Ultrasound Obstet Gynecol 2002; **20**: 142–153

Clinical implications of fetal magnetocardiography

H. W. P. QUARTERO*, J. G. STINSTRA†, E. G. M. GOLBACH*, E. J. MEIJBOOM‡ and M. J. PETERS†

**Department of Obstetrics and Gynecology, Medisch Spectrum Twente, Enschede, †Faculty of Applied Physics, Institute for Biomedical Technology University of Twente, Enschede and ‡Pediatric Cardiac Center and Department of Obstetrics and Gynecology, University Medical Center Utrecht, the Netherlands*

KEYWORDS: Congenital heart defect, Fetal arrhythmia, Fetal magnetocardiography, M-mode ultrasound

ABSTRACT

Objectives *To test the usefulness and reliability of fetal magnetocardiography as a diagnostic or screening tool, both for fetuses with arrhythmias as well as for fetuses with a congenital heart defect.*

Methods *We describe 21 women with either a fetal arrhythmia or a congenital heart defect discovered during prenatal evaluation by sonography. Four fetuses showed a complete atrioventricular block, two an atrial flutter, nine ventricular extrasystole, and one a complete irregular heart rate. Five fetuses were suspected to have a congenital heart defect. In all cases magnetocardiograms were recorded.*

Results *Nine fetuses with extrasystole showed a range of premature atrial contractions, premature junctional beats or premature ventricular contractions. Two fetuses with atrial flutter showed typical flutter waves and four fetuses with complete atrioventricular block showed an uncoupling of P-wave and QRS complex. One fetus showed a pattern suggestive of a bundle branch block. In three of four fetuses with confirmed congenital heart defects the magnetocardiogram showed abnormalities.*

Conclusion *Fetal magnetocardiography allows an insight into the electrophysiological aspects of the fetal heart, is accurate in the classification of fetal arrhythmias, and shows potential as a tool in defining a population at risk for congenital heart defects.*

INTRODUCTION

The diagnosis of fetal arrhythmias and congenital heart defects (CHDs) has gradually improved and is currently performed with sonography, including three-dimensional imaging and Doppler echocardiography. The atrial contraction rate can be determined by means of M-mode echocardiography, while the ventricular contraction rate can be determined with the use of M-mode and/or echo Doppler[1]. These techniques have allowed the study of the structure of the fetal heart and the evaluation of rate as well as rhythm based on the mechanical performance of the heart. However, the actual electrophysiological phenomena are not directly recorded. Fetal electrocardiography by means of electrodes attached to the maternal abdomen is not always feasible, the signal-to-noise ratio is poor and it is impossible to distinguish the P-wave in the time traces, which complicates the precise interpretation of the signals[2]. Over the last decade magnetocardiography has been applied to obtain electrophysiological information in adults, but also in the fetal setting. A fetal magnetocardiogram (MCG) is a recording of the magnetic field generated by the electrical activity of the fetal heart. As it is generated by the same sources as the electrocardiogram (ECG), the heart complexes will have the typical waveforms found in ECGs, such as the P-wave and the QRS complex. Fetal magnetocardiography can be used for the detection and classification of arrhythmias, such as the detection of supraventricular and ventricular ectopic beats, brady- and tachycardias, and the classification of atrioventricular (AV) blocks[3–6]. Moreover, fetal magnetocardiography can be used for the diagnosis of a prolonged QT-syndrome[7,8]. One case study has been reported of a fetus with a CHD, namely ectopia cordis[9].

METHODS

Twenty-one women were recruited to the study. Diagnosis of fetal arrhythmia or CHD was made by ultrasound. Sixteen fetuses showed an arrhythmia: two an atrial flutter, four a third-degree AV block, nine ventricular extrasystole, and one a completely erratic pattern associated with caffeine abuse. Five fetuses had a suspected CHD: one a hypoplastic left heart, one endocardial fibroelastosis with critical aortic stenosis, one an atrioventricular septal defect (AVSD) with transposition of the great arteries, one an AVSD, and one fetus showed an abnormal position of the apex and asymmetrical four-chamber view, but without a clear structural defect. Hydrocephaly was also present.

Correspondence: Dr H. W. P. Quartero, Department Ob/Gyn, Medisch Spectrum Twente, POB 50000, 7500 KA Enschede, the Netherlands (e-mail: h.quartero@interstroom.nl)

Presented at The Fetal Medicine Foundation's meeting on Research and Developments in Fetal Medicine, London, August 30th–September 1st 2001.

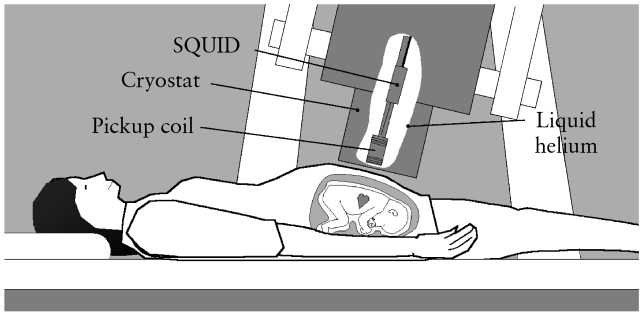

Figure 1 Experimental set-up: woman in supine position beneath the magnetometer system.

The fetal MCG is recorded from just outside the maternal abdomen. Usually, the component of the magnetic field that is perpendicular to the maternal abdomen is recorded with the mother in the supine position underneath the magnetometer. As the magnetic field generated by the fetal heart has an extremely low magnitude, special sensors that have to be cooled by liquid helium are required for the detection of these fields. The helium is contained in a vessel (cryostat), which is positioned a few cm above the maternal abdomen. The technique is non-invasive and carries no risk. The experimental set-up is depicted in Figure 1.

Fetal MCG measurements were carried out in a magnetically shielded room using a custom-made 19-channel magnetometer system. In fetal MCG recordings, activity generated by both the maternal heart and the fetal heart is present. To allow differentiation of the maternal heart signal from that of the fetus, a maternal ECG was recorded simultaneously. After identifying the maternal signal in the MCG trace, the maternal signal was averaged (i.e. individual complexes were aligned along their R-peaks, summed, and divided by the number of complexes) and the averaged MCG maternal complex was subtracted from the fetal MCG recordings. In the fetal MCG time traces, the time instants of the individual fetal R-peaks were used to determine the fetal heart rate and to construct an average fetal complex. From these averages the duration of the various waves was obtained.

Our reference range can be viewed on the Internet (http://bct.tn.utwente.nl/database).

The hospital's ethics committee approved the research in accordance with the Helsinki guidelines. Fetal MCGs were measured following written and informed consent from the mother. No adverse effects in mothers or fetuses were encountered. Fourteen of the 21 patients will be discussed in detail.

RESULTS

Complete atrioventricular block

Four women with a pregnancy complicated by a complete AV block were studied. The first (Patient A) was referred in the 27th week of pregnancy with a persistent bradycardia. With ultrasound a complete AV block was diagnosed and Sjögren syndrome-B (SS-B) antibodies were found. Fetal MCGs were measured in week 35 of gestation. After subtraction of the maternal complexes, fetal QRS complexes and P-waves could be observed. In Figure 2a, the ventricular and atrial contraction rates over a 100-s period are shown during which an abrupt change in both rates occurred. In the first period of 40 s, the P-waves and QRS complexes were coupled with a mean RR interval of 784 ms (77 bpm) and a mean PP interval of 397 ms (152 bpm), suggesting a two to one block (Figure 3a), whereas during the next 60 s, they were uncoupled with an entirely irregular PR interval, suggesting complete AV block (Figure 3b). The averaged signals were calculated using the R-peak for the alignment of the complexes. Figure 4 shows the averaged complexes. When a P-wave was found in the averaged signal, it was concluded that the P-wave and R-peak were coupled in time. Note that two P-waves were found, one preceding the QRS complex and

