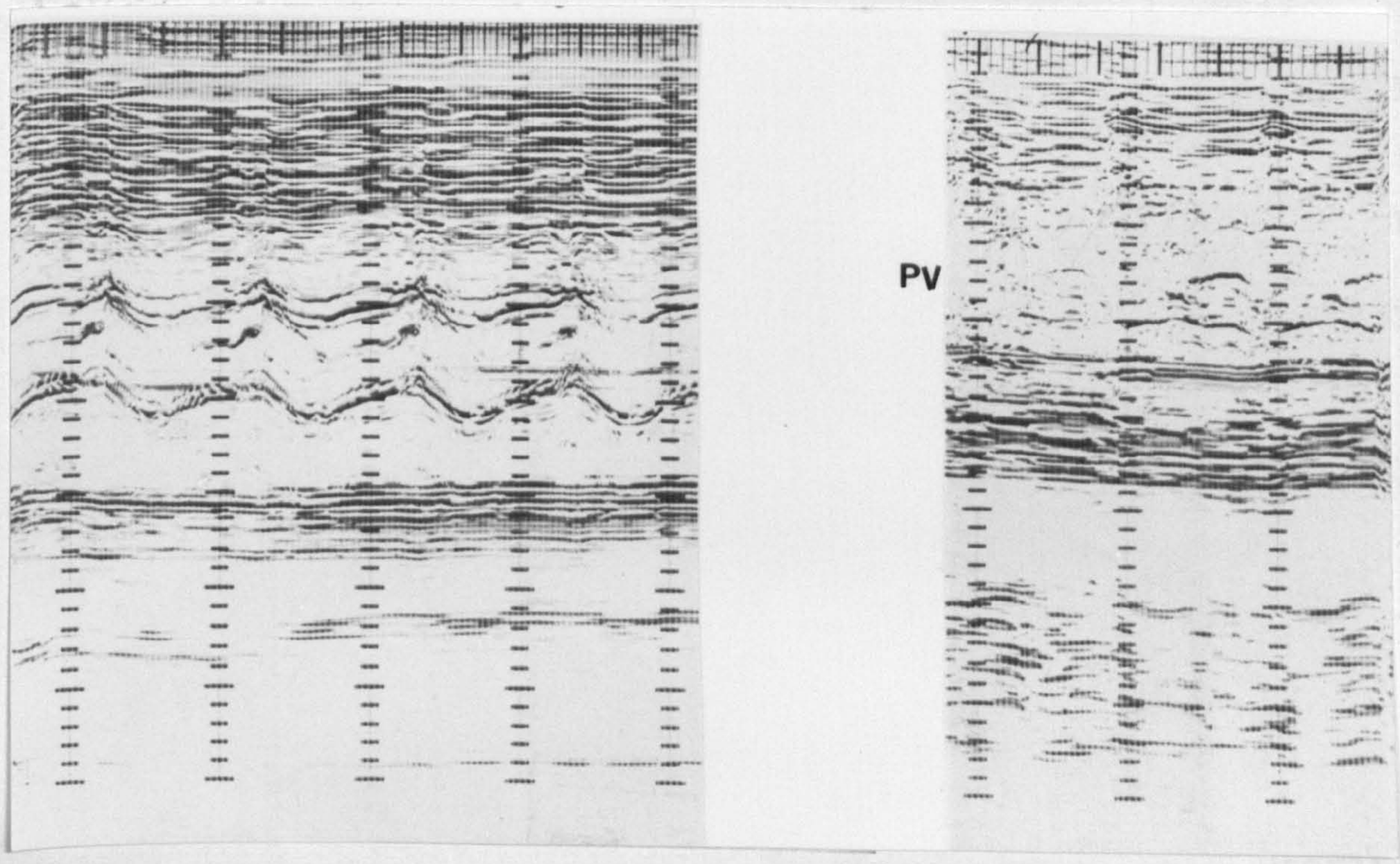


Figure 11.4. M mode echocardiogram in Case 2.

(a) The aorta is dilated, the aortic closure line appears thickened.

(b) The pulmonary valve could not be seen to open although something could be recorded moving where the pulmonary valve should have been.

TABLE V

Case No.	Gestation at presentation (weeks)	Reason for Study	Suspected -echocardiographic diagnosis	Type of follow-up
11.1	34	Fetal ascites	Aortic stenosis (retrospective)	Anatomy
11.2	32	Hydrocephaly	Pulmonary atresia, VSD	Anatomy
11.3	35	Fetal ascites	Right ventricular hypertrophy	Anatomy
11.4	35	Hydronephrosis	Tetralogy of Fallot	Anatomy
11.5	32	Growth retardation	Tetralogy of Fallot	Anatomy
11.6	19	Previous neonatal death from CHD	Mitral atresia	Anatomy
11.7	28	Previous neonatal death from CHD	Truncus arteriosus	Catheterization
11.8	27	Fetal ascites	Cardiac tumor	Autolysed intrauterine death
11.9	24	Hydronephrosis	VSD (retrospective)	Anatomy
11.10	19	Previous two infant deaths from CHD	?VSD	Clinical and echocardiographic
11.11,12, 13,14,15	20-25	Previous neonatal death from CHD in 3 maternal diabetes in 2	?VSD	Clinical and echocardiographic

was examined by a paediatric cardiac morphologist. The report stated that there was absence of the infundibular septum, atretic pulmonary valve and hypoplasia of the pulmonary arteries. Figure 11.5. The aorta lay overriding a ventricular septal defect. These autopsy findings therefore confirmed the echocardiographic diagnosis.

Case 11.3. Case 11.3 presented at 35 weeks gestation because of polyhydramnios. Gross fetal ascites was also present. The right ventricle was found to be dilated and hypertrophied echocardiographically. No obstructive lesion could be detected to account for this finding. The fetus was still born at 37 weeks gestation. No definitive cause of hydrops was found on autopsy. The fetal heart specimen confirmed the echocardiographic findings namely a thick walled, dilated right ventricle but no other structural cardiac anomaly. Figure 11.6.

Case 11.4. Case 11.4 presented at 35 weeks gestation. The referring ultrasonographer had suggested the presence of fetal ascites. No fetal ascites was found to be present, but an obstructive uropathy with marked hydronephrosis, ureteric dilatation and bladder enlargement was seen in the fetal abdomen. There was oligohydramnios. Examination of

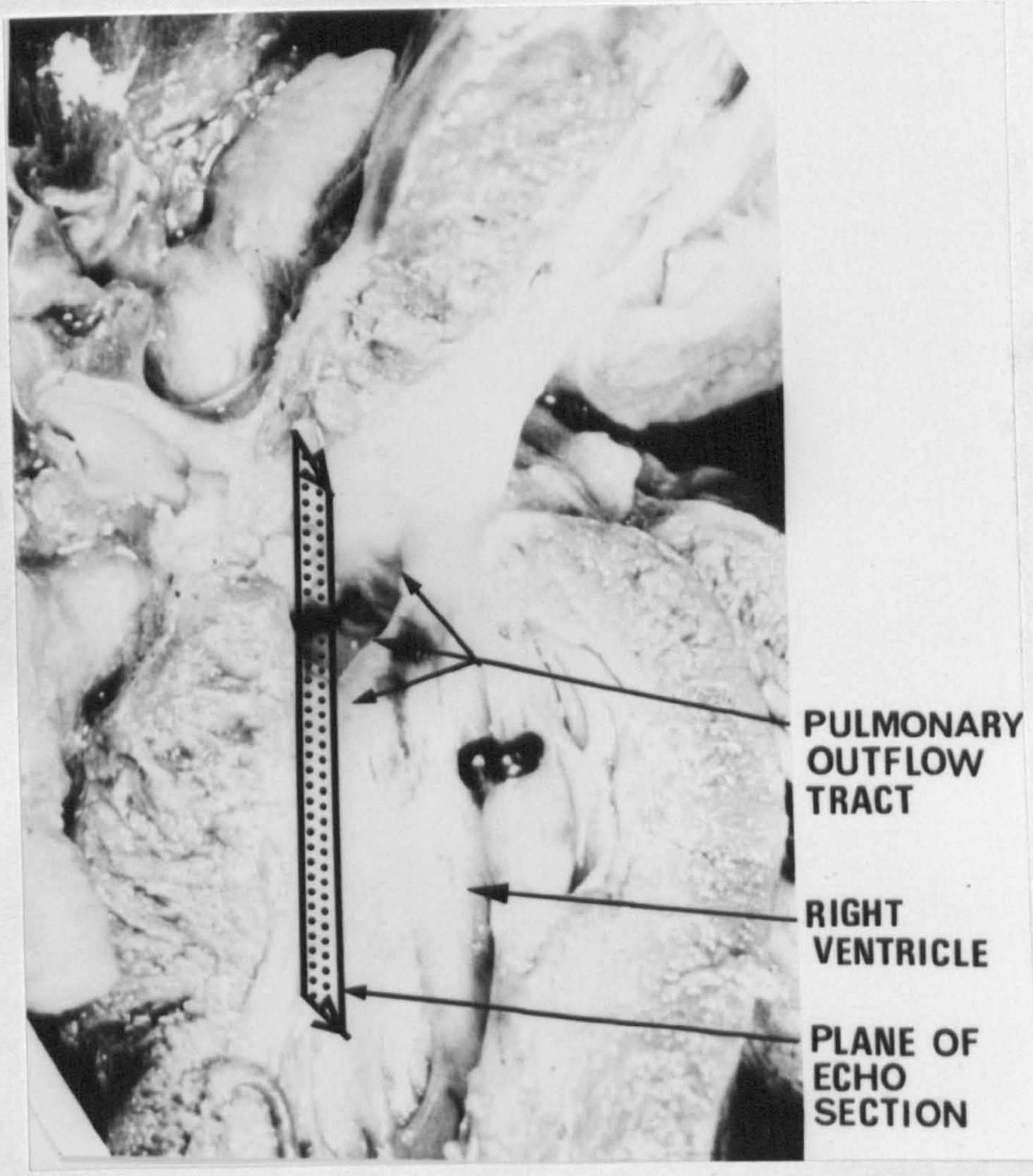
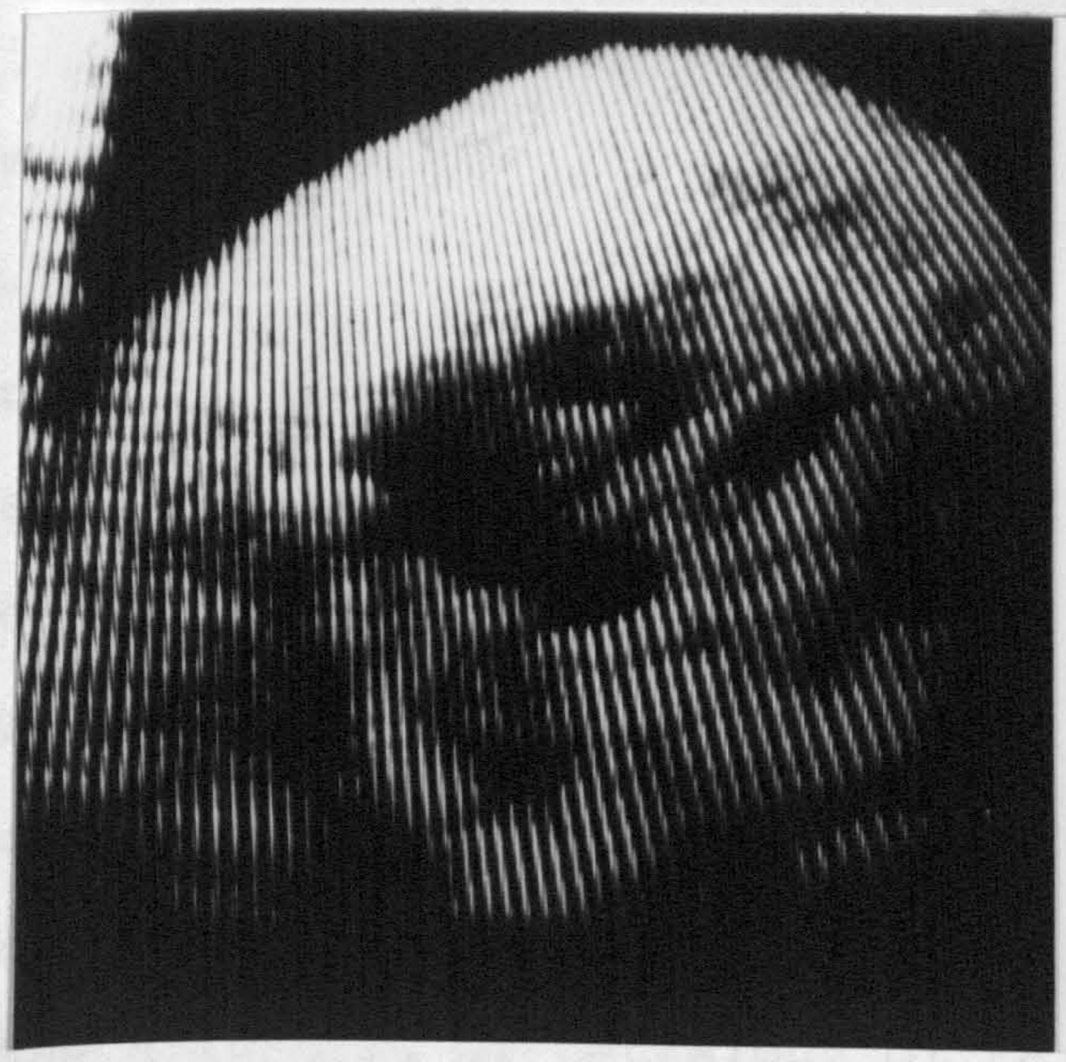


Figure 11.5. Case 2. The front of the right ventricle is incised and elevated to display the narrowed pulmonary outflow tract. The plane of the echocardiographic section marked is that seen in Figure 11.2. cutting through the pulmonary outflow tract with the left ventricle behind.



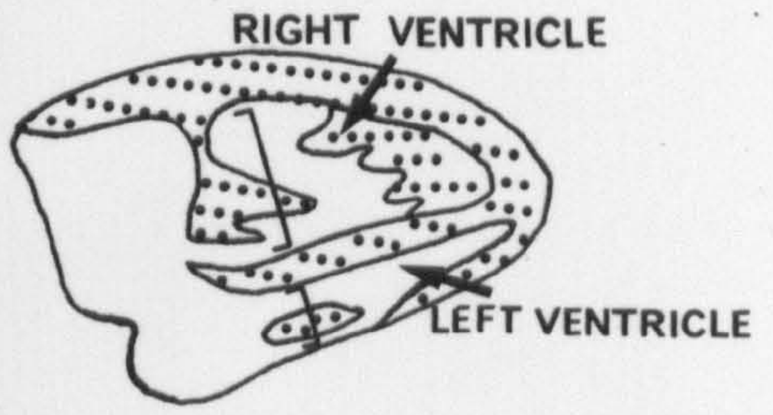


Figure 11.6. Case 3. The heart is seen in four chamber projection.
The right atrium and ventricle are dilated.
The right ventricle appears thick walled.

the fetal heart showed the aorta overriding a large ventricular septal defect, which extended down into the inlet septum. The pulmonary outflow tract showed narrowing in the infundibular region. The echocardiogramsobtained in this case, illustrating these points, are seen in Figures 11.7,8,9,10. The diagnosis of Tetralogy of Fallot was suspected. The association of the abnormality in the renal system with congenital heart disease aroused the suspicion of a chromosomal abnormality. The fetus was delivered at 38 weeks gestation. He was found to have Trisomy 18, and died a week later. A postnatal examination correlated well with the prenatal findings (Figure 11.7) and examination of the cardiac specimen at autopsy confirmed the diagnosis of tetralogy of Fallot.

Case 11.5. This case presented within a few weeks of Case 4, but with apparent growth retardation at 32 weeks gestation. Ultrasonic examination of the fetal abdomen demonstrated the identical appearance of an obstructive uropathy that was seen in Case 4. Examination of the fetal heart also showed similar findings to those seen in the previous case. There was a ventricular septal defect with aortic override. There was infundibular stenosis (Figures 11.11,11.12). A diagnosis of Tetralogy of Fallot was made. The combination of abnormalities in two systems again

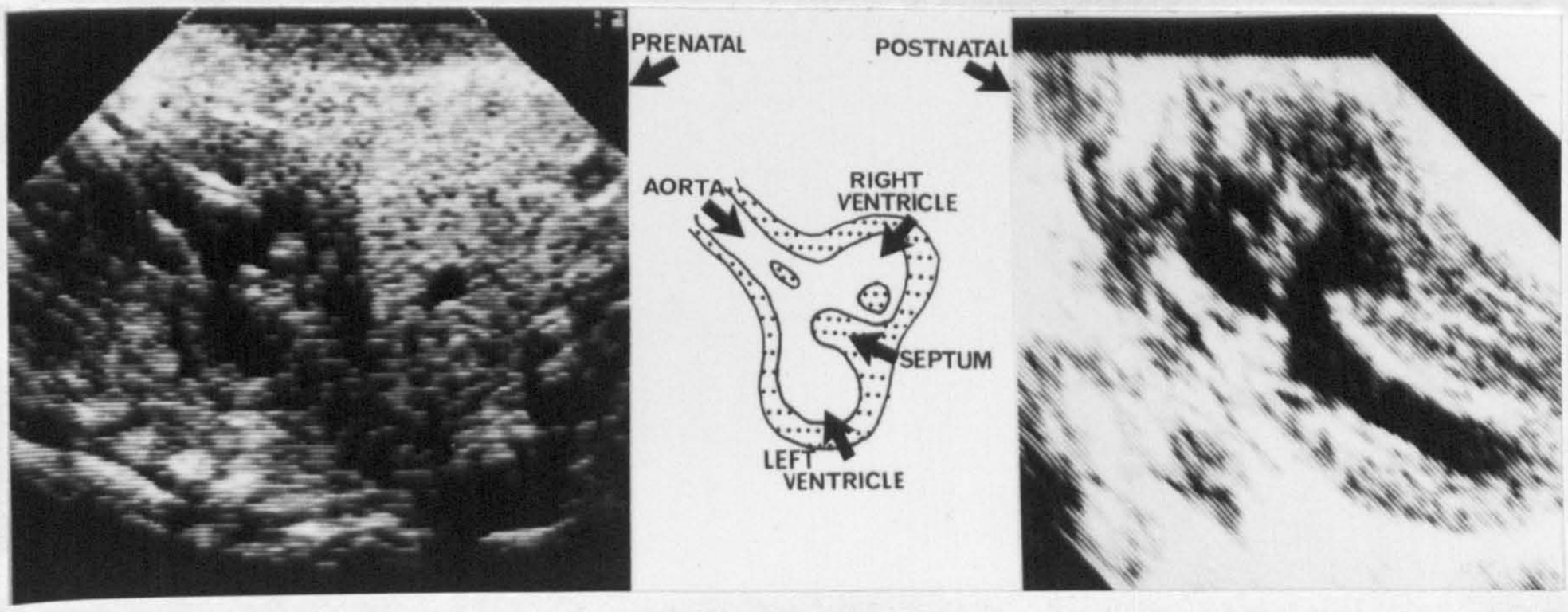


Figure 11.7. Case 4. The same projection prenatally and postnatally to show a ventricular septal defect and the aorta arising astride both ventricles.

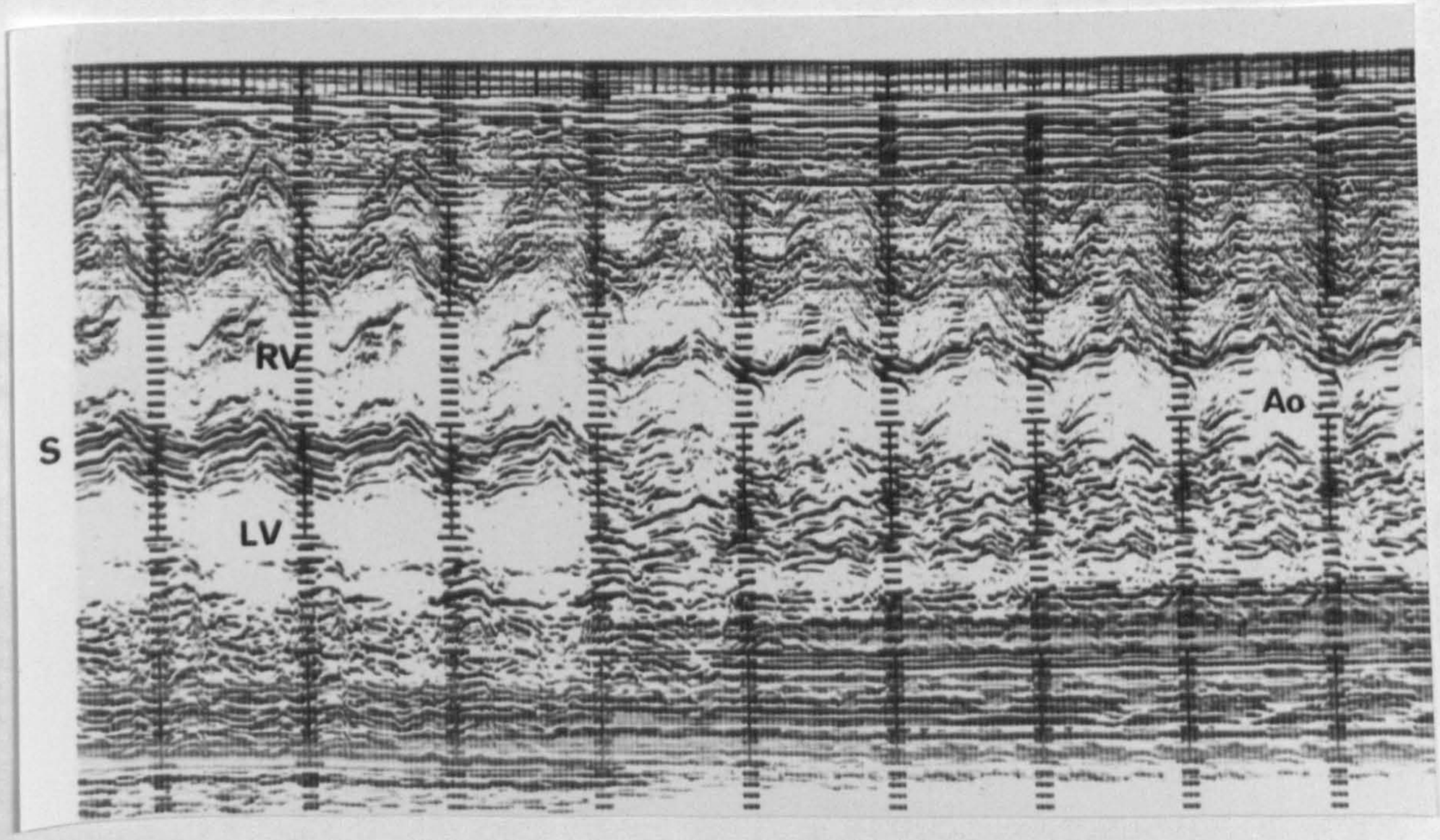


Figure 11.8. Case 4. The prenatal M mode echocardiogram. The aorta appears to arise mainly from the right ventricle.

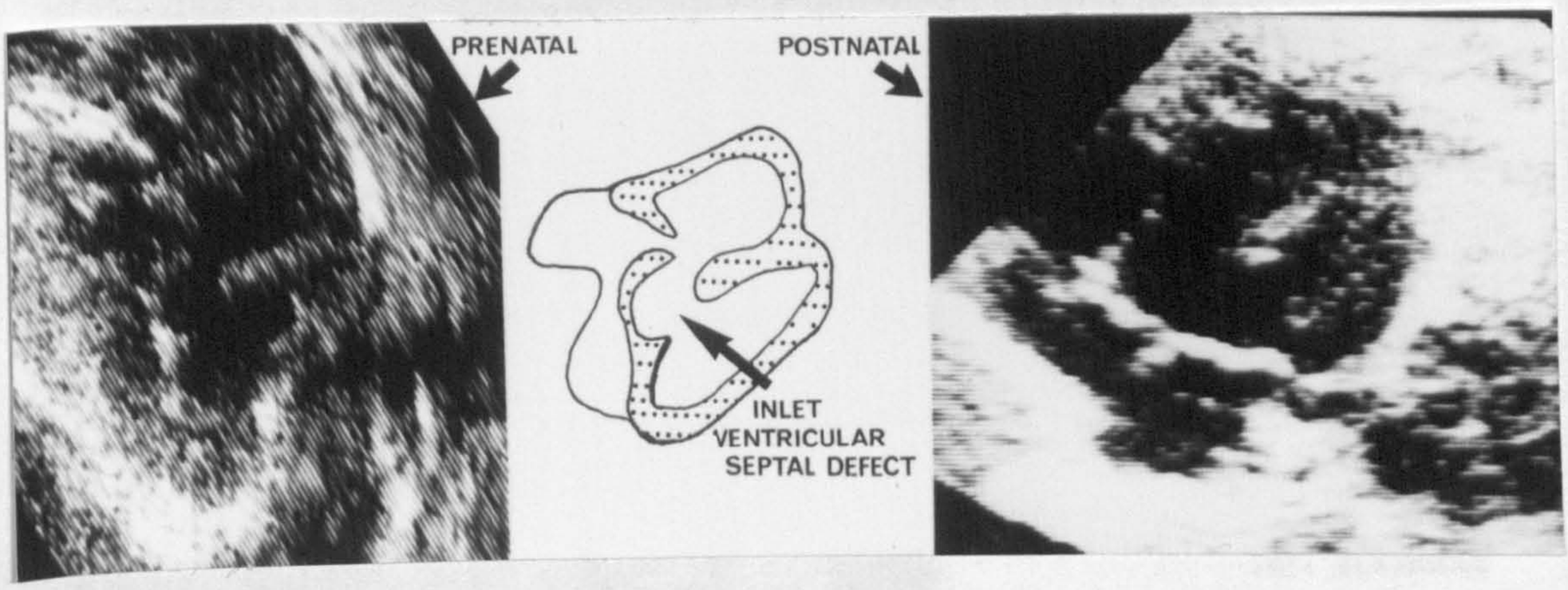


Figure 11.9. Case 4. The heart is seen in four chamber projection prenatally and postnatally. Both atrioventricular valves appear to insert at the same point in the ventricular septum. There appears to be a large inlet ventricular septal defect.

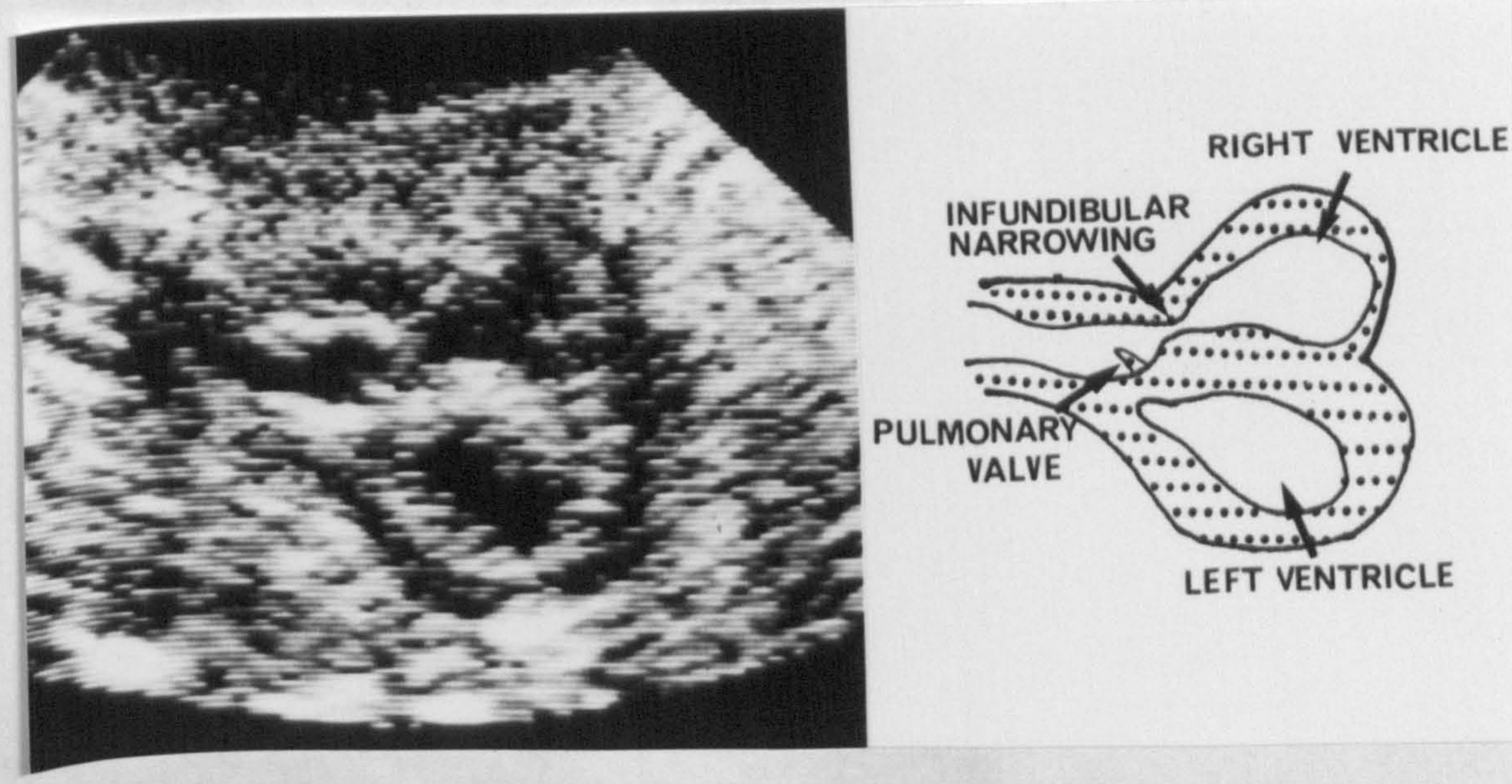


Figure 11.10. Case 4. The pulmonary artery is seen arising from the right ventricle. The infundibulum appears narrow. There appears to be a pulmonary valve within the pulmonary artery.

