Guideline

Guidelines for fetal echocardiography

Edited by the Fetal Echocardiography Guidelines Committee

Japanese Society of Fetal Cardiology and Japan Association of Pediatric Cardiology and Cardiac Surgery

Congenital heart defects have been reported to occur in 1 out of every 100 births but, because this statistic does not include miscarriages or stillbirths, it can be inferred that the actual number of fetuses with heart defects is almost fivefold greater than that reported.1 Approximately one-third of such patients have serious heart defects, which is the major cause of infant mortality. These congenital defects, however, are the most difficult to diagnose prenatally. Screening for heart defects is performed in only a low percentage of cases.2 In addition, 90% of heart defects occur in low-risk infants with no clear indication of a congenital anomaly on prenatal examination.3,4

Goals

Prenatal diagnosis of congenital heart disease is common throughout the world. Improved survival rates, fewer complications, and lower medical costs are characteristic of centers where prenatal screening for heart defects is performed. Prenatal screening of congenital heart disease is rapidly becoming more commonplace in Japan, but at present it is limited in accuracy and efficacy. According to reports from the UK, prenatal screening for congenital heart disease varies widely from region to region.

Correspondence: Gengi Satomi, MD, PhD, Department of Cardiology, Nagano Children’s Hospital, 3100 Toyoshina, Azumino, Nagano 399–8288, Japan. Email: g3_satomi8688@bc4.so-net.ne.jp

Principal Author
Gengi Satomi, Department of Pediatric Cardiology, Nagano Children’s Hospital, Azumino, Nagano, Japan

Team Leader
Gengi Satomi, Department of Cardiology, Nagano Children’s Hospital, Azumino, Nagano, Japan

Team Members
Motoyo Kavataki, Department of Neonatology, Kanagawa Children’s Medical Center, Yokohama, Kanagawa, Japan
Makoto Nishibatake, Department of Pediatrics, Kagoshima Seikyo Hospital, Kagoshima, Kagoshima, Japan
Yasuki Maeno, Department of Pediatrics, Kurume University School of Medicine, Kurume, Fukuoka, Japan

External Evaluation Committee Members
Noriyuki Suehara, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka, Japan
Makoto Nakazawa, Department of Pediatric Cardiology, Tokyo Women’s Medical University, Tokyo, Japan
Michiya Natori, National Center for Child Health and Development, Tokyo, Japan

This article is based on a study first reported in Pediatric Cardiology and Cardiac Surgery 2006; 22: 591–613.

The copyright line for this article was changed on 7 August 2015 after original online publication.

Received 12 May 2014; accepted 10 July 2014.

Effectiveness

Reports from Japan and throughout the world discuss the advantages and disadvantages of prenatal screening using fetal echocardiography. Some reports conclude that prenatal screening does not offer many advantages with respect to the incidence of congenital heart defects.5,6 This study takes issue with this viewpoint, asserting that prenatal screening offers many benefits to patients and their families.

Hypoplastic left heart syndrome, one of the most severe types of congenital heart defects, provides a good example of the effectiveness of prenatal diagnosis. In undiagnosed cases left to follow the natural course, infants die of shock as a result of closure of the arterial duct within 1 week of birth. When oxygen is given for cyanosis, it triggers closure of the arterial duct, thus worsening the situation. In a study by Satomi et al., among the infants for whom prenatal screening was performed, no oxygen was given, no shock was observed, and the infants were immediately transferred to a facility where surgery could be performed between 1 and 15 days after birth (average, 7 days). In contrast, among 10 infants for whom no prenatal screening was performed, four (40%) suffered shock and two (20%) required oxygen between 1 and 10 days (average, 3 days) before they were transferred to a facility where surgery could be performed. Surgery was performed between 9 and 24 days (average: 19 days) after birth. Therefore, health status was lower for infants in this latter group. In contrast, health status was better for infants in the group that underwent prenatal screening and early surgery.

Satomi et al. concluded that prenatal screening contributed to improved outcome in cases of congenital heart defects.6

Tworetsky et al. compared 33 cases of congenital heart defects diagnosed prenatally with 55 diagnosed postnatally in terms of the effect on surgical outcome. They found that the postoperative survival rate of infants in the prenatal diagnosis...
group was 100%, whereas that of infants in the postnatal diagnosis group was 66%. Therefore, prenatal diagnosis of congenital heart defects clearly had a beneficial effect on postoperative survival rate.1 Bonnet et al. compared 68 cases of transposition of the great vessels diagnosed prenatally with 250 diagnosed postnatally in terms of time before hospitalization, preoperative mortality rate, and postoperative mortality rate. They found that infants in the prenatal diagnosis group were hospitalized within an average of 2 h, whereas those in the postnatal diagnosis group were diagnosed within an average of 73 h. The preoperative mortality rate was 0% in the prenatal diagnosis group and 6% in the postnatal diagnosis group, whereas the postoperative mortality rate was 6% in the prenatal diagnosis group and 8.5% in the postnatal diagnosis group.10 This indicates that in cases of transposition of the great vessels, prenatal diagnosis can prove beneficial. In cases of persistent truncus arteriosus,11 a correlation was reported between stenosis of the truncal valve and surgical results. In cases of aortic stenosis, the condition of infants who were diagnosed through prenatal screening was more stable ($P < 0.01$) than that of infants who did not undergo prenatal screening, and a higher survival rate was observed in the former ($P < 0.05$) than in the latter.12 Prenatal diagnosis of tetralogy of Fallot has been reported to aid in the determination of a prospective course of treatment.13 All these reports indicate that prenatal diagnosis of congenital heart disease can be highly beneficial to patients in terms of outcome and survival.

Prenatal diagnosis elucidates previously unknown medical conditions, allows for planning in the perinatal period, and contributes to the formulation of clinical treatment strategies. In cases of transposition of the great vessels, closure of the foramen ovale and arterial duct occurs with extremely severe consequences. Maeno et al. examined cases of congenital closure of the arterial duct. In such cases, closure of the foramen ovale is highly likely if balloon atrial septostomy is not performed immediately after birth. If the delivery team is not prepared to perform this procedure, infants with transposition of the great vessels may not survive. Prenatal screening can lead to an improved prognosis in such cases.14

These guidelines also discuss the default settings for ultrasonic devices used in prenatal diagnosis of congenital heart defects. The Doppler method has advantages and disadvantages. First, it yields only 2-D echocardiograms, and it may have a large impact on the fetus.15 In contrast, it results in improvements in diagnostic accuracy16 and is effective in analyzing fetal circulation.17 Like all modalities used to examine living organisms, ultrasonography may also have detrimental effects on the fetus. Despite these possible effects, the benefit of using this diagnostic method outweighs the risk of not using it, and it is not superior to other available diagnostic methods. In one study, in 77 out of 171 cases (45%) of congenital heart defects diagnosed prenatally, the parents opted to terminate the pregnancy.1 The rate of abortion of fetuses with congenital heart defects differs among countries according to the religious and social/cultural environments. When heart disease is detected at an early stage of pregnancy with a high degree of precision, however, the issue of abortion is unavoidable.

Summary

These fetal echocardiography guidelines are divided into the following three sections: discussion of prenatal diagnosis of congenital heart disease; prenatal diagnosis of arrhythmia; and ethical issues associated with prenatal screening. In section I, technical guidelines for standard fetal echocardiography used for the prenatal diagnosis of heart defects are presented and the representative characteristic findings of congenital heart diseases are described. Guidelines are delineated for childbirth and postnatal care in the case of congenital heart defects diagnosed prenatally. Section II discusses a few atypical cases of fetal arrhythmia that were diagnosed prenatally and treated accordingly. The standard methods of diagnosis of and drug therapies for fetal arrhythmia are laid out in this section of the guidelines. Section III distinguishes the prenatal diagnosis of congenital heart disease from chromosome banding and prenatal diagnosis at the genetic level. The primary difference is that prenatal diagnosis of congenital heart disease involves a heart that is completely developed. Some parents do not necessarily desire a prenatal diagnosis, and others do not want to learn of the existence of congenital heart disease. These guidelines respect the rights of these parents while guiding other parents to the most appropriate choices for the fetus at the time of diagnosis. Emotional support for parents after a prenatal diagnosis is made is also addressed.

Prenatal diagnosis is accomplished through two levels of procedures. Level I involves screenings performed by obstetricians. Level II procedures are performed on the recommendation of an obstetrician and are indicated in the case of fetal cardiovascular disease, requiring more detailed examination and a definitive diagnosis by a specialist. Statistical estimates indicate that all of the approximately 1.2 million infants born annually in Japan should be subjected to level I prenatal screening. Of the screened cases, slight to severe congenital heart disease would be identified in approximately 1% (or 12,000 infants). In approximately half these cases, fetal arrhythmia would be detected, with an annual estimated total of 18,000 fetuses with congenital heart defects. In practice, because extremely slight heart defects are impossible to detect in utero, the actual number of infants identified with heart defects through level II prenatal screening is estimated to be half that number. These guidelines have been created on the basis of these statistics in order to facilitate the use of level I screening for heart defects as a routine fetal examination performed by obstetricians. The guidelines consider the time required to perform this screening and the need for it to be highly effective in detecting heart defects. Level II screening is presumably performed by heart specialists whose knowledge of congenital heart disease and arrhythmia can ensure a high level of accuracy and prevent the overlooking of illness during the examination.