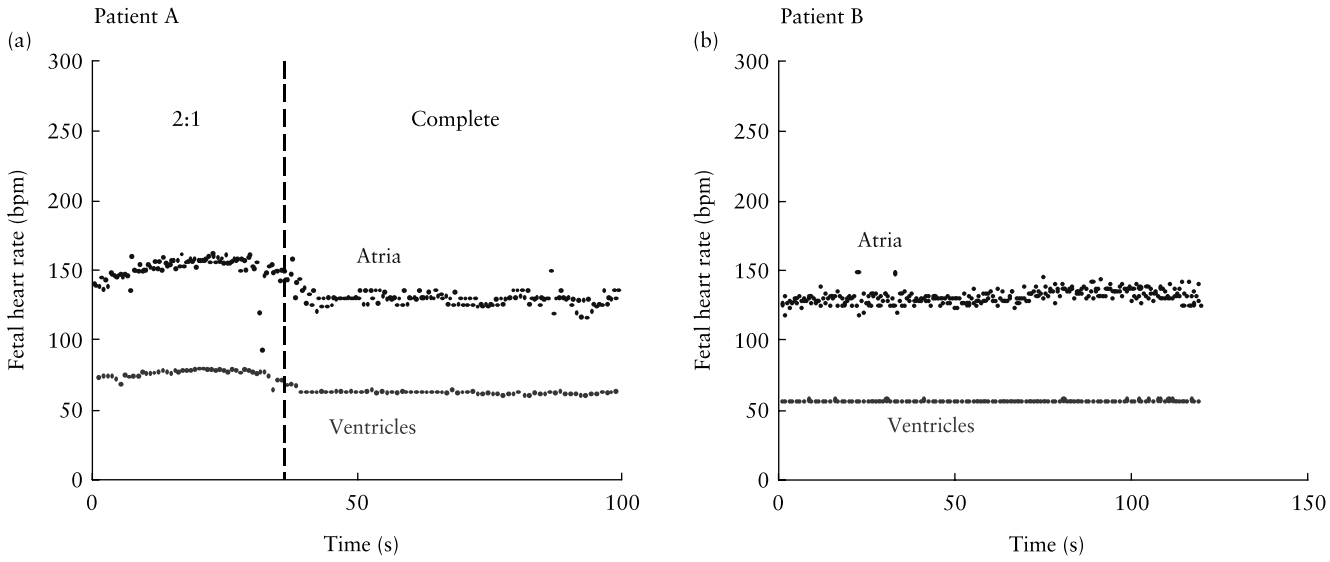

Figure 2 Fetal heart rate of Patient A at 35 weeks' gestation (a) and Patient B at 31 weeks' gestation (b). Note how in Patient A the rate changes abruptly; during the first 40 s the AV block is second degree and in the next 60 s it is a complete AV block.

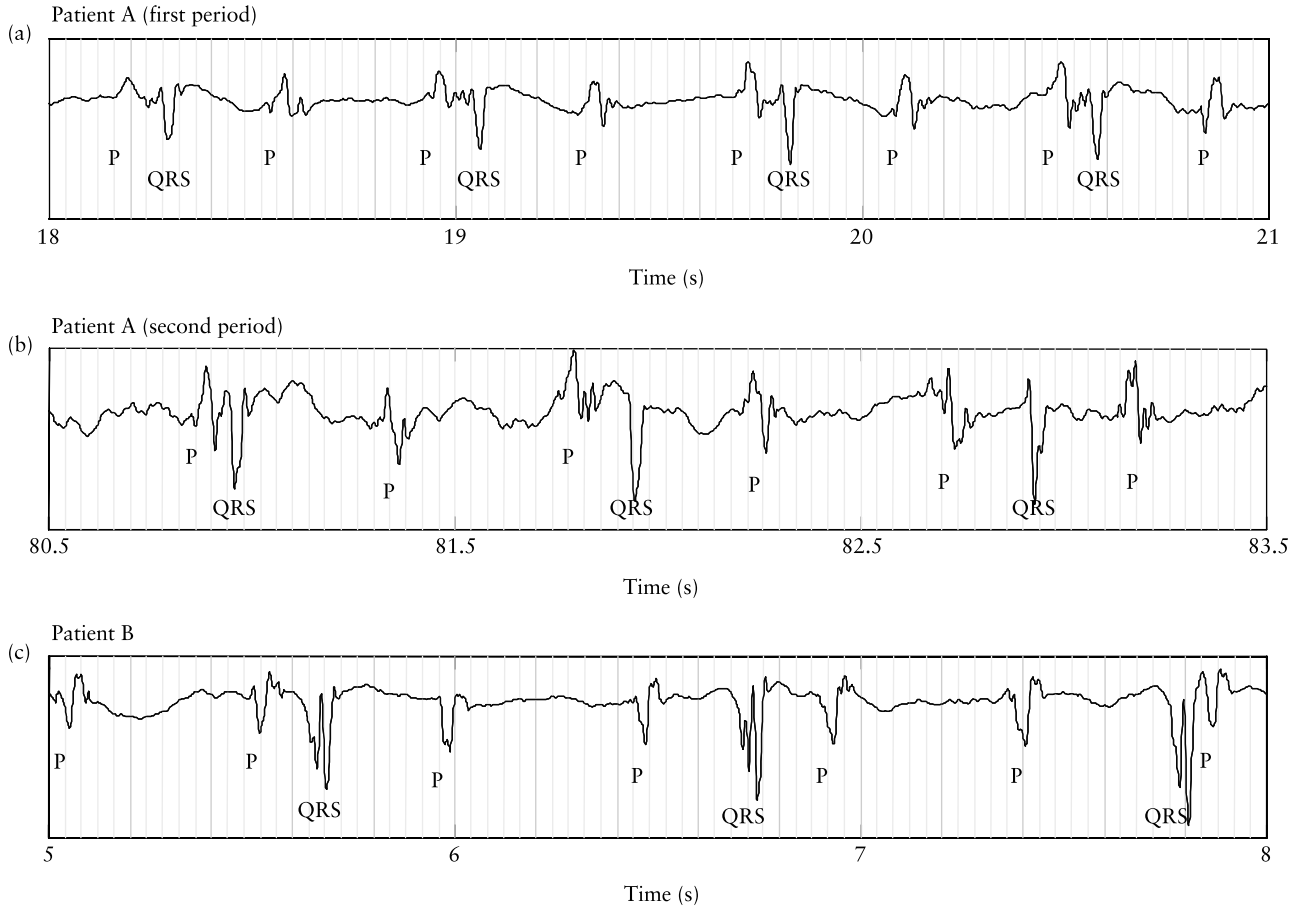

Figure 3 Magnetocardiogram time traces of two fetuses after band-pass filtering and subtraction of the maternal signal. The P-waves and QRS complexes are indicated. Shown are traces of Patient A at 35 weeks during a period of a second degree AV block (2 : 1) (a) and during a complete AV block (b), and of Patient B at 31 weeks (c).

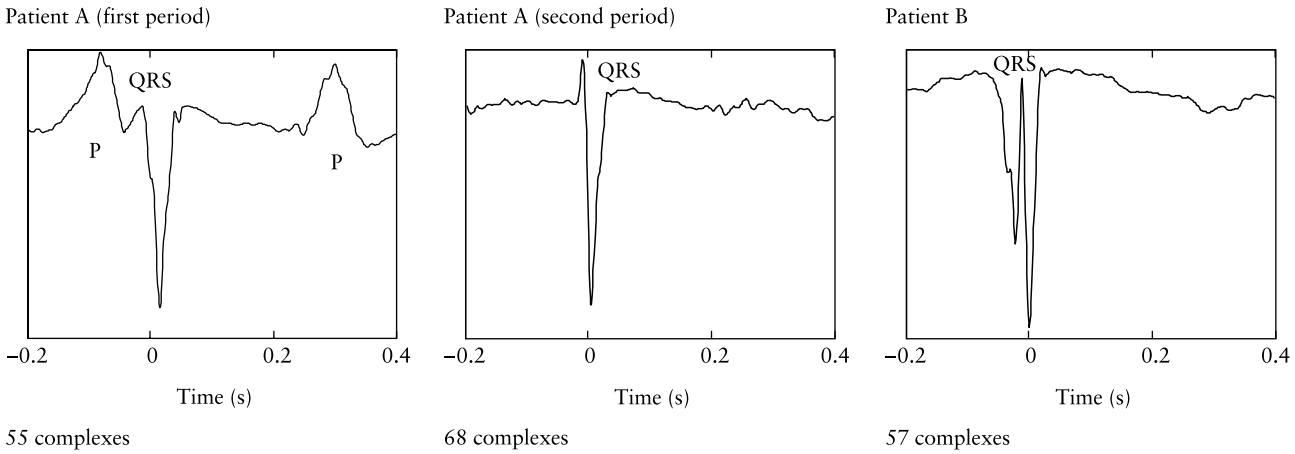

Figure 4 Averaged fetal magnetocardiogram traces from Patient A in a period of second degree AV block (a) and complete AV block (b); note that in (a) a P-wave is present in the averaged signal, because it is coupled to the QRS complex, while in (b) the P-wave is not present in the averaged signal, because it is not coupled in time to the QRS complex. (c) shows the averaged trace from Patient B. The number of complexes taken for each average is as indicated below the trace.