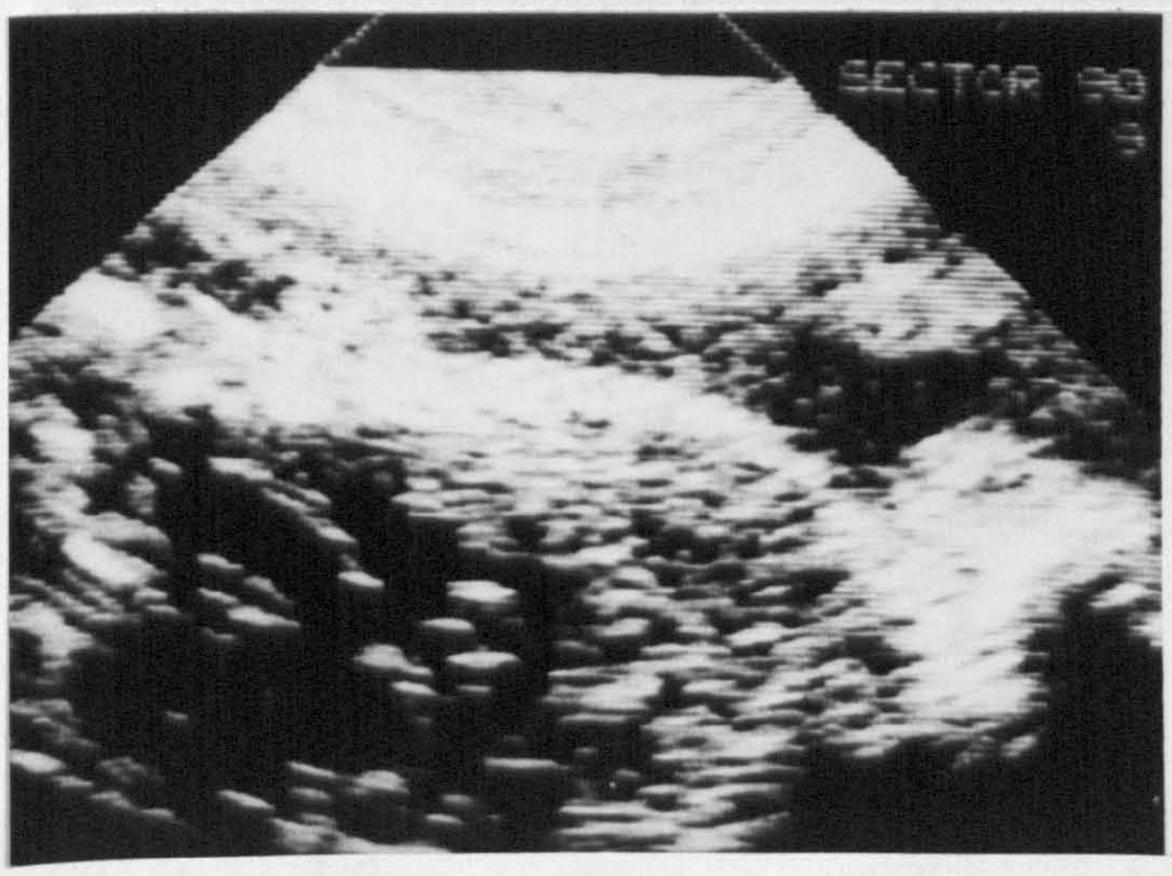


Figure 11.11. Case 5. The aorta is seen to be arising astride the ventricular septum. The ventricular septal defect is seen.

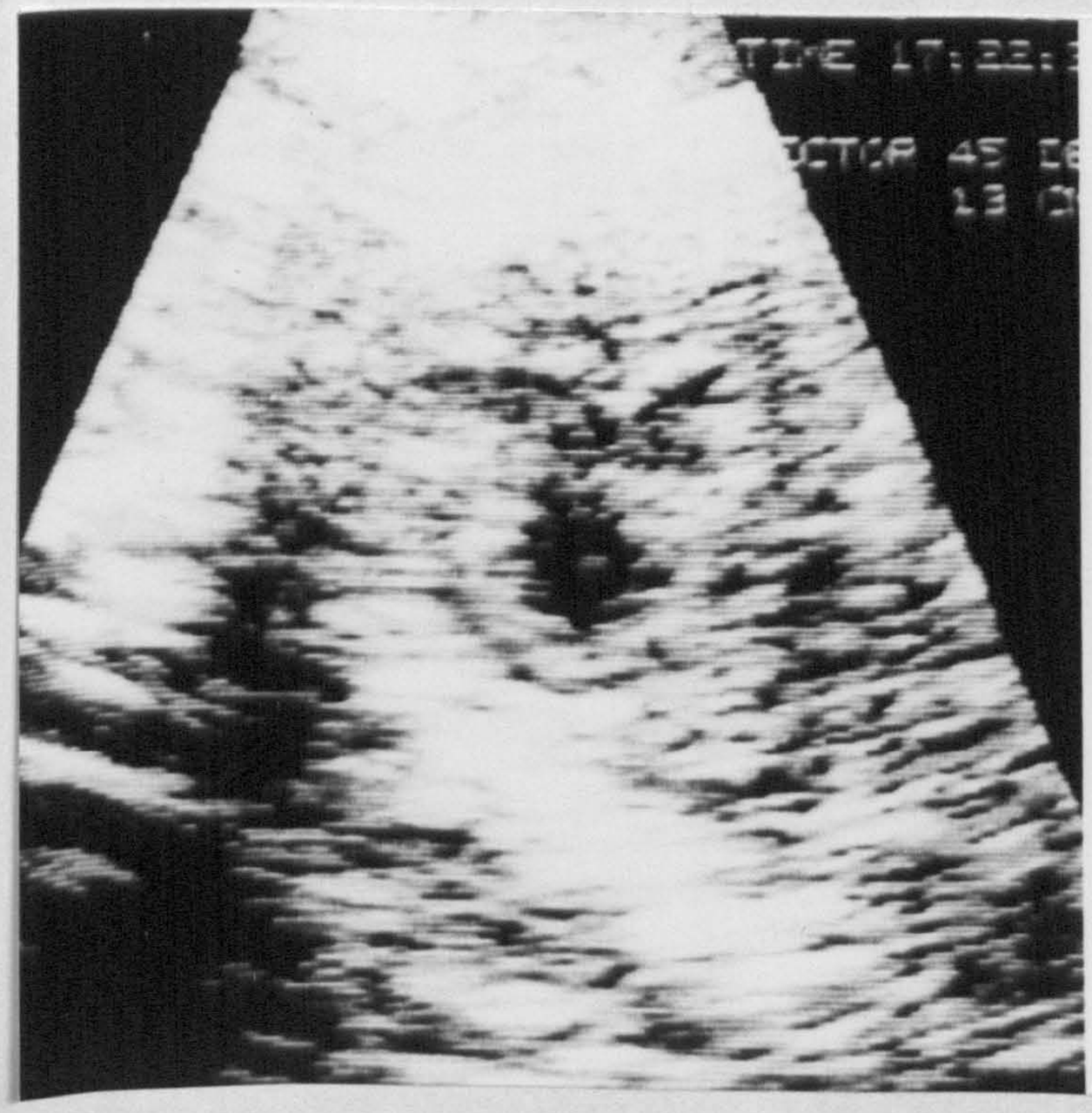


Figure 11.12. Case 6. The heart is seen in the short axis left ventricular plane. The pulmonary outflow tract is seen to be narrowed in the infundibular region.

suggested a chromosomal anomaly. The pregnancy was induced at this stage. Trisomy 18 was clinically apparent at birth and confirmed by chromosome culture. The baby died at a few hours old. Anatomical dissection of the cardiac specimen confirmed the diagnosis of Tetralogy of Fallot.

Case 11.6. This case presented at 19 weeks gestation. The mother had lost a previous baby at the age of four weeks with a univentricular heart, transposition of the great arteries and possible total anomalous pulmonary venous drainage. The cardiac catheterization information was incomplete and no autopsy had been performed on this previous child. On initial presentation in this second pregnancy there was a unilateral pleural effusion (Figure 11.13). The heart could not be well visualised because of this but abnormality was suspected. On re-examination of this patient at 22 weeks gestation the pleural effusion had disappeared and no other extracardiac anomaly could be seen on detailed scanning (By Professor S. Campbell). The heart however was abnormal. There appeared to be a large single anterior ventricle with a slit like posterior one, figure 11.14 a and b. Only one atrioventricular valve was seen entering the main chamber, from which the two great arteries arose. The aorta was anterior to the pulmonary artery. Figure 11.15. The diagnosis of mitral atresia and double outlet right ventricle was

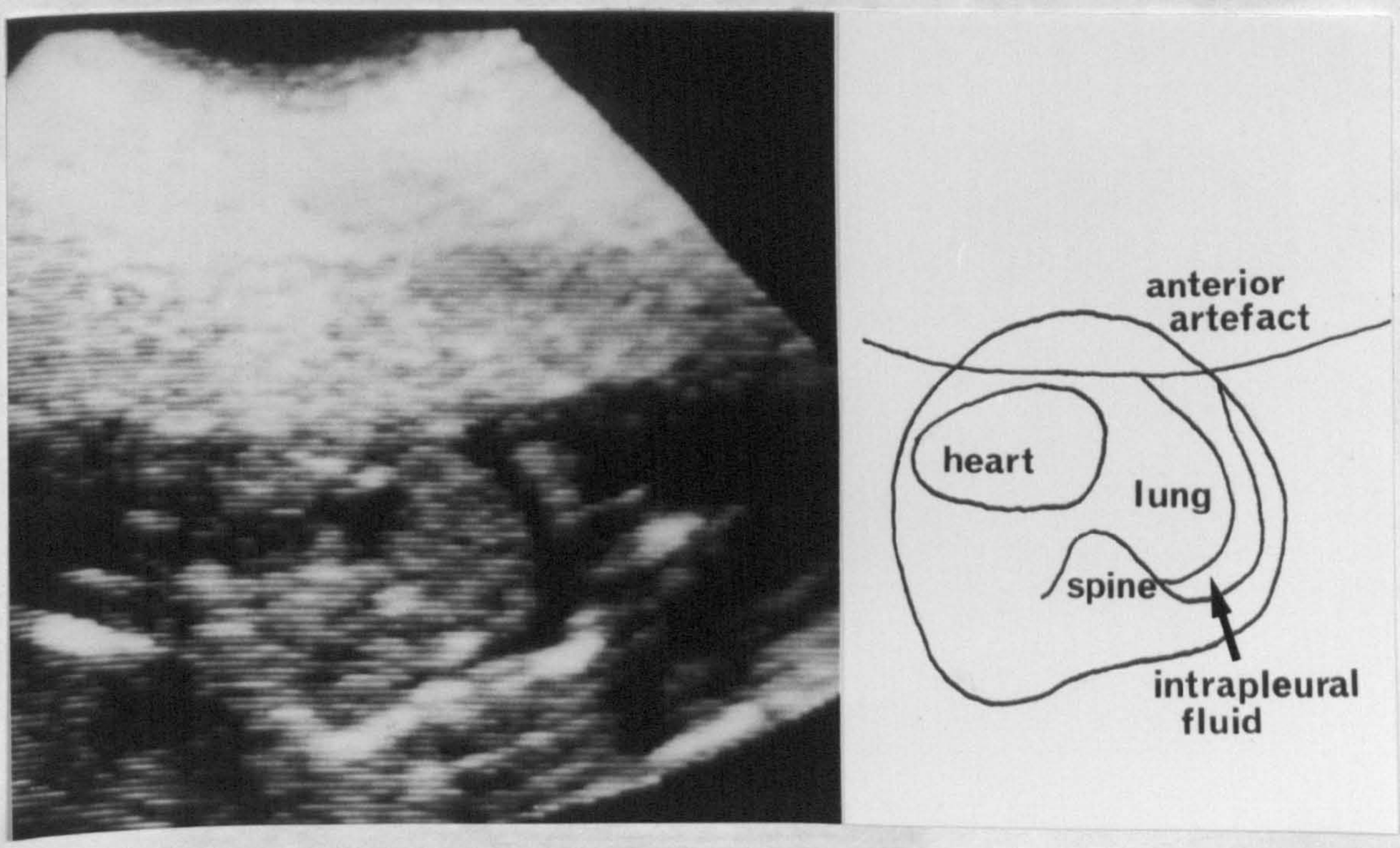


Figure 11.13. The fetal thorax is seen in cross section. The heart is seen in the four chamber projection. The rim of intra pleural effusion is seen on the right side of the chest.

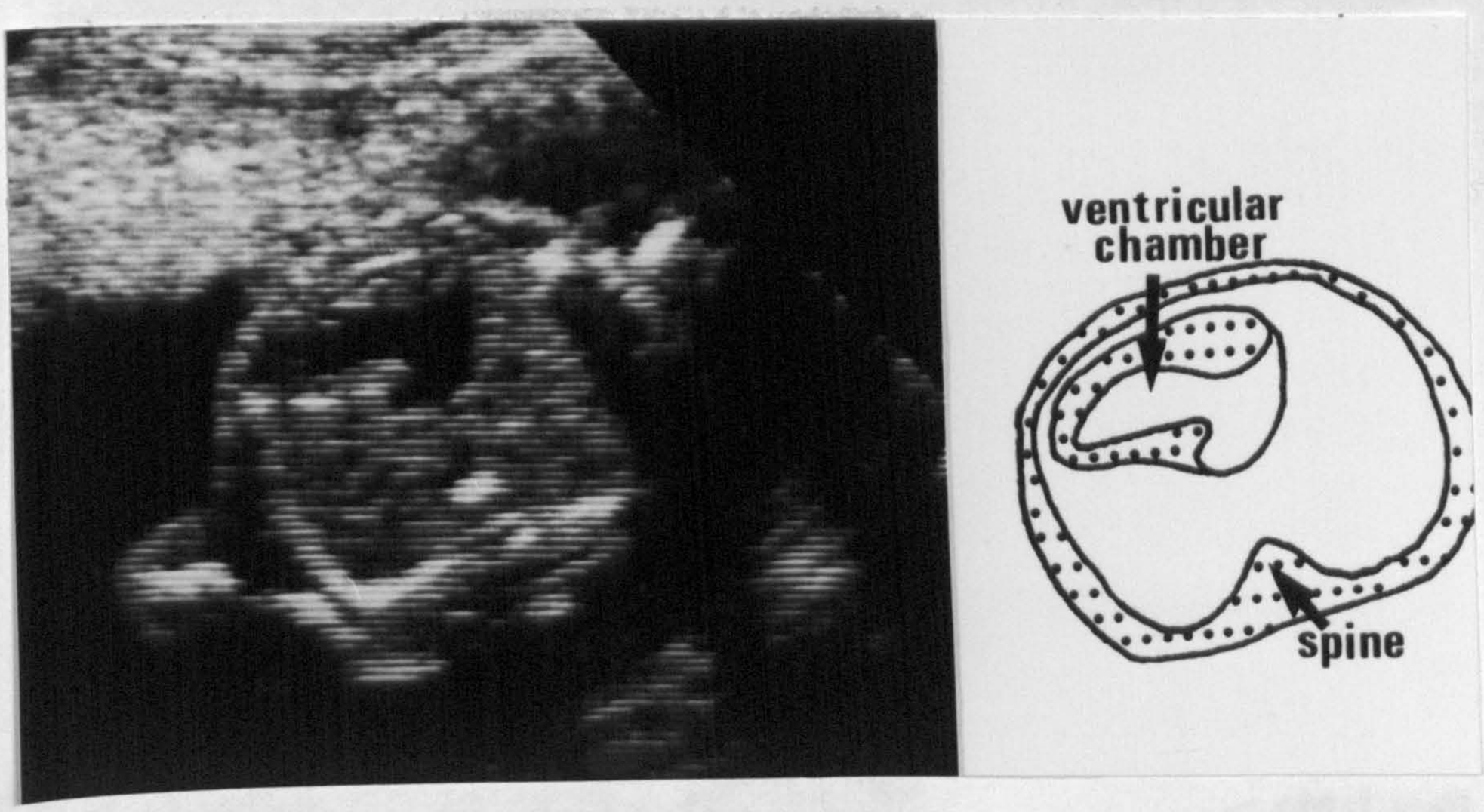


Figure 11.14a. The fetal heart is seen in a transverse section of the thorax but only one ventricular chamber is seen. Only one atrioventricular valve could be found. There appears to be a common atrium.

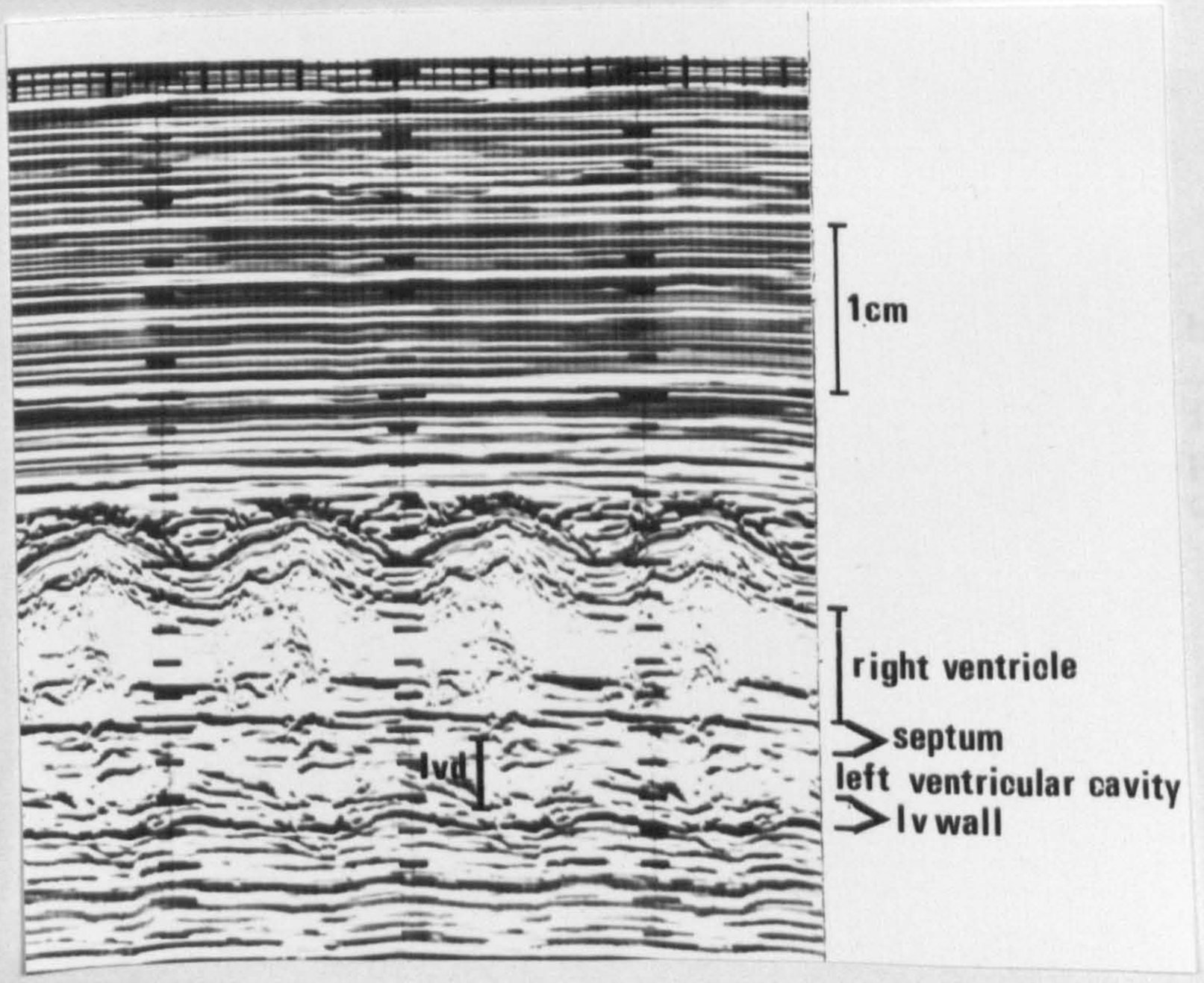


Figure 11.14b. The M mode echocardiogram demonstrates a large anterior ventricle with a small posterior cavity. No atrioventricular valve could be found entering this chamber.

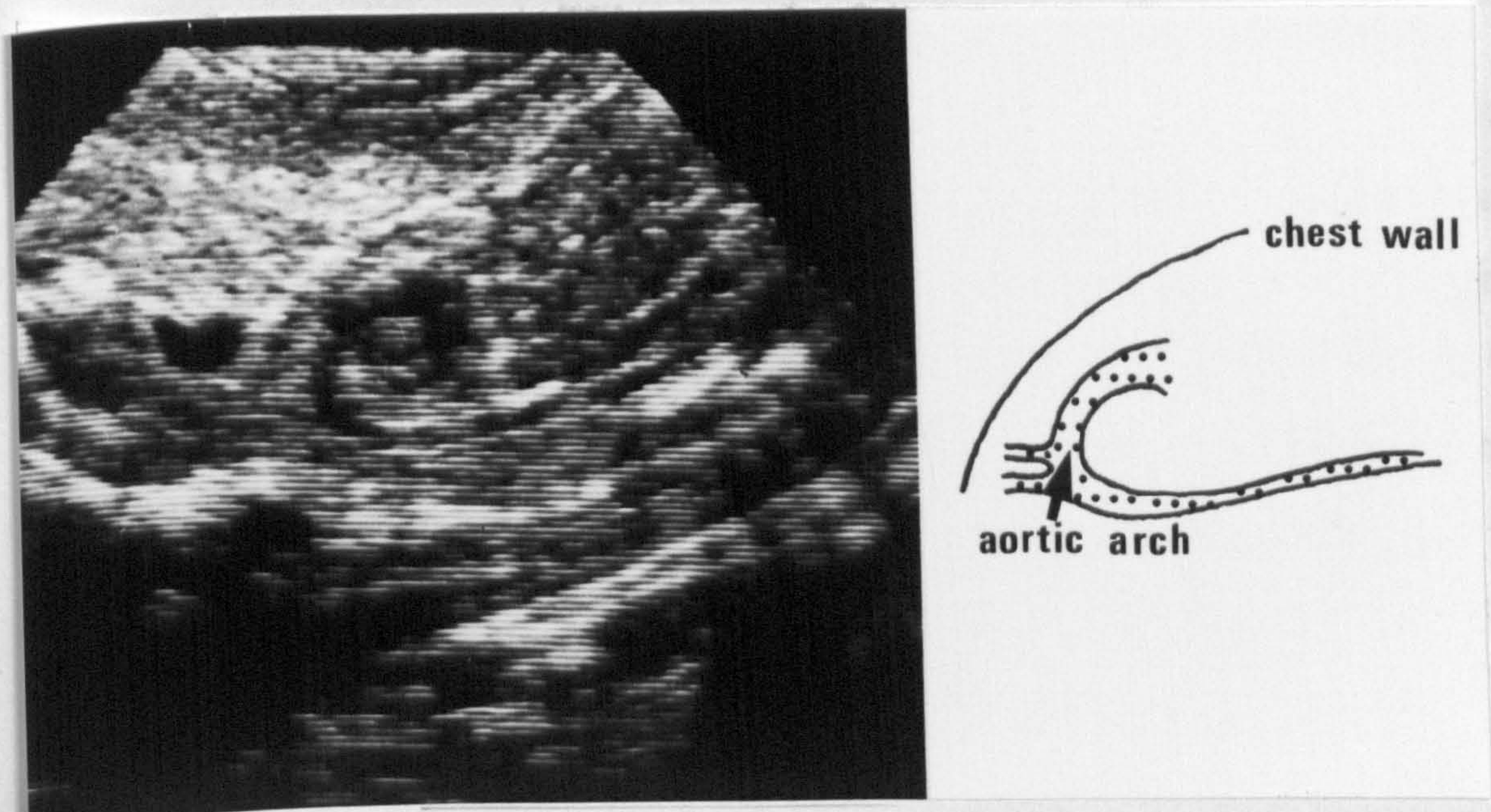


Figure 11.15. The aortic arch is seen to arise from the heart much closer to the anterior chest wall than normal. The pulmonary artery was found posterior to the aorta suggesting transposed great arteries. Both great arteries arose from the main chamber.

suspected at this stage. The patient was warned that a major cardiac abnormality was suspected. The unexplained unilateral pleural effusion raised the possibility of multiple congenital anomalies. The effusion appeared and disappeared twice during the course of this pregnancy. Repeated examination of the pregnancy throughout its course reconfirmed the early cardiac findings. Picture quality however was always poor because of maternal obesity. The patient was delivered at term. The postnatal echocardiogram confirmed the intracardiac findings but also demonstrated dextrocardia and total anomalous pulmonary venous drainage. Cardiac catheterization confirmed mitral atresia, double outlet right ventricle, total anomalous pulmonary venous drainage and also demonstrated right atrial isomerism. The diagnosis of asplenia (Ivemarks syndrome) was suspected. All these findings were confirmed at autopsy at 3 weeks of age.

Case 11.7. Case 7 presented at 28 weeks gestation. The mother had lost a previous baby, in 1973 in New Zealand, at a few weeks of age during surgical operation for congenital heart disease. No details of the previous anomaly were available at the time of referral. The aortic root was enlarged for the gestational age when compared to the growth charts. It measured 1.2 cms. at 27 weeks (normal aortic root dimension at this gestational age is 0.6 ± 0.15 cms). Figure 11.16. It overrode the ventricular septum and vent-

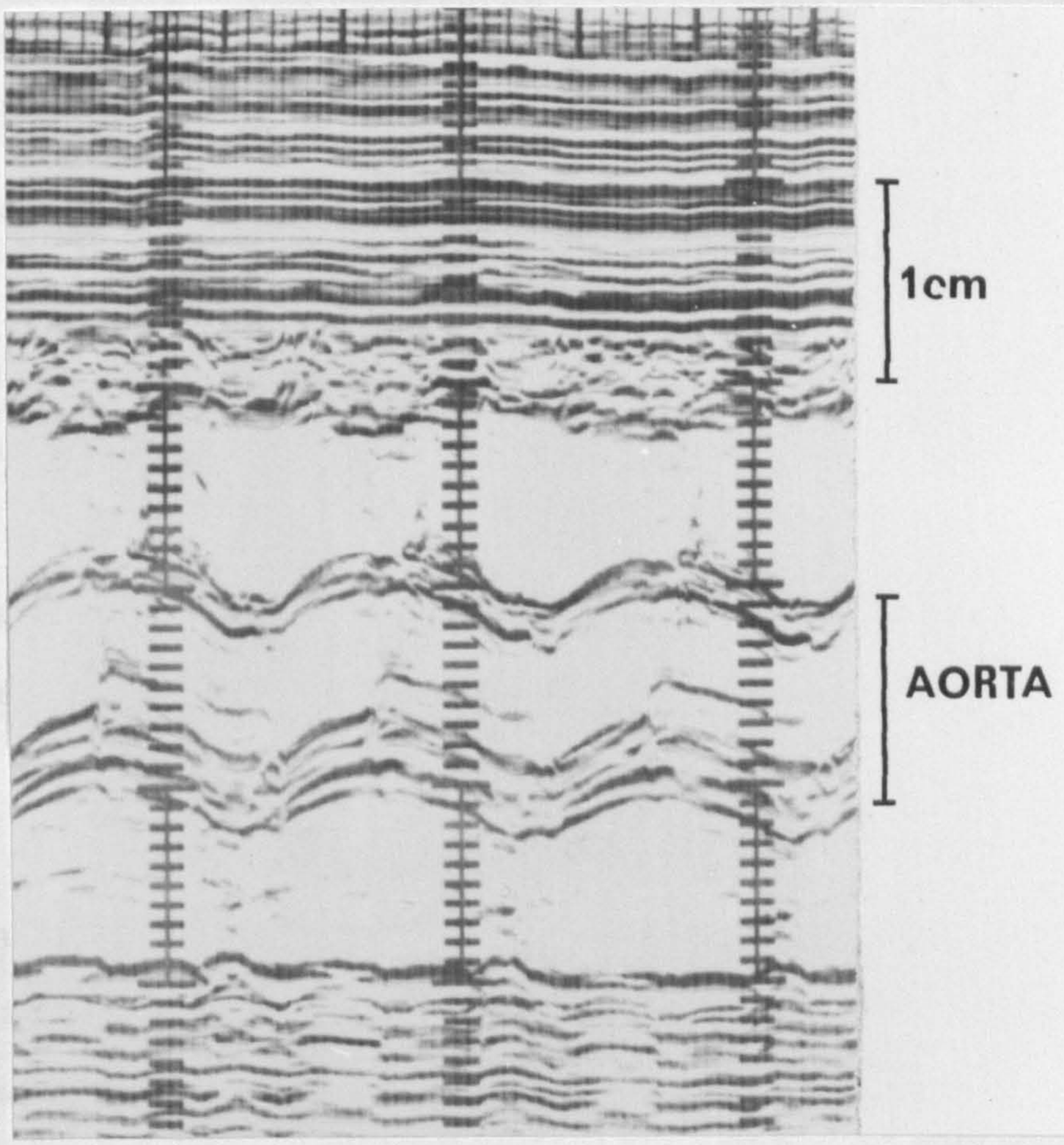


Figure 11.16. The aortic root can be measured on the M mode echocardiogram. The measurement of 1.1 cms. at 27 weeks gestation when this recording was made is much greater than expected. (See Chapter 8, Figure 8.5).

ricular septal defect. Figure 11.17. No pulmonary valve could be detected. The main pulmonary artery could be seen to arise from the posterior aspect of the aorta and divide into right and left pulmonary arteries (Figure 11.18). A diagnosis of truncus arteriosus was made. These observations were confirmed at 32 weeks gestation. The findings have been confirmed by catheterization after delivery. The details of the anomaly found in the first baby have since been discovered. This consisted of truncus arteriosus (Type I) the same as was found in the second child, but the previous child had in addition partial anomalous pulmonary venous drainage.