Prenatal diagnosis of congenital heart disease

As mentioned, fetal echocardiography is currently performed at two levels in Japan.

© 2015 The Authors. Pediatrics International published by Wiley Publishing Asia Pty Ltd on behalf of Japan Pediatric Society
Fetal heart screening (level I)

Level I fetal heart screening can, in principle, be performed on all pregnant women, but pregnant women with risk factors indicating a higher risk of fetal congenital heart disease require more careful screening compared with pregnant women at low risk. High-risk pregnancies are described in Table 1.18

Frequency and timing of screening

Although the detection rate improves with an increased frequency of screening, too many screenings impose major time and financial burdens on both pregnant women and obstetricians. In order to maximize the efficacy of fetal heart screenings in the limited time available for examination, screenings should be conducted at certain weeks during pregnancy rather than performing brief screenings at each visit. Most serious heart defects can be detected between week 18 and early week 20.19 Semilunar valve stenosis and backflow of the atrio-ventricular valve, however, cannot be detected until week 30 or later. Therefore, another heart screening should be performed at or around week 30.20 Given that the amount of amniotic fluid decreases near the end of pregnancy, the fetus becomes fixed in the prone position and the skeleton becomes calcified. Observation of the fetal heart becomes difficult under these conditions. In addition, when fetal heart screening reveals abnormalities at this point, insufficient time remains for subsequent detailed examinations of the fetal heart or provision of adequate explanations to parents. For these reasons, we recommend that fetal heart screenings be performed first between week 18 and early week 20 and repeated around the 30th week of pregnancy.

Examiner

Level I fetal heart screenings should be performed by the attending obstetrician, licensed ultrasonographers, clinical technologists, radiological technologists, nurses, or midwives who have experience in performing fetal screenings. If the attending obstetrician is unable to perform an adequate heart screening for patients with the risk factors listed in Table 1, the screening should be performed by another obstetrician or an experienced pediatric cardiologist.

Table 1  Risk factors for congenital heart disease

| 1. Family history |
|-------------------|
| Congenital heart disease (siblings, parents) |
| Malformation syndromes thought to have a strong correlation with heart defects |
| 2. Maternal diseases |
| Diabetes, collagen disease, phenylketonuria |
| 3. Exposure to teratogens during pregnancy |
| Chemicals (alcohol, amphetamines, anticonvulsant drugs, lithium, vitamin A, warfarin) |
| Infectious diseases (rubella virus, cytomegalovirus, Coxsackie virus, parvovirus) |
| Radiation |
| 4. Fetal abnormalities |
| Intrauterine growth retardation, discordant twins, nuchal translucency positive |
| Fetal arrhythmia, extracardiac malformations |

Gain. Gain should be adjusted to allow the best possible image quality. The lighting in the examination room should be dimmed appropriately.

Zoom. In order to make detailed internal observations of the small fetal heart, the zoom should be used and the image display on the screen should be enlarged.

Frame rate. The frame rate indicates the number of images created per second. When the image movement is jerky because of a low frame rate, the angle of the view should be decreased and the interval between the scan lines should be increased. Observations cannot be made if the frame rate cannot keep up with the quick movements of the fetal heart. Therefore, the minimum frame rate required that will allow accurate observation is between 20 and 40/s.

Persistence. Persistence, a function designed to make images clearer, is effective when used on immobile organs. It is therefore widely used for abdominal or obstetric observations. Because of
its movement, however, the heart is difficult to observe with this function. Therefore, persistence should be switched off during screening for congenital heart defects.

**Focus.** In order to facilitate observation and obtain clear images of the heart, the focus should be adjusted for the required plane of the heart. Use the dial to change the depth (cm) at which the device focuses. For example, to view the ventricles, set the focus around 5 cm.

**Frame-by-frame advance or slow playback.** Because the fetal heart is small and moves extremely quickly, its movements are difficult to follow in real time. Whenever possible, the image should be frozen and each frame should be observed individually using frame-by-frame advance or slow playback. This method is particularly important for observations of the end of the ventricular diastole and the end systole.

**Video.** Because the heart is a moving organ, still images alone cannot record clinical findings accurately. Moving images should be recorded and compared with previously recorded moving images. These videos can be used during consultations with specialists in fetal cardiovascular diseases. They may also be useful for postnatal diagnosis.

**Views and points to observe**

Copel *et al.* suggested that diagnosis is possible in 96% of cases that require echocardiography using solely the four-chamber view.24 Kirk *et al.*, however, reported that screening using only the four-chamber view yields accurate screening results in ≤50% cases.25–27 Fetal heart screening should not be restricted to the four-chamber view alone; rather, the abdominal section and outflow tract views should also be utilized. Observation using a wide range of views will improve screening results.2,5,9,28,29

**Confirming position.** When the apex and stomach are not on the left, situs inversus or visceral heterotaxy are indicated and the risk of complications due to heart defects is high. Observations must be made after confirmation of the position of the fetus (Fig. 1). No standard method has been established for identification of the dorsal, ventral, left, and right sides. One generally used method is described here.

1. Use the long axis view of the fetus (the sagittal section of the fetus). Either adjust the probe so that the fetus’s head is on the right side of the screen or use the button on the device to switch the views from left to right.
2. Rotate the probe 90° counterclockwise. This will allow the observer to view the horizontal section of the fetus from above.
3. Confirm the dorsal, ventral, left, and right positions from the horizontal section of the fetus’s chest. Imagine a clock face and place the dorsal column at 12 o’clock, the sternum at 6 o’clock and facing forward, the left side at 3 o’clock, and the right side at 9 o’clock. In most cases, this will position the heart in the fetus’s horizontal section and allow a four-chamber view.

**Abdominal section.** Move the horizontal section along the abdomen and confirm the location of the stomach. When the stomach is on the right or the location of the stomach and heart are inconsistent, a heart defect is a strong possibility (Fig. 2).

**Four-chamber view.**

1. Cardiac position: set the point where the interatrial septum contacts the rear wall of the atrium as point P. When point P is normal, it is almost exactly in the center of the trunk (Fig. 3). From deviations of point P, cardiac malposition in the thoracic cavity can be determined and screening for a causative space-occupying lesion can be performed. Space-occupying lesions (e.g. diaphragmatic hernia, congenital cystic adenomatoid malformation, pulmonary sequestration, bronchogenic cyst) cause respiratory disorders immediately after birth.
2. Cardiac axis: The cardiac axis is the angle formed by the straight line between the spinal column and the sternum and the straight line between the interatrial septum and the interventricular septum (Fig. 4). Normally, this angle is 45 ± 20° (25°–65°). Abnormalities in cardiac axis are useful in screening for complicated heart defects.30–32
3. Cardiac size: (i) total cardiac dimension (TCD) and (ii) cardiothoracic area ratio (CTAR). TCD is the measure of the
distance between the attachment point of the mitral valve on the epicardium to the attachment point of the tricuspid valve on the epicardium (Fig. 5). The normal TCD is the measure in millimeters that corresponds to the week of pregnancy after week 22. Because TCD prior to week 22 is smaller than the number of gestational weeks, the normal value must be

Fig. 2  Horizontal section of the fetal trunk viewed from above.

Fig. 3  Cardiac position. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.
(Reproduced with permission from: Russ PD, Weingard JP: Cardiac malposition, in Drose JA: Fetal Echocardiography. Philadelphia, WB Saunders, 1998; p. 60).

Fig. 4  Cardiac axis. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.
(Reproduced with permission from: Russ PD, Weingard JP: Cardiac malposition, in Drose JA: Fetal Echocardiography. Philadelphia, WB Saunders, 1998; p. 60).

Fig. 5  Total cardiac dimension (TCD) vs gestational week (mean ± 1.5 SD) in a normal fetus.
(Reproduced with permission from: Shigeki Izumi. The relation between total cardiac diameter and gestational age in normal fetus. Perinatal medicine 1955: 25 (Suppl.): 247).
checked for each week or CTAR must be measured. When the estimated weight of the fetus does not correspond to the week of pregnancy, TCD cannot be used as a guide (Fig. 5). CTAR is a percentage figure that results from dividing the area of the thorax by the area of the heart (Fig. 6). The area of the heart is obtained by tracing the exterior of the pericardium. The area of the thorax is obtained by tracing the exterior of the thorax, including the ribs and spinal column, but, because manual tracing that does not include the skin and muscles is both complicated and time-consuming, the ellipse method, which entails tracing an ellipse that approximates the area, is often used. The ellipse method gives nearly the same result as a manual measurement (Fig. 6).

Cardiac lateral differences: placement of the center line (the line connecting the interatrial septum and the interventricular septum) in the middle makes the heart divide almost perfectly into its left and right sides and this allows the examiner to compare the sides to determine the size of the atria, the diameter of the annulus of the atrio-ventricular valve, ventricular size, the characteristics and thickness of the ventricular walls, and the contractility of the ventricular walls.33

Observation of outflow tracts. Two methods of observation are utilized during fetal echocardiography. In one, the examiner moves the probe from the four-chamber view toward the head in a parallel translation (Figs 7,8). In the other, the examiner tilts the view toward the fetus’s head (Fig. 9). Moving toward the head in a parallel translation allows observation of the major blood vessels in a short axis view and simultaneous observation of both the pulmonary artery and the aorta in a single view. Therefore, confirmation of the position and size of these two structures in relation to each other is possible. When the view is tilted toward the fetus’s head, the left ventricular outflow tract becomes visible. As the probe continues to tilt, the right ventricular outflow tract comes into view. The connection between the ventricle and major arteries and the major arteries in their entirety can be observed in the long-axis view.