one following it, clearly showing the presence of two P-waves for each QRS complex. When no P-wave was found, it was concluded that the P-wave and R-peak were uncoupled in time. Figure 2 shows the fetal heart rates. The fetal heart rate shows the abrupt change from a second degree (2 : 1) to a complete AV block. The change in AV conduction coincided with a change of the ventricular rhythm from 77 to 62 bpm. A similar change in atrial depolarisation rate was observed from 152 to 130 bpm. The variability of the ventricular contraction rate was less than that of the atrial contraction rate. The atrial variability showed a larger variability during the second-degree AV block. The duration of the QRS complex

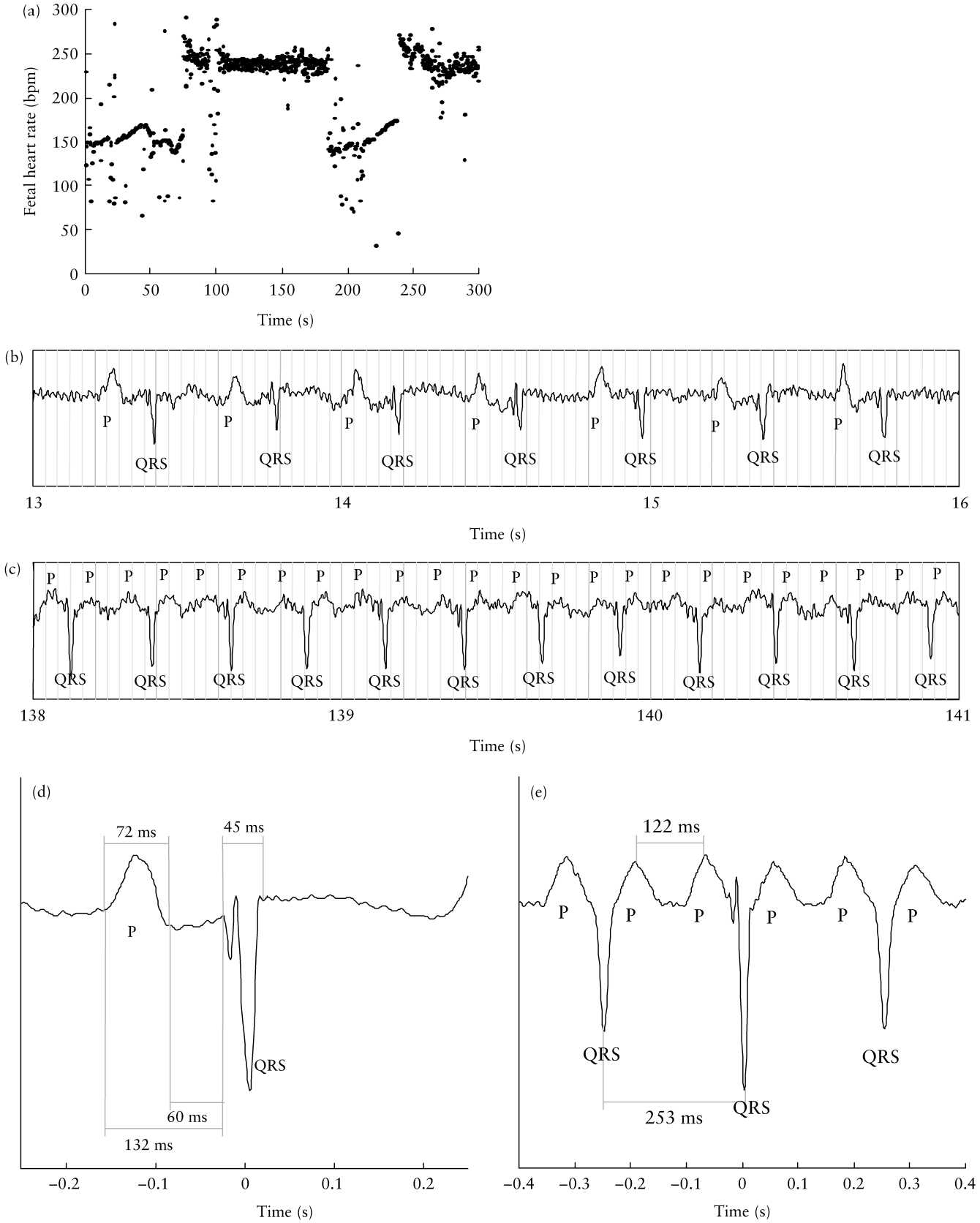

Figure 5 Magnetocardiographic results of a fetus diagnosed with periods of atrial flutter, measured in the 36th week of gestation. In (a), the fetal heart rate shows periods of 150 bpm (normal sinus rhythm) and 250 bpm (atrial flutter). The fetal magnetocardiograms were recorded during a period of sinus rhythm (b) and during a period of atrial flutter (c) and averaged during sinus rhythm (d) and atrial flutter (e).

was 58 ms and the duration of the P-wave was 85 ms during the period with a complete AV block; the duration of the QRS complex was 53 ms and that of the P-wave was 65 ms during the 2 : 1 AV block. The neonate was delivered at a gestational age of 38 weeks and a complete AV block was confirmed by means of ECG. The postnatal condition was good: the atrial pace was 136 bpm and the ventricular pace was 64 bpm. No postnatal pacing was required.

Patient B, with systemic lupus erythematosus, was referred in her third pregnancy. Her first child was delivered with a complete AV block having a ventricular contraction rate such that a pacemaker was not required. In her current pregnancy, ultrasound showed a complete AV block. Fetal MCGs were recorded in week 31 of gestation. Again it was possible to detect both the P-waves and R-peaks (Figure 3c). The P-wave was notched and had a duration of 71 ms and the atrial depolarisation rate varied between 120 and 150 bpm with an average of 131 bpm. The duration of the QRS complex was 75 ms and it showed several notches. The ventricular depolarisation rate was very stable at a rate of 56 bpm. After delivery at 38 weeks of gestation, a complete AV block was confirmed, with an atrial depolarisation rate of 121 bpm and a ventricular depolarisation rate of 50–60 bpm. A pacemaker was applied in the first week of life.

The third patient (Patient C) was diagnosed with a complete AV block in week 25. SS-A antibodies were found. Fetal MCGs were measured repeatedly, in weeks 25 and 27 of gestation. In the MCGs recorded in the 25th week of gestation, only a few P-waves were recognizable. From their position in relation to a neighboring QRS complex, it could be concluded that the PR interval was irregular. It was not possible to average sufficient P-waves and to determine the depolarisation rate of the atria. The QRS duration was 54 ms and the ventricular depolarisation rate 62 bpm. Fetal MCGs measured in week 27 showed clear P-waves. The ventricular depolarisation rate varied between 55 and 65 bpm and the atrial depolarisation rate was 138 bpm. As the pace of the waves was independent, the diagnosis of a complete AV block could be confirmed. The P-wave had a duration of 63 ms and the QRS complex a duration of 50 ms. At 40 weeks of pregnancy the neonate was delivered in a good general condition. A postnatal ECG confirmed the diagnosis of a complete AV block, with a ventricular depolarisation rate of 65 bpm. No pacemaker was required.

The fourth pregnancy with a complete AV block was measured by magnetocardiography in week 34 of gestation. The mother had Sjögren's syndrome and SS-A and SS-B antibodies were found. From the fetal MCGs the atrial depolarisation rate was determined to be 100 bpm, a ventricular depolarisation rate of 45 bpm, and a duration of the P-wave of 89 ms, being clearly prolonged. Postnatally a pacemaker was required.