Case 11.8. This case presented at 27 weeks gestation. The referring ultrasonographer had found fetal ascites and had suggested a diagnosis of intracardiac tumor. On examination there was fairly marked fetal ascites. Figure 11.19. There was a tumor within the left atrium. It, although mobile, was obstructing the mitral valve and the left ventricular outflow tract. Figure 11.20,21. The fetus did not move during the period of study which is unusual and it was suspected that fetal death was imminent. The most likely histology for a tumor in this position in the heart is left atrial myxoma although this is very rare indeed in children. It is potentially operable but operation was thought not likely to be successful at 27 weeks gestation. The administration of diuretics to the mother was tried in an attempt

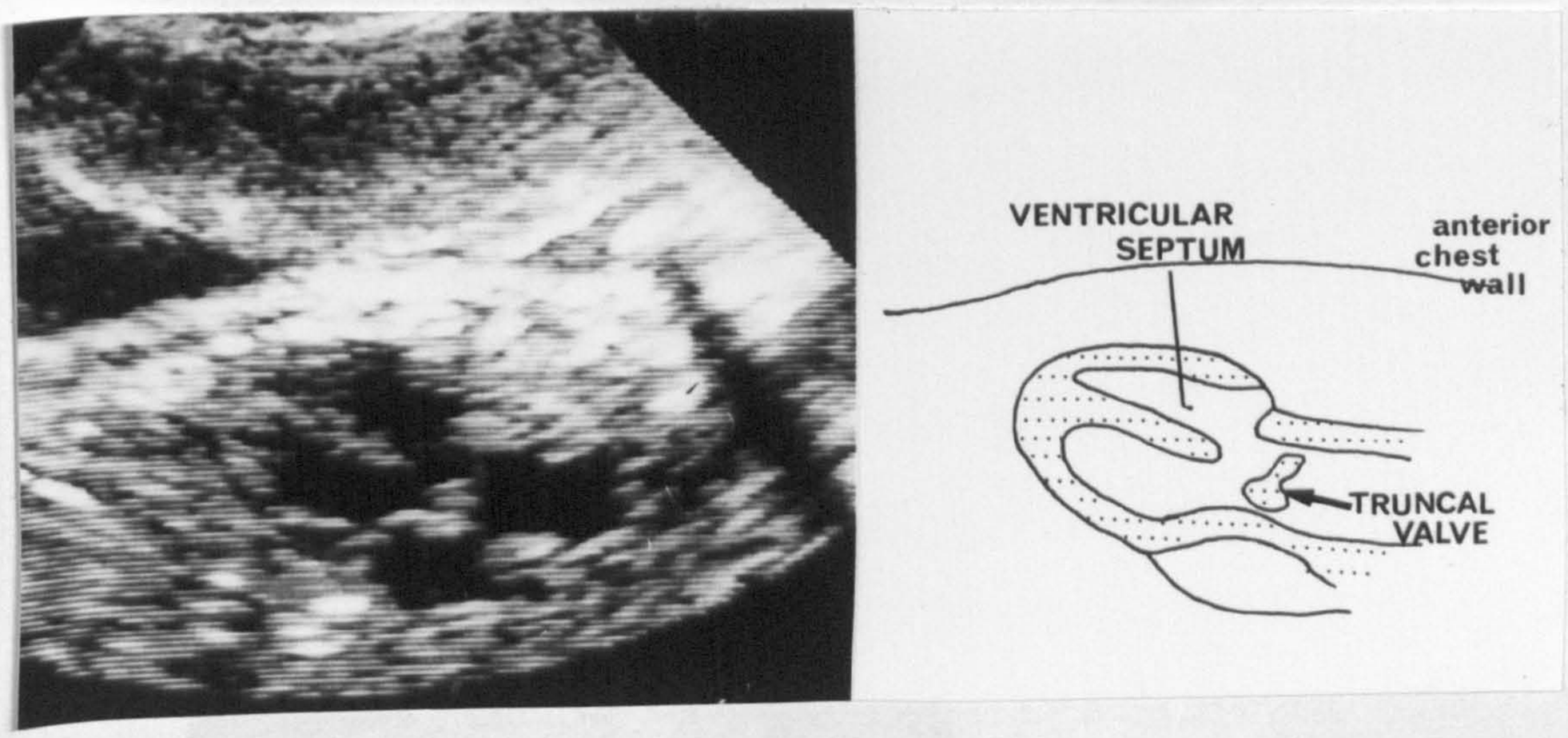


Figure 11.17. The fetal heart is seen in the long axis. Only one main artery can be seen. This arises astride the ventricular septum and a ventricular septal defect. The truncal valve appears abnormal.

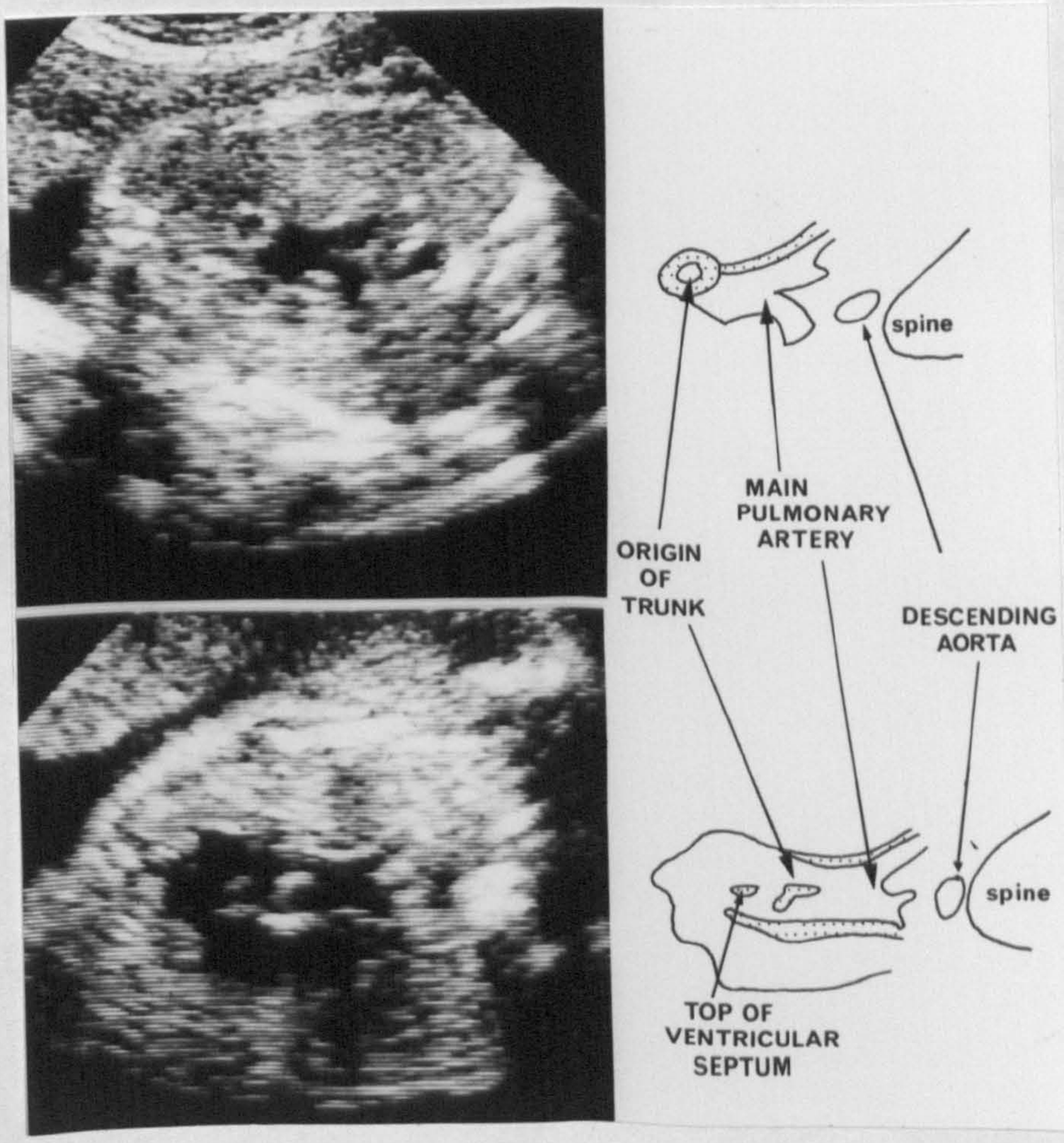


Figure 11.18. Transducer angulation from Figure 11.17. allows the main pulmonary artery to be seen arising from the posterior aspect of the aorta. The pulmonary artery branches can be clearly visualized. The moving image allows these connections to be followed in a continuous manner.

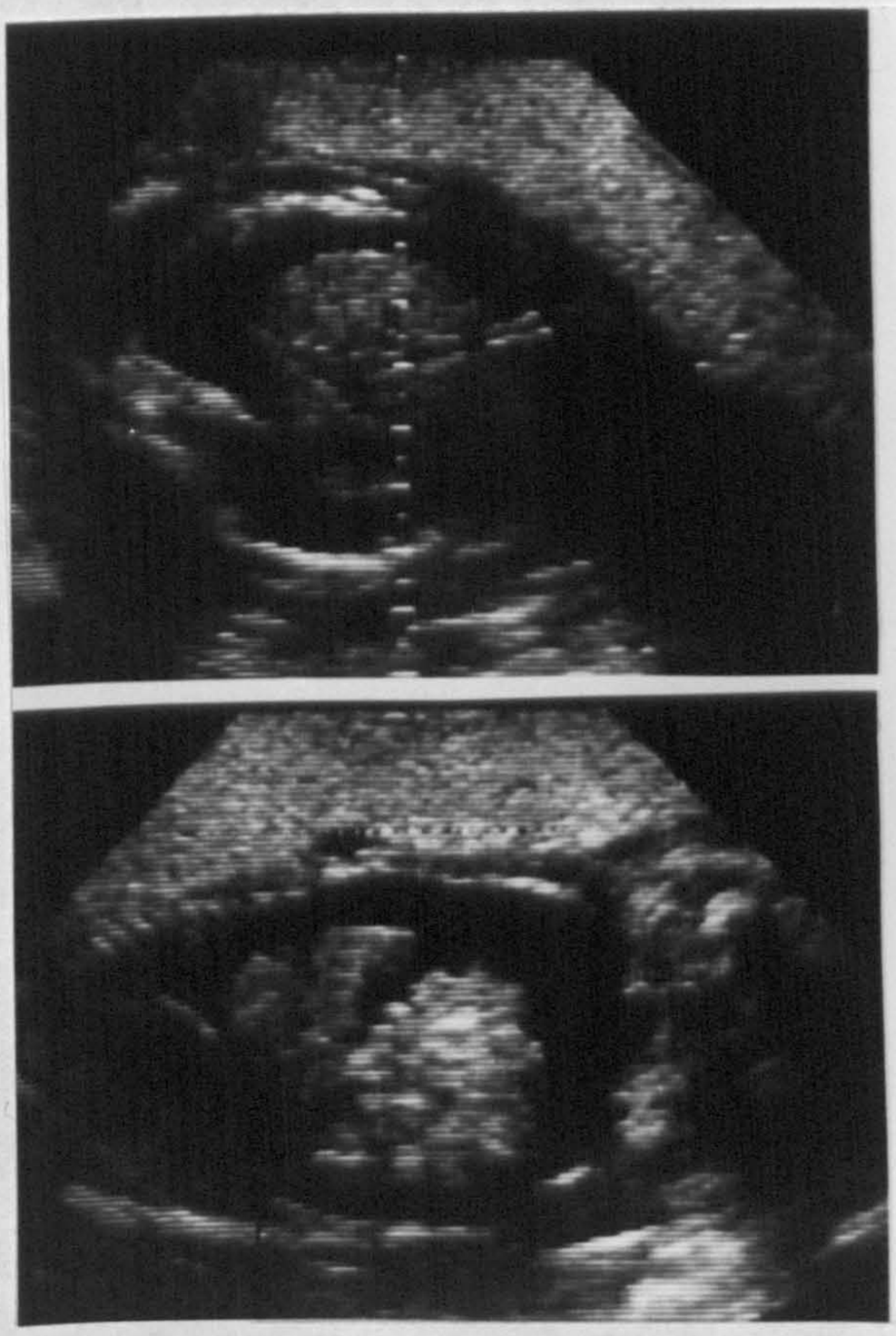


Figure 11.19. The top picture shows the fetal abdomen in transverse section with fluid surrounding the liver and outlining the umbilical vein. The lower picture shows a longitudinal section of the fetus with intra abdominal fluid compressing the intra abdominal contents.

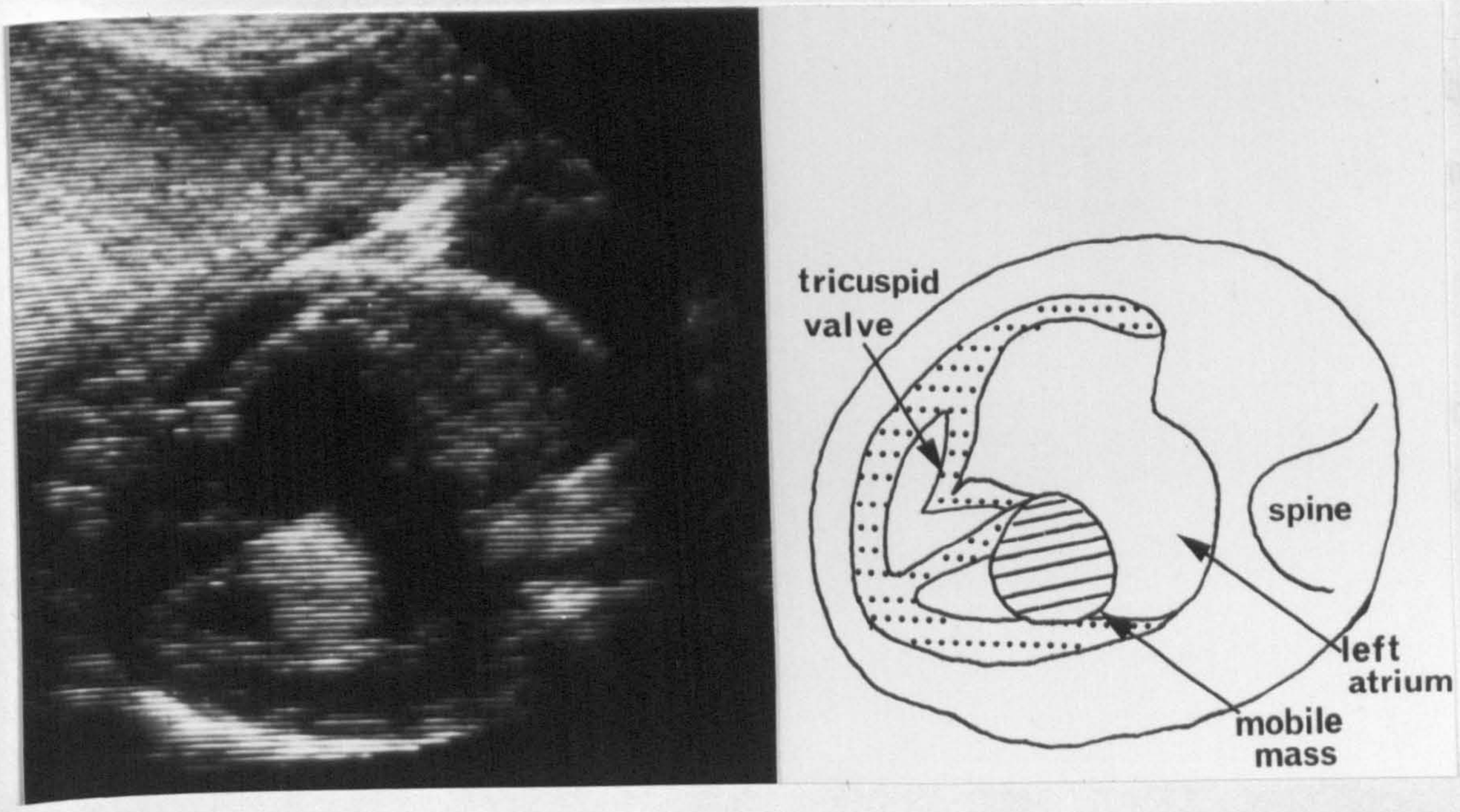


Figure 11.20. The heart is seen in the four chamber projection. The right ventricle is dilated. The left side of the heart is seen to contain a tumor. This appeared to lie in the mitral valve orifice and be mobile on real time scanning.

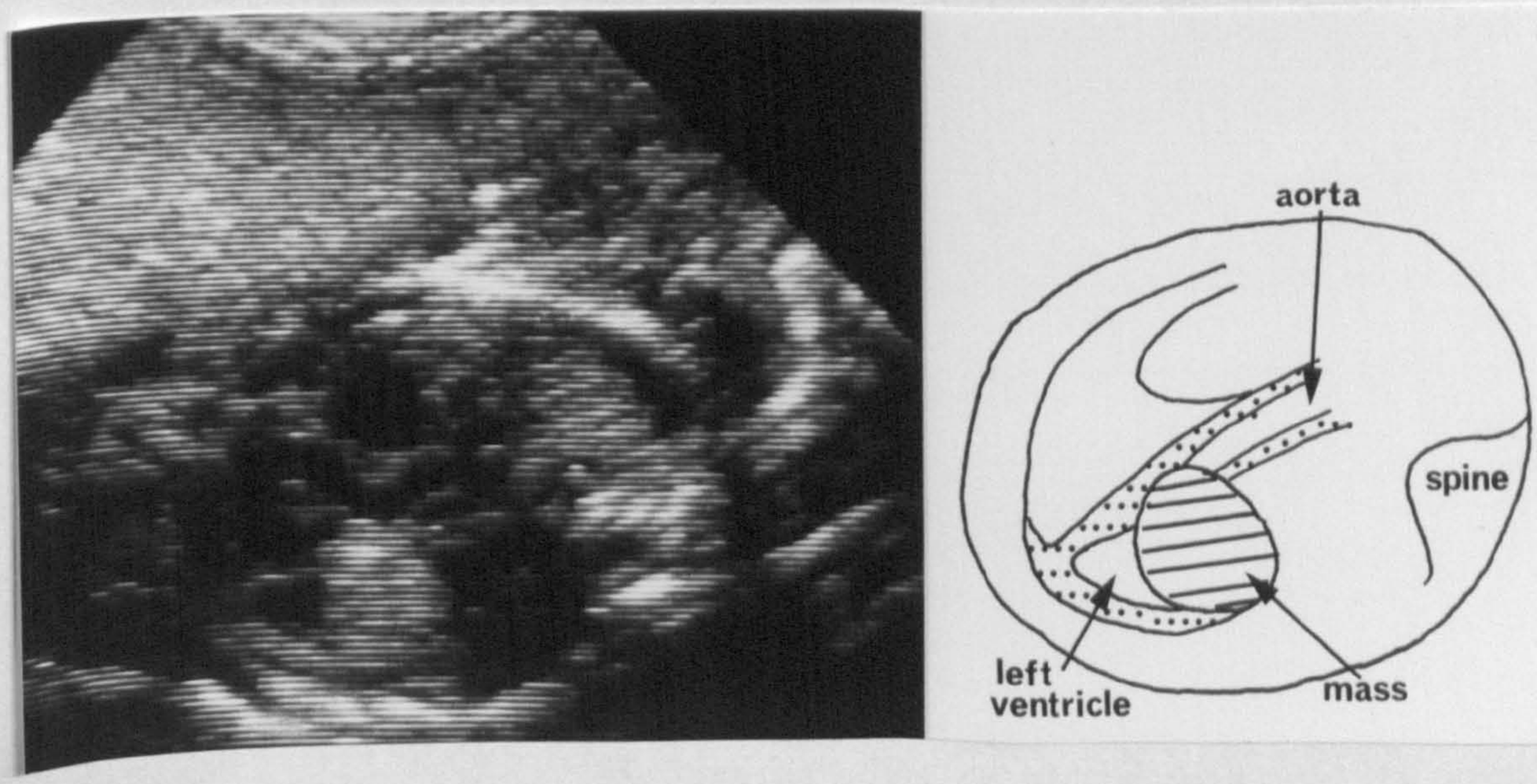


Figure 11.21. The fetal heart is seen in the four chamber aortic root plane. The tumor mass can be seen obstructing the left ventricular outflow tract.

to improve the cardiac failure, however, the fetus died three days later. Histological examination of the cardiac tumor suggested rhabdomyoma although the tumor did arise in the left atrium.

Case 11.9. This case presented at 24 weeks gestation with an obstructive uropathy. Hydronephrosis, ureteric and bladder dilatation were present but not thought severe. There was no oligohydramnios and apparently adequate renal tissue seen. Examination of the fetal heart revealed no structural anomaly. The fetus was not re-examined by us and was delivered at term. He died within three weeks of birth of his renal abnormalities. At autopsy a small perimembranous ventricular septal defect was found. Re-examination of the intrauterine pictures allowed retrospective identification of this defect. Figure 11.22.

Case 11.10. Case 11.10 presented at 19 weeks gestation. The patient had lost one previous baby with tetralogy of Fallot. A second baby died in infancy, during surgery to close a ventricular septal defect. On the first examination no gross structural defect could be detected. Re-examination at 24 weeks gestation showed what appeared to be a perimembranous ventricular septal defect. The observer was not convinced of its presence, it did not appear large and therefore

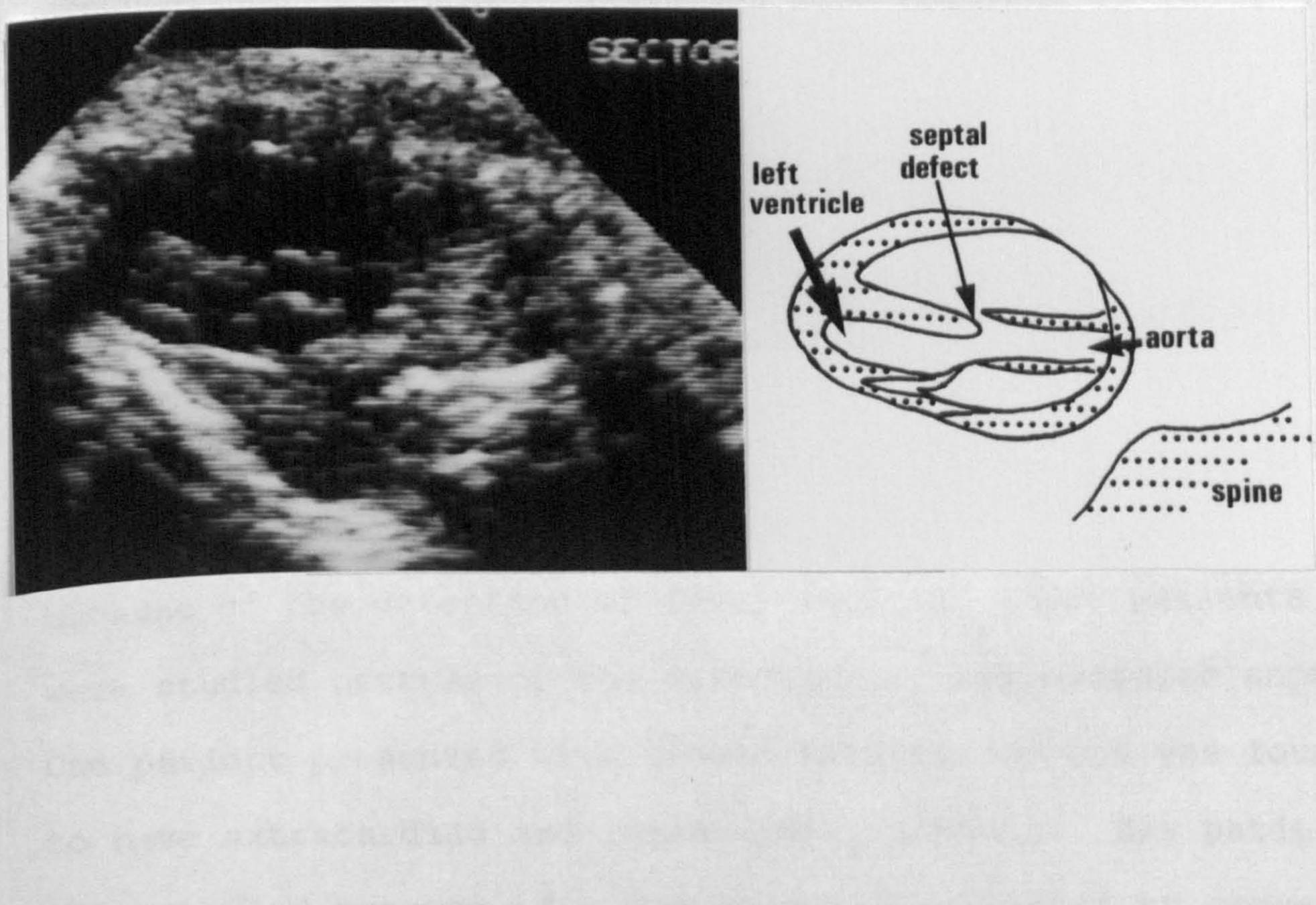


Figure 11.22. The fetal heart is seen in the long axis of the left ventricle. There is an apparent defect in the perimembranous region of the ventricular septum.

the patient was not informed of this doubt. She was re-examined at 36 weeks gestation and the perimembranous area carefully searched for a defect. No defect could be seen. Figure 11.23. Postnatal clinical and echocardiographic examination at two months of age revealed no abnormality.

Case11.11-15. This identical sequence has been observed in a further five cases. Specifically, a doubt about the integrity of the perimembranous septum has been present at 20-25 weeks gestation, and the septum has appeared intact at 36 weeks gestation. Another of these cases is illustrated in Figure 11.24.