There are three points to observe when viewing the outflow tracts: two major arteries of approximately the same size, two major arteries that intersect in space, and the connection of one major artery to each of the ventricles.

Detailed examination of the fetal heart (level II)

Subjects

Detailed examinations must be performed by a physician familiar with fetal heart disorders in order to confirm the diagnosis in cases in which the patient has undergone prenatal screening. In addition, when adequate level I screening cannot be performed in infants at high risk of congenital heart disease, specialist screening must be treated as the equivalent of a level II examination on request of the obstetrician.

Timing and number of examinations

Detailed examination should be performed immediately after the referral of the patient by the obstetrician. Because changes in fetal position may obscure the view, it is desirable to perform two or more fetal echocardiograms on different occasions before drawing any conclusions.

Examiners

A physician familiar with fetal heart disorders should perform the level II examination upon referral from the physician who performed the level I screening.

© 2015 The Authors. Pediatrics International published by Wiley Publishing Asia Pty Ltd on behalf of Japan Pediatric Society
Ultrasonic wave functions

The settings on the ultrasonic diagnostic equipment and supplemental observational conditions are the same as those described for level I screenings. In addition to 2-D echocardiogram, color Doppler, pulsed Doppler, continuous wave Doppler, and M-mode Doppler images are used. When the sample speed exceeds the limits of pulsed Doppler, continuous wave Doppler should be used.

Points to observe

In addition to the points observed in a level I screening, the following points should also be observed.

Confirmation of the position. Confirm the position of the descending aorta and the superior vena cava.

Four-chamber view. Observe the blood flow of the mitral and tricuspid valves using color Doppler imaging to evaluate atrioventricular valve insufficiency. Confirm the inflow from the four pulmonary veins into the left atrium using color Doppler imaging. Confirm bimodal blood flow (two-peak blood flow) into the tricuspid and mitral valves using pulsed Doppler imaging. When an upper ventricular septal defect is suspected on the basis of 2-D echocardiography, use color Doppler and pulsed Doppler imaging to confirm that the blood flow crosses the interventricular defect.

Outflow tract view. Using the outflow tract view, characteristic branching pattern of the two great arteries must be identified. The pulmonary artery branches into a Y pattern. In contrast, the aorta has three major branches and is located closer to the head than is the pulmonary artery. Doming of the valves and post-stenotic dilation of the pulmonary artery and aorta can be observed in addition to mosaic patterns using color Doppler imaging.

Three-vessel view. The three-vessel view can be obtained by either moving the plane from the four-chamber view toward the head in a parallel fashion or by slightly tilting the plane. The pulmonary artery (PA), aorta (Ao), and superior vena cava (SVC) will be aligned in a straight line. In normal patients, the sizes of

---

Fig. 8 Tilting the probe from the four-chamber view toward the head. (a) Four-chamber view; (b) three-vessel view; (c) three-vessel trachea view. aAo, ascending aorta; DA, ductus arteriosus; dAo, descending aorta; LA, left atrium; LPA, left pulmonary artery; LV, left ventricle; MPA, main pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RV, right ventricle; SVC, superior vena cava.

Fig. 9 Representative pictures obtained when moving the probe from the four-chamber view toward the head.
these vessels are as follows, in decreasing order: PA > Ao > SVC (Fig. 10).

Three-vessel trachea view. The three-vessel trachea view can be obtained by either moving the plane further toward the head in a parallel fashion or by tilting further. The ductus arteriosus connects the pulmonary artery to the descending aorta, and the aortic arch connects the ascending aorta and the descending aorta and these three vessels form a V shape. The ductus arteriosus and the aortic arch are similar in size, and blood flows through both vessels (ductus arteriosus and aortic arch) go in the same direction. In normal patients, the elliptical trachea can be observed behind and to the right of the aortic arch (Fig. 11).

Views of the aortic and ductal arches. Aortic arch: originates from the left ventricle and forms a convex arch as it moves toward the head; branches three vessels.

Ductal arch: originates from the right ventricle and forms an arch of the same size as the main pulmonary artery, ductus arteriosus, and descending aorta. These two arches are normally observed together in utero.

Continuous flow observed in either the aorta or the pulmonary artery is abnormal.

A proposal has been made to standardize fetal echocardiography in Japan. Diagnostic fetal echocardiography may be performed as part of pediatric echocardiography. Please refer to the references section for more detail.34–36

Points to screen for each disease

The major congenital heart defects to be screened and the views and observational points necessary to make diagnosis are listed in Table 2.

Procedures for perinatal management

Prenatal management

Notification. Notification of the mother only should be avoided whenever possible. Instead, both parents should be notified when possible. The following points should be included: (i) details of the illness detected in the fetus (explain using detailed diagrams); (ii) the anticipated intrauterine progression of the disease and resultant change in the fetal condition until delivery (explain using detailed diagrams); (iii) assuming delivery is successful, the anticipated progression of the illness if medical care is not provided after birth (the natural progression of the illness); (iv) the anticipated progression of the illness if medical care is not provided after birth (the natural progression of the illness); (v) the available medical procedures to treat the patients and the changes in hemodynamics that can be achieved via these treatments (explain using detailed diagrams); (vi) the quality of life that can be expected as a result of intervention; and (vii) the risks that accompany intervention
Fetal cardiac malformations can complicate diseases detectable through screening by view examination must be conducted to detect extra-cardiac malformations. Because extra-cardiac malformations can have a major effect on prognosis, a detailed prenatal examination must be conducted to detect extra-cardiac malformations. A detailed examination must be conducted to detect extra-cardiac malformations. Because extra-cardiac malformations can have a major effect on prognosis, a detailed prenatal examination must be conducted to detect extra-cardiac malformations.

### Table 2 Diseases detectable through screening by view

| View                                | Malformations                                                                 |
|-------------------------------------|-------------------------------------------------------------------------------|
| Abdominal view                      | Heterotaxia (congenital asplenia syndrome, polysplenia syndrome), visceral inversion |
| Cardiac axis                        |                                                                                   |
| Abnormalities of the aortic and ductal arches | premature closure of the arterial duct, premature constriction (narrowing) |
| Abnormalities of the great arteries  | premature closure of the arterial duct, premature constriction (narrowing) |
| Arrangement of outflow tracts (parallel orientation) | Macrocardiomyopathy, cardiomegaly, etc. |
| Connection between the ventricles and great arteries | Heterotaxia, atrio-ventricular septal defect, ventricular septal defect |
| Abnormalities of the aortic and ductal arches | Aortic stenosis/atria, coarctation of the aorta/interrupted aortic arch |

CTAR, cardiothoracic area ratio; TCD, total cardiac dimension.

**Malformations.** Fetal cardiac malformations can complicate extra-cardiac malformations. Because extra-cardiac malformations can have a major effect on prognosis, a detailed prenatal examination must be conducted to detect extra-cardiac malformations.

When abnormalities in the fetal heart are detected on screening, the patient should be referred to perinatal facilities, where detailed examinations of cardiac and extra-cardiac malformations can be performed. Postnatal care can also be provided at such facilities.

**Multidisciplinary conference.** The case should be discussed in a multidisciplinary conference where an obstetrician, neonatologist, pediatric cardiologist, cardiac surgeon, nurse, and case-worker are in attendance. The diagnosis of cardiac malformation, any extra-cardiac malformations, the treatment plan and support for the family should be fully addressed in this conference. The family’s privacy must be respected and a sufficient time must be allotted to discuss the diagnosis. The discussion should include the exact diagnosis and long-term prognosis. All the family’s questions should be answered, and emotional support should be provided after the notification.

**Premature birth and low birthweight.** Premature birth and low birthweight often make the treatment of heart disease difficult. One of the important goals of prenatal care is the avoidance of premature birth.

**Delivery.**

Unless elective cesarean section provides a clear advantage, vaginal birth should be chosen even for infants with fetal heart disease. Elective cesarean section with immediate postpartum treatment is appropriate, however, when an emergency surgical procedure such as pacemaker implantation or balloon valvuloplasty is required.

**Prenatal diagnosis and treatment of arrhythmia**

**Introduction.**

Many types of congenital illnesses and heart diseases are now diagnosed during the fetal stage. The pre- and postnatal prognosis of arrhythmia is often determined by the perinatal care provided. Prenatal treatment of fetal tachyarrhythmia has been demonstrated as effective, although diagnosis, treatment, and perinatal care must be performed with great precision.

**Diagnostic methods.**

When fetal arrhythmia is suspected, a comprehensive series of decisions must be made, including accurate diagnosis and appropriate course of management (Table 3). These decisions should be made by a care team at a facility that is able to perform a Level II fetal examination.