Atrial flutter

Two cases of atrial flutter were studied by means of fetal magnetocardiography. In the first case, episodes of tachycardia were discovered in the 36th week of pregnancy during a routine prenatal evaluation. Ultrasound analysis showed no evidence of fetal structural anomalies, particularly no cardiac anomalies. Thus far, the pregnancy had been uncomplicated. An atrial contraction rate of 400 bpm was observed and a ventricular contraction rate of 280 bpm. No signs of congestive heart failure or fetal hydrops were noticed. Fetal MCGs were obtained in weeks 36 and 37 of gestation. The data presented in Figure 5 are from the 36th week. The fetal heart rate (Figure 5a) was irregular, showing episodes of a ventricular pace of about 150 bpm as well as abrupt changes to episodes of 240 bpm. Examples of fetal MCG time traces with a length of 3 s recorded during different episodes are given in Figures 5b and c. The first trace (Figure 5b) shows the MCG during an interval when the heart rate was about 150 bpm. The second (Figure 5c) was recorded during a period with a heart rate of about 240 bpm. The averaged fetal MCG recorded during an episode of tachycardia (Figure 5e) shows waves that are typical for atrial flutter. For each QRS complex two P-waves can be seen (2 : 1 AV block) with a mean RR interval of 253 ms and PP interval of 122 ms. The first and third QRS complexes shown are seemingly smaller than the middle one. However, this is due to the averaging procedure and can be explained by the fact the RR interval was not perfectly regular during this episode of atrial flutter. The average calculated during the episode of normal sinus rhythm is shown in Figure 5d. From this figure it follows that neither atrial flutter waves nor a 2 : 1 AV block were present.

At 39 weeks of gestation a healthy neonate was delivered with a regular sinus rhythm alternated with episodes of atrial flutter and a 2 : 1 AV block. The ventricular rhythm varied between 200 and 250 bpm. The infant was treated with 8 mg tds sotalol and the episodes of tachycardia diminished. Finally the patient had a sinus rhythm of 130 bpm. A small cerebral infarction was noticed on postnatal cerebral ultrasound.

The second case was referred to the hospital in the 29th week of gestation with a 2-day history of vaginal bleeding. Ultrasound evaluation showed no placental pathology, but did show episodes of fetal tachycardia (230 bpm) alternating with episodes of bradycardia (70–80 bpm). There was neither evidence of fetal structural anomalies nor obvious signs of fetal hydrops or congestive heart failure. The pregnancy had been otherwise uncomplicated. Treatment with 80 mg tds sotalol was initiated, resulting in a fetal heart rate of approximately 114 bpm as established by ultrasound. Unfortunately, episodes of tachyarrhythmia recurred intermittently. Fetal MCG was performed at 32 weeks of gestation. The results are shown in Figure 6. The fetal heart rate during a period of 120 s (Figure 6a) showed an RR interval of about 270 ms (220 bpm) intermittently interrupted by an RR interval of 510 ms (110 bpm). In Figure 6b, a time trace of the fetal MCG is shown. An averaged fetal MCG is shown in Figure 6c based on those complexes that had an RR interval of 270 ms between three consecutive R-peaks. From this figure one can conclude that an atrial flutter was present with a 2 : 1 AV block. The duration of a flutter wave is more than 1.5 times the duration of a P-wave found in uncomplicated pregnancies[10]. The duration of the QRS complex was difficult to estimate due to the overlap of P-wave and QRS complex, but amounted to 67 ms, which is prolonged[11]. In Figure 6d, an averaged fetal MCG is shown

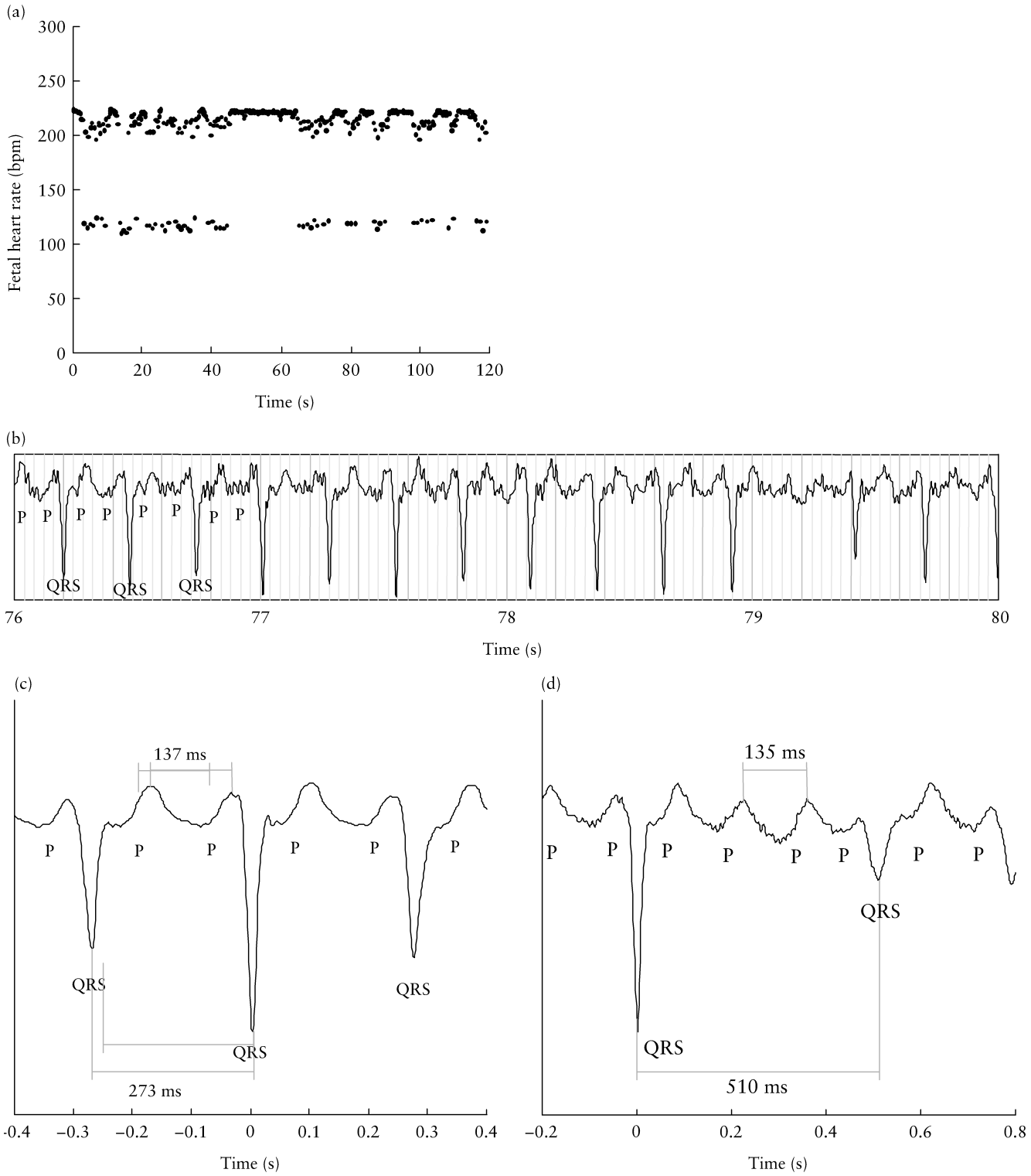

Figure 6 Magnetocardiographic results of a fetus diagnosed with periods of atrial flutter, measured in the 32nd week of gestation. (a) shows the fetal heart rate during atrial flutter; the beats of about 120 bpm correspond to a 4 : 1 AV block and the others to a 2 : 1 AV block. Also shown are the fetal magnetocardiogram (b), and the averaged fetal magnetocardiogram during a period of atrial flutter with a 2 : 1 AV block (c) and during a period of atrial flutter with a 4 : 1 AV block (d).

based on complexes with an RR interval between the previous R-peak and the present one of 270 ms and an RR interval of 510 ms between the present R-peak and the next one. In this figure a 4 : 1 AV block is seen.