Discussion

The cases described illustrate the type of patient referred or included in our study, as being at high risk of congenital heart disease. Three patients were studied because of the detection of fetal ascites, three patients were studied because of the detection of extracardiac anomaly. One patient presented with growth retardation and was found to have extracardiac and intracardiac anomaly. Six patients were studied because of a previous baby affected by congenital

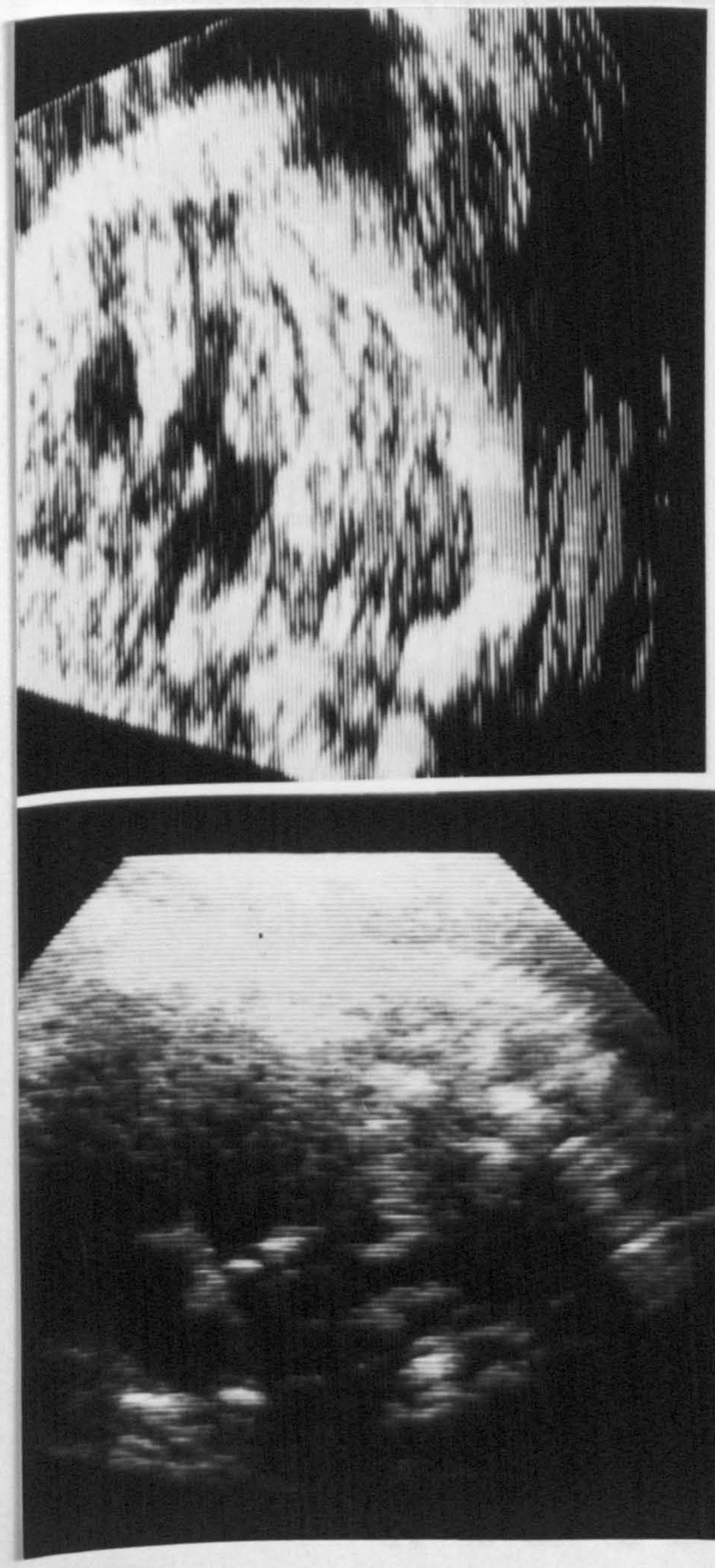
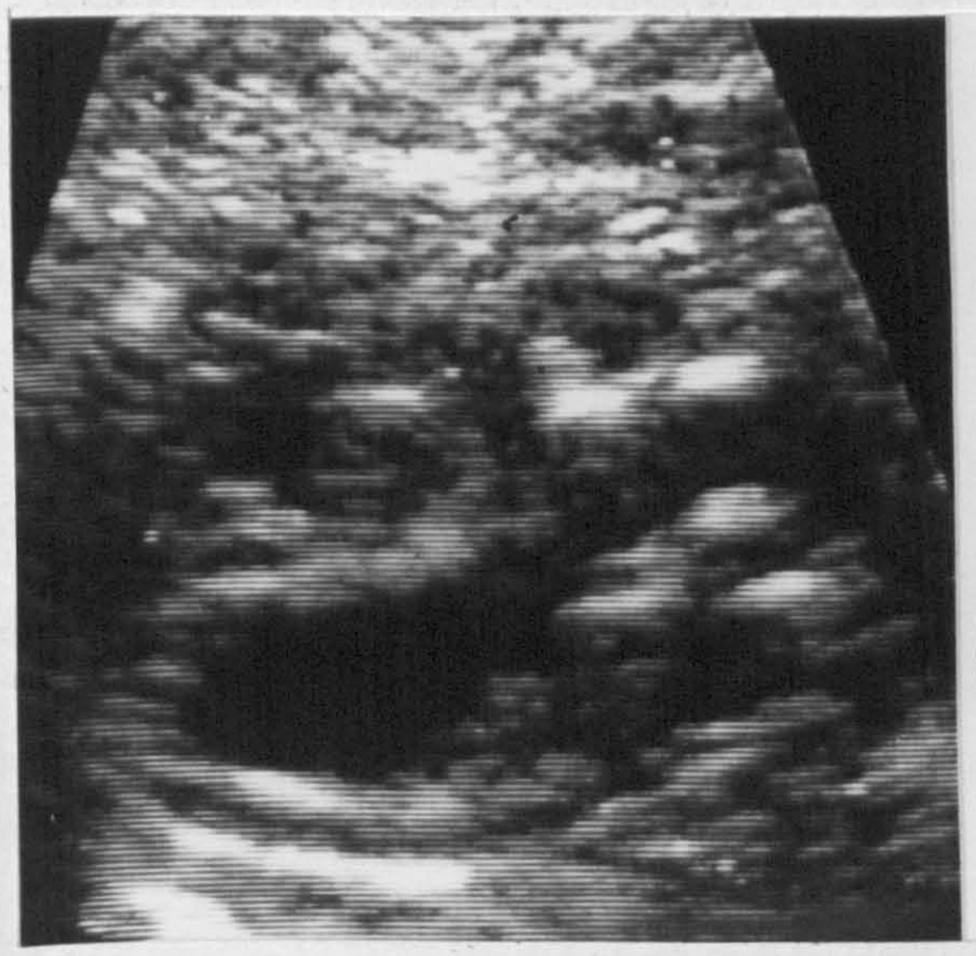


Figure 11.23. The top picture taken at 24 weeks shows an apparent defect in the perimembranous part of the ventricular septum similar to that seen in Figure 11.22. The heart is seen in the same projection at 36 weeks in the lower frame. There is no defect detectable in the perimembranous region.



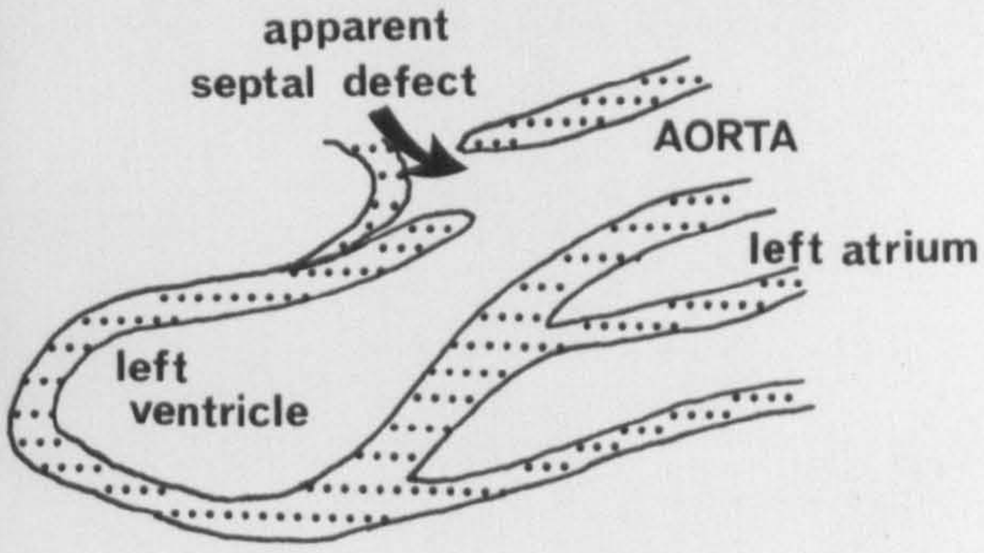


Figure 11.24. The fetal heart is seen in the long axis projection at 22 weeks gestation. There is an apparent perimembranous ventricular septal defect. No defect was detectable at 36 weeks in the same projection.

heart disease. Two patients in the "possible" ventricular septal defect group were studied because of maternal diabetes.

Six apparent ventricular septal defects were seen early in pregnancy. One was detected postnatally. The natural history of ventricular septal defects in postnatal life is of spontaneous closure, occurring in between 34 (161) to 58% (168) of cases. It is not unreasonable to suppose that this process of closure of the ventricular septum is occurring also, throughout intrauterine life, in a small number of cases. Our incidence of detection of defects was six cases out of 637 pregnancies studied. Mitchell et al, however, suggested that ventricular septal defects are between 3-4 times as common in premature infants as in full term infants. The expected incidence of ventricular septal defects in liveborn infants would be 1 in 532. (169). Mitchell found a clinically apparent ventricular septal defect in 25% of premature infants of less than 2,000 gm., and in 87% of autopsied infants less than 2,500 gm., an isolated ventricular septal defect was found. If these figures are real, we should perhaps have found a higher incidence of ventricular septal defect in intrauterine life. However, as defects less than 2 mm in size are not detectable with present imaging techniques, (170,171) it is possible that the majority of defects in the fetus are impossible to

visualize echocardiographically. Canale et al. found that defects of about half the internal dimension of the aortic root, had a shunt ratio of 2:1 and were therefore of functional significance (173). But the aortic root is only 0.4 ± 0.14 mm at 20 weeks gestation. A potentially functionally significant ventricular septal defect of 2 mm in size would therefore be overlooked at this gestation. For this reason we altered our policy of the timing of fetal echocardiography during our study. The initial examination at 18-20 weeks gestation excluded abnormalities of connection and our second study, which initially had been at 22 weeks gestation, was deferred until 26 weeks when particular attention was paid to the integrity of the ventricular and atrial septa. Even if a defect is suspected in fetal life, it may close, as it appeared to in five of our cases, and serial observations throughout pregnancy should demonstrate the progress of a defect.

The cases of structural cardiac abnormality detected during the study, and described in this chapter, demonstrate that congenital cardiac malformations can be detected prenatally. The accuracy of definition of all the components of each defect increased as the study progressed and greater experience gained in interpretation. As the prenatal and postnatal echocardiogram of the normal heart are not identical,

so abnormalities in the fetal heart are not necessarily identical to the appearance of the same abnormality post-natally. It is important therefore that each abnormality suspected be followed up clinically and echocardiographically, or anatomically where appropriate, so that the interpretation of prenatal echocardiographic appearances are validated.

CHAPTER 12

RESULTS:

Cardiac arrhythmias detected in fetal life and studied echocardiographically

Introduction: Cardiac arrhythmias found in children or in fetal life fall into three main categories. Irregularity of rhythm, which may be due to atrial or ventricular premature beats, tachyarrhythmias or bradycardias. Structural cardiac abnormality may alter or interrupt the course of the electrical conducting pathways, or there may be accessory communications in addition to, or in place of, the usual pathways (173). However, arrhythmias are found much more commonly in structurally normal hearts.

A persistently irregular rhythm is very rarely associated with structural abnormality but may be associated with a cardiomyopathy. Much more commonly it is due to an undefined abnormality of the intra cardiac conduction or impulse formation. A cardiomyopathy can be detected echocardiographically and therefore excluded prenatally. Thorough elucidation of an irregular rhythm requires a complete electrocardiogram and often invasive His Bundle studies when indicated in children. As has been described in Chapter 9, although the fetal electrocardiogram can be obtained, no P wave can be detected and between 28 and 36

weeks gestation even the R wave is unobtainable. Prenatally therefore, echocardiographic study of a fetal heart with an irregular rhythm, is mainly to exclude a cardiomyopathy or structural cardiac anomaly.

Tachyarrhythmias again are rarely associated with structural cardiac abnormalities. They may originate in the sinus node, atria, or ventricles, or they may be atrio-ventricular reciprocating tachycardias (174). Antenatally their origin can best be documented from the echocardiogram as the limitations to the fetal electrocardiogram described above, applies equally to the elucidation of all fetal dysrhythmias. The echocardiogram can record left atrial and left ventricular wall motion and this should help to distinguish the tachyarrhythmias.

Bradycardias, in the fetus a persistent rate of below 100 beats per minute, are more commonly associated with structural defects than the other arrhythmias. In one study of 90 cases of congenital heart block, 25.5% were associated with structural anomaly (175). If complete heart block is present it can be associated with an atrioventricular septal defect or congenitally corrected transposition of the great arteries, or indeed any congenital cardiac anomaly. However, it is still more common to find complete heart block in a structurally normal heart.

Case Material: Nine cases were studied in this series of fetal arrhythmias. They are summarised in Table VI. There were four cases of an irregular rhythm, one case of sinus bradycardia, one of atrial flutter and three cases of heart block. Two of the cases of heart block had a structural abnormality.

Cases 12.1,2,3 and 4 presented for fetal echocardiography because a persistently irregular fetal heart rhythm had been detected. Case 12.1. In Case 12.1,presenting at 34 weeks gestation,there was maternal diabetes present. No structural cardiac abnormality was found and the arrhythmia was seen to be due to frequent premature beats, one beat present in every ten beats. The mother's diabetes was poorly controlled at the time of the study. The extrasystolic beats decreased when the control of maternal diabetes improved. At no time was there septal hypertrophy on septal measurement (176) or any other cardiac abnormality found.

Case 12.2. Case 12.2. presented at 39 weeks during labour with frequent premature beats. Again no structural abnormality was found before or after delivery. Left ventricular function was normal on two dimensional examination. The arrhythmia disappeared within a few days of life.

TABLE VI

Case No.	Arrhythmia	Echocardiographic findings	Gestational age at first study (weeks)	Outcome
Cases 12.1, 2,3,4.	Irregular rhythm	Structurally normal heart	34,39,28,35	Normal heart on delivery
Case 12.5	Sinus brady-cardia 90/min	RV dilatation. Small aortic root? Aortic stenosis	34	Small aortic root. Systolic murmur. VSD. Left atrial isomerism.
Case 12.6	Atrial flutter	Structurally normal heart	34	Normal heart. Once cardio-verted to sinus rhythm.
Case 12.7	Complete heart block	RV dilatation ? normal mitral valve	34	Poor LV funct-ion. Poor MV function.
Case 12.8	Complete heart block	Atrioventricular defect Double outlet right ventricle	38	DORV and AV canal on cath. Left atrial isomerism.
Case 12.9	2:1 heart block	Ostium primum A.S.D. Abnormal cardiac orientation and hypertrophy	21	Termination of pregnancy. O.P.A.S.D. and left at-rial isomerism confirmed. Aortic inter-ruption also found.

Case 12.3. Case 12.3 presented at 28 weeks with persistent cardiac irregularity. Coupled beats or bigeminy was found. Again no structural abnormality was found. Left ventricular function was normal on cross-sectional appearance and on M mode measurement. The arrhythmia persisted postnatally but has required no treatment or further investigation to date.

Case 12.4. Case 12.4 presented at 35 weeks gestation. Premature beats were noted to occur within every ten beats. No structural cardiac abnormality was found. The arrhythmia disappeared postnatally.

Case 12.5. Case 12.5 presented at 34 weeks gestation with a sinus bradycardia of between 90 and 100 beats/min. The mother had a previous baby with tetralogy of Fallot surviving, as yet uncorrected, at 4 years of age. The right ventricle was dilated as seen in Figure 12.1. The aortic root was small in relation to the rest of the heart (Figure 12.2) and M mode measurement of the aortic root was 0.6 cm., below the 5th percentile for this gestational age. Figure 12.3. There also appeared to be post stenotic dilatation of the aortic root, Figure 12.4. A diagnosis of aortic stenosis, possibly severe, was suspected and the right ventricular dilatation was thought to represent incipient right

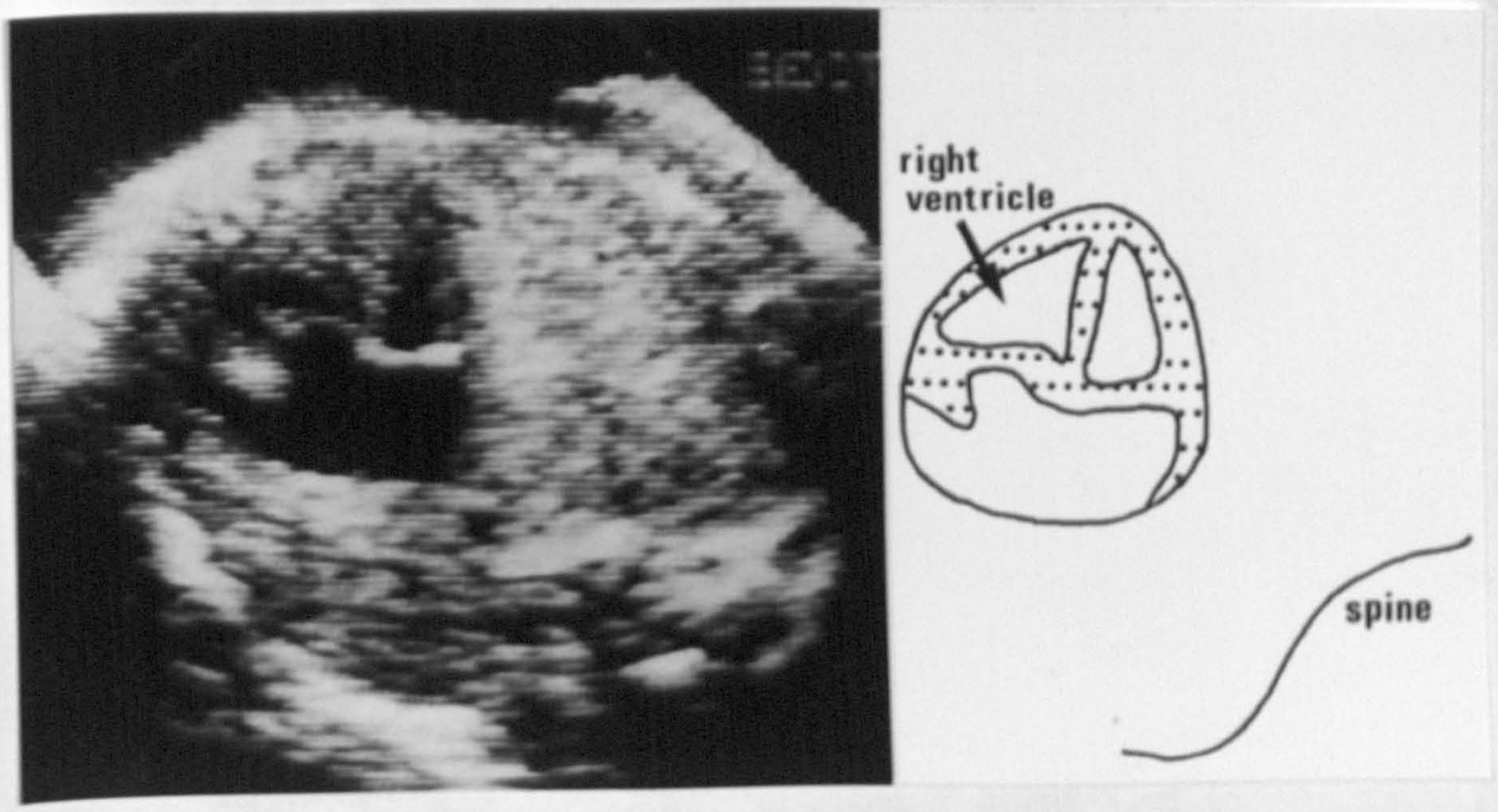


Figure 12.1. Case 5. The right ventricle is dilated and greater in internal diameter than the left seen in the four chamber view.

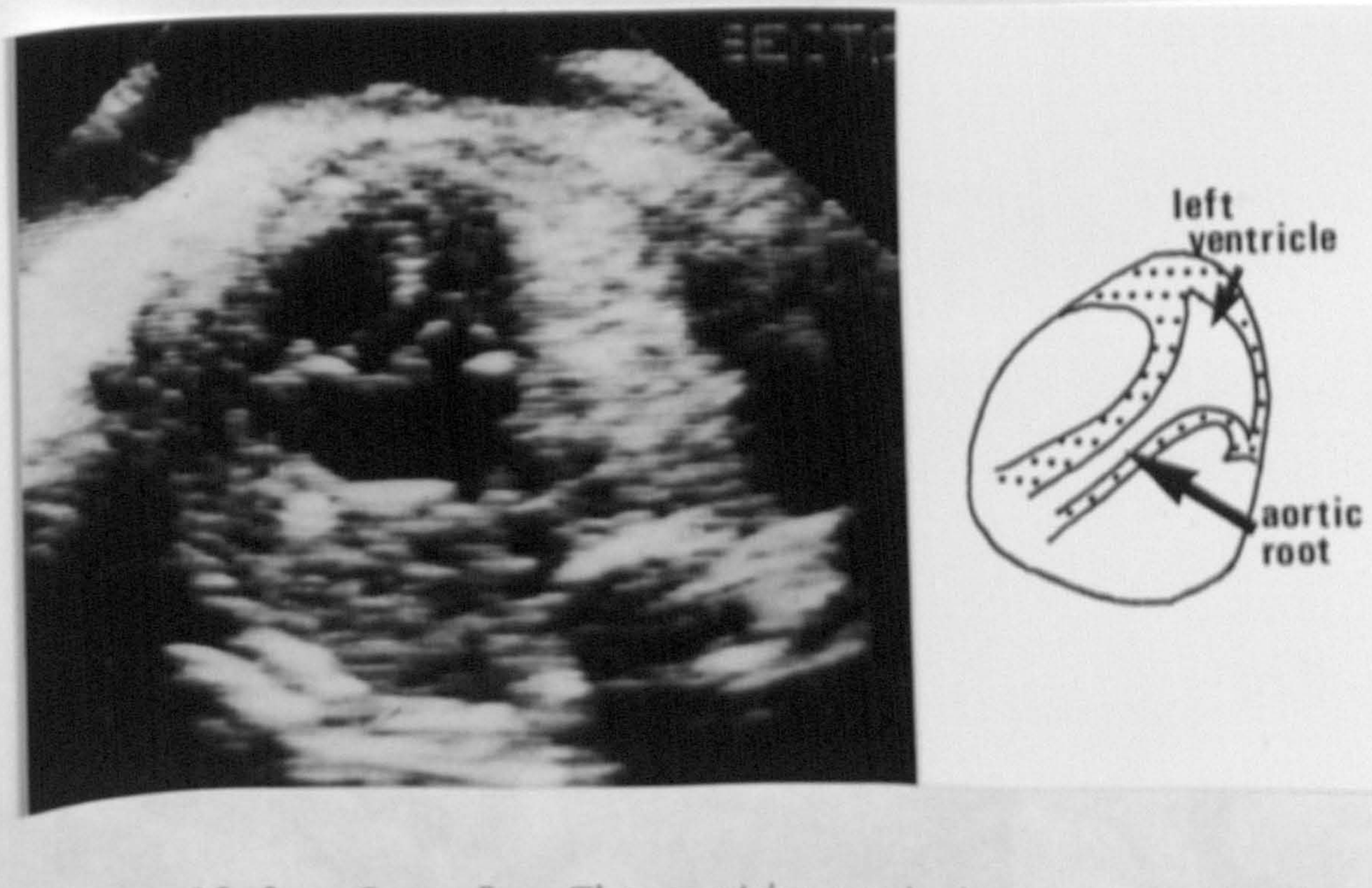


Figure 12.2. Case 5. The aortic root is seen arising from the left ventricle. It appears disproportionately small relative to right and left ventricles. The left atrium which lies between the aorta and the spine appears dilated.

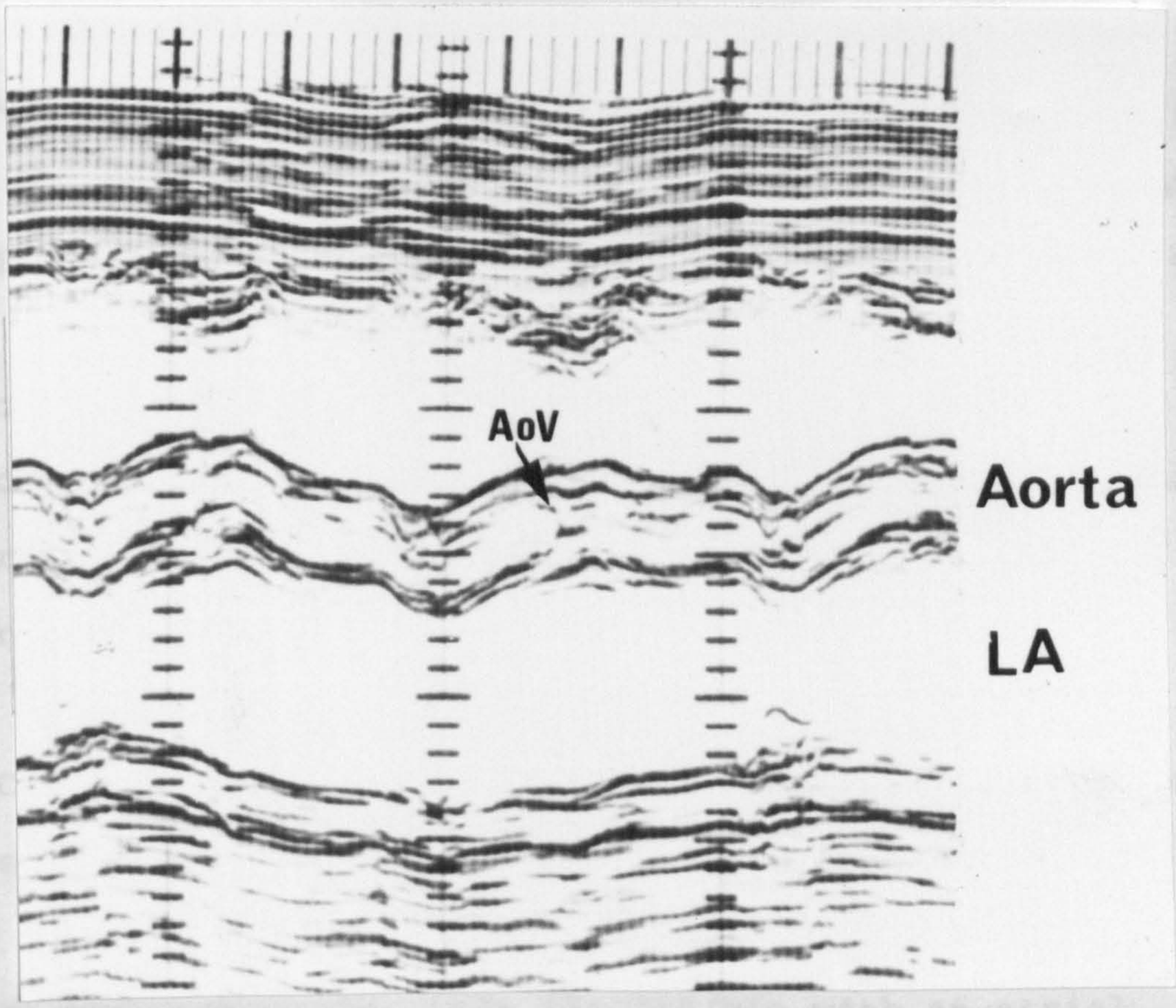


Figure 12.3. The M mode echocardiogram in Case 5. The aorta has a lumen and contains a valve which can be seen to open. The aortic root size is smaller than normal for this gestational age at 0.6 cms. The left atrium is dilated at 1.6 cms.

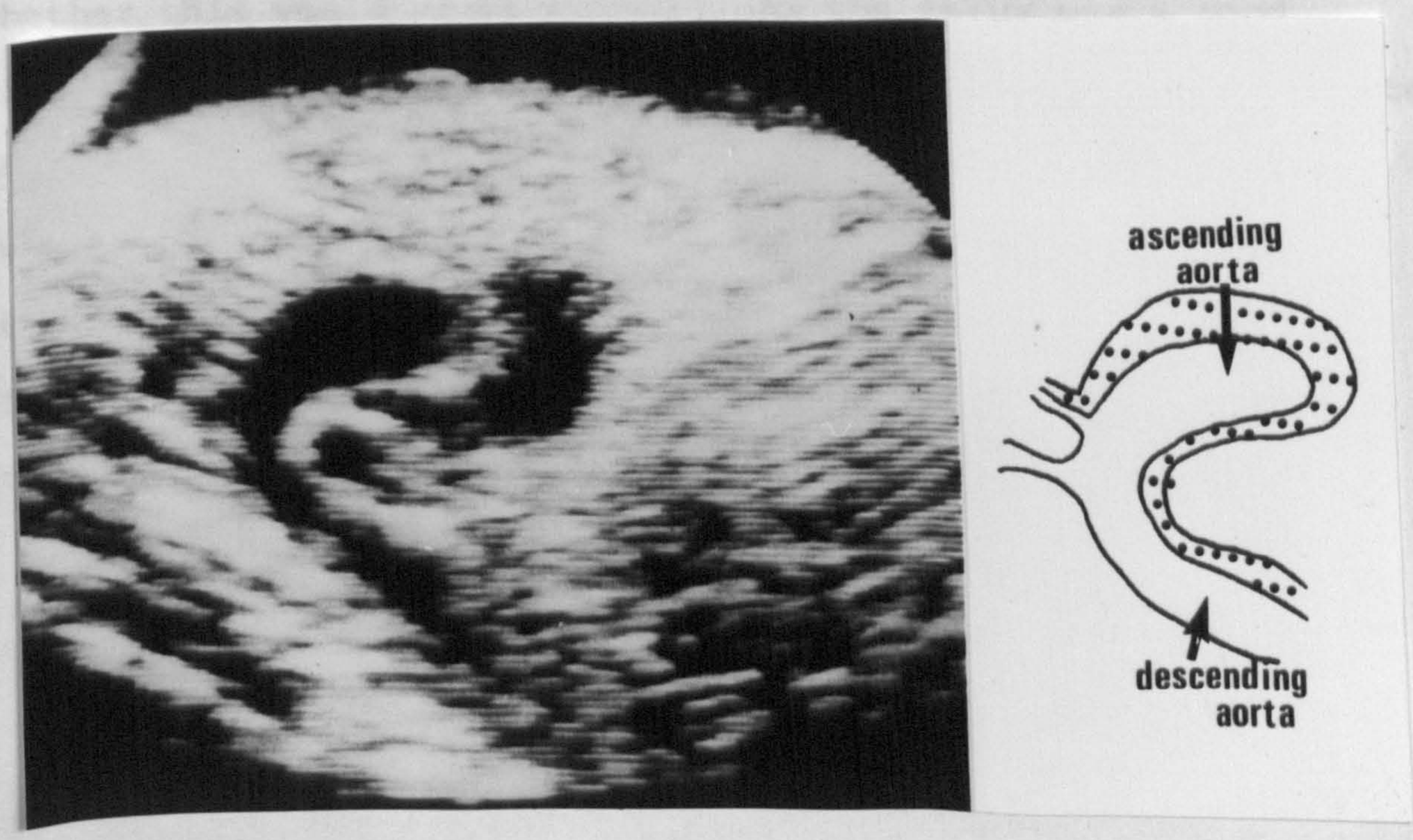


Figure 12.4. Case 5. The aortic arch view shows a narrow aortic orifice, and an apparently dilated ascending aorta.

ventricular failure. The patient was followed throughout the rest of her pregnancy but fetal ascites did not develop. At delivery there was a soft systolic murmur and confirmation of a small aortic root but the diagnosis of aortic stenosis could not be confirmed. At catheterization the child was found to have a perimembranous ventricular septal defect and left atrial isomerism with azygous continuation of the inferior vena cava.