M-mode and Doppler echocardiography are effective tools for diagnosis of fetal arrhythmia. The number of contractions for each ventricle and atrium and the time phase relation between contractions must be established. The corresponding P and QRS waves can then be calculated and the arrhythmia analyzed. Diagnostic tools such as fetal electrocardiography from the mother’s abdominal surface, direct fetal electrocardiography, or magnetocardiography may also be used. These methods, however, are not standardized at present in the clinical setting.
M-mode assessment of the fetal heart rhythm is achieved by interrogating the fetal heart from the apex or base. The cursor is placed so that atrial and ventricular wall motion is recorded simultaneously. Capturing the movements near the atrio-ventricular valve in both the ventricle and atrium results in a clear image of the contractions (Fig. 12).

Setting the cursor in a position to pass both the aortic valve and the left ventricle (a view that is normally used for measuring the left atrial/aorta ratio on the long axis of the left ventricle) facilitates imaging of the opened aortic valve as the ventricle contracts (Fig. 13).

Using Doppler imaging, the user samples the space between the mitral valve and the aortic valve and records the wave form of the inflow of the left ventricle while simultaneously recording the wave form of the outflow of the left ventricle into the aorta as the ventricle contracts. In recent years, echocardiography using tissue Doppler has been developed and improved to evaluate the contractions of the myocardium itself. In future practice, this method may prove very useful in the diagnosis of fetal arrhythmia.

When diagnosing arrhythmia, the examiner should search for complicating congenital cardiac structural anomalies, other congenital malformations, and fetal hydrops. Fetal hydrops can be identified by any one of the following: subcutaneous edema, pleural fluid, abdominal dropsy, and pericardial effusion. After identification of these symptoms, fetal progress should be monitored.

**Fetal bradyarrhythmia**

Pathological fetal bradycardia is most often caused by an atrio-ventricular block wherein the timing of ventricular and atrial

---

**Table 3** Checklist for diagnosis of fetal cardiac arrhythmia

| 1. Record the relationship between contraction of the ventricles and atria using M-mode or Doppler echocardiography. Then categorize the arrhythmia. |
|---|
| **M-mode:** |
| 1. Simultaneously record the contraction of the ventricles and atria. |
| 2. Then simultaneously record the contraction of the atria and the opening and closing of the aortic valve. |
| **Doppler:** |
| 1. Simultaneously record the wave form of the mitral valve inflow and the wave form of the left ventricular outflow. |
| 2. Search for complicating heart malformations and extra-cardiac malformations. |
| 3. Search for signs of fetal hydrops. |
| 4. Measure the duration of arrhythmia using a fetal heart rate monitor. |

**Definitions**

- Fetal bradycardia: Fetal heart rate <100 beats/min
- Fetal tachycardia: Fetal heart rate ≥200 beats/min or periods of paroxysmal heart rate increase
- Extrasystoles: Sudden premature contractions compared to normal sinus rhythm

---

**Fig. 12** (a) Analysis of arrhythmia using M-mode echocardiography: setting the four-chamber view and M-mode cursors placed through the atrium and ventricle. (b) Recorded M-mode image: the forward movement of the right atrial wall shows atrial contraction. Backward movement of the interventricular septum shows ventricular contraction. IVS, interventricular septum; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

**Fig. 13** Analysis of arrhythmia using M-mode echocardiography: setting the M-mode cursor to pass through the aortic valve and left ventricle. AV, aortic valve; LA, left atrium; RV, right ventricle.
Progression to fetal hydrops is common when the rate of atrio-ventricular block is disassociated (Fig. 14; Table 4).\textsuperscript{37–39,42} Sinus bradycardia, in which the atrial to ventricular conduction is in a 1:1 ratio, is most often a temporary condition accompanying compression of the umbilical cord, or uterine contractions. Occasionally, however, sustained bradycardia is identified when the general condition of the fetus is poor.\textsuperscript{37} Although rare, cases of sinus bradycardia and sinus node dysfunction manifesting as arrhythmia have been reported.\textsuperscript{39,43}

\textbf{Atrio-ventricular block}

Atrio-ventricular block accounts for 33–50\% of cases of congenital heart disease (mostly polysplenia syndrome and corrected transposition of the great arteries). Therefore, practitioners should be aware of this complication during examinations.\textsuperscript{37,39,42,44}

When the cardiac structure is normal, more than half the cases of atrio-ventricular block are caused by maternal autoantibodies (SSA-antibody).\textsuperscript{45–48} Therefore, even if no symptoms of maternal collagen disease are evident, testing for autoantibodies (including the SSA antibody) must be performed. Of the two types of SSA antibody, 52 kD and 60 kD, the one responsible for ventricular block in most cases is 52 kD.\textsuperscript{49} The SSA antibody is not currently included in standard tests, but we will include this test, especially for the 52 kD type, in these guidelines as a necessary future addition.

\textbf{Intrauterine cardiac insufficiency}

The prognosis for severe arrhythmia is generally poor because it causes fetal hydrops, which leads to cardiac insufficiency.\textsuperscript{37,39,42} Therefore, arrhythmia must be treated before it develops into fetal hydrops or when early signs of hydrops have been detected. In cases of pericardial effusion alone, when fetal bradycardia is caused by the mother’s antibodies, accumulation can occur because of myocarditis unrelated to fetal hydrops. Therefore, exercise of caution is necessary to correctly determine the presence or absence of cardiac insufficiency.

Progression to fetal cardiac insufficiency is caused by advanced bradycardia, atrio-ventricular valve regurgitation (especially when complicated with congenital heart disease), and cardiac dysfunction (due to myocarditis or endocardial fibroelastosis caused by maternal antibodies). In these cases, cardiac output drops and the condition progresses to fetal hydrops.\textsuperscript{48} Progression to fetal hydrops is common when the rate of ventricular contraction is <55/min.\textsuperscript{34,47} A relatively large number of cases have been reported, however, in which no hydrops developed even when the rate dropped to approximately 45 contractions/min.\textsuperscript{48} In contrast, hydrops can develop even when the rate of ventricular contraction is as high as 60/min, as seen in cases of atrio-ventricular valve regurgitation and cardiac dysfunction.\textsuperscript{44,48} Fetal hydrops is often observed in cases in which the heart rate decreases over time.\textsuperscript{47}

In addition, cumulative evidence from fetal echocardiography of blood flow velocity in the aorta,\textsuperscript{37} cardiomegaly, and the fetal condition can be gathered using the biophysical score and other methods.

\textbf{Differential diagnosis}

\textit{Non-conducted premature atrial contraction resulting in bigeminal rhythm.} Premature atrial contractions block the signals to the ventricle and cause non-conducted premature atrial contraction, resulting in a bigeminal rhythm. When this occurs, a...
heartbeat resembling a 2:1 ventricular block will occur. Differentiation between the two is important. Differentiation can be accomplished by observing the interval between ventricular contractions. In cases of atrio-ventricular block, the interval is stable.

Long QT syndrome. A 2:1 atrio-ventricular block is sometimes observed in cases of long QT syndrome. When sudden occurrences of tachycardia are observed in the fetal stage, long QT syndrome should be particularly suspected. Sudden death in the early neonatal stage is associated with long QT syndrome. Therefore, electroencephalography should be performed soon after birth in infants with normal heart structure and negative autoantibodies.

Intrauterine treatment

In some cases of fetal bradycardia due to maternal autoantibodies, β-agonists or steroids to the mother have been reported as effective. Direct implantation of a fetal pacemaker is currently in the experimental stage and has been conducted only for research purposes.

Transplacental β-agonists (class IIa). Transplacental β-agonists such as ritodrine hydrochloride (Utemerin), terbutaline (Bricanyl), and salbutamol (Venetol) increase the fetal heart rate by 10–20%, improve heart function, and alleviate fetal hydrops. Maternal side-effects (heart palpitations, liver dysfunction, leukopenia), however, have been reported. This treatment method facilitates observation of fetal progress, but may precipitate a late delivery.

Transplacental steroids. This treatment may be used when the fetus has tested positive for the mother’s autoantibodies.

(1) Atrio-ventricular block (class IIb): normally, autoantibodies pass through the placenta around gestational week 18, destroying the atrio-ventricular node and causing bradycardia. Transplacental steroid (4 mg oral dexamethasone per day) immediately on diagnosis of the condition will improve the blockage.

(2) Myocarditis (class IIb): transplacental steroid (4 mg oral dexamethasone per day) is effective in cases of cardiac dysfunction and accumulation of pericardial effusion due to autoantibody-induced myocarditis. In these cases, steroids may also be given as prophylaxis against myocarditis. Issues concerning postnatal dilated cardiomyopathy and endocardial fibroelastosis in autoantibody-positive cases have recently attracted attention. Steroid may aid in prevention of these conditions, but this has yet to be confirmed.

(3) Prophylactic use (class IIb): large-scale epidemiological surveys conducted outside Japan have reported that the frequency of atrio-ventricular block is between 1% and 7.5% in anti-SSA-positive cases. The frequency of atrio-ventricular block in the second pregnancy is between 15% and 18%. At present, the efficacy and safety of steroid treatment for the mother, which is based on a positive test result for anti-SSA antibodies alone, are uncertain. In contrast, steroid treatment for the mother in the early stages of pregnancy with the second child has been reported as effective in cases in which the first child had atrio-ventricular block. Some reports show steroids having an effect on adrenal suppression and fetal brain development in cases of intrauterine growth restriction. Steroid treatment of atrio-ventricular block requires further study.