At 36 weeks of gestation the neonate was delivered with an atrial flutter. The atrial depolarisation rate was more than 400 bpm and a 2 : 1 AV block was observed. The child was treated with sotalol and digoxin after which normal sinus rhythm was restored for most of the time; however, daily periods of tachycardia were still observed. At the age of almost 3 years, the atrial flutter switched to an AV re-entrance tachycardia. During electrophysiological examination a

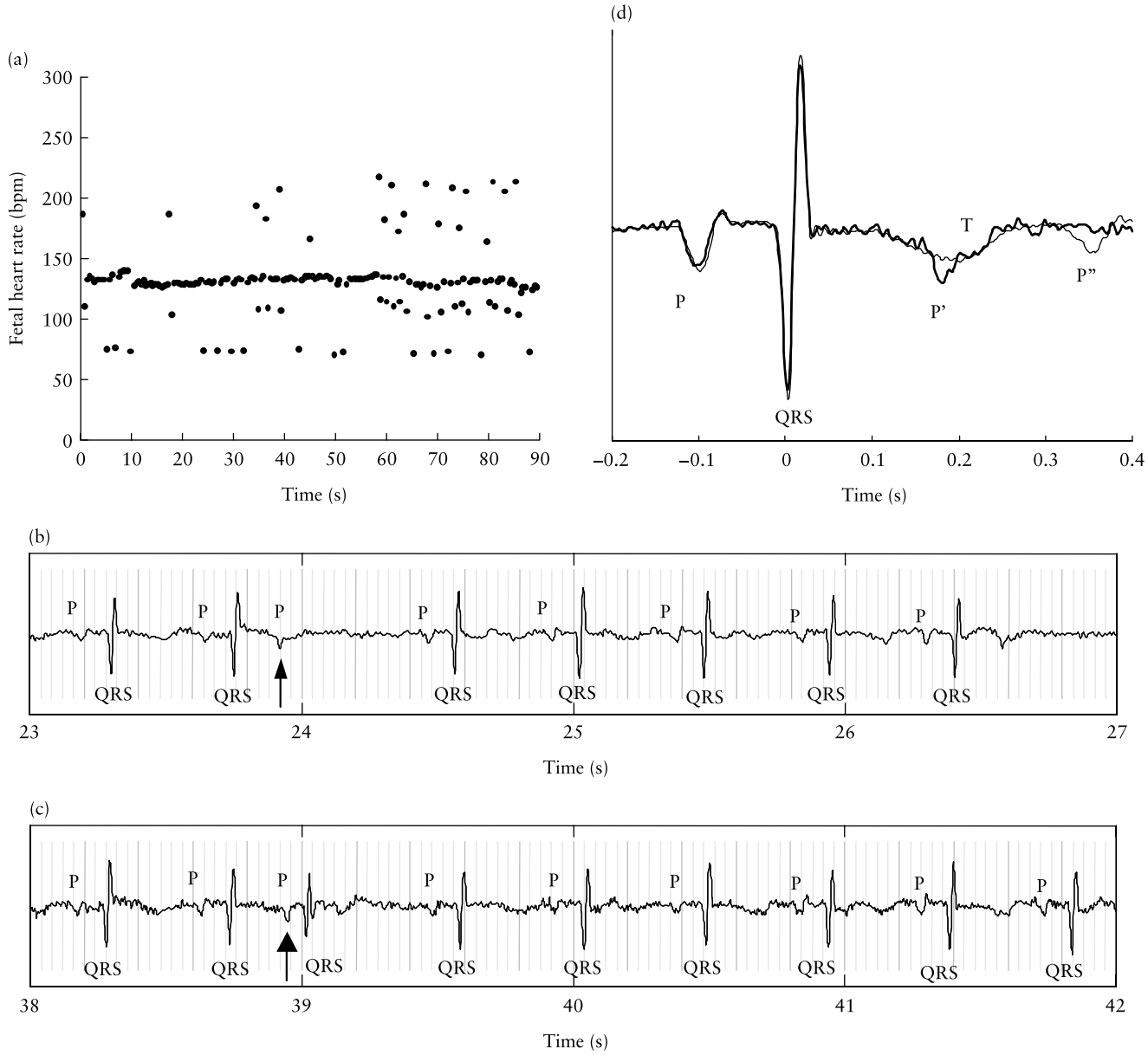

Figure 7 Magnetocardiographic results of a fetus diagnosed with periods of arrhythmia, measured in the 38th week of gestation. (a) shows the fetal heart rate. Also shown are fetal magnetocardiograms with a premature atrial contraction without (b) and with (c) a QRS complex succeeding the P-wave, and two averaged magnetocardiograms superimposed (d), one during a period of normal beats showing a T-wave (bold line) and one for beats followed by a premature atrial depolarisation (fine line).

concealed pathway was found and was treated by catheter ablation, after which normal sinus rhythm was restored.

Various arrhythmias

Nine cases of fetuses with ventricular extrasystole and one with a completely erratic heart rate were investigated by fetal magnetocardiography, three of which will be presented here in detail. The first patient was referred at 37 weeks of gestation with episodes of fetal arrhythmia. The pregnancy had been uncomplicated and the arrhythmia was discovered on a routine antenatal visit. Ultrasound analysis showed no evidence of structural fetal anomalies. Some extrasystolic beats with compensatory pauses were observed. No signs of fetal hydrops were noticed. Fetal magnetocardiography was performed at 38 weeks' gestation. The fetal heart rate as shown in Figure 7a was irregular and showed a mean RR rate of 140 bpm. Two time traces are depicted in Figure 7b and c. P-waves are distinguishable in both traces. Most complexes in these time traces show a sinus rhythm although some premature P-waves are observable, as indicated by arrows. In Figure 7b, the premature P-wave indicated by an arrow is not followed by a QRS complex, whereas in Figure 7c it is. In Figure 7d two averaged fetal MCGs are superimposed, one calculated for normal beats and the other for beats followed by a premature atrial depolarisation. The first PQRS waveforms are identical, whereas in the normal trace a T-wave is seen while in the other trace the premature P-wave coincides with the T-wave. A healthy neonate was delivered after 40 weeks of pregnancy. An

ECG was performed in the hospital and showed no signs of rhythm disturbance.

The second patient had a pregnancy complicated by vaginal bleeding during the second trimester. During repeated ultrasound evaluations premature fetal heart beats were observed. There was no evidence of structural fetal anomalies. Fetal magnetocardiography was performed at 38 weeks of gestation. The fetal heart rate displayed a mean RR rate of about 130 bpm but was otherwise very irregular. The rhythm could be described as two normal beats followed by a premature atrial depolarisation after which the pattern repeated. Most of the time the premature beats were followed by a normal QRS complex; however, sporadic abnormal complexes occurred. The normal and abnormal waves were averaged separately, showing a different shape and polarity of the P-wave. Therefore, the premature atrial beats originated from somewhere outside the sinoatrial node. A healthy neonate was delivered after 39 weeks of pregnancy. A postnatal ECG 4 days after delivery showed a normal sinus rhythm alternated with some premature atrial beats followed by a normal QRS complex and a compensatory pause. No abnormal complexes were found.

The third patient, a 32-year-old woman in her second pregnancy, was referred to the hospital for severe fetal arrhythmia at 24 weeks of gestation. A careful examination of her history revealed that the woman had developed a craving for caffeine during her pregnancy, resulting in an intake of 10 cups of coffee and 3–4 L cola a day. Detailed ultrasound analysis showed no evidence of structural cardiac defects, but a completely erratic contraction pattern was observed. M-mode ultrasound analysis was of no benefit for the classification of the disorder. No fetal hydrops was present. The woman was advised to stop her intake of caffeine-containing beverages. Within a few weeks the fetal arrhythmia disappeared. Fetal magnetocardiography was performed at 24, 34 and 38 weeks of gestation. The fetal MCG obtained in the 24th week of gestation showed a fetal heart rate that was erratic as illustrated in Figure 8a. The fetal MCG time trace recorded in the 24th week of gestation (Figure 8b), showed a chaotic pattern in which quite often a regular depolarisation was followed by a second fast depolarisation. The period between both depolarisations was highly variable and was sometimes as short as 50 ms. These fast depolarisations disappeared when the caffeine intake ended, as shown in the time trace recorded in week 34 (Figure 8c). In the 38th week, a fetal ECG was recorded simultaneously with the fetal MCG. Although the signal-to-noise ratio of the fetal ECG measured by electrodes attached to the maternal abdomen was very low, the ECG could be averaged using time information obtained from the fetal MCG (Figure 8d). From the averaged fetal MCG and ECG, complexes were extracted with a duration of the QRS complex of 77 ms. A comparison of this value with those found in uncomplicated pregnancies shows that this value exceeds the 99th centile. The QRS showed a RR'R''. Based on these findings a diagnosis of a bundle branch block was made. After 40 weeks of pregnancy the neonate was delivered. An ECG recorded within 30 min after delivery is shown in Figure 8e. The postnatal diagnosis was ambiguous, namely a Wolff Parkinson White syndrome or a bundle branch block. At the age of 2 years a final diagnosis of an incomplete right bundle branch block was made.