Case 12.6. Case 12.6 presented at 34 weeks gestation. A persistent tachycardia had been noted at antenatal examination for 2 or 3 weeks. No structural cardiac anomaly was found but the ventricular rate was 200/min with an atrial rate of 400/min. Figure 12.5 a.b. This was thought to be atrial flutter with 2:1 block. If at any time all the atrial beats were conducted, it was thought that the fetus could not long survive a ventricular rate of 400/min. It was unknown whether this would occur or not. As the fetus was a good size for 34 weeks and the lecithin-sphingomyelin ratio suggested adequate lung maturity, the fetus was delivered by Caesarian section. Atrial flutter was confirmed electrocardiographically and sinus rhythm established in the first few days of life after cardioversion. There was no clinical or postnatal evidence of structural congenital cardiac disease.

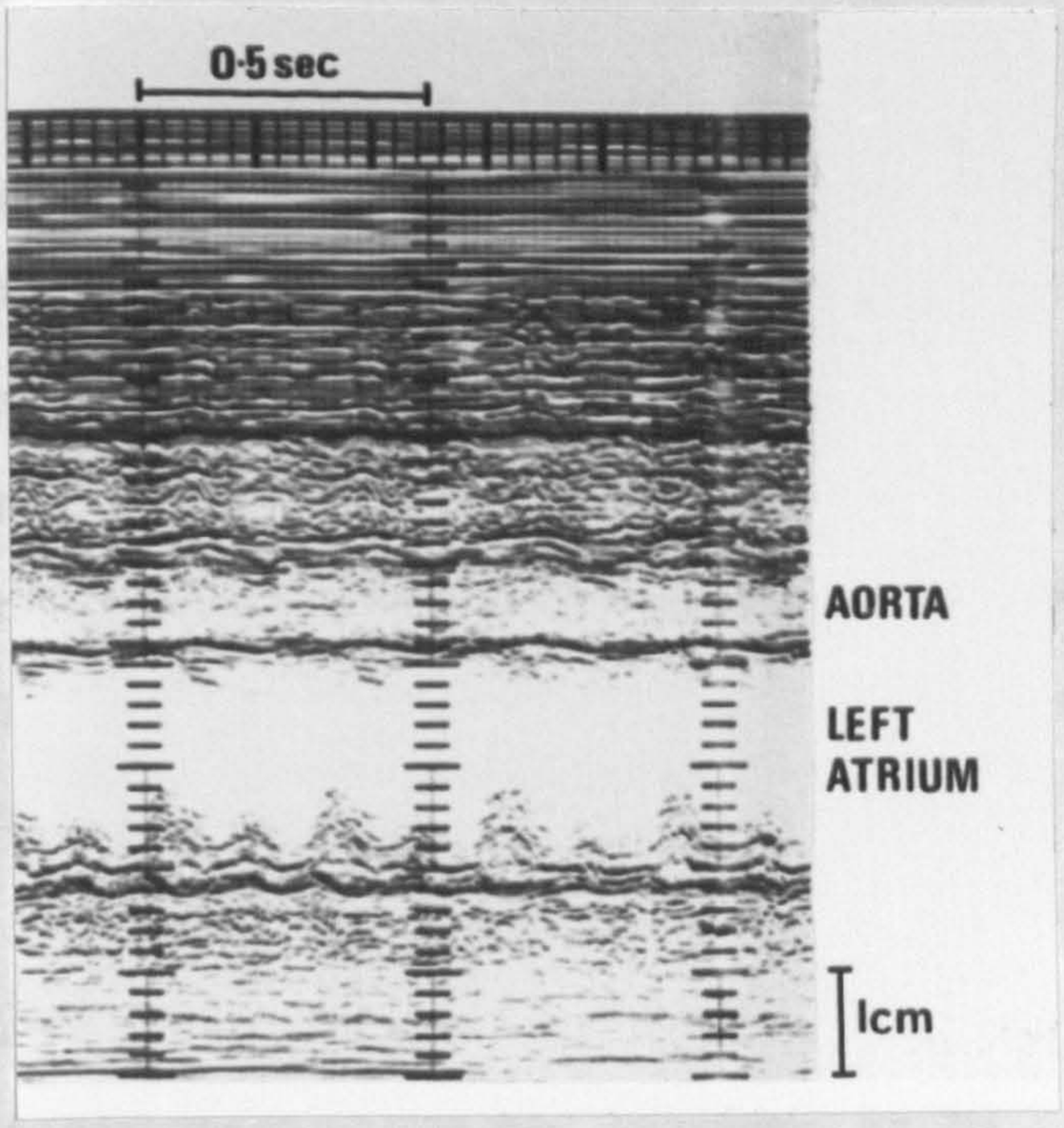


Figure 12.5. (a) Case 6. M mode echocardiogram across aorta and left atrium. Study of left atrial wall motion shows an atrial rate of 400/min.

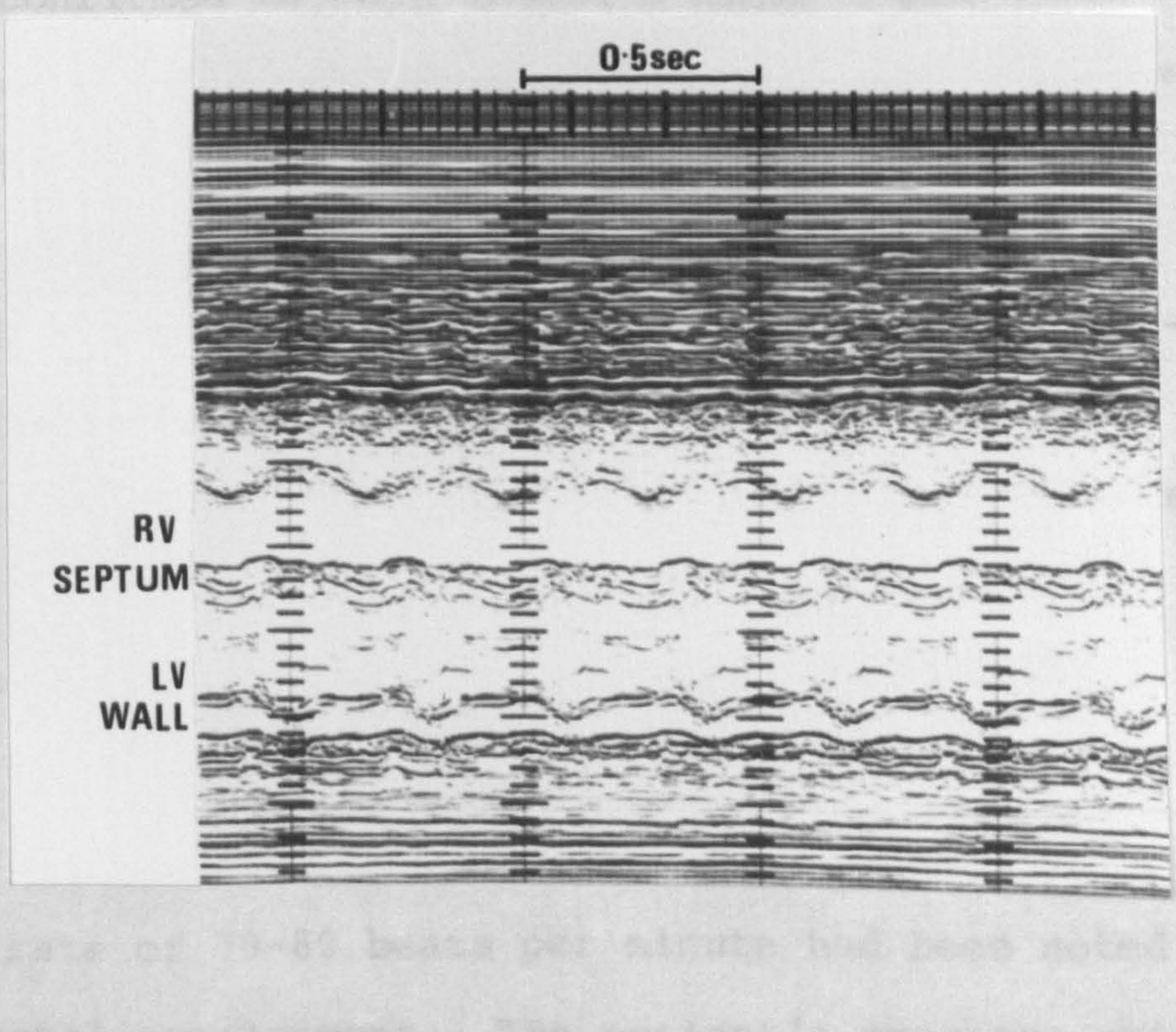


Figure 12.5. (b) Case 6. M mode echocardiogram across both ventricular chamber shows a simultaneous ventricular rate of 200/min. Note diminished movement of left ventricular wall.

Case 12.7. Case 12.7 presented at 34 weeks gestation. A persistent bradycardia had been noted of 80 beats/min. This was seen to be complete heart block, the atrial contraction occurring unrelated to ventricular contraction. There was right ventricular dilatation and paradoxical septal motion (Figures 12.6,7). The left ventricle and aortic root was below the normal size for the gestational age at 1.0 and 0.7 cms. respectively. Careful examination of the mitral valve on cross-sectional and M mode scanning, could not demonstrate movement of the mitral valve (Figure 12.8). An abnormality of the mitral valve, either stenosis or atresia was suspected. After delivery at 38 weeks gestation, the fetus was confirmed to have complete heart block. The mitral valve was present and opening, although excursion was diminished. The mitral valve ring was small, as was the left ventricle and aortic root. Left ventricular function was diminished. Cardiac catheterization confirmed the postnatal echocardiographic findings and diminished left ventricular function. There was no gradient however, across the mitral valve. In the six months since delivery, left ventricular function has become normal echocardiographically.

Case 12.8. Case 12.8. presented at 38 weeks gestation. A fetal heart rate of 70-80 beats per minute had been noted at a recent antenatal appointment. The patient's previous child had just died aged 4 years from subacute bacterial endocarditis

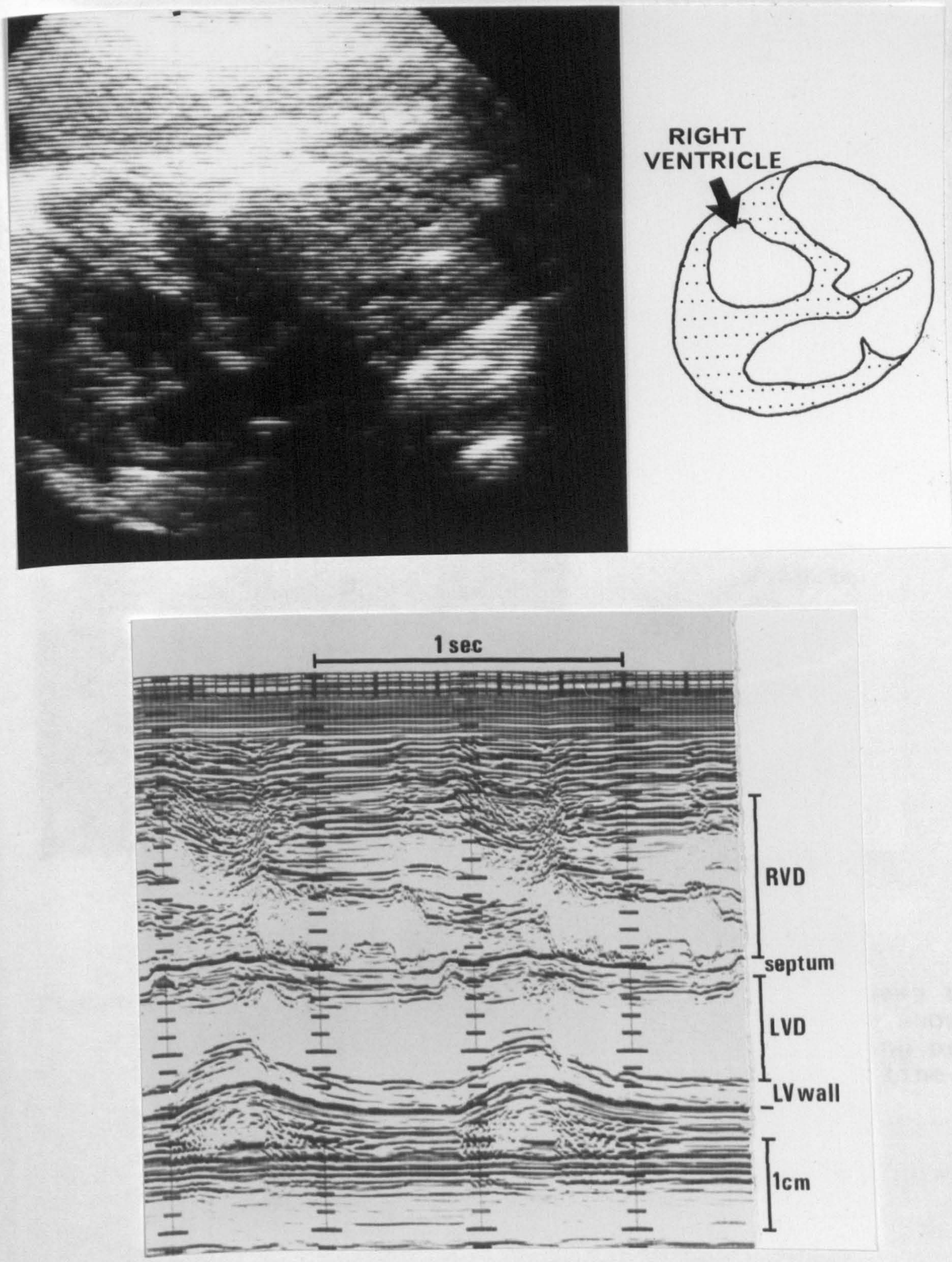


Figure 12.6 (top) Case 7 shows the two dimensional image in the four chamber view illustrating right ventricular dilation.

Figure 12.7(below) The M mode confirms this and demonstrates paradoxical septal motion.

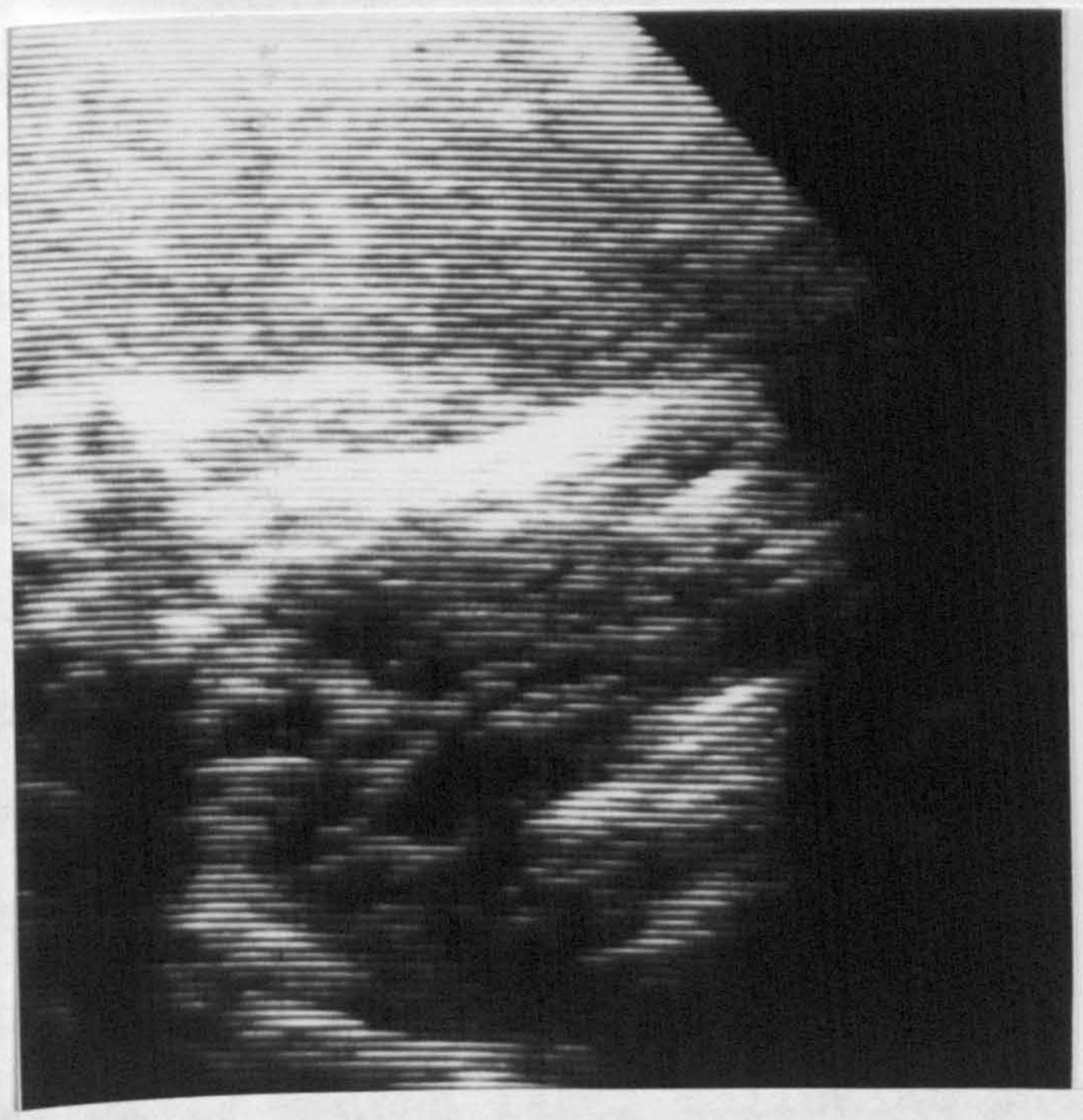


Figure 12.8. Case 7. Although the mitral valve is seen and appears normal it could not be shown to open on two dimensional scanning or sweeping across it with the M line.

She had had a double inlet univentricular connection to a chamber of left ventricular type with concordant ventriculo-arterial connection. Fetal cardiac scanning of the second pregnancy showed complete heart block, a complete atrio-ventricular septal defect and the aorta arising from the right ventricle. The pulmonary artery could not be seen antenatally but poor quality pictures were obtained. The atrioventricular defect is illustrated in Figure 12.9. Postnatally the atrioventricular septal defect was confirmed echocardiographically and at cardiac catheterization. Double outlet right ventricle with pulmonary stenosis was seen echo-cardiographically, prior to catheter confirmation. Left atrial isomerism was also found with azygous continuation of the inferior vena cava, which could be seen retrospectively on the prenatal scan (Figure 12.10). The patient is still alive 18 months later following palliative surgery.

Case 12.9. Case 12.9 presented at 20 weeks gestation with a bradycardia, which had been noticed since early in pregnancy. There was an atrial rate of 140/min and a ventricular rate of 70 beats/min. As this was very consistent it was thought to represent 2:1 heart block. The heart was found to lie in the centre of the chest and both ventricular chambers were excessively thick walled (Figure 12.11). The posterior left ventricular wall measured 0.4 cm. (normal range at this age is between 0.15 ± 0.07cms). There was an

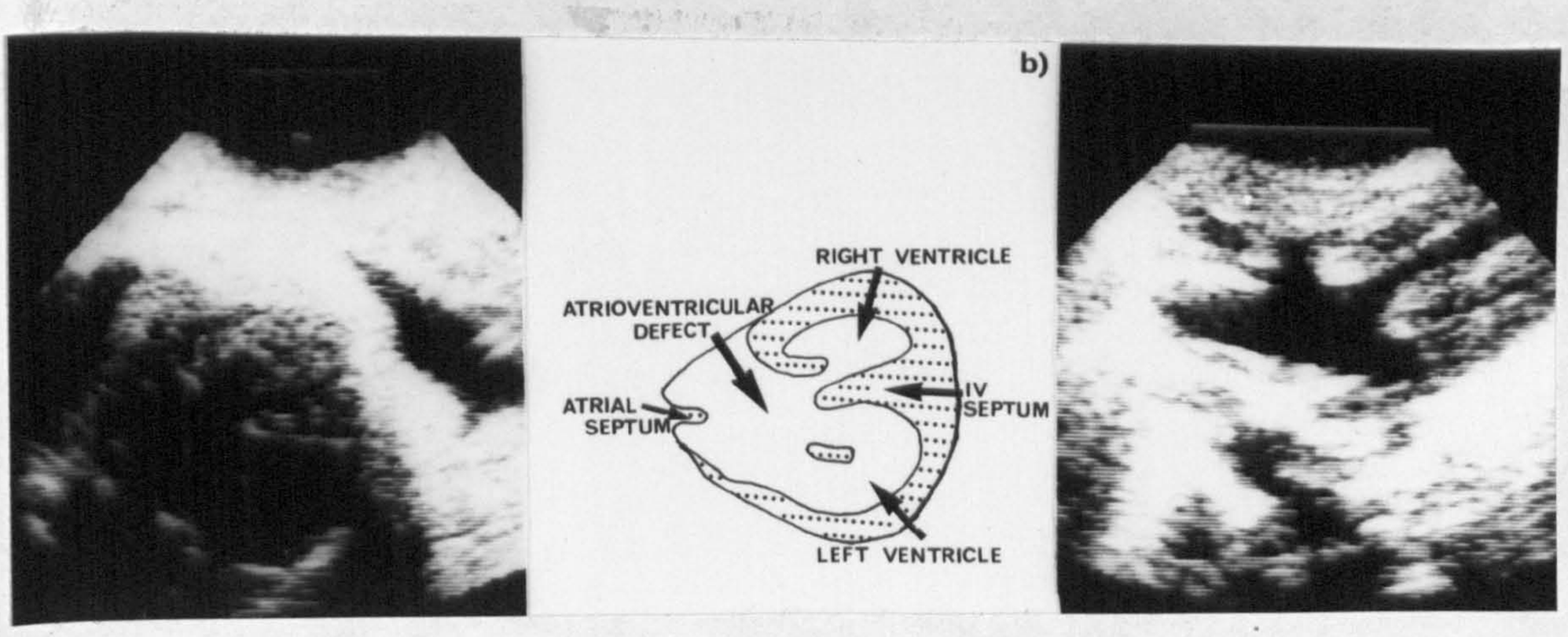


Figure 12.9. Case 8. The heart is seen in a four chamber projection in the prenatal and postnatal scan. The complete atrioventricular defect can be seen. There was a common bridging atrioventricular valve leaflet.