Timing and mode of delivery

The obstetrician and neonatologist must decide the timing of delivery after weighing the risks of continuing intrauterine treatment versus the risks of premature delivery and treating an underdeveloped fetus outside the womb. In cases in which β-agonist treatment results in an increase in fetal heart rate and improvement of fetal hydrops, timing of delivery should not be decided by the presence of fetal hydrops alone. Conversely, an early delivery allows the temporary surgical attachment of myocardial electrodes for external pacing of the heart. Delivery must occur before fetal hydrops develops to a critical point and effects prognosis.

As part of the decision regarding timing of delivery, cardiac insufficiency must be assessed, as mentioned earlier. The assessment must be made over time using several indices.

No standard guidelines exist regarding the choice between vaginal delivery and cesarean section in cases of ventricular block. Practitioners should be aware, however, that vaginal delivery may preclude assessment of the fetal heart rate using a fetal heart rate monitor.

Postnatal care

Early postnatal echocardiography and electrocardiography can be performed for assessing cardiac structure, function, and arrhythmia. Long QT syndrome may cause torsades de pointes immediately after birth. Echocardiography should be used to examine and identify this syndrome in the postnatal stage.

Patients with confirmed fetal hydrops may develop postnatal cardiac insufficiency. Therefore, temporary external pacing should be done via a venous catheter inserted in the inguinal region. Insertion of electrode catheters in patients weighing <2 kg, however, may result in myocardial perforation. In such cases external pacing should be performed by attaching invasive myocardial electrodes. In less severe fetal hydrops and in those cases in which preparations can be made on an emergency basis, an internal pacemaker may be implanted in a single surgery.

In patients not complicated with fetal hydrops, a comprehensive decision must be made regarding the need for internal pacemaker implantation. Even in the absence of fetal hydrops, pacemaker implantation is considered appropriate if cardiac output cannot be sufficiently maintained. The American College of Cardiology/American Heart Association and Japanese guidelines set the minimum required heart rate in the neonatal stage as 50–55 beats/min. Pacemaker implantation is also appropriate in cases of higher heart rate but poor cardiac function or heart malformation. When sufficient cardiac output cannot be maintained, an alternative method is to increase the heart rate and stabilize the patient’s condition using isoproterenol. If this procedure is successful, the dose may be gradually decreased and...
the heart rate monitored. When the patient is crying and no increase in heart rate is observed even when echocardiography indicates adequate QRS width, pacing is considered appropriate. A multifacility Japanese study showed that pacing was performed in all neonatal cases of heart rate <60 beats/min.

In the long term, dilated cardiomyopathy and endocardial fibroelastosis may develop in cases of neonatal arrhythmia. Monitoring of heart function over time is important, even in cases of stable heart rate during the neonatal and infant stages or cases in which an internal pacemaker has been implanted.

**Fetal tachyarrhythmia**

Intrauterine treatment is effective in cases of fetal tachyarrhythmia (Table 5). However, for cases of intractable arrhythmia, the proper treatment may be difficult to determine. More effective and safer treatment for this disease are reported every year. Accurate diagnosis and assessment of the patient’s condition facilitate treatment planning using the latest methods.

**Diagnosis of fetal tachyarrhythmias**

Fetal tachycardia is diagnosed when the fetal heart rate is ≥200 beats/min. Paroxysmal tachycardia may be diagnosed, however, if transient increases in heart rate are observed, even when the heart rate is <200 beats/min. Changes in heart rate during tachycardia must be evaluated for accurate diagnosis. M-mode and Doppler echocardiography can be used to classify paroxysmal tachycardia by observation of the relation between ventricular and atrial contractions, but it should be noted that these methods do not reflect electrical phenomena, and electrocardiography is necessary after birth to elucidate the detailed mechanisms of tachycardia.

**Key points**

**Duration of tachycardia.** In cases of intermittent paroxysmal tachycardia, the duration of tachycardia can be recorded using echocardiography or long-term fetal heart rate monitoring. When tachycardia is present for ≥50% of the total time, the risk of circulatory insufficiency is increased and treatment is considered appropriate. The longer the duration of tachycardia, the more likely is the development of fetal hydrops. In contrast, fetal hydrops may develop in some cases even when tachycardia is observed <50% of the time. In these cases, careful observation of the fetus is required. Impairment of cardiac function due to sustained tachycardia is a more important factor in the development of fetal hydrops compared with fetal heart rate.

**Complicating congenital heart anomalies.** Although rare, Ebstein’s anomaly and other congenital heart disease may complicate paroxysmal tachycardia. The incidence of complicating congenital heart anomalies is especially high in cases of atrial flutter.

**Fetal hydrops.** As heart failure advances, fetal hydrops (pericardial effusion, pleural effusion, ascites and subcutaneous edema) develops, and treatment strategy should be modified.

**Cardiac function.**

1. **Atrio-ventricular valve insufficiency:** because atrio-ventricular valve insufficiency can occur as a result of decreased cardiac function and annular dilatation due to tachycardia, grade of tachycardia can be an index for decline in cardiac function. Venous backflow caused by atrio-ventricular valve regurgitation will increase, leading to fetal hydrops (class IIA).

2. **Cardiomegaly:** the development of cardiomegaly is an index for the development of heart failure (class IIA).

3. **The reverse flow (preload index) in the inferior vena cava can sometimes be used to assess heart failure.** In many cases of tachycardia, however, the reverse flow appears in the early phase, making its use as an index for the progress of heart failure uncertain (class IIb).

4. **Heart rate:** early studies reported that heart rate ≥230 beats/min indicates a high risk for fetal hydrops, but many recent studies have found no association between fetal heart rate and development of fetal hydrops.

**Types of fetal tachycardia**

**Supraventricular tachycardia.** In cases of tachycardia with 1:1 atrio-ventricular conduction, atrio-ventricular reentrant...
In rare cases, atrio-ventricular (AV) tachycardia (AVRT) due to Wolff–Parkinson–White syndrome is most frequently diagnosed. In cases of atrio-ventricular nodal reentrant tachycardia, ectopic atrial tachycardia (EAT), permanent junctional reciprocating tachycardia (PJRT), or junctional ectopic tachycardia (JET) are diagnosed. Also, ventricular tachycardia with retrograde conduction must be differentiated. Measurement of the ventriculo-atrial intervals using M-mode or Doppler echocardiography would be helpful to differentiate these arrhythmias.

(1) Measurement of ventriculo-atrial time interval: ventriculo-atrial time interval can be measured using M-mode or Doppler echocardiography. Doppler, which can simultaneously record the blood flow of both in the superior vena cava and in the descending aorta, provides more accurate assessment, but M-mode is easier to perform.

The ventriculo-atrial time interval is the time between a ventricular contraction and the following atrial contraction. When the ventriculo-atrial time interval is shorter than the atrio-ventricular time interval, short VA tachycardia, that is, most frequently AVRT, is indicated. This is similar to atrio-ventricular reciprocating tachycardia (Fig. 15). In contrast, when the ventriculo-atrial time interval is longer than the atrio-ventricular time interval, long VA tachycardia, that is, other types of supraventricular tachycardia (SVT) including EAT and PJRT, is indicated.

(2) AVRT: this is the most common type of fetal tachycardia with a 1:1 atrio-ventricular conduction. It is characterized by an accessory conduction pathway such as the bundle of Kent, through which reentry occurs, and short ventriculo-atrial time. It is confirmed postnatally by delta waves and often diagnosed as Wolff–Parkinson–White syndrome, and even if delta waves are not present, concealed Wolff–Parkinson–White syndrome cannot be excluded. In rare cases, it may be complicated with congenital heart anomalies other than Ebstein’s anomaly. In some cases, intermittent paroxysmal or sustained tachycardia is observed.

**Atrial flutter.** Atrial flutter is indicated by tachycardia with atrial and ventricular contractions in a 2:1 or 3:1 ratio, as identified using M-mode echocardiography. When atrio-ventricular conduction becomes a 1:1 ratio, the heart rate increases remarkably, the overall condition deteriorates rapidly, and fetal death is possible. Therefore, treatment of atrial flutter is required regardless of the presence or absence of fetal hydrops. Atrial flutter can be complicated by congenital heart anomalies.

**Multifocal atrial tachycardia.** Multifocal atrial tachycardia is characterized by unmistakable irregularities both in the ventricular and atrial contractions and a high heart rate. Definitive diagnosis is made on postnatal electrocardiography. Because of the high risk of rapid progression of heart failure, this irregular rhythm must not be attributed to only frequent occurrence of premature atrial contraction.

**Ventricular tachycardia.** Ventricular tachycardia is characterized by disassociated ventricular and atrial contractions with increased ventricular rate. If ventricular tachycardia occurs without retrograde conduction, atrial contractions dissociate with ventricular contractions. JET can show sequences. When retrograde conduction occurs with a 1:1 ventriculo-atrial conduction, differentiation between ventricular tachycardia and SVT is necessary. Ventricular tachycardia is rare in fetal life. Standard treatment for ventricular tachycardia in the fetus has not been established. Each case must be treated individually after thorough investigation of the patient’s condition.

**Treatment of fetal tachycardia**

**Basic plan.** Fetal tachyarrhythmias include SVT, atrial flutter, multifocal atrial tachycardia, and ventricular tachycardia. The treatment of fetal tachyarrhythmias should be managed with the cooperation of pediatric cardiologists in a hospital equipped to perform level II fetal echocardiography. The safety of the mother is of paramount importance. In particular, the mother should be hospitalized and her condition thoroughly evaluated (i.e. echocardiography, underlying conditions, electrolytes, K+, use of other drugs) when procedures involving the fetus are performed.