Congenital heart defects

A 30-year-old woman in her third pregnancy was referred to the hospital in the 19th week of gestation on suspicion of a cardiac abnormality detected during a routine ultrasound. Detailed ultrasound evaluation showed critical CHD: coarctation of the aorta, a possible ventricular septal defect and mitral valve atresia. The right atrium and ventricle contracted, but the left atrium and ventricle did not. The diagnosis finally made in two different hospitals was fibroelastosis of the left side of the heart and a critical aortic stenosis. Congenital endocardial fibroelastosis is a serious and life-threatening heart disease and occurs with a frequency of 1 in 5000–6000 births[10]. Most children die in the first week of life, usually due to cardiac failure. Following counseling, the parents elected to continue the pregnancy, but to refrain from postnatal surgical intervention. Fetal MCGs were recorded in weeks 21 and 30. A fetal MCG measured in the 30th week of gestation is shown in Figure 9a. The averaged fetal heart complex showed a biphasic P-wave of 62 ms and a PR and PQ interval of 131 ms and 69 ms, respectively. Compared to uncomplicated pregnancies, such a PR interval is larger than the 95th centile. The QRS complex was 49 ms and indicated the presence of a RR'. At 42 weeks of pregnancy the neonate was delivered. Postnatal cardiac ultrasound confirmed the prenatal diagnosis of a left hypoplastic heart and a stenotic aorta. It also showed a mitral valve of 5 mm (Z-4), and a hyperdense left side of the septum in keeping with endocardial fibroelastosis. Both the right ventricle and the pulmonary artery were widened. The size of the aortic annulus was 3–4.5 mm, which is small. The ascending aorta had a diameter of 3–4 mm. The ductus arteriosus was still open with a right to left shunt. The foramen ovale was open and showed a left to right shunt. A minor tricuspid valve insufficiency was noticed as well as a minimal mitral valve insufficiency. The aorta showed no antegrade flow, but backflow was noticed. The parents declined surgical intervention and the child died at the age of 3 days. Postmortem examination was not permitted by the parents.

The second patient, a 37-year-old woman in her third pregnancy, was referred to our prenatal assessment unit with suspected fetal anomalies found at biometry for suspected growth restriction. Detailed ultrasound evaluation showed a progressively growth-restricted fetus. An abdominal wall defect in the form of an omphalocele was noticed. The spinal column showed a severe kyphoscoliosis and lordosis, with no evidence of a neural tube defect. The intracranial anatomy showed several choroid plexus cysts. The heart showed a transposition of the great arteries, an AVSD and an abnormal position of the apex. Karyotyping showed trisomy 18. The parents declined the option of a termination of pregnancy. Fetal magnetocardiography was performed in weeks 30 and 34. The averaged signal (Figure 9b) showed a small P-wave of 40 ms, which is below the 1st centile. Compared to uncomplicated pregnancies, the PR (136 ms) and PQ (96 ms)

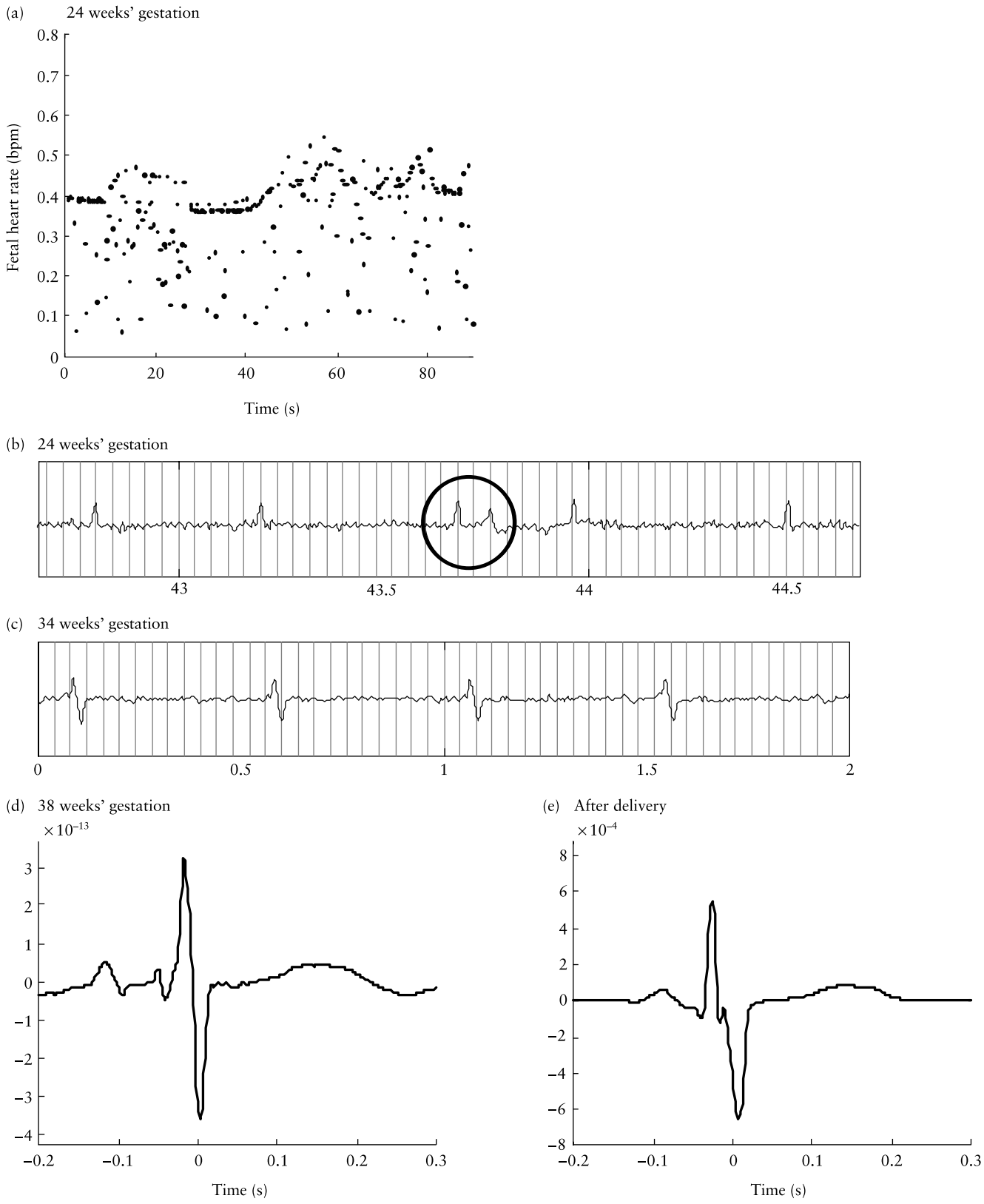

Figure 8 Magnetocardiographic results of a pregnancy complicated by caffeine intoxication and a suspected fetal bundle branch block measured in the 24th, 34th and 38th weeks of gestation. Shown are: the RR interval during the first 100 s of the measurements in week 24 (a); fetal magnetocardiogram time traces in week 24 showing the fast beats (b) and in week 34 showing normal sinus rhythm (c); averaged fetal magnetocardiogram measured in week 38 (d); averaged postnatal electrocardiogram recorded 30 min after delivery (e).