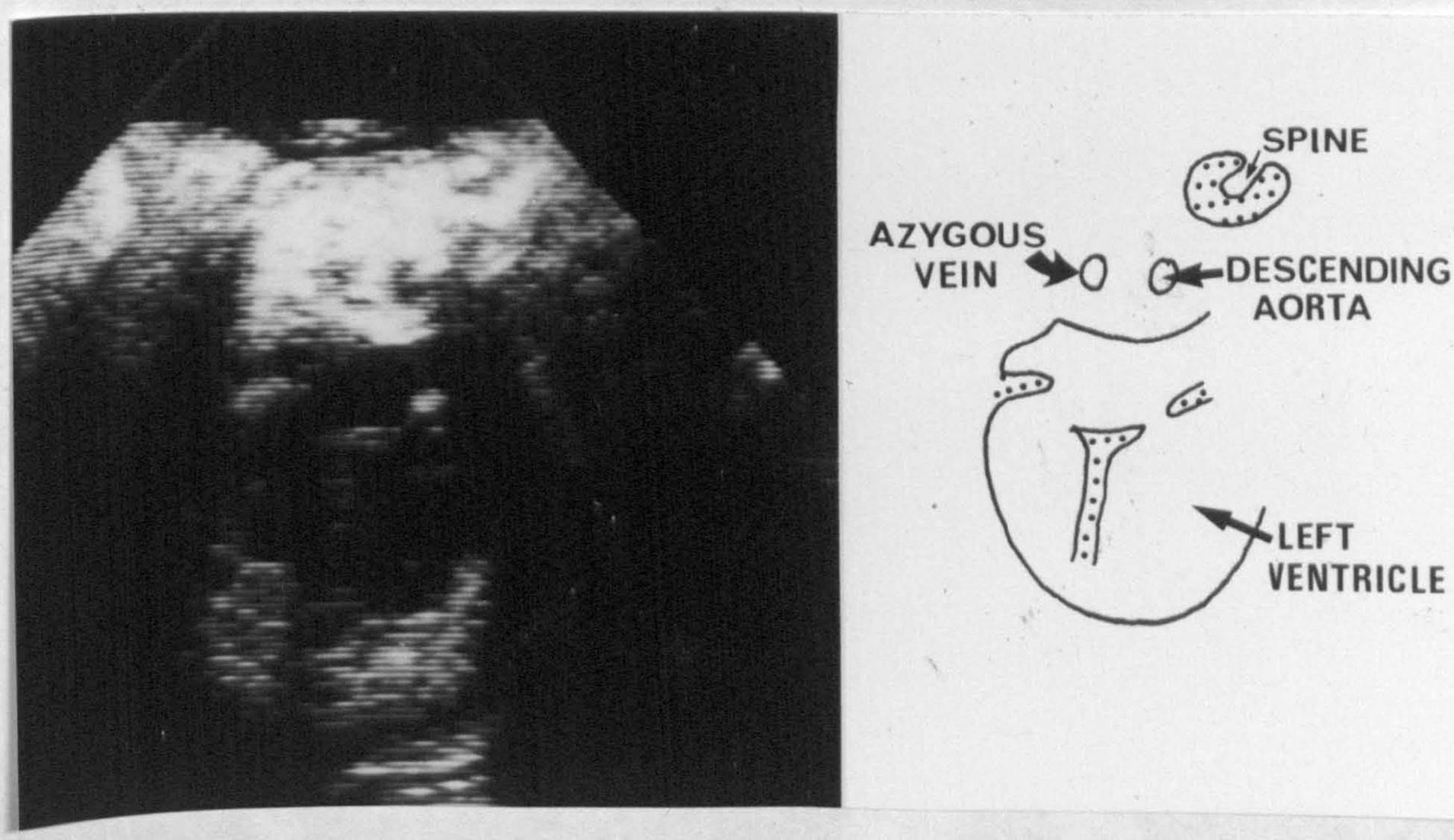
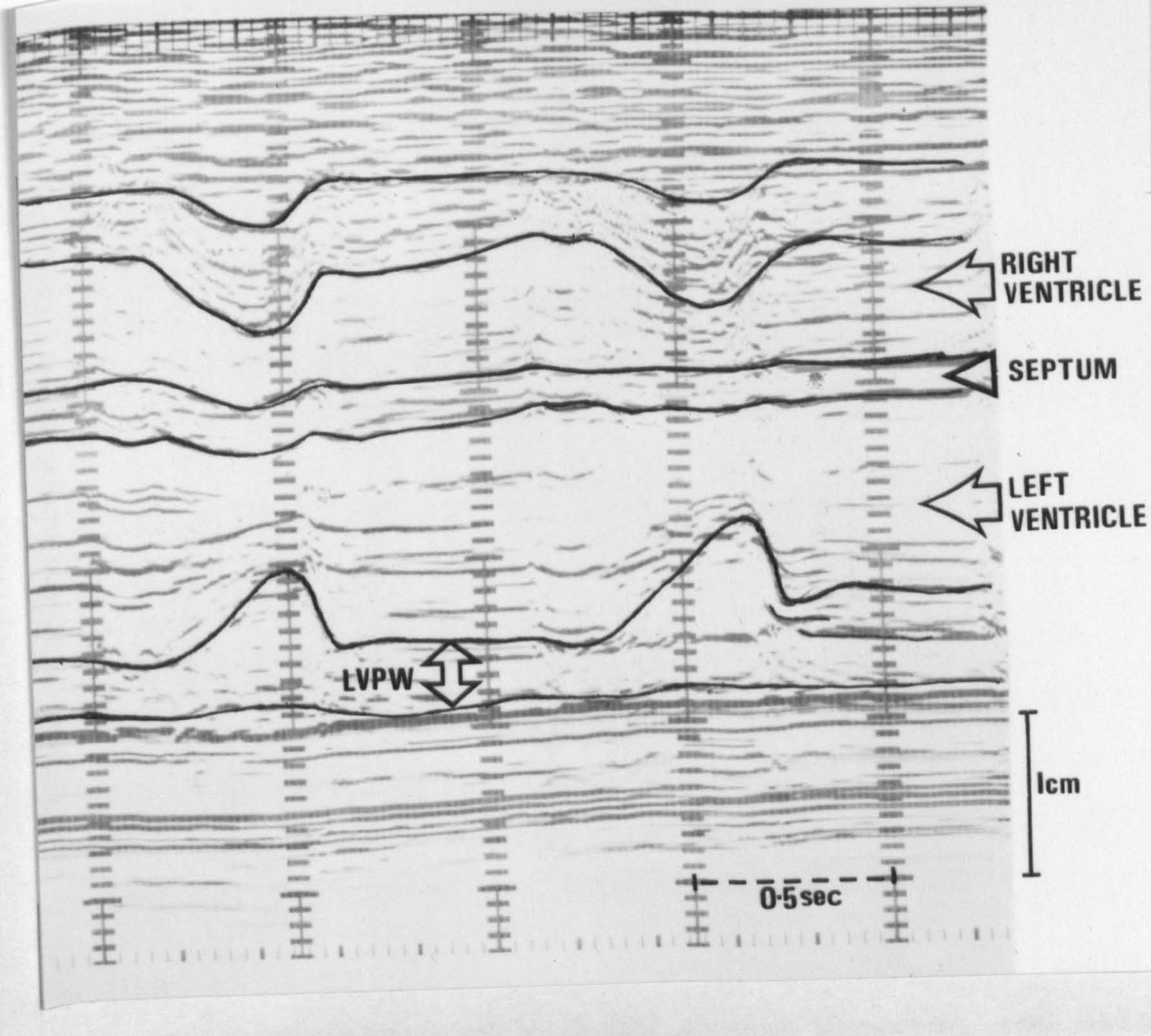
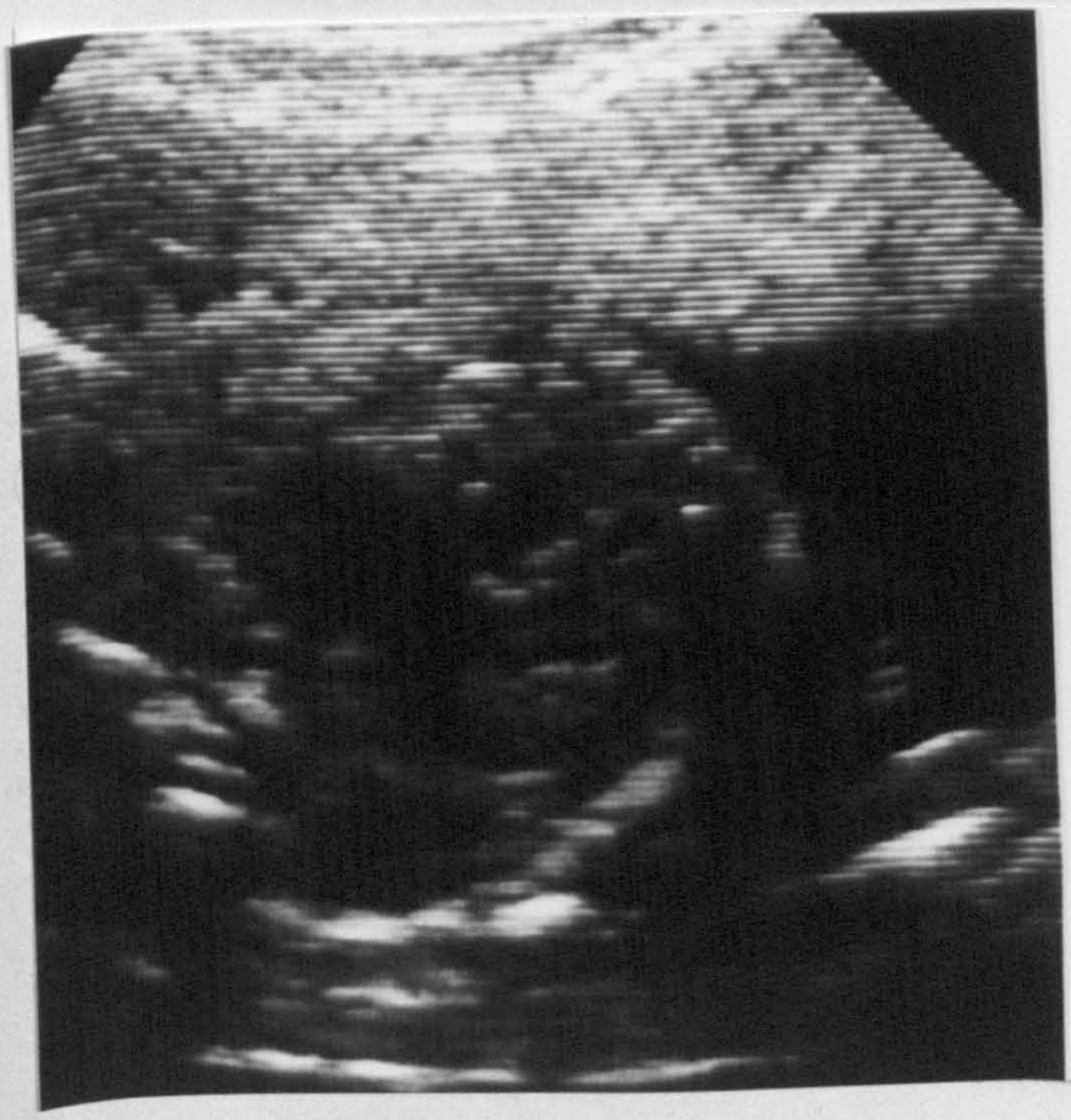


Figure 12.10. Case 8. There are two vessels seen behind the heart in cross section as circles. Normally only the descending aorta is seen lying between the left atrium and the spine. The vessel to the right of the aorta is the azygous vein.





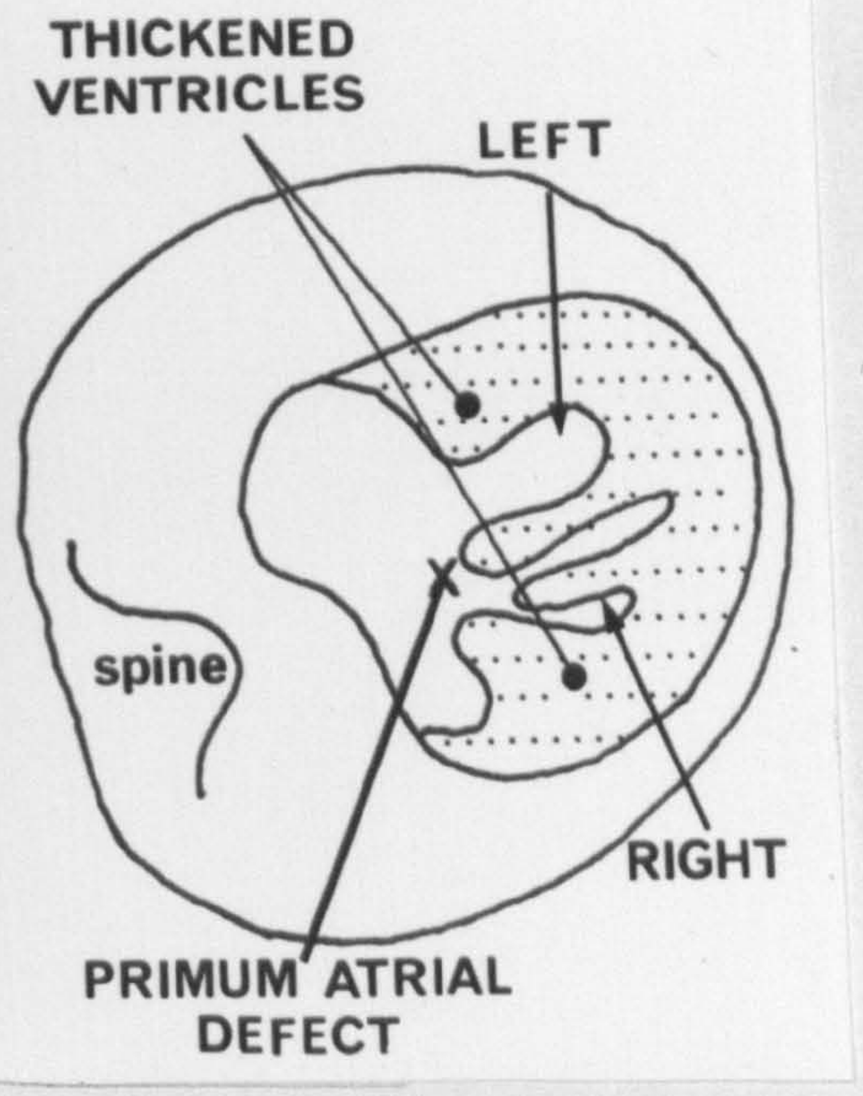


Figure 12.11 (top) Case 9. The M mode is recorded across both ventricular chambers. Both chambers are thickened.

Figure 12.12 (below) The two dimensional image is seen in the four chamber projection. The heart is seen to lie in the middle of the chest. The ventricular walls are thickened. The ostium primum atrial septal defect is seen.

ostium primum atrial septal defect Figure 12.12. The pulmonary artery arose from the right ventricle anterior to the aorta but parallel to it. The aorta was just below the mean for this gestational age at 0.4 cms. Figure 12.13. (normal range 0.45 ± 0.1 cms). The aorta was thought to arise from the right ventricle also. The arch of the aorta could not be visualized but the unusual orientation of the whole heart was thought to account for this. A diagnosis of ostium primum atrial septal defect with double outlet right ventricle was suspected. The association of this combination of abnormalities in addition to the positional abnormality of the heart was thought to indicate a diagnosis of left atrial isomerism and polysplenia (177). Termination of pregnancy was carried out at 22 weeks gestation. At autopsy multiple splenunculi were found in the abdomen, and bilateral left bronchial anatomy. Left atrial isomerism, ostium primum atrial septal defect and right and left ventricular hypertrophy were confirmed (Figure 12.14,15). Azygous continuation of the inferior vena cava was found. In addition to these abnormalities, interruption of the aortic arch was found between the left common carotid and left subclavian arteries (Figure 12.16).

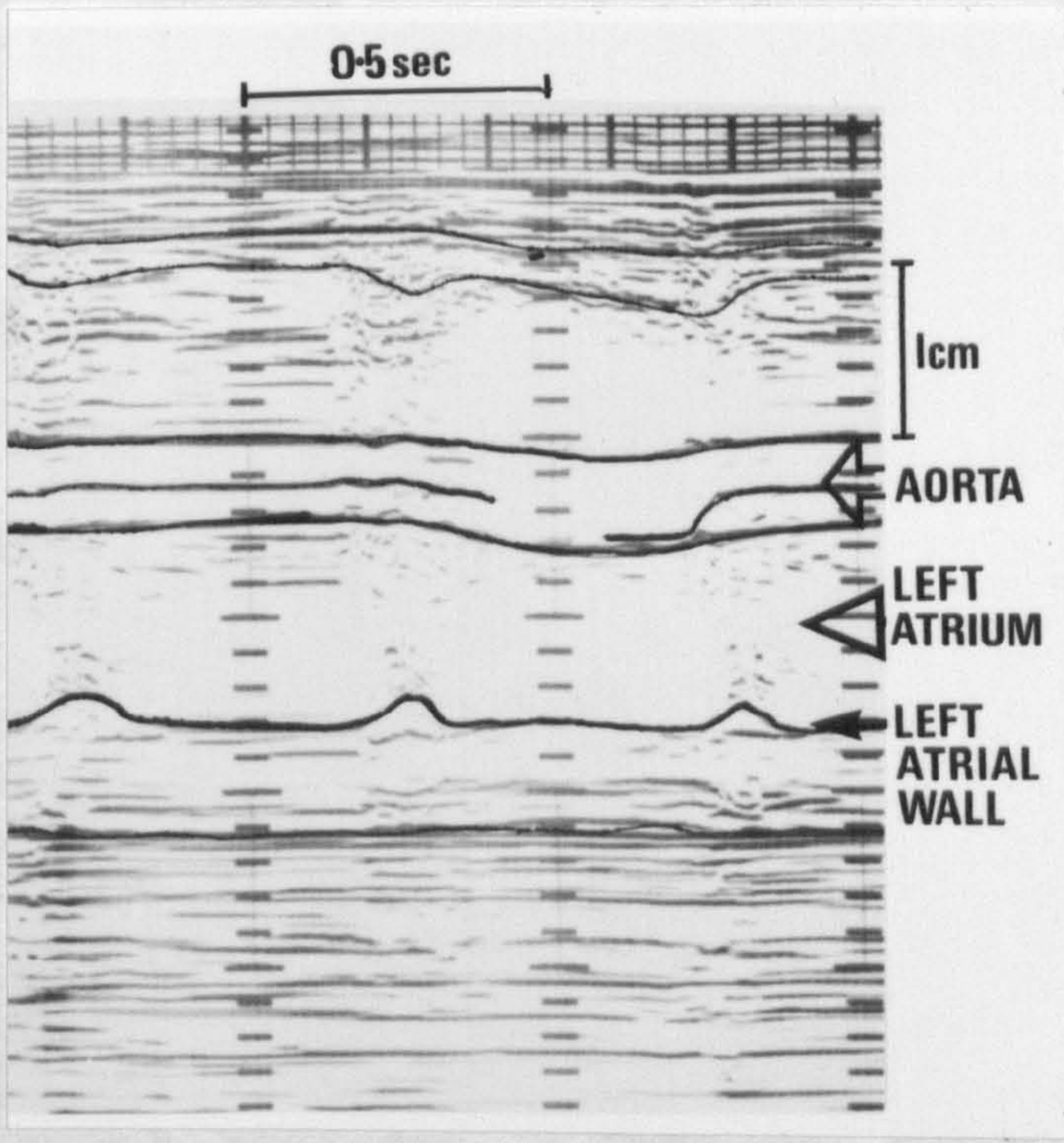


Figure 12.13. Case 9. The aortic root and left atrium are seen in M mode. The atrial contraction can be seen to be at twice the ventricular rate.

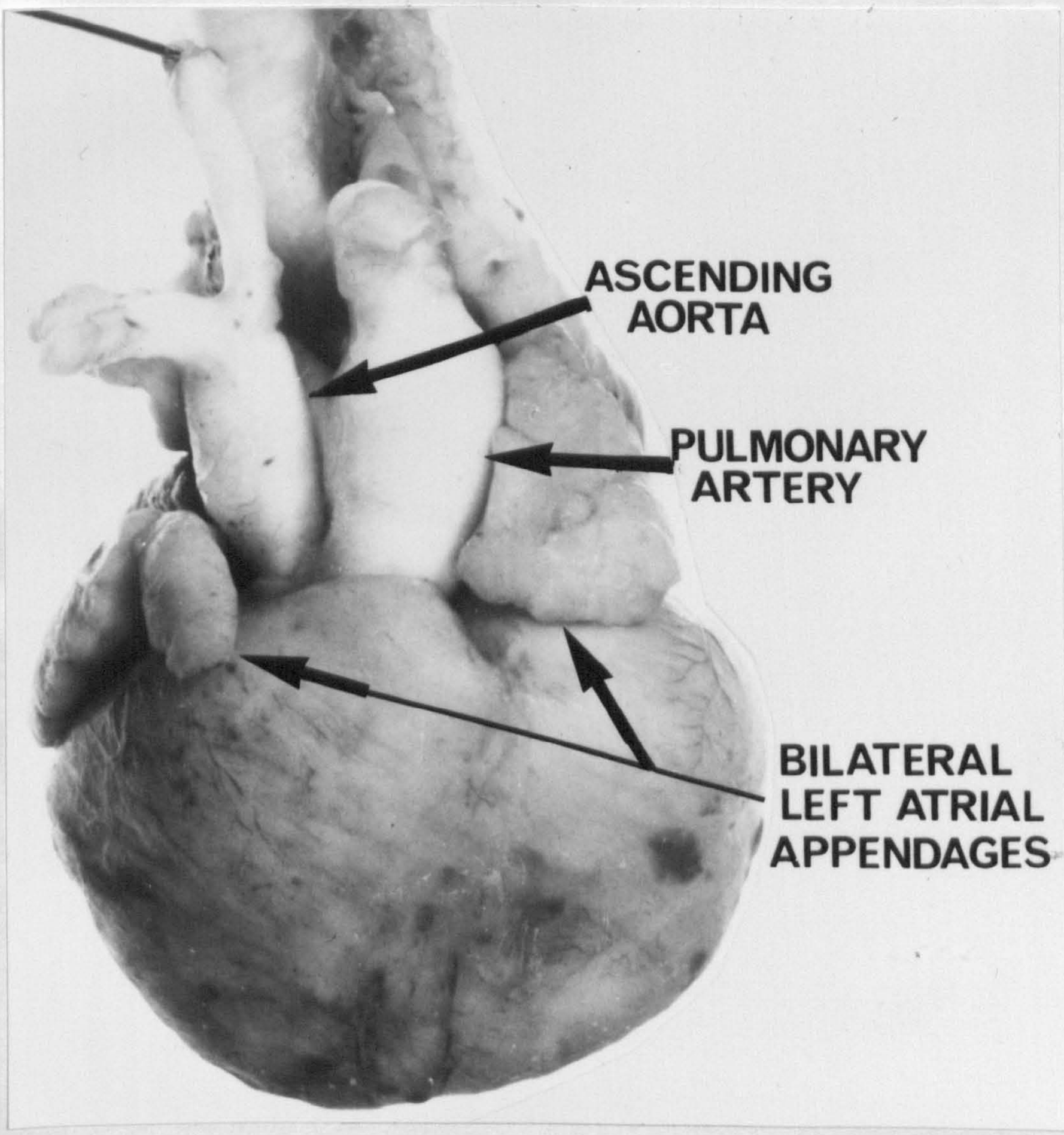


Figure 12.14. Case 9. The heart is seen unopened. Bilateral left atrial appendages can be seen. The ascending aorta is seen to be short and to divide into 4 branches. The aorta is smaller than the pulmonary artery lies behind and to the right of it.

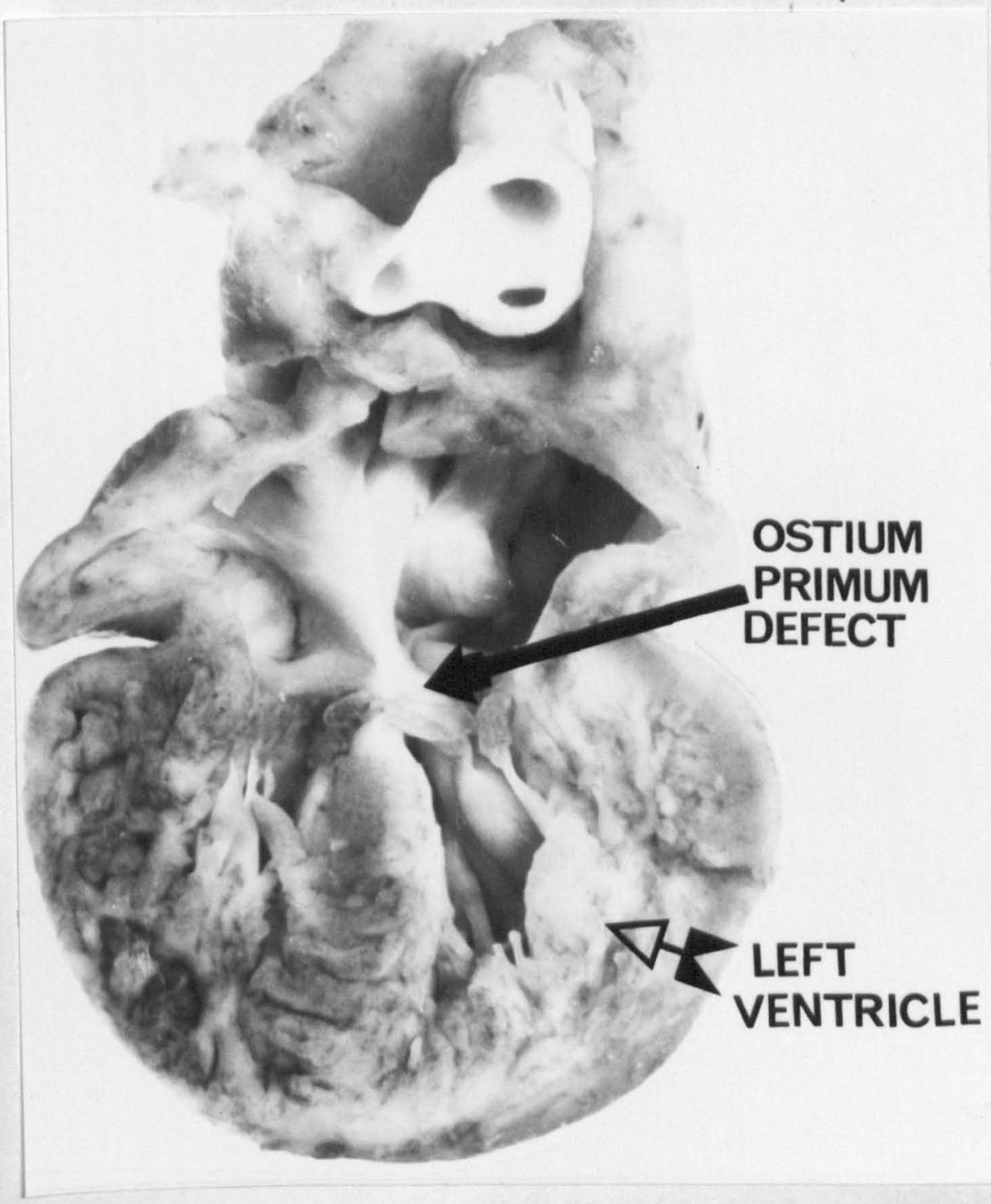


Figure 12.15. Case 9. The heart is opened to show the bilateral ventricular hypertrophy and the ostium primum atrial septal defect.

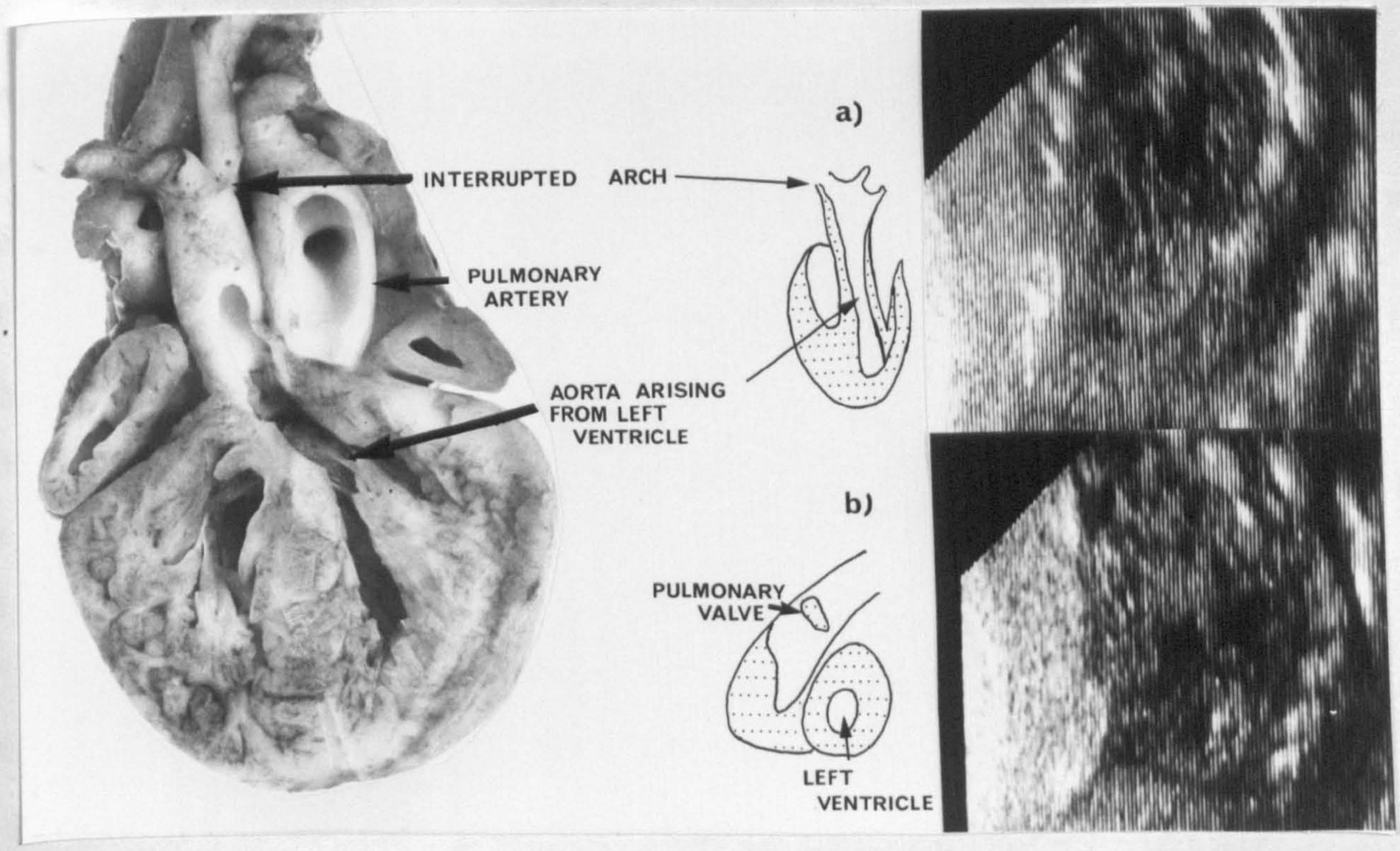


Figure 12.16. Case 9. In the anatomical specimen the continuity between left ventricle and aortic root is displayed and in (a) the same section is displayed echocardiographically.
(b) demonstrates the normal appearance of the infundibulum of the right ventricle supporting the pulmonary valve with the left ventricle seen as a concentric structure behind. The normality of arterial connections therefore is demonstrable on the echocardiogram although incorrectly interpreted at the time. The short branching posterior great artery was incorrectly thought to be the pulmonary artery.

Discussion

Arrhythmias presenting during fetal life are an important group to be studied echocardiographically. The limitations of the electrocardiogram in fetal life, detailed in Chapter 9, mean that the echocardiogram is the only way of elucidating an arrhythmia. The "P" wave of the electrocardiogram is impossible to record non invasively in prenatal life. However, atrial and ventricular wall motion can be recorded on the M mode echocardiogram. The relationship of atrial to ventricular contraction will provide clues to the type of arrhythmia present. Cardiomyopathies and structural cardiac anomalies can be readily excluded. Documentation of the tachyarrhythmias can be performed and managed according to the circumstances. In our case the fetus was sufficiently mature for delivery. However, if this had not been the case or there was suspicion that the fetus was compromised as a result of the arrhythmia, the mother could have been digitalised. Fetal decompensation would have been evidenced by right heart dilatation or the development of ascites. There is good placental transfer of digoxin, similar concentrations having been found immediately after birth, in maternal and fetal blood. (178).

It is interesting that two of our cases in which a slow heart rate was recorded, Case 12.5 and Case 12.6, showed similar abnormal echocardiographic findings; namely right

heart dilatation with left ventricular and aortic root measurements below the mean for gestation. In one case, Case 12.7, with complete heart block, the mitral valve could not be shown to open in intrauterine life. Decreased left ventricular blood flow in intrauterine life may restrict left ventricular and aortic root development, but the mechanism of diminished left heart flow is as yet undefined.

Three of our cases, Case 12.5, 12.8 and 12.9 had left atrial isomerism and polysplenia, in association with structural cardiac malformations. In each case, azygous continuation of the inferior vena cava was present. Atrial isomerism is usually, but not invariably, associated with splenic anomalies (179). Right atrial isomerism is associated with asplenia and more major cardiac anomalies, left atrial isomerism with polysplenia and slightly less severe cardiac malformations (177) although over 60% of children with left atrial isomerism die in the first year of life. Cases 12.8 and 12.9 had severe malformations. It is important to note atrial situs as these isomeric syndromes may have a different recurrence rate from other forms of congenital heart disease (180).

CHAPTER 13

RESULTS:

Abnormal echocardiographic appearances secondary to extra-cardiac abnormality.

Unusual echocardiographic appearances probably representing normal variation.

This chapter describes abnormal echocardiographic appearances which probably do not represent primary cardiac disease. These echocardiographic findings are important to interpret accurately. Table VII summarises the cases discussed in this chapter.