The treatment of fetal tachycardia includes intrauterine treatment and that after birth following early delivery. In many cases, transplacental treatment of fetal tachycardia with anti-arrhythmic drugs to the mother is effective. Several limitations and problems, however, are known to be related to intrauterine treatment. In some cases, early delivery is preferable. The choice of intrauterine treatment or early delivery should take into account gestational age, the type of fetal tachycardia, the presence or absence of fetal hydrops, and the effectiveness and risks of treating the...
fetus. The choice should be made after the family has been fully informed of all issues associated with both options.

In clinical settings, each case is different, and the choice between intrauterine treatment and early delivery is often difficult. No definitive and established treatment exists at present. Each country and facility has its own protocols, and the experience of each case provides opportunities for new treatment strategies to be studied and reported each year. For these reasons, the efforts of obstetricians, neonatologists, and pediatric cardiologists must be coordinated, detailed information must be provided to the family, and then treatment options must be carefully chosen. The following is our view of the points that should be considered when making these decisions.

Gestational age. When facilities for premature infants are available, the first choice is early delivery and postnatal treatment. This treatment option allows direct monitoring using electrocardiography, direct treatment of anti-arrhythmic drugs to infants without exposing the mother to danger. Furthermore, DC shock or i.v. adenosine triphosphate is available with more immediate effects. In cases of sustained tachycardia, however, delivery via cesarean section is preferable because vaginal delivery makes it difficult to monitor the fetal heart rate. For this reason, the risk of anti-arrhythmic drugs to the mother should be thoroughly explained. Digoxin, which poses low risk to the mother, can be used as one of the first-line drugs for transplacental treatment. Once sinus rhythm is established, vaginal delivery becomes a more viable option. For cases in which digoxin is ineffective, however, early delivery is a more feasible option with lower risk compared with additional treatment with other anti-arrhythmic drugs that may cause side-effects in the mother.

When delivery is inadvisable due to prematurity of the baby, intrauterine treatment should be selected. If sinus rhythm is not obtained by a variety of anti-arrhythmic drugs, and if circulatory insufficiency progresses, delivery induction and external treatment should be chosen. It should be noted that, if prematurity is combined with circulatory insufficiency, life expectancy, neurological prognosis and quality of life could deteriorate.

Types of fetal tachycardia. Because the risk of heart failure progression and the effectiveness of intrauterine treatment depends on the type of arrhythmia, the patient management strategy must be decided after considering all these variables.

Fetal hydrops. Signs of fetal hydrops, progressive cardiomegaly, and atrio-ventricular valve regurgitation indicate that tachycardia-induced collapse of fetal circulation is imminent, and that the time available for intrauterine treatment is limited. Some reports showed that the mortality rate for patients complicated with fetal hydrops is between 12% and 35%, which is far higher than the mortality rate of 0–4% in patients without this complication. In cases in which intrauterine treatment improves tachycardia, however, a dramatic improvement in fetal hydrops may also be observed. Even in cases of fetal hydrops, fetal death is rare during the first 1–2 weeks required for conversion of tachycardia in utero. If early delivery is selected on the basis of the presence of fetal hydrops due to tachycardia, the prognosis may be worsened by complications resulting from the prematurity of the newborn. Many reports recommend intrauterine treatment with a combination of digoxin and a second-line drug from the beginning of treatment in cases of fetal hydrops.

Drugs for intrauterine treatment of tachycardia.

Digoxin. The following is the pharmacokinetics of digoxin and rationale for its usage. In most cases of fetal tachycardia, digoxin is considered the first-line drug of choice (Table 6), but, because its placental transportation is limited, the fetal blood concentration of this drug is approximately 80% that of the maternal blood concentration. Therefore, 2–3 days are required for digoxin to reach this concentration in the fetus. In cases of fetal hydrops, placental transportation of the drug is further decreased, necessitating more time for it to reach the target concentration, and its effectiveness in inhibiting tachycardia and restoring sinus rhythm is reduced. Digoxin is widely accepted as the drug of first choice, however, for several reasons. First, it is easy to use, because monitoring the blood concentration of digoxin is easy and its effective and toxic concentration ranges are well known.

| Name          | Saturation dosage | Dosage | Maintenance dosage | Effective blood concentration | Problems                                      |
|---------------|-------------------|--------|-------------------|-----------------------------|-----------------------------------------------|
| Digoxin       | 1.0 mg 2 × po (1st day) or 0.5 mg i.v. 8 h later 0.25 mg i.v. ×2 (every 8 h) | 0.5–0.75 mg 2 × po or 0.25 mg 2–3 i.v. | 1.5–2.0 ng/mL               | Digoxin toxicity (mother)                     |
| Propranolol   | 1000 mg in a slow i.v. infusion at 20 mg/min. | 4000 mg 4 × po | 4–8 µg/mL            | Hypoglycemia                                |
| Flecainide    | 160 mg/day        | 200–400 mg 2–3 × po | 20–100 µg/mL          | Proarrhythmia (long QT syndrome)              |
| Sotalol       | 160–320 mg 2 × po | 400–800 mg 2 × po | 300–800 ng/mL         | Proarrhythmia (long QT syndrome) Fetal death is reported |
| Amiodarone    | 800–2400 mg 2 × po (2–5 days) | 400–800 mg 2 × po | 1.0–2.5 µg/mL         | Hypothyroidism (cease in 3 weeks) Pulmonary fibrosis (in neonates) |

© 2015 The Authors. Pediatrics International published by Wiley Publishing Asia Pty Ltd on behalf of Japan Pediatric Society
addition, the high pulse rate caused by sustained tachycardia triggers deterioration in cardiac function. Unlike other anti-arrhythmic drugs, which suppress cardiac function, digoxin is widely used because of its side-effects of improving cardiac function.

With regard to the actual method of treatment, the normal oral maintenance dosage may be used in the absence of signs of fetal hydrops or other circulatory insufficiency. When a more rapid increase in blood concentration is needed, however, rapid digitalization via oral or i.v. treatment to the mother should be selected. As already mentioned, the target concentration of digoxin in fetal blood is achieved 2–3 days later than in maternal blood. When it is necessary to achieve the desired blood concentration in the fetus more quickly, direct i.m. injection of digoxin is effective. Because of its large volume of distribution, however, digoxin 0.75 mg per day might be necessary in order to maintain the effective concentration range. Because the effective blood concentration of digoxin is 1–2 ng/mL, a blood concentration close to 2 ng/mL should be maintained in the mother in order to avoid toxicity.68

Drugs of second choice. Currently, flecainide, sotalol, amiodarone, procainamide, and propranolol, and so on, are reported to be effective second-line drugs for the intratutine treatment of fetal tachycardia. The merits and demerits of these drugs and their effectiveness when used in combination, however, have not yet been established.37,59,62,66,67,69–76 Studies have shown that the placental transportation of these drugs is satisfactory even in the presence of fetal hydrops. Verapamil, which was used for the treatment of fetal tachycardia previously, has a strong suppressive effect on fetal or neonatal cardiac function, therefore, it is no longer used (class III).36,62 Care must be taken to avoid proarrrhythmia in the mother when these drugs are used. The mother should be regularly monitored using electrocardiography, particularly for prolongation of QT intervals.

No standard protocol has been established for discontinuing drugs once tachycardia has resolved and regular sinus rhythm has been established. Many reports recommend that drugs other than amiodarone should be given continually until delivery. Because amiodarone suppresses thyroid function, this drug must be discontinued in 2 weeks.

Treatment of fetal tachyarrhythmias.

Paroxysmal SVT. As mentioned in the section of diagnosis, the course of intratuterine treatment depends on the underlying type of SVT diagnosed by measurement of the ventriculo-atrial time interval.

(1) AVRT: when a short ventriculo-atrial time interval is detected, probability of AVRT is high,54,65 and intratuterine treatment is effective in such cases. The first-line drug is digoxin (class I). When no improvement in tachycardia is observed after 3–4 days of digoxin treatment, and fetal hydrops or cardiac dysfunction develops, an anti-arrhythmic second-line drug should be used (class I). Many reports indicate that, when fetal hydrops is not progressing, digoxin alone should be maintained without an addition of second-line drug for 2 weeks with monitoring (class IIa) to avoid maternal side-effects. In contrast, because the placental transportation rate of digoxin decreases when fetal hydrops is present, it is recommended by some researchers to use digoxin with a second-line drug from the beginning of treatment (class IIa). For those fetuses who do not show conversion of SVT into sinus rhythm under fetal hydrops early in the pregnancy, one second-line drug should be used. If this drug is ineffective after 3–4 days of treatment, another second-line drug should be considered.7

(2) Other types of SVT: for fetal tachycardia with 1:1 atrio-ventricular conduction and a long ventriculo-atrial time interval, digoxin may be ineffective. Treatment with one of the second-line anti-arrhythmic drugs from the beginning will be more effective (class IIa).64,65 When safe for the fetus, early delivery should be considered. Transplacental intratuterine treatment should be chosen when the gestational age rules out early delivery. When this is ineffective, one of the second-line drugs should be used. Heart failure, however, may develop and, if it progresses, treatment should continue until early delivery and postnatal treatment. Fetal tachycardia with long ventriculo-atrial time interval has a poor prognosis. Treatment must be chosen and carried out after a thorough explanation of the situation has been provided to the family.