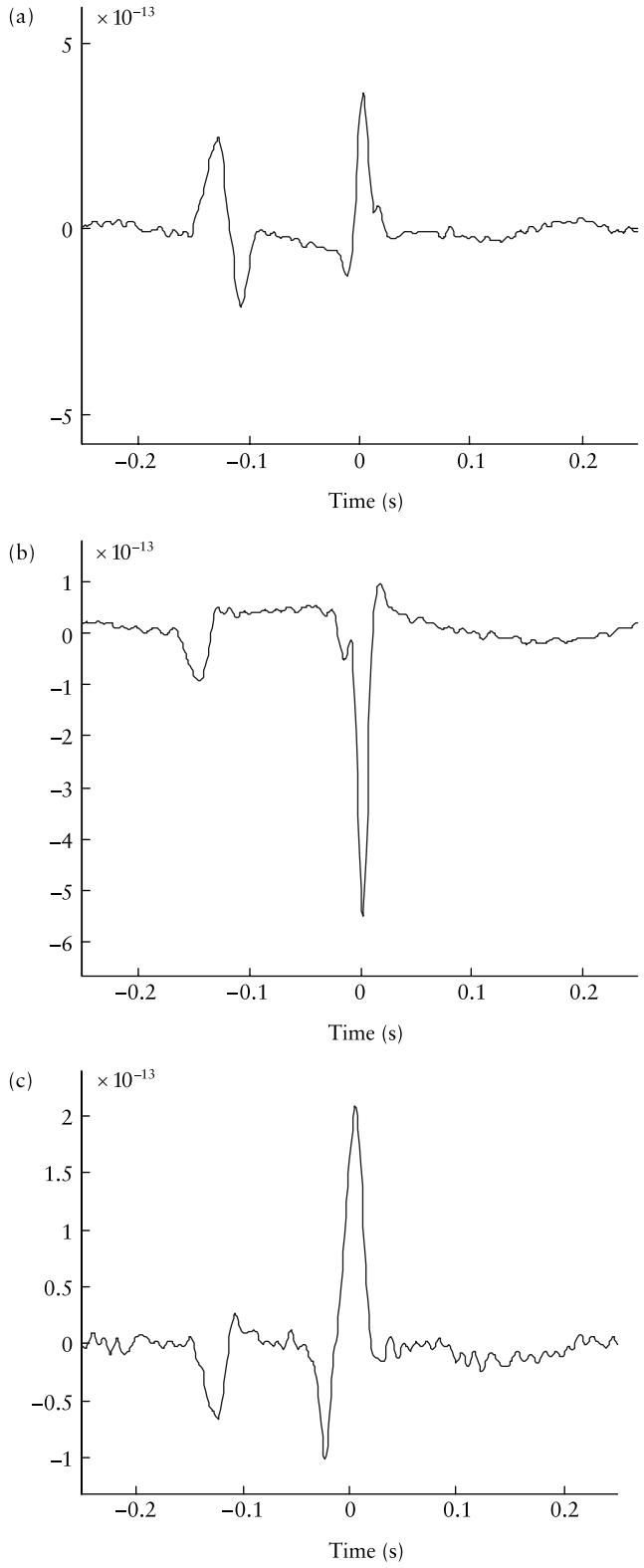

Figure 9 Averaged fetal complexes obtained by fetal magnetocardiography. (a) shows results of a fetus diagnosed with a hypoplastic left heart and a stenosis of the aorta, measured in the 30th week of pregnancy; the averaged signal shows a biphasic P-wave and RR' in the QRS complex. (b) shows results of a fetus diagnosed with trisomy 18, measured in the 34th week of pregnancy; the averaged signal shows an RR' in the QRS complex. (c) shows results of a fetus diagnosed with a hypoplastic left heart, measured in the 33rd week of pregnancy; the averaged signal shows a broad QRS complex of 70 ms.

intervals were above the 97th and 96th centiles, respectively,[11]. The QRS width was 60 ms, which is around the 94th centile, and showed an RR'. At 37 weeks of pregnancy intrauterine fetal death occurred. Postmortem examination was not permitted by the parents.

The third patient, a 29-year-old woman in her third pregnancy with a past obstetric history of fetal bilateral renal agenesis, was referred for nuchal translucency screening. Obvious edema (nuchal translucency thickness, 6 mm) was visible on the first ultrasound. Chorionic villus sampling showed a normal karyotype. Detailed evaluation in the 17th and 20th weeks of pregnancy showed a cleft lip and cleft palate, a right dysplastic kidney and underdevelopment of the left side of the heart. The aorta and pulmonary artery both originated from the right ventricle (double outlet right ventricle). The parents declined the option of termination of pregnancy. Fetal magnetocardiography was performed in the 33rd week of pregnancy. The averaged fetal signal (Figure 9c) showed a broad QRS complex of about 70 ms. Compared to uncomplicated pregnancies such a QRS value is greater than the 99th centile. After 38 weeks of pregnancy the neonate was delivered. The prenatal diagnosis of a hypoplastic left ventricle, a ventricular septal defect, transposition of the great arteries and abnormal location of the pulmonary veins was confirmed by means of cardiac ultrasound. One month after birth the child died. Again, no postmortem was allowed.

The fourth patient was referred following ultrasound examination at 30 weeks' gestation for suspected growth restriction. Detailed ultrasound evaluation showed an AVSD. Karyotyping showed trisomy 21. Fetal magnetocardiography was performed at 32 weeks' gestation but showed no abnormalities. Following delivery at term the ultrasound diagnosis was confirmed. Surgical correction was uneventful.

The fifth patient was referred at 20 weeks' gestation with suspected hydrocephaly. Detailed ultrasound evaluation confirmed the hydrocephaly, but also showed an assymmetrical four-chamber view, with an abnormally positioned apex. No clear structural defect could be established. Karyotyping was normal. Fetal magnetocardiography showed normal PQRS complexes. The parents elected to continue the pregnancy, but at 37 weeks' gestation intrauterine death occurred. Postmortem examination showed multiple central nervous system malformations, but no evidence of CHD.

DISCUSSION

Today, devices to perform fetal magnetocardiography are expensive. A magnetically shielded room is needed, and skilled personnel are required to handle the liquid helium. For this reason, only a few laboratories have a facility for fetal magnetocardiography. However, this may change in the near future because instruments not requiring liquid helium as a coolant for the superconducting quantum interference device (SQUID) sensors and designed to be used in normal hospital surroundings are under development.

Fetal MCG traces provide not only the fetal heart rate with a beat-to-beat accuracy, but also the duration of the P-wave, PR interval, and QRS complex[12,13]. These time intervals can be used to classify arrhythmias. Although an occasional

tracing could be obtained from as early as 12 weeks' gestation, reliable and reproducible fetal MCGs can be expected only from 20 weeks' gestation onward.

We found that fetal MCGs of fetuses with a complete AV block, a condition that is manifest in 1 in 20 000 live births[14], could be measured. A separate atrial contraction rate could not be determined earlier than 27 weeks, as the signal-to-noise ratio was too low. The fetal MCG of Patient A showed the P-wave to be prolonged compared to those measured during uncomplicated pregnancies[11]. This finding is consistent with the experimental animal data of Alexander *et al.*[15]. The fetal MCGs in Patient A were remarkable: first a 2 : 1 block at 35 weeks' gestation was encountered and this later progressed to a complete AV block. The period in which a second-degree AV block develops into a third-degree block might be the optimal time gap for anti-inflammatory therapy. Figure 2 shows ventricular depolarisation rate tracings with a minimal beat-to-beat variability while the atrial contraction rate tracings show a more dispersed pattern. This straight pattern has been documented previously in cardiotocograms[16]. In all four patients with a complete AV block it was possible to detect P-waves in the fetal MCG time traces.

Fetal magnetocardiography was found to be an adequate method for diagnosing atrial flutter, which is a serious and life-threatening rhythm disorder of the human fetus, especially when the fetus is hydropic[17]. The diagnosis is important in order to initiate treatment to obtain a conversion to sinus rhythm. The acute changes of heart rate and rhythm are well documented in MCG tracings. They may give rise to a disturbance in cerebral perfusion, which can lead to neurological damage. Therefore, MCGs may be instrumental in the etiology of neurological damage in patients with atrial flutter[18].