Abnormal echocardiographic appearances secondary to extra-cardiac abnormality.

The first group consists of four cases and all presented because of fetal ascites. Case 13.1. This case was first seen at 20 weeks gestation. Fetal ascites was very marked and the right ventricle was seen to be grossly dilated. The appearance is seen in Figure 13.1. The right atrium and right ventricle were dilated although the fibrous tricuspid valve ring remains fairly narrow. The whole cardiac size seemed to occupy more than half the thorax, although normally it fills only a third. Despite extensive viral and antibody

TABLE VII

	Echocardiographic finding	Gestational age	Associated Abnormalities	Outcome
Case 13.1	Right ventricular dilatation	20/52	Fetal ascites	IUD 27/52 Leukaemia
Case 13.2	Right ventricular dilatation	22/52	Fetal ascites Cystic hygromata	Termination XO fetus
Case 13.3	Right ventricular dilatation	22/52	Fetal ascites	Normal baby at term
Case 13.4	Right ventricular dilatation	30/52	Fetal ascites	Normal
Case 13.5	Right ventricular dilatation	32/52	Fetal ascites	Normal baby at term
Case 13.6	Right ventricular dilatation	22/52	Fetal ascites Rh isoimmunisation	Gross anaemia on delivery Normal after exchange transfusion
Case 13.7	Right ventricular dilatation	35/52	Rh isoimmunisation	Gross anaemia on delivery. Normal after exchange transfusion.
Case 13.8	Whole cardiac dilatation Poor LV function	28/52	Growth retardation	Intrauterine death. 24 hours later
Case 13.9, 10, 11, 12	Echogenic body within left ventricle	22,24 19 weeks 19 2eeks	None	Normal babies at delivery

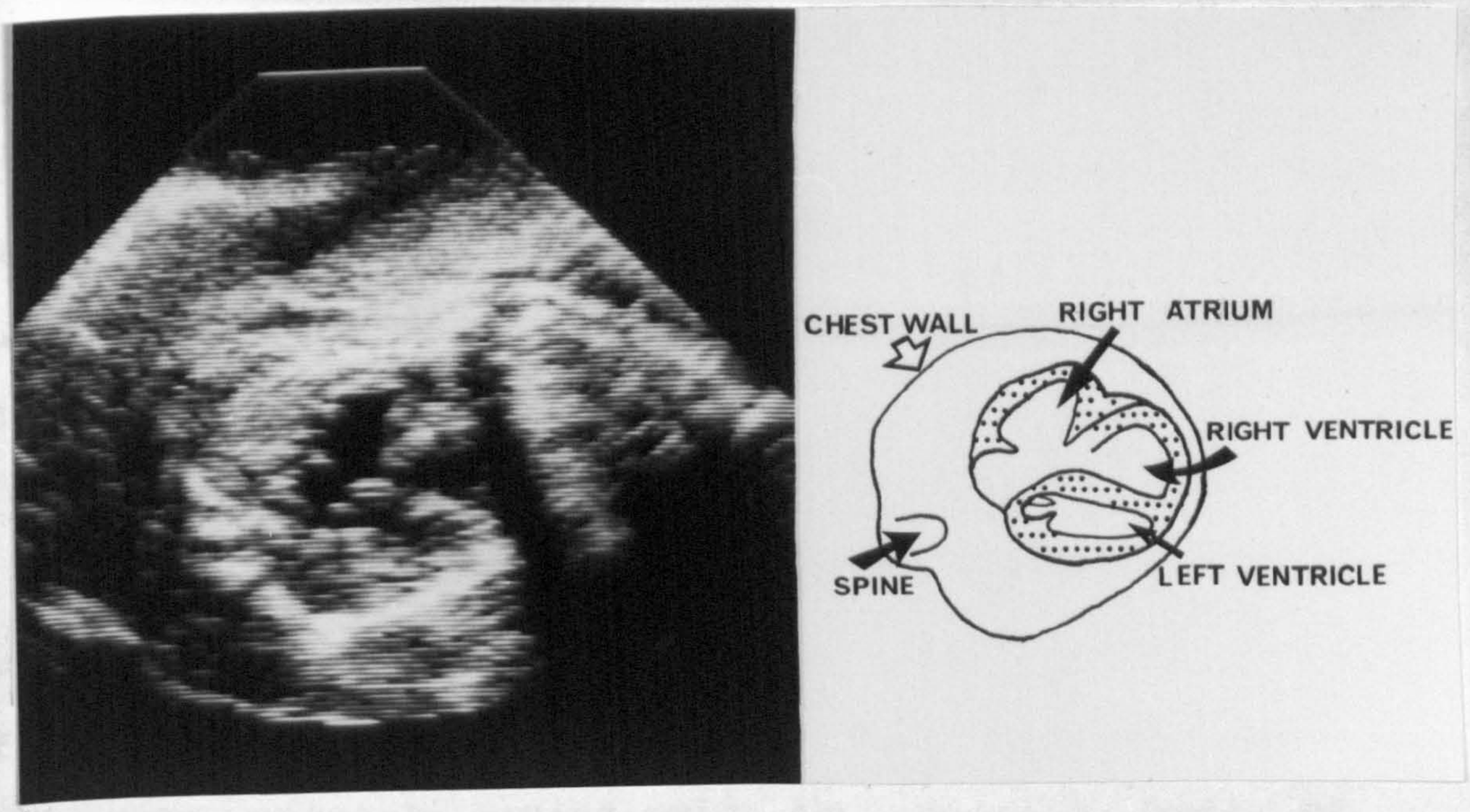


Figure 13.1. Case 13.1 The heart is seen in a four chamber projection. The right atrium and right ventricle are dilated with the tricuspid valve ring remaining fairly narrow. The whole heart appears enlarged.

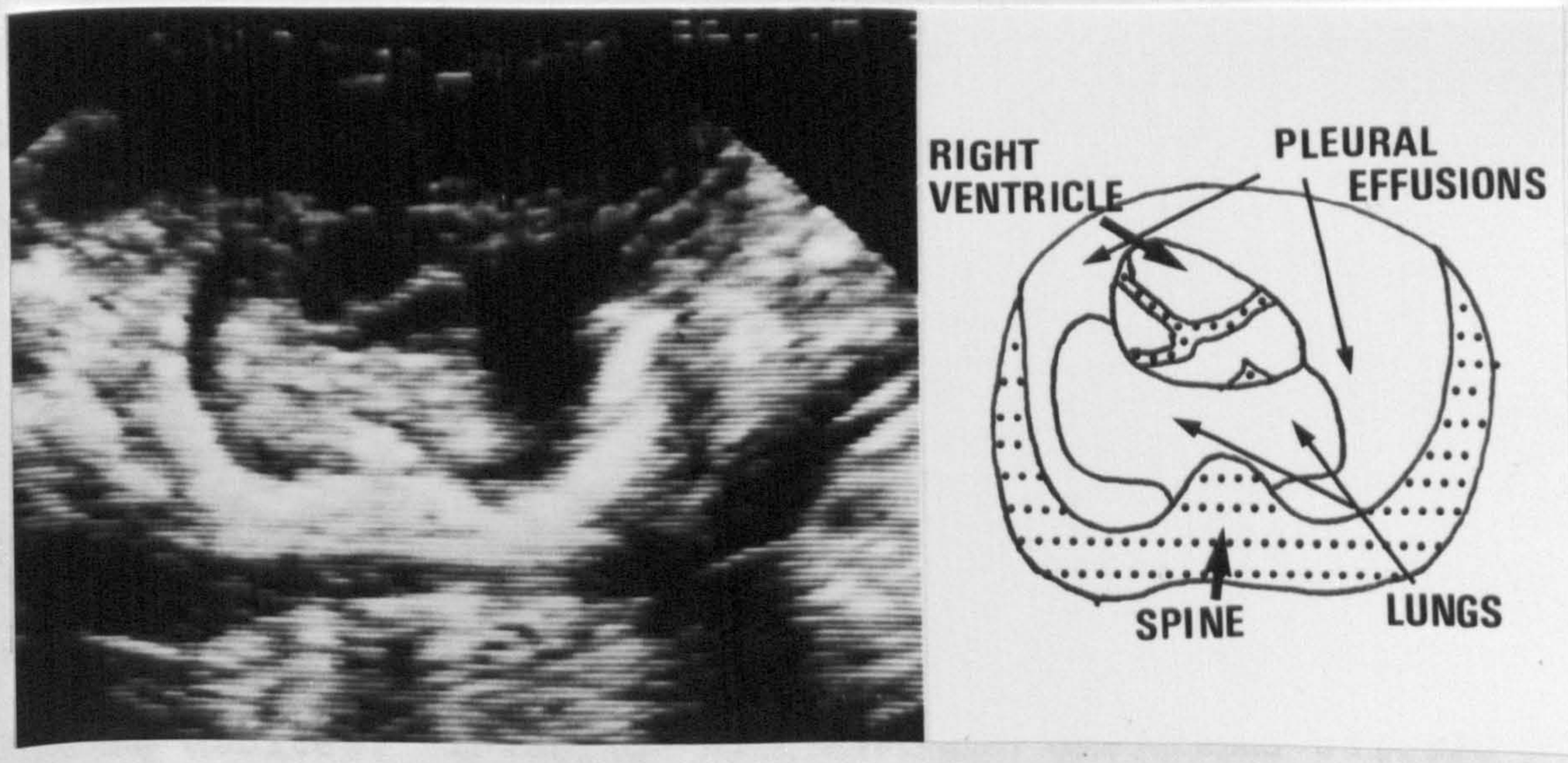
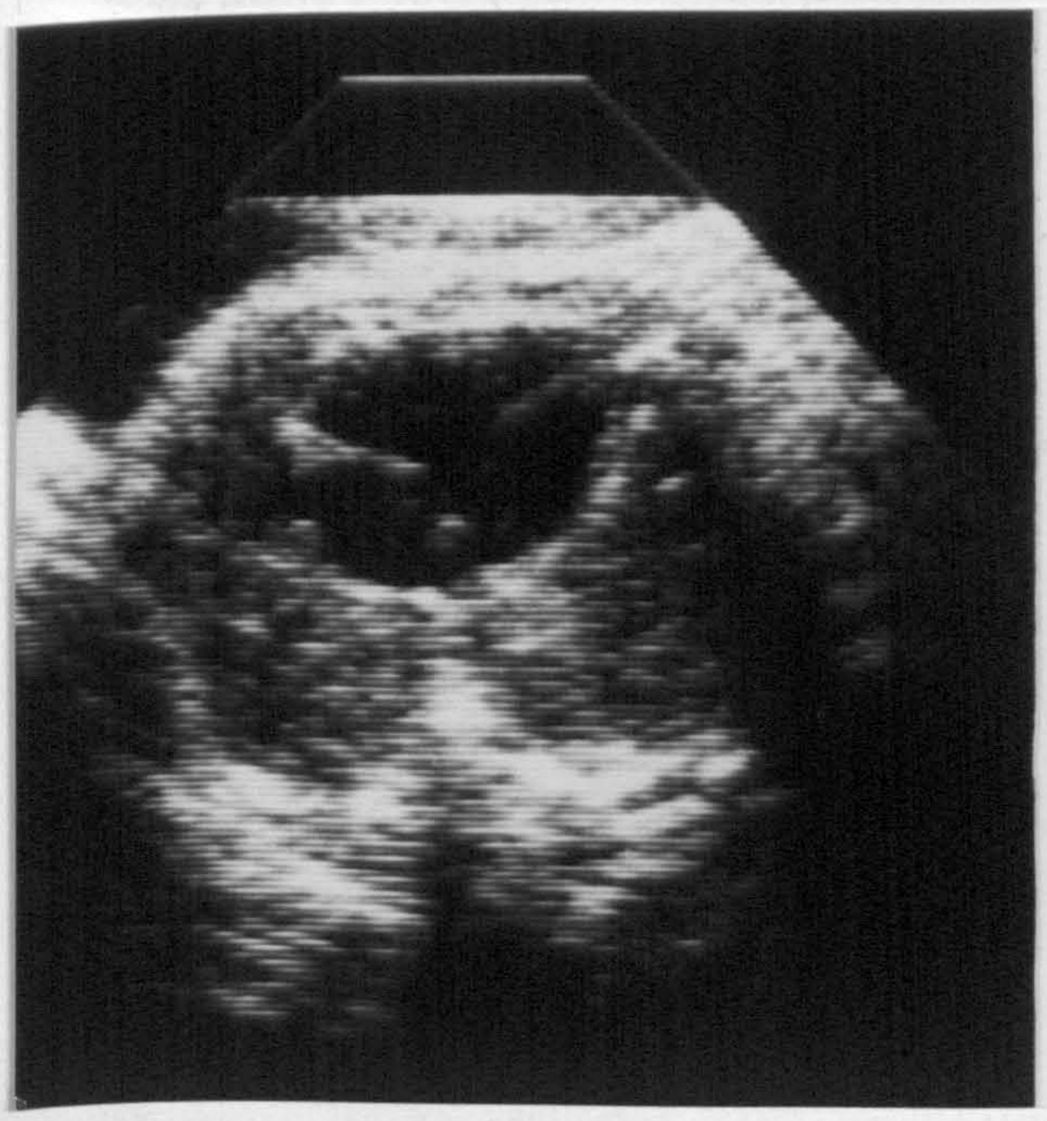


Figure 13.2. Case 13.2 The heart is again seen in the four chamber view. The right side is dilated and there are bilateral pleural effusions.

testing, including chromosome culture of the amniotic fluid, no cause of the fetal ascites could be detected. No other fetal organ could be seen to be abnormal. Intra-uterine death occurred at 27 weeks gestation. Autopsy discovered a monocytic leukaemia.

Case 13.2. Case 13.2 presented at 27 weeks gestation with gross fetal ascites. This case is illustrated in figure 13.2. The right ventricular dilatation was marked, the right ventricle having twice the internal diameter of the left. No structural abnormality of the heart could be seen. Bilateral pleural effusions could also be seen in this case. (Figure 13.2). This fetus showed large cystic hygromata on both sides of the neck. The diagnosis of Turner's syndrome was suspected, and the pregnancy was terminated. The diagnosis was confirmed by chromosome analysis of a fibroblast culture of the fetal specimen. Apart from the nonspecific right ventricular dilatation found echocardiographically, there were no other abnormal findings within the heart at autopsy.

Case 13.3, 13.4, 13.5. Three presented at 22,30 and 32 weeks respectively. There was marked fetal ascites and right ventricular dilatation in each. Despite thorough investigation, no cause could be found for either fetus having ascites. Investigation included chromsome culture



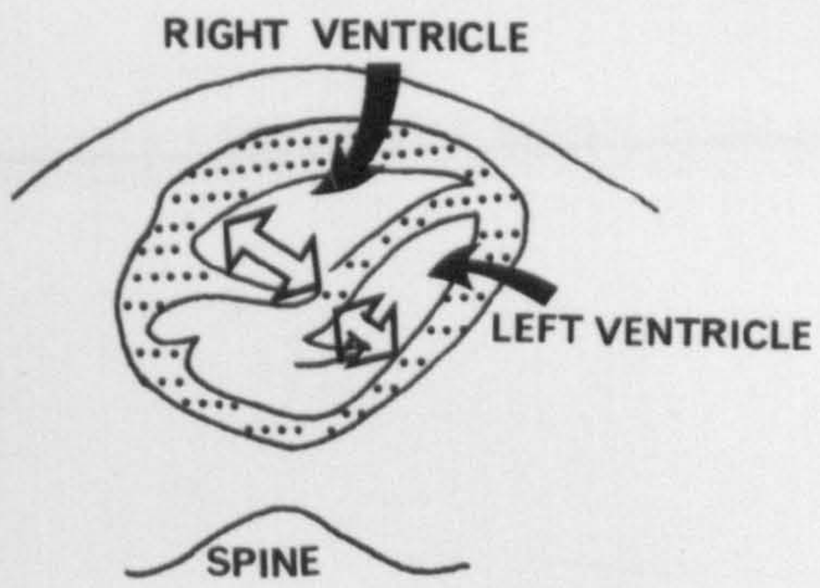


Figure 13.3. Case 13.7. The heart is seen in the four chamber projection with the spine posterior. The right heart is uniformly dilated.

of the amniotic fluid, bacteriological and viral screening, antibody testing, and in case 13.3, fetoscopy was performed. The only abnormality found in the fetal blood specimen was a marginally low serum albumin. A transfusion of albumin was given and regression of fetal ascites coincided with this. Fetoscopy was not performed in cases 13.4 or 13.5. All three cases appeared to be of the same severity and ran a similar course. The fetuses appeared otherwise normal. They were delivered close to term, by which time the ascites had completely resolved in Case 13.3, and almost completely in cases 13.4 and 13.5. The right ventricular dilatation decreased in parallel with the diminution of ascites. Postnatally no abnormality could be detected in any of the babies apart from mild dysmaturity.

Rhesus isoimmunisation. Cases 13.6 and 13.7. There were two cases known to have rh-isoimmunisation (Cases 13.6 and 13.7). Case 13.6 was first seen at 23 weeks gestation. The right ventricle was slightly dilated. An exchange transfusion was performed. Two weeks later, the right ventricle was more dilated and there was seen to be a rim of fetal ascites. Exchange transfusion was again performed. This sequence was repeated weekly until 28 weeks gestation, with fetal ascites reaccumulating more quickly each time after exchange transfusion. The size of the right ventricle was consistently twice the size of the left ventricle after the

development of fetal ascites. At delivery, at 28 weeks gestation, the haemoglobin was 5.4 gms. The right sided dilatation of the heart regressed after correction of the anaemia. Case 13.7. Case 13.7 presented at 35 weeks gestation with diminished fetal movement. The right ventricle was slightly dilated. The patient was found to have very raised anti-Rh antibodies. Twenty four hours later right ventricular dilatation was noted to have increased dramatically. This case is illustrated in Figure 13.3. No fetal ascites had as yet developed. The patient was delivered by caesarian section and the fetus was found to have a haemoglobin of 5 gms. After exchange transfusion, the baby's condition rapidly improved and the echocardiographic abnormalities resolved.

Placental Insufficiency: Case 13.8. One case, Case 13.8, presented at 28 weeks gestation with intrauterine growth retardation. On examination of the pregnancy there was oligohydramnios. The biparietal diameter and abdominal circumference measurements were below the 5th percentile for the gestational age. The fetus was noted to be immobile. The heart, however, was beating, though dilated and occupying more than one half of the fetal thorax. The enlargement seemed to involve all four cardiac chambers in the four chamber view. (Figure 13.4). Left ventricular function was

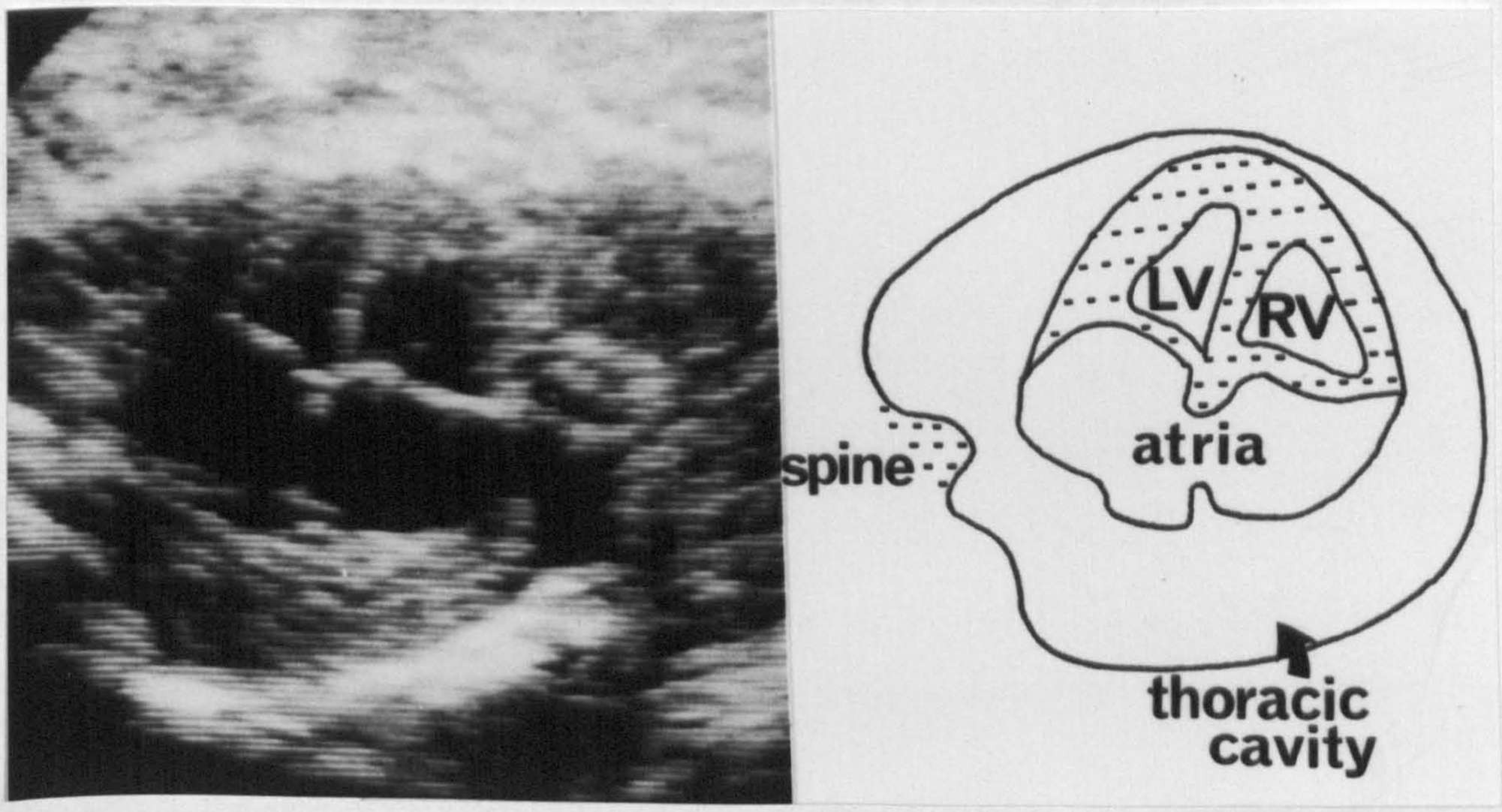


Figure 13.4. Case 13.8. The fetal heart is seen in the four chamber projection. The heart appears to occupy more of the fetal thorax than usual (c.f. e.g. Figure 12.5). Both ventricular chambers appear equally dilated.

decreased with poor posterior left ventricular wall movement. Shortening fraction was 16.6%, VCF 0.69 circ./sec. Twenty four hours later, no fetal heart beat was detected and delivery of the fetus was induced. Severe placental insufficiency was found. No structural abnormality of the fetus or of the fetal heart was found. This dilated, poorly functioning fetal heart was thought to be part of severe oxygen deprivation of the fetus, just prior to its death.

Unusual echocardiographic appearances probably representing normal variation

Papillary body: Cases 13.9, 10, 11, 12. These cases all showed identical appearances when studied initially at 22,24,19 and 19 weeks respectively. Each was followed closely during pregnancy and examined at least three times, the last time at around 36 weeks gestation. The appearance was of an intraventricular echogenic body within the cavity of the left ventricle (Figure 13.5). It seemed to be related to the papillary muscles of the mitral valve but in no case was the mitral valve thought abnormal on the two dimensional or M mode scan. Both the left ventricle and left atrium were a normal size in each case. Cases 13.9,10,11,12 have all been followed up postnatally. Case 13.12 is illustrated in Figure 13.6. The clinical examination postnatally, in

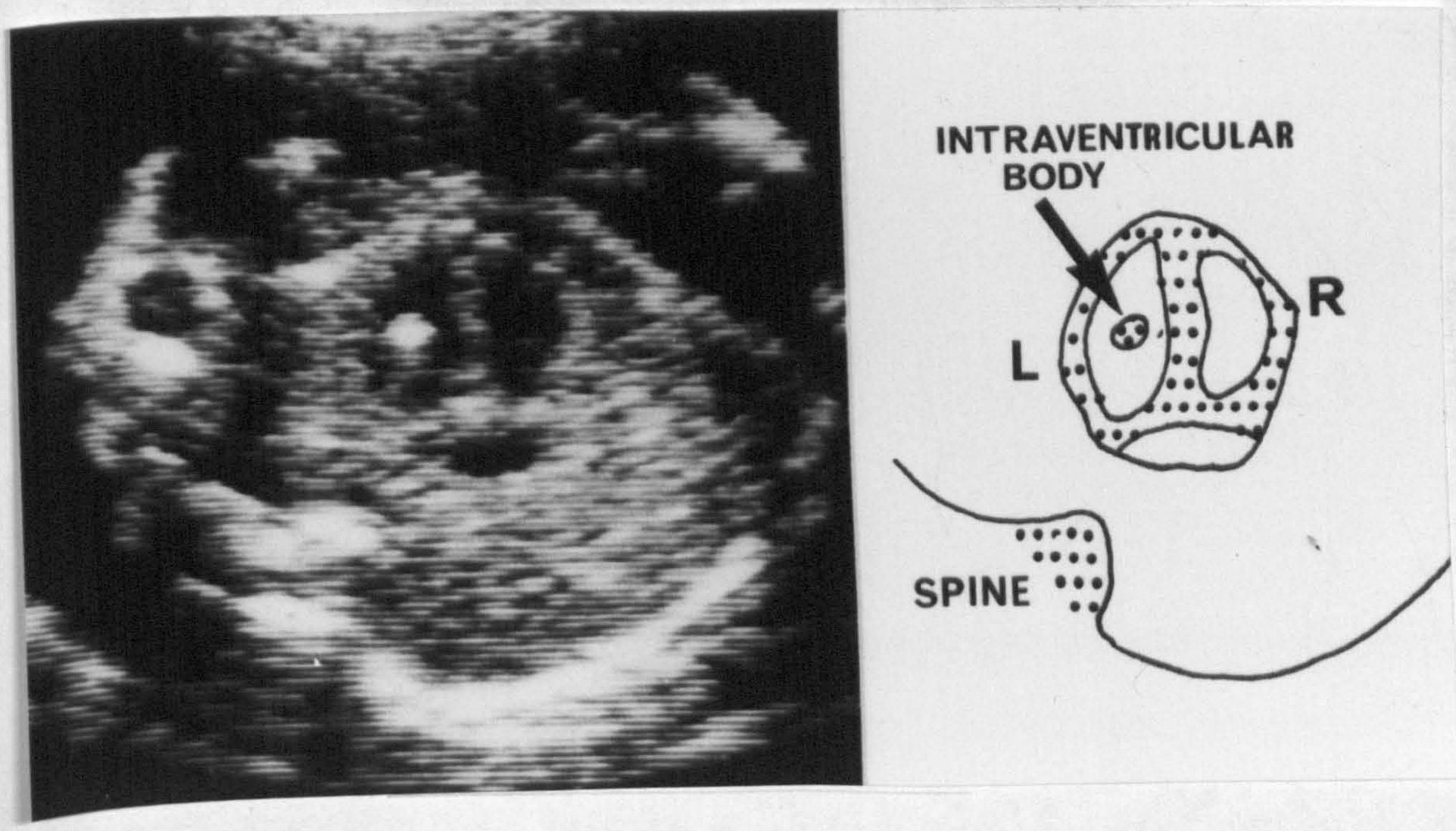


Figure 13.5. Case 13.9. The heart is seen in the four chamber projection at 22 weeks gestation. There is a densely echogenic structure within the cavity of the left ventricle. This was best seen in this projection but was visible in all views that visualised the left ventricular cavity.