Atrial flutter. In cases of atrial flutter, atrio-ventricular conduction rate is commonly 2:1–3:1, but, because of the risk of sudden worsening of circulation66 when the conduction ratio becomes 1:1, intratuterine treatment is the better option regardless of the presence of fetal hydrops (class IIa). Digoxin is the drug of choice. If a regular sinus rhythm is not established in 3–4 days, one of the second-line drugs should be used.62 If digoxin lowers the ventricular rate, it may be expected that fetal hydrops/heart failure improves without conversion of flutter into sinus rhythm. Some studies report that the effectiveness of digoxin is lower for atrial flutter than for AVRT.66,67

Postnatal care of infants with fetal tachycardia

A 12-lead electrocardiogram should be obtained without delay for accurate postnatal diagnosis of arrhythmia. Cases of fetal tachycardia should be monitored carefully soon after birth in case of recurrence. In cases of fetal AVRT, intractable tachycardia may develop during the neonatal stage. Beyond the neonatal period, however, episodes of tachycardia typically decrease drastically, allowing cessation of treatment with prophylactic drugs.59,62 In some cases of atrial flutter, postnatal recurrence may be observed immediately after birth; in most of these cases, however, tachycardia resolves quickly. Recurrence of resolved neonatal atrial flutter is rare in the post-neonatal period. Studies have shown that drug treatment as a prophylactic measure against atrial flutter is unnecessary.66,67

In some cases of fetal paroxysmal tachycardia causing fetal hydrops, postnatal encephalopathy has been reported. Therefore, brain imaging and careful observation of the development of the baby are necessary.

© 2015 The Authors. Pediatrics International published by Wiley Publishing Asia Pty Ltd on behalf of Japan Pediatric Society
Long-term prognosis requires future study, but some cases in which tachycardia recurred at school age or older have been reported. Therefore, education of the family about the illness, and long-term observation is recommended.36

Premature contraction

When premature contraction is detected, accurate diagnosis should be obtained at a facility that is able to perform level II fetal echocardiography. In addition, complicating congenital heart diseases should be screened for.32,36 In the fetal stage, premature atrial contraction is common, while premature ventricular contraction is infrequent.

Premature atrial contraction

In cases of premature atrial contraction, M-mode echocardiography can record an atrial contraction before an irregular ventricular contraction. When a premature atrial contraction occurs shortly after the preceding sinus rhythm, the atrio-ventricular node has not recovered from the refractory period, and following ventricular contraction does not occur. Therefore, the interval between ventricular contractions is prolonged. This type of premature atrial contraction, which is called non-conducted premature atrial contraction, is relatively common in fetal life.

Continuous monitoring is unnecessary in cases of sporadic premature atrial contraction without cardiac malformation, but tachycardia may subsequently develop in rare cases.37 If fetal movement decreases, further examinations should be performed. When premature atrial contractions occur frequently (≥10/min), a level II examination should be conducted in order to distinguish between monofocal and multifocal atrial tachycardias. In such cases, even if the possibility of multifocal atrial tachycardia is eliminated, evaluations should be repeated in order to determine the progress of heart failure. In addition, an accurate postnatal diagnosis should be made using electrocardiography.

Premature ventricular contraction

In cases of premature ventricular contraction, an underlying heart defect is often suspected. The patient should be referred to a facility that is able to perform level II fetal echocardiography. Observations should be made for ≥30 min using a fetal heart rate monitor in order to exclude ventricular tachycardia. Even in the absence of ventricular tachycardia, as in cases of premature atrial contraction, the mother should be instructed to visit a medical facility if fetal movement decreases. Postnatal screening of ventricular tachycardia or long QT syndrome using 12-lead electrocardiography and 24 h electrocardiography is advisable.

Ethical issues

Among many changes in today’s society, one is the transition from physicians deciding on patients’ treatment to patients themselves obtaining information from many resources and using them to make their own decisions. Doctors are now required to provide understandable explanations to make sure their patients understand the planned treatment before they undergo medical treatments. These explanations include the possible risks (adverse events and undesirable results for patients), which may result from examination or treatment.

Prenatal medical care, however, is not yet widely recognized, and fetal examination and treatment is not covered by health insurance. The fetal examination itself is not approved. Therefore, the whole of fetal medicine is left in a difficult position, in the gap between social demands for fetal care and the health insurance system.

Diagnosis of fetal heart diseases, like that of other fetal organ diseases, now takes place earlier in pregnancy than ever before. But the ethical aspects of examination have not developed along with it. The most important principle of bioethics is autonomy or self-determination, but a fetus is unable to make its own decisions and the parents are required to make decisions on behalf of the unborn child. The medical staff carrying out the examination are urged to recognize the fetus as a patient. Given here are our indications regarding the ethics of examination and the treatment of fetal heart diseases, with special attention to informed consent.

Choosing an appropriate course of treatment

Although the fetus is an independent life-form from its mother, it does not exist without her. Therefore, medical care provided to a fetus must also meet the needs of the mother. When fetal abnormalities are found, several choices must be made soon after diagnosis (Table 7). These choices can be classified into four categories:

(i) continuation or termination of pregnancy;
(ii) location of delivery (transportation issues);
(iii) method of delivery (cesarean section, induced vaginal delivery, or spontaneous delivery); and
(iv) timing of delivery.

Pre-examination explanation and informed consent

Unlike the pre-implantation imaging or diagnosis using fetus-derived markers, most parents wish to bring their baby to full term when diagnostic imaging detects cardiac anomalies. The unexpected, unfavorable results of abnormality would be told to the parents using only healthy baby images (Table 8).

Different policies between screening and referral

Screening (level I). In general, fetal ultrasonography is a routine examination in prenatal check-up. No particular informed consent is obtained in most cases, because examiners do not expect to find abnormality or pathological condition, but they

Table 7 Establishing treatment policies on the basis of fetal examination

1. Continuation or termination of pregnancy
2. Location of delivery (mother transportation)
3. Method of delivery (cesarean section, induced vaginal delivery, or spontaneous delivery)

Whether to continue or terminate the pregnancy is a critical issue after level II screening before 22 weeks of gestation. It is essential to obtain informed consent before examination.
should inform the expecting mothers of the possibility of finding abnormalities even with the screening.

**Referral for detailed examination (level II).** In most cases, any forms of abnormality are already noted. Therefore, there is a higher possibility that detailed examination would identify an abnormality and patients (expecting mother and father of the fetus, and other family members) may have a variety of anxieties with the examination. In those cases, careful explanation should be provided and consent must be obtained beforehand.

Written consent is still controversial. At present, the health insurance system does not cover fetal diseases (including suspected diseases). This situation calls for prudence with regard to obtaining written consent, which may raise legal responsibility for the medical institution despite the fact that they are not financially insured.

**Details of informed consent (level II)**

Informed consent for level II examinations should include the following.

**Uncertainty and reasons for possible errors.** Parents must be informed about the limitation of accuracy with fetal heart disease examinations. The limiting factors are ductus arteriosus, which closes shortly after birth, and the communication between the two atria (foramen ovale). In addition, the fetus’ spinal column or humerus may interfere with a clear view. And the fetus is examined through the maternal abdominal wall, uterus, and placenta.

When the examination is performed early in pregnancy, the fetus would change its figure with gestational weeks. It is highly recommended to explain these facts and do multiple examinations.

**Parents’ rights.** It is the right of expecting mothers to have the examination and be informed of the results. They may opt to refuse the examination or remain uninformed of the results. There should be options in which the hospital or the family members of the expecting mother may be informed of the diagnosis and bear responsibility for deciding upon the best course of treatment for the fetus, and it is recommended to explain this to the expecting mothers.

**Purpose of examination.** The purpose of examination is to consider the best course of action for the wellbeing of the fetus on the basis of the diagnosis. In case of fetal examination before 22 weeks of gestation, examination is done to determine the best option rather than to decide on termination of pregnancy.

**No coverage by health insurance.** Fetal examination is currently not covered by health insurance (July 2004). Each institution has its own policy and fees. Therefore, it is recommended to mention this before the examination.

**Fetal diagnosis before 22 weeks of gestation (level II)**

This is halfway through the whole pregnancy period. The fetus is changing, and it is difficult to predict the outcome. For example, even when the examination shows no abnormality at this point, the decrease of blood flow from the left atrium to the left ventricle by premature foramen ovale closure may lead to hypoplastic left heart disease. Therefore examination at 30 weeks of gestation is recommended even in the case of no abnormality at the first screening.

Fetal examination is performed for the benefit of the fetus, not to decide on continuation or termination of the pregnancy, but it is necessary to discuss choice of termination before or after the examination.

**Who explains the result, to whom?**

Obstetrician or pediatric cardiologist? When level II examination is performed as a referral, a discussion should be held beforehand on who would explain the result, to which extent.

The pre-exam explanation should be given to both parents (expecting mother and her partner). This allows both of them to hear the same explanation, and the presence of another person facilitates full understanding.

**Post-exam diagnosis and deciding the policy**

A second examination is recommended even when the result of level I examination indicates no abnormality. We list guidelines for the abnormality cases (Table 9).