It was found that the amplitudes of the atrial flutter waves were enhanced compared to P-waves found during uncomplicated pregnancies. These effects may be explained by assuming hypertrophied atria. In the patient described in Figure 6, the existence of large P-waves was confirmed by the postnatal ECG.

Isolated extrasystoles, particularly premature atrial contractions, rarely cause hemodynamic problems and almost always disappear before term or shortly after birth. Van Leeuwen *et al.*[4] observed different types of abnormal rate and rhythm in about half of 155 MCG recordings. We observed nine cases of ventricular extrasystole. If the P-waves are not visible in the MCG time traces, normal and premature beats can be averaged separately. The resulting averages also offer the possibility to determine whether the premature beats are preceded by a P-wave. Premature atrial contractions belong, in contrast to atrial flutter, to rhythm disorders that are regarded as innocent and that constitute the majority (80–90%) of all fetal arrhythmias. Clinically relevant heart insufficiency during pregnancy usually does not occur and therefore treatment is not necessary. The fetuses who suffer from premature atrial contractions have a 1% risk of developing a sustained supraventricular tachycardia[19].

The fetal MCG described in Figure 8 showed a prolonged QRS complex accompanied by a RR'. This was also found in ECGs measured both prenatally and postnatally. Based on these findings a diagnosis of bundle branch block was made. The association of the fetal bundle branch block with a high caffeine intake may be entirely coincidental, but this should be viewed with some caution with the Barker hypothesis in mind, which associates adverse pregnancy conditions with cardiovascular disease in adult life[20]. The risk of spontaneous miscarriage, low birth weight, changes in fetal heart rate and neurobehavioral changes associated with caffeine use in pregnancy have been reviewed elsewhere[21].

As we have shown, three out of four fetuses with a CHD had an abnormal MCG. These preliminary results indicate that fetal magnetocardiography may be of help in the early intrauterine detection of congenital heart anomalies. Whereas the eventual diagnosis will remain an ultrasound diagnosis, fetal magnetocardiography, once developed as a technique as simple as an adult ECG, may have potential as a screening tool.

M-mode sonography, currently the standard to evaluate fetal arrhythmias, is an indirect way to assess the electrophysiological phenomena in the fetal heart. Simultaneous recordings of M-mode ultrasound and ECG in fetal lambs showed a significant prolongation of the PR interval using M-mode[22], and information more specific than intervals from atrial contraction to next ventricular contraction, and vice versa, cannot be obtained. Equally, although a good intraobserver variability has been observed, reliability decreases with more than one observer[1].

In conclusion, fetal magnetocardiography provides a safe tool in the diagnosis of fetal tachycardia and allows new insight into the electrophysiology of the human fetus. In fetal complete congenital AV block, the MCG reveals atrial contraction rate, ventricular contraction rate, depolarization aspects and the lack of ventricular contraction rate variability. In the diagnosis of fetal arrhythmia it is superior to (M-mode) ultrasound. With abnormal MCG recordings being observed in three out of four fetuses with confirmed CHD, provided this trend holds true with larger numbers, fetal magnetocardiography may have a future as a tool in defining a population at risk for CHD.

REFERENCES

1 Fouron JC, Proulx F, Miró J, Gosselin J. Doppler and M-mode ultrasonography to time fetal atrial and ventricular contractions. *Obstet Gynecol* 2000; 96: 732–6
2 Piéri JF, Crowe JA, Hayers-Gill BR, Spencer CJ, Bhogal K, James DK. Compact long-term recorder for the transabdominal foetal and maternal electrocardiogram. *Med Biol Eng Comput* 2001; 39: 118–25
3 Achenbach S, Moshage W, Menéndez T, Beinder E, Bittl A, Hofbeck M, Kollert A, Singer H, Bachmann K. Investigation of fetal cardiac arrhythmias by magnetocardiography. *Biomed Tech* 1997; 42: 253–6
4 van Leeuwen P, Hailer B, Bader W, Geissler J, Trowitzsch E, Grönemeyer DH. Magnetocardiography in the diagnosis of fetal arrhythmia. *Br J Obstet Gynaecol* 1999; 106: 1200–8
5 Wakai RT, Leuthold AC, Cripe L, Martin CB. Assessment of fetal rhythm in complete congenital heart block by magnetocardiography. *Pacing Clin Electrophysiol* 2000; 23: 1047–50
6 Hosono T, Chiba Y, Shinto M, Miyashita S, Muramaki K, Kandori A, Tsukada K. A case of fetal complete heart block recorded by magnetocardiography, ultrasonography and direct fetal electrocardiography. *Fetal Diagn Ther* 2001; 16: 38–41

7 Hamada H, Horigome H, Asaka M, Shigemitsu S, Mitsui T, Kubo T, Kandori A, Tsukada K. Prenatal diagnosis of long QT syndrome using fetal magnetocardiography. *Prenat Diagn* 1999; 19: 677–80
8 Menéndez T, Achenbach S, Beinder E, Hofbeck M, Schmid O, Singer H, Moshage W, Daniel WG. Prenatal diagnosis of QT prolongation by magnetocardiography. *Pacing Clin Electrophysiol* 2000; 23: 1305–7
9 Wakai RT, Lengle JM, Leuthold AC. Transmission of electric and magnetic fetal cardiac signals in a case of ectopia cordis: the dominant role of the vernix caseosa. *Phys Med Biol* 2000; 45: 1989–95
10 Veille JC, Sivakoff M. Fetal echocardiographic signs of congenital endocardial fibroelastosis. *Obstet Gynecol* 1988; 72: 219–22
11 Golbach EGM, Stinstra JG, Grot P, Peters MJ. Reference values for fetal MCG/ECG recordings in uncompicated pregnancies. In: Nenonen J, Ilmoniemi RJ, Katila T, eds. *Biomag 2000, Proceedings of the 12th International Conference on Biomagnetism*, Helsinki University of Technology, Espoo, Finland, 2001: 595–8
12 Horigome H, Takahashi MI, Asaka M, Shigemitsu S, Kandori A, Tsukuda K. Magnetocardiographic determination of the developmental changes in PQ, QRS and QT intervals in the foetus. *Acta Paediatr* 2000; 1: 64–7
13 Leuthold A, Wakai RT, Martin CB. Noninvasive in utero assessment of PR and QRS intervals from the fetal magnetocardiogram. *Early Hum Dev* 1999; 54: 235–43
14 Olah KS, Gee H. Fetal heart block associated with maternal anti-Ro (SS-A) antibody: Current management. *Br J Obstet Gynaecol* 1991; 98: 751–5
15 Alexander E, Buyon JP, Provost TT, Guarnieri T. Anti-Ro/SSA antibodies in the pathophysiology of congenital heart block in neonatal lupus syndrome, an experimental model: in vitro electrophysiologic and immunocytochemical studies. *Arthritis Rheum* 1992; 35: 176–89
16 Somville T, Morgenstern J. Fetal arrhythmias. In: van Geijn HP, Copray FJA, eds. *A Critical Appraisal of Fetal Surveillance*. Amsterdam: Elsevier Science, 1994: 297–302
17 Lisowski LA, Verheijen PM, Benatar AA, Soyeur DJ, Stoutenbeek P, Brenner JI, Kleinman CS, Meijboom EJ. Atrial flutter in the perinatal age group. Diagnosis, management and outcome. *J Am Coll Cardiol* 2000; 35: 771–7
18 Schade RP, Stoutenbeek P, de Vries LS, Meijboom EJ. Neurological morbidity after fetal supraventricular tachyarrhythmia. *Ultrasound Obstet Gynecol* 1999; 13: 43–7
19 Kleinman CS, Copel JA, Weinstein EM, Santulli TV, Hobbins JC. In utero diagnosis and treatment of fetal supraventricular tachycardia. *Semin Perinatol* 1985; 9: 113–29
20 Barker DJ. Fetal origins of cardiovascular disease. *Ann Med* 1999; 1 (Suppl.): 3–6
21 Eskanazi B. Caffeine—filtering the facts. *N Engl J Med* 1999; 341: 1688–9
22 Dancea A, Fouron JC, Miro J, Skoll A, Lessard M. Correlation between electrocardiographic and ultrasonographic time-interval measurements in fetal lamb heart. *Pediatr Res* 2000; 47: 324–8