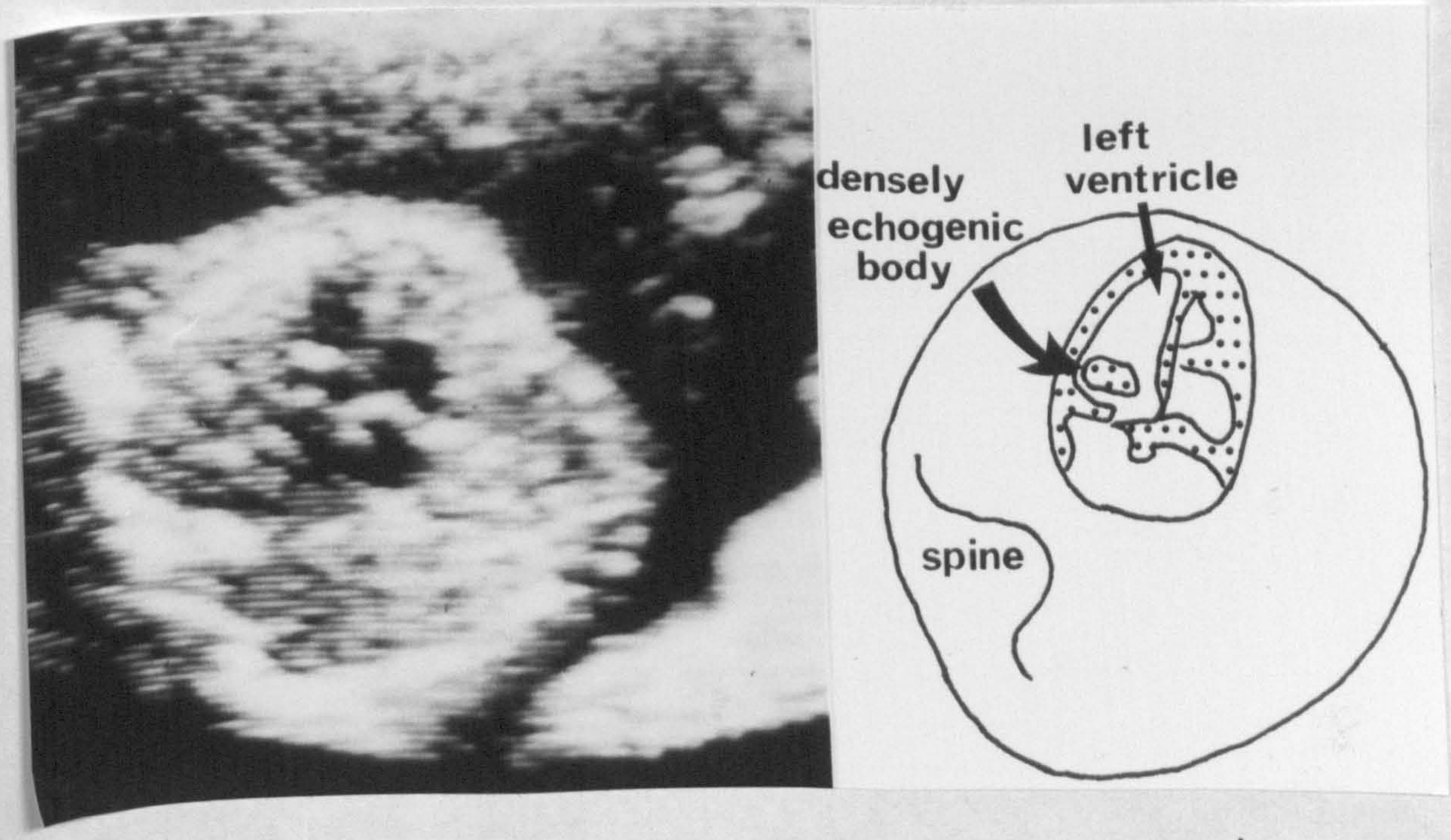


Figure 13.6. Case 13.11. An almost identical appearance as case 9 in a 19 week fetus. An echogenic body, that moved with cardiac motion was seen within the left ventricular cavity. There is no left atrial dilatation suggesting that this lesion does not appear to obstruct the mitral valve although closely related to it.

each case, was completely normal. The postnatal echocardiogram again demonstrated the echogenic body within the left ventricular chamber, and showed it to be related to one of the papillary muscles supporting the mitral valve. This finding is thought to represent a variation of normality, unassociated with functional disability.

Discussion

Case 13.1 had severe anaemia in association with a monocytic leukaemia and this is the probable cause of cardiac failure in this case. Cases 13.3,4 and 5 were all similar in their course and ultrasound findings; that is, they all presented with unexplained fetal ascites and associated cardiac signs, namely right heart dilatation. The echocardiographic findings all regressed in parallel with the fetal ascites. In each case a normal baby, although small for dates, was the outcome. It is thought that some form of intrauterine infection, perhaps viral, produced these findings, the infective event or fetal insult being expressed in the long term by growth retardation. The infection could have affected the heart causing right heart failure, which resolved, or alternatively the infection could have caused a severe anaemia or hypoalbuminaemia, which produced cardiac failure. This transitory fetal ascites has been described by other authors (181). Etches and Lemons,

reviewing 22 cases of non-immune hydrops, recorded seven cases of "idiopathic" hydrops (182). Kleinman (183) found no cases of idiopathic hydrops in his series of 13 cases and suggests that fetal tachycardia, undiagnosed, produces hydrops and subsequent fetal death. Autopsy in these cases would not elucidate this cause of fetal ascites. In one of our cases fetoscopy was performed. No anaemia was found although mild hypoalbuminaemia was present. An intrauterine transfusion of albumin was performed and regression of the fetal ascites coincided with this therapy but could have been unrelated. In the other two similar cases recovery occurred spontaneously. It may be that these three cases are not a homogeneous group. Right heart dilatation is not an invariable accompaniment of fetal ascites; five cases of fetal ascites have been seen where no cardiac signs were detected. It is thought that in these cases fetal ascites was secondary to some cause other than cardiac failure.

The cardiac signs are unexplained in Case 13.2 where right heart dilatation and fetal ascites were seen in association with Turners syndrome.

Case 13.6 and 13.7 where right heart dilatation was found in association with the severe anaemia of rhesus isoimmunisation seems readily explicable. In Case 13.6 the

recurring anaemia produced cardiac failure and fetal ascites. In Case 13.7 the pregnancy was interrupted before right heart failure could become established and thus before the signs of ascites had developed. It is quick and simple to measure and monitor right ventricular size in rhesus iso-immunisation and this may prove to have useful predictive value in relation to the degree of anaemia present. However rate of development of anaemia may also be an important factor in causing cardiac failure in this condition. Five further cases of rhesus isoimmunisation have been studied and followed. In once case the anaemia was more severe prior to each exchange transfusion than in either of the cases described above, that had cardiac signs. Despite this, neither right ventricular dilatation, nor ascites developed. In the other four cases the anaemia was less severe than Cases 13.5 and 13.6. Measurement of the right ventricular internal dimension may therefore give a useful, although not absolute guide, to the degree of anaemia present. Perhaps more importantly it may predict the ability of the individual fetus to tolerate anaemia. Variation in placental function and oxygenation may modify the ability of an individual fetus to tolerate anaemia. This hypothesis requires to be tested using larger numbers of cases but severe rhesus iso-immunisation inthis country is now a rare disease. It is interesting to note that cardiac failure in the fetus appears

to affect mainly the right ventricle. This observation has been made by other authors (184). It may be that the right ventricle is unable to withstand sudden changes in volume or pressure it is required to handle in utero and therefore fails preferentially. The right ventricle is more compliant than the left, particularly in fetal life (185).

In case 13.8, whole cardiac dilatation was seen just prior to fetal death from placental insufficiency. It is thought that this may be nonspecific sign of severe oxygen deprivation in the fetus. Signs of poor cardiac muscle function, expressed by decreased left ventricular functional measurements, are consistent with this hypothesis.

The last four cases demonstrate an unusual echocardiographic finding which could easily be wrongly interpreted by the inexperienced observer as representing a structural abnormality. The body seen within the left ventricular cavity is very densely echogenic. It could be mistaken for a cardiac tumor, the most common in children being a rhabdomyoma or fibroma. However rhabdomyoma are commonly multiple and always associated with tuberose sclerosis (186). The site of this body in the papillary muscle would be most unusual for a fibroma or myxoma. It would be very unlikely

to have seen four cardiac tumors in a series of 647 patients. Cardiac tumors form only 0.086 percent of heart disease in children (187). Tumor size might also change during pregnancy and cause some functionally observable effects. However, none has caused any functional disability or clinical signs on postnatal follow up.

In summary therefore, abnormal echocardiographic findings may indicate extracardiac disease. Where no primary cardiac cause can be detected to account for these echocardiographic appearances, disease elsewhere in the fetus, in the mother, or in the placenta, should be specifically sought. Where unusual echocardiographic appearances are seen with no apparent functional disability these should not be assumed to represent abnormality. The documentation of normal variation in the appearance of cross-sectional scanning is at an early stage in adults and children and this is even more so in the fetus.

CHAPTER 14

RESULTS:

Follow Up Studies

It was essential to include in the project follow-up studies which would allow assessment of the accuracy and reliability of prenatal echocardiography. The method of follow-up depended on the outcome of the pregnancy. It also depended on the initial reason for studying the pregnancy.

In every case in which there was an anatomical specimen, a determined attempt was made to obtain the specimen for study by the author and the same cardiac morphologist (RHA). Cooperation from pathologists was not always achieved and some specimens were not made available to us. In 12 of these the referring hospitals pathologist's report had to suffice. In 3 cases the heart was apparently not examined at autopsy and no report became available. Several patients were referred for fetal echocardiography or obstetric scanning from a long distance. In these cases also the local pathologists report was all that became available. In all the remaining cases in which an abnormality was suspected, and the fetus did not survive, the anatomical dissection was carried out in the presence of the author by the same morphologist (RHA), with the exception of case 11.2 as indicated in the text.

The method of follow-up in the surviving fetuses, the vast majority, falls into one of two categories. In all these patients, studied because of a family history of congenital heart disease, the babies were examined clinically and echocardiographically at around two months of age. The majority (96)were examined by the author and the same paediatric cardiologist (MJT); some (16) were examined by the paediatric cardiologist at other centres and a report sent. The remaining fetuses which had been studied echocardiographically were examined clinically by a paediatrician (477 cases) and no indication for further examination or echocardiography was thought to be present except in three cases. Cyanotic congenital heart disease was suspected in three cases in the immediate postnatal period but all were found to have a structurally normal heart on echocardiography. Table VIII summarises the number of patients in each group and the method of follow-up. The anatomical findings, in each case suspected of an abnormality, have been discussed throughout the text. False positives and false negatives and possible reasons for them have also been discussed at the appropriate part of the text. In no other case to date where the heart was thought to be echocardiographically normal was the surviving fetus found to have congenital heart disease.

It is acknowledged that some defects, even major defects, may have been overlooked by the paediatrician at immediate postnatal examination. Because of the number of pregnancies studied however, it was impossible to examine all the babies postnatally echocardiographically. The majority of severe congenital heart disease presents within the first six months or certainly the first year of life (188). The study has now been in progress for three years. No baby examined prenatally and judged to be normal has presented to the cardiac clinic at an older age. This is not an absolute guarantee that none has congenital heart disease but the antenatal catchment area for the two hospitals concerned should be the same area served by the paediatric cardiac clinic.

Throughout the text, deficiencies in the prediction of abnormalities have been stated and discussed. More complete and exact prediction of abnormality can only improve with greater experience of prenatal scanning coupled with thorough postnatal or anatomical correlation. The follow-up studies however, do suggest that the prediction of normality is reliable and accurate, once the appearance of the normal fetal heart is thoroughly understood.

TABLE VIII

		Number
Anatomical Follow-Up	Total	58
RHA and LDA		42
Others		16
Paediatric examination		477
Clinical & echocardiographic examination	Total	112
MJT & LDA		96
Others		16
Total no. of cases studied		647

Summary of abnormalities found in groups of pregnancies studied

During the three year period 647 pregnancies were studied. The number in each group of pregnancies and the abnormalities seen in each are summarised in Table IX. Two hundred normal pregnancies were studied initially to familiarise the author with normal cardiac anatomy. These subjects were randomly selected from the routine antenatal ultrasound clinic and no high risk factor was present. No structural cardiac anomalies were seen or are known to have been overlooked in this series. As described in the first part of this chapter the offspring of this group were examine postnatally by a paediatrician. Only three cases were thought to require further investigation, none was found to have heart disease, and no case has since presented although fetal echocardiography in this group took place over two years ago. A further 54 normal pregnancies were studied when the feasibility of M mode echocardiography was being assessed during the cross-sectional study.

The largest high risk group studied, 198 subjects, were those with a family history of congenital heart disease. In 186 of these, the mother had had a previous child with congenital heart disease, in 172 the previous child had not

survived. In three cases the family history of congenital heart disease was in a second degree relative. These were four cases of parental congenital heart disease, two maternal, two paternal. In three of the four patients where a parent had congenital heart disease surgical correction of the lesion had taken place in childhood; one mother had had a shunt procedure for cyanotic congenital heart disease to enable her to embark on the pregnancy. Four cases were referred because of Marfan's syndrome in a parent, one maternal, three paternal.

One hundred and sixty patients in this group were seen twice, initially at 18-20 weeks gestation. If picture quality was good, they were re-examined at 24-26 weeks. If picture quality was poor on the initial examination, re-study was at 21-22 weeks gestation. Twenty three patients in this group, were examined three times during their pregnancy. Of these, twenty were studied at the outset of the project and three examinations were performed to reassure the author that all structures had been adequately identified. Two cases, in which a V.S.D. was suspected early in pregnancy, were studied three times, the last examination being at 36 weeks gestation. In neither case was a defect seen at 36 weeks (See Chapter 11). In one further case adequate visualisation of the aortic arch had not been achieved in the early studies, and as the previous child had had

coarctation of the aorta restudy of the aortic arch took place at 36 weeks gestation and was normal. Fifteen patients were examined only once. In three cases of 20-21 weeks gestation, image quality was so good restudy was judged unnecessary. In three cases of over 28 weeks gestation picture quality was adequate and restudy judged unnecessary. Nine patients had been referred from too great a distance for restudy to be practical (Greece, Spain, Scotland, Ireland etc.) In seven of those picture quality was acceptable at the initial examination. In two cases the patient returned later on the same day by which time fetal movement had occurred and adequate pictures were obtained.

Four structural abnormalities were seen in the 198 patients with a family history of congenital heart disease; namely double outlet right ventricle with absent left atrioventricular connection (one), truncus arteriosus (one), atrioventricular septal defect and double outlet right ventricle (one) and left atrial isomerism with a ventricular septal defect in one.

The fetal heart was examined in 86 pregnancies complicated by maternal diabetes. All the patients were well controlled except one patient seen in late pregnancy. This patient had multiple premature ectopic beats and was

discussed in Chapter 12. Good diabetic control was established in most cases prior to conception and carefully monitored throughout pregnancy. All 86 patients were studied initially between 18-22 weeks gestation, when normal cardiac connections were identified. The patients were then restudied between 32 weeks gestation and delivery. At this second examination an M mode echocardiogram was recorded in addition to the cross-sectional study with particular attention paid to measurement of the ventricular septum and posterior left ventricular wall. In no case was a structural abnormality found.

Ten cases of fetal cardiac arrhythmia were studied and are discussed together in Chapter 12. Four showed irregularity of rhythm, one atrial flutter, one sinus bradycardia and four complete heart block. The case with sinus bradycardia and two of the cases with complete heart block showed structural cardiac abnormality.

Seventeen cases with fetal ascites were studied. Two were cases of rhesus isoimmunisation. In four cases structural cardiac malformation was seen; aortic stenosis (1 case) hypoplastic aortic arch (1 case) right ventricular hypertrophy (1 case) and a cardiac tumour (1 case). In thirteen of the seventeen cases, including both of those with immune hydrops fetalis, right ventricular dilatation was seen.

That the right ventricle appears to fail preferentially in utero, has been noted by other workers (189). In six cases of hydrops the heart was completely normal; the causes of hydrops in these six included intra thoracic tumor (1 case) cystic hygromata (2 cases) neck teratoma (1 case) a large encephalocoele (1 case) and listeria monocytogenes (1 case). In the five remaining cases of non-immune fetal hydrops the aetiology included leukaemia (1 case) idiopathic (three cases) cystic hygromata in Turner's syndrome (1 case).

Fifty eight cases were studied because an extra-cardiac fetal anomaly had been detected. This group included chromosomal anomalies (12 cases) renal anomalies (15 cases), neural tube defects (19 cases) omphalocoele (5 cases) gastrointestinal tract anomalies (4 cases) and limb reduction deformities (3 cases). Eight cardiac malformations were seen in this group; a primum atrial septum defect in a case of trisomy 21, a hypoplastic aortic arch in an XO fetus, tetralogy of Fallot in 2 cases of trisomy 18, tetralogy of Fallot in association with hydrocephalus and three cases of hypertrophic cardiomyopathy seen in association with renal anomalies.

Fifteen cases of intrauterine growth retardation were studied. In no case had an extracardiac abnormality been detected to account for poor growth. In only one case was

there an echocardiographic abnormality seen. This was whole heart dilatation with diminished left ventricular function. There was an intrauterine death in this case within 24 hours of the echocardiographic study.

Three cases were referred because the mother had been exposed to viral infection in early pregnancy, mumps (one case) and rubella (two cases). Mumps virus in early pregnancy is said to affect the fetal heart (190). The commonest effect of rubella virus on the heart is to damage the wall of the ductus arteriosus such that it does not close spontaneously on delivery (191). This would be impossible to predict prenatally as the ductus arteriosus is always seen. However, occasionally, rubella virus can cause more extensive cardiac damage (192). No abnormality was detected in any of these three cases.

Six cases were referred because of possible damage to the fetus by drug ingestion. The drugs were taken in the first twelve weeks of pregnancy and included lithium (two cases) oestrogens (2 cases) epanutin (one case) and a mixture of phenobarbitone and oestrogens in an overdose (one case). All were associated with an increased incidence of congenital heart disease (193). Lithium ingestion is particularly associated with Ebstein's malformation in the fetus (194). No cardiac abnormality was detected in this group.

Discussion

The numbers of subjects in each group of pregnancies studied are summarised in Table IX. The detection of cardiac abnormalities in each group are ennumerated. Some structural abnormalities detected had more than one "high risk" reason for study; for example, an extracardiac anomaly and ascites detected in the same fetus.

The finding of four cardiac abnormalities out of 195 cases where there was a first degree relative with congenital heart disease on the face of it seems to bear out the expected recurrence rate commonly quoted for congenital heart disease, of 2% (195,196). However, as 172 of the mothers had lost the previous baby this suggests that these siblings had more severe lesions. These tend to be complex and rarer lesions, and thus should have a lower recurrence rate than 2% (197). Three out of the four cases had atrial isomerism sometimes called asplenia or polysplenia syndromes, in the second sibling. In one case this was right isomerism, two cases left isomerism. In none of these cases was catheterization or autopsy data detailed enough on the first sibling, to ascertain atrial situs. It may be that these families were at a different risk from recurrence if both siblings had atrial isomerism. Both have been described in sibships (198) and some geneticists suggest a recessive form of

inheritance (199). In the fourth case, that of truncus arteriosus, the same anomaly had been present in the previous sibling. This has been described previously (200).

In the diabetic mothers, there was no evidence of hypertrophic cardiomyopathy in any of the fetuses in the last trimester of pregnancy. An increased incidence of structural cardiac abnormality (201) and signs of hypertrophic cardiomyopathy, have been described in the offspring of diabetic mothers (202). The incidence of fetal abnormality in maternal diabetes has been correlated with the adequacy of control (203). It is also suggested that the transient cardiomyopathy in the newborn is seen more commonly where there has been poor diabetic control in the last trimester of pregnancy (204). This may account for our failure to identify any abnormalities in this group.

Four cases of cardiac anomaly, seen out of 15 cases of non-immune hydrops is consistent with autopsy findings in hydrops fetalis. (205,206). Kleinman et al (1982) (207) found 10 structural cardiac anomalies out of 13 cases of fetal ascities. This may reflect a difference in the mode of referral between the two centres. Three of our cases were of idiopathic hydrops fetalis, a condition well described by other authors (208), but which Kleinman et al suggest is

is not a real entity. However, all of our three cases showed severe fetal hydrops in the midtrimester but all three babies survived, and no abnormality was found at birth. It is difficult to call this condition anything other than idiopathic hydrops.

Eight cases of structural cardiac anomaly were found in 58 cases with fetal extracardiac anomaly. This incidence will vary with the type of fetal anomaly studied. Autopsy studies show an increased incidence of heart malformation in fetuses with other anomalies, some abnormalities,such as chromosomal defects,being more strongly associated with congenital heart disease than others (209). Conversely,the incidence of associated abnormalities in patients with congenital heart disease lies between 25 (210) and 30 percent (211). It is interesting that three cases of hypertrophic cardiomyopathy were seen in association with renal anomalies. This condition has been described postnatally in patients with renal failure (212). It may reflect hypertension in the fetus producing a hypertensive cardiomyopathy mimicking the appearance of hypertrophic obstructive cardiomyopathy.

The lack of structural cardiac abnormalities in small-for-dates fetuses is not surprising. A recent study in Toronto found that the presence of congenital heart disease did not significantly affect the mean birth weight (213).

The one case, in which a dilated poorly functioning heart was found in a growth retarded fetus, was followed by intrauterine death within the next 24 hours. This cardiac appearance may have been secondary to fetal hypoxia.

In summary, the scattter of abnormalities found perhaps illustrates our present inadequate knowledge and misconceptions, rather than confirming accepted thinking. The genetic factors affecting the recurrence of congenital heart disease may be more complicated than current concepts suggest. Control of maternal diabetes may be a factor in prevention of congenital heart disease in these subjects. The dynamics of cardiac function and cardiac failure in utero are poorly understood at the present time, as the cases of fetal ascites and hypertrophic cardiomyopathy suggest.

TABLE IX

Group of pregnancy	No. of Subjects	No. of structural abnormalities detected.
Normal	254	None
Family history of CHD		
- previous child with CHD	186	4
- 2nd degree relative CHD	3	None
- Marfans syndrome in one parent	4	None
- One parent (of fetus) with CHD	4	None
- Total	198	4
Maternal diabetes	86	None
Fetal arrhythmia	10	3
Fetal ascites non-immune	15	4
Fetal ascites immune hydrops	2	None
Extracardiac fetal anomaly	58	8
Intrauterine growth retardation	15	1
Miscellaneous - drugs	6	None
Maternal mumps	1	None
Maternal rubella	2	None

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CHAPTER 15

DISCUSSION AND CONCLUSIONS

Summarised conclusions from the results

From the initial studies of the normal fetal heart in unselected pregnancies the echocardiographic description of normal cardiac connections was found to be feasible between 16 weeks gestation and term. Because of the differences in the extent of visualisation of the fetal heart, from the heart in postnatal life, and thus difficulties in interpretation of cardiac sections, validatory direct and indirect anatomical studies were performed. Some intrinsic anatomical differences, between the prenatal and postnatal heart, resulting from the differences in circulatory physiology, were observed on the echocardiogram. The cross sectional echocardiogram could be used to display the structural anatomy of the fetal heart, the cross-sectionally directed M mode beam providing further information concerning the normal heart. The M mode echocardiogram was used to define valve and chamber wall motion, for the acquisition of measurement data and the derivation of functional characteristics. It also proved possible to record the fetal electrocardiogram with the M mode tracing to time events within the cardiac cycle. During the course of the study of the fetal heart in 647 pregnancies, 41 abnormalities of cardiac structure or function were suspected. These cases are described in the

text. The discussion of each case includes the method of confirmation of each prediction and the accuracy of prediction. There were three false negative diagnoses and one false positive. In the remaining 602 pregnancies the fetal heart was correctly predicted to be normal. As the echocardiographic appearance of the normal fetal heart was found to be slightly different from the postnatal heart, so structural anomalies were not found to have echocardiographic appearances identical with those in postnatal life. Although a scatter of examples of congenital heart malformations have been seen by no means all anomalies of the heart are as yet described in fetal life. Further experience of detection of structural cardiac abnormality in the fetus will allow greater accuracy in prenatal prediction of anomalies, paralleling the improving accuracy and reliability of the echocardiogram in the diagnosis of congenital heart disease in paediatric practise. Improved selection of high-risk pregnancies and concentration of experience in a referral centre should optimise the accuracy of the technique. It may be some, potentially severe, congenital heart defects are not possible to visualise in early prenatal life; for example the thin membrane involved in discrete coarctation of the aorta may be impossible to detect allowing this diagnosis to be missed. Only further experience will confirm or deny this. The limitation of the technique that we have demonstrated is the inability to detect atrial or ventricular

septal defects in the small fetal heart. Such defects may become larger, and thus functionally significant, as the heart grows. However, advances in the resolution of ultrasound imaging techniques should improve the capability of defining smaller defects. At the same time this will allow the anatomy of smaller and younger hearts to be visualised, thereby extending the technique.

Future research areas

Firstly, the inheritance of congenital heart disease requires re-examination. It is probable that the mode of inheritance of most congenital heart disease cannot be homogeneously grouped as multifactorial, as is currently accepted thinking. Different forms of congenital heart disease may have different patterns of recurrence and therefore a different recurrence rate. Once a test for prenatal diagnosis is introduced, genetic counselling with accurate prediction for recurrence becomes more important. It is therefore essential that this field receives renewed attention.

Echocardiographic techniques allow the non-invasive investigation of cardiac function in utero, a field of study as yet undocumented in the human fetus. Some aspects of normal cardiac function are introduced here, but further investigation with other techniques, such as Doppler echo-

cardiography, or investigation of cardiac function in the non-resting state, are examples of future possible work. Cardiac function in labour or under stress conditions, during maternal drug therapy or during smoking, would be interesting to study.

The natural history of intrauterine arrhythmias is as yet unknown. The frequency of arrhythmias, whether they require treatment, whether they are related to unexplained intrauterine deaths, or the development of non-immune hydrops fetalis, whether they disappear spontaneously or are the precursor of postnatal arrhythmias, all require further investigation and experience.

These are some examples of possible areas of extension of research arising from the study. Doubtless many other ideas will occur to other workers once fetal echocardiography is recognised to be feasible and accurate.

The Potential application of fetal echocardiography

Up to the present time fetal echocardiography has been a specialised technique confined to a few individual workers and applied to selected high risk pregnancies. But increasing prenatal ultrasound scanning in routine obstetric cases

using continually improving methods of imaging is rapidly changing this fact. Once the ultrasonographer understands fetal cardiac anatomy it becomes possible to include the heart in a routine real-time cross-sectional investigation, and differentiate a heart that appears normal from the malformed heart. Within the last three years this peripheral screening "sieve" of ultrasonographers familiar with cardiac scanning has greatly expanded such that referrals from this, already screened population, have a high incidence of abnormality. This enables, not only a much larger antental population to be screened for congenital heart disease, but also concentration of experience of abnormality in a specialised centre. This is an ideal way of extending the technique which, it is hoped, will continue in the future.

The concentration of experience in a referral centre will not only be to increase accuracy of diagnosis but increase experience of the antenatal management of cardiac abnormalities. As discussed in Chapter One the main application of the technique is in the prediction of a defect allowing delivery of the infant in a specialised centre. This will avoid delay in diagnosis and the high morbidity and mortality in infancy associated with congenital heart disease. An important part of the antenatal management of a patient, in whom a fetal cardiac anomaly has been detected will include counselling, support and preparation for an affected infant. In the long term future, when the accuracy of echocardiography

has been more completely assessed in both prenatal and post-natal life, prevention of the birth of fatally or severely physically handicapped infants, by mid trimester termination of pregnancy, will become a further application of the technique. This is a controversial area, with difficult ethical considerations, which needs to be cautiously approached. Advice on the management of an affected pregnancy will be influenced by the individual defect present, with consideration given to the confidence limits of the particular diagnosis and can only be given by those routinely involved in the care of children with congenital heart disease. Only such a team of physicians and surgeons can accurately infer operability, morbidity and mortality based on the echocardiographic appearances of an anomaly. In summary, therefore, study of the fetal heart by echocardiography is an exciting technical advance which will have wide ranging implications to the future practise of paediatric cardiology, once greater experience has allowed a more complete assessment of the accuracy and reliability of fetal echocardiography.

APPENDIX I

SPECIFICATION OF FETAL ELECTROCARDIOGRAM

General System Specification:

Line voltage requirements	220 V AC RMS	(±10%)
Line frequency	59 Hx	
Line power consumption	< 15 VA	(max.)
Ambient temperature (operating)	10 - 40°C	
Integral power lead length	3 m	
Electrical instrument class type	II B (HTM8), IICF(BS5724)	

Preamplifier Functional Specification:

Frequency response (DC mode, -3dB)	DC - 10 kHZ	
(AC mode, -3dB)	1 Hz - 10 kHz	
Gain (G) nominal	1000	
Common mode rejection ratio (G=1000, R_s=0,F=50Hz)	100dB	(min.)
Differential input impedance	100 Mohm	(min.)
Common mode input impedance	100 Mohm	(min.)
Differential input range	± 10/G V	(max.)
Common mode input range	± 10 V	(max.)
Output impedance	560	(nom.)
Offset voltage	20 mV	(max.)
Noise 1 Hz - 10 kHz	10 µV RMS	(typ.)
1 Hz - 1 kHz	3 µV RMS	(typ.)
1 Hz - 100 Hz	1 µV RMS	(typ.)

Filter Unit Specification:

Gain (variable)	0 - 10	(nom.)
Frequency response (normalised, OdB at 100Hx) TO 1 Hz	+24dB/octave	(nom.)
1 Hz to 100 Hz	+6dB/octave	
100 Hz to 250 Hz	-12dB/octave	
250 Hz to 10 kHz	-18dB/octave	
49.5 Hz to 50.5 Hz	-20dB	(min.)

Calibration signal		
Pulse repetition frequency	300 p.p. min	(nom.)
Pulse width	40mS	(nom.)
Pulse amplitude (referred to input of pre-amp)	12mV	

Safety Specification:

Isolation voltage (input to output)		
Continuous	2 kV	(pk.)
Non-repetitive (10mS)	5 kV	(max.)
Input connector leakage current		
250 V RNS supply	10 μ A	(max.)

Dimensions (each unit);

Case size (W x H x D)	205 x 75 x 140 mm	(approx.)
Materials (excluding front and back panels)	High Impact ABS	
Front and back (pre amp)	Plastic laminate	
Front and back (filter unit)	Brushed aluminium alloy	
Weight	1.5 Kg.	(max.)

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