**Who will explain the result?**

In most cases it is the physician who performed the examination or the obstetrician in charge, and the key is the patient–doctor relationship. In critical cases, it is advised to obtain help from the counselors, midwives, nurses, and neonatologists in order to provide a better explanation.

**In principle, explain to the expecting mother and the father of the fetus**

As mentioned in the pre-exam explanation, it is important that not only the expecting mother but another person hear the abnormality result at the same time. It is desirable to have an emotional
**Table 9** Explanation of the results and the treatment options (level II)

| Explanation of the result | Treatment options |
|--------------------------|-------------------|
| Multiple examinations should be recommended even when the first one indicates no abnormality | |
| When abnormality is diagnosed: | |
| - The explainer should be selected based on their relationship with the expecting mother up to that point | |
| - In a critical case, the explanation should be given after medical staff have decided upon a course of action | |
| - In principle, the explanation should be given to the expecting mother and the father of the fetus | |
| - The explanation should include: main diagnosis, anticipated progress with gestational weeks and after birth, necessity of the treatment and the prognosis, alternative treatment, next examination and recommendation for a second opinion | |
| Support for the expecting mother and the family after the explanation of the result | |
| Follow-up support after diagnosing cardiac abnormality with poor prognosis | |

**Support after a poor outcome**

**Pathological autopsy.** Pathological autopsy is recommended in any of intrauterine fetal death, termination of pregnancy or postnatal death. The result is important to reconfirm the diagnosis and following counseling.

**Mental counseling.** Counseling for poor prognosis is the least developed area of domestic medical care. It is better to provide it a few days after the fetal diagnosis has been made.

**Fetal examination of the subsequent pregnancy.** Parents are anxious about the following pregnancy after losing a baby. Special consideration is required for fetal and genetic examination in the next pregnancy.

**Effects and safety of ultrasound examination**

While there is little evidence that M-mode and 2-D ultrasound have adverse effects on the fetus, the exposure must be kept as low as possible.

The possibility of fetal morphogenesis during the middle of the pregnancy has not been ruled out, especially for Doppler and color Doppler modes. Therefore, blood flow examination must be performed as quickly as possible.

The ultrasound equipment is pre-set to minimum output for fetal examination compared to the adult and pediatric modes. It is recommended to use the fetal pre-set mode determined by the manufacturer’s default.

This guideline is set by the Guideline Committee of the Japanese Society of Fetal Cardiology for the Japan Society of Pediatric Cardiology and Cardiac Surgery.

**Acknowledgments**

In the process of publication of the English version of this guideline as the second publication, the following Board Members of the Japanese Society of Fetal Cardiology contributed to checking the translation style into English: Hitoshi Horigome, MD, Tomoaki Ikeda, MD, Yukiko Kawazu, MD, Kenji Suda, MD, Kenji Harada, MD, Hitoshi Yoda, MD, Kiyohiro Takigiku, MD, and Satoshi Yasukochi, MD.

**References**

1 Hoffman JIE. Incidence of congenital heart disease. II. Prenatal incidence. *Pediatr. Cardiol.* 1995; 16: 155–65.
2 Horger EO, Tsai CC. Ultrasound and the prenatal diagnosis of congenital anomalies: A medicolegal perspective. *Obstet. Gynecol.* 1989; 74: 617–19.
3 Allan LD. A practical approach to fetal heart scanning. *Semin. Perinatol.* 2000; 24: 324–30.
4 Achiron R, Glaser J, Gelernter I et al. Extended fetal echocardiographic examination for detecting cardiac malformations in low risk pregnancies. *BMJ* 1992; 304: 671–4.
5 Bull C. Current and potential impact of fetal diagnosis on prevalence and spectrum of serious congenital heart disease at term in the UK. *British Paediatric Cardiac Association. Lancet* 1999; 354: 1242–7.
6 Montana E, Khoury MJ, Cragan JD et al. Trends and outcomes after prenatal diagnosis of congenital cardiac malformations by...
fetal echocardiography in a well defined birth population, Atlanta, Georgia, 1990–1994. *J. Am. Coll. Cardiol.* 1996; 28: 1805–9.

7 Smythe JF, Copel JA, Kleinman CS. Outcome of prenatally detected cardiac malformations. *Am. J. Cardiol.* 1992; 69: 1471–4.

8 Satomi G, Yasukochi S, Shimizu T et al. Has fetal echocardiography improved the diagnosis of congenital heart disease? Comparison of patients with hypoplastic left heart syndrome with and without prenatal diagnosis. *Pediatr. Int.* 1999; 41: 782–32.

9 Tworetzky W, McElhinney DB, Reddy VM et al. Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. Circulation 2001; 103: 1269–73.

10 Bonnet D, Coltii A, Butera G et al. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation 1999; 99: 916–18.

11 Duke C, Sharland GK, Jones AM et al. Echocardiographic features and outcome of truncaus arteriosus diagnosed during fetal life. *Am. J. Cardiol.* 2001; 88: 1379–84.

12 Franklin O, Burch M, Manning N et al. Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. *Heart* 2002; 87: 67–9.

13 Pepas LP, Savis A, Jones A et al. An echocardiographic study of tetralogy of Fallot in the fetus and infant. *Cardiol. Young* 2003; 13: 240–47.

14 Maeno YV, Kamenri SA, Sinclair B et al. Prenatal features of ductus arteriosus constriction and restrictive foramen ovale in transposition of the great arteries. Circulation 1999; 99: 1209–14.

15 Huhta JC. Uses and abuses of fetal echocardiography: A pediatric cardiologist’s view. *J. Am. Coll. Cardiol.* 1996; 8: 451–8.

16 Silverman NH, Kleinman CS, Rudolph AM et al. Fetal atrioventricular valve insufficiency associated with nonimmune hydrops: A two-dimensional echocardiographic and pulsed Doppler ultrasound study. Circulation 1985; 72: 825–32.

17 Tulger G, Kowsathit P, Gudmundsson S et al. Diastolic function of the fetal heart during second and third trimester: A prospective longitudinal Doppler-echocardiographic study. *Eur. J. Pediatr.* 1994; 153: 151–4.

18 Buskens E, Stewart PA, Hess J et al. Efficacy of fetal echocardiography and yield by risk category. *Obstet. Gynecol.* 1996; 87: 423–8.

19 Sharland GK, Allan LD. Screening for congenital heart disease prenatally. Results of a 2 1/2-year study in the South East Thames Region. *Br. J. Obstet. Gynaecol.* 1992; 99: 220–25.

20 Hornberger LK, Sanders SP, Rein AJJ et al. Left heart obstructive lesion and left ventricular growth in the midtrimester fetus: A longitudinal study. Circulation 1995; 92: 1531–8.

21 Chauoi R, McEwing R. Three cross-sectional planes for fetal color Doppler echocardiography. *Ultrasound. Obstet. Gynecol.* 2003; 21: 81–93.

22 DeVore GR, Medearis AL, Bear MB et al. Fetal echocardiography: Factors that influence imaging of the fetal heart during the second trimester of pregnancy. *J. Ultrasound Med.* 1993; 12: 659–63.

23 Comstock CH. What to expect from routine midtrimester screening for congenital heart disease. *Semin. Perinatol.* 2000; 24: 331–42.

24 Copel JA, Pilu G, Green J et al. Fetal echocardiographic screening for congenital heart disease: The importance of the four-chamber view. *Am. J. Obstet. Gynecol.* 1987; 157: 648–55.

25 Kirk JS, Comstock CH, Lee W et al. Sonographic screening to detect fetal cardiac anomalies: A 5-year experience with 111 abnormal cases. Obstet. Gynecol. 1997; 89: 227–32.

26 Anderson N, Boswell O, Duff G. Prenatal sonography for the detection of fetal anomalies: Results of a prospective study and comparison with prior series. *AJR Am. J. Roentgenol.* 1995; 165: 943–50.

27 Buskens E, Grobbee DE, Frohn-Mulder IM et al. Efficacy of routine fetal ultrasound screening for congenital heart disease in normal pregnancy. Circulation 1996; 94: 67–72.

28 Kirk JS, Riggs TW, Comstock CH et al. Prenatal screening for cardiac anomalies: the value of routine addition of the aortic root to the four-chamber view. Obstet. Gynecol. 1994; 84: 427–31.

29 DeVore GR. The aortic and pulmonary outflow tract screening examination in the human fetus. *J. Ultrasound Med.* 1992; 11: 345–8.

30 Comstock CH, Smith RS, Lee W et al. Right fetal cardiac axis: Clinical significance and associated features. Obstet. Gynecol. 1998; 91: 495–9.

31 Smith R, Comstock CH, Kirk JS et al. Ultrasonographic left cardiac axis deviation: A marker for fetal anomalies. *Obstet. Gynecol.* 1995; 85: 187–91.

32 Shipp TD, Bromley B, Horneriker JK et al. Levorotation of the fetal cardiac axis: A clue for the presence of congenital heart disease. Obstet. Gynecol. 1995; 85: 97–102.

33 Kirk JS, Comstock CH, Lee W et al. Fetal cardiac asymmetry: A marker for congenital heart disease. Obstet. Gynecol. 1999; 93: 189–92.

34 Satomi G, Yasukochi S, Iwasaki Y et al. Standardization and advantages of fetal echocardiography. In: Imai Y, Momma K (eds). *Proceedings of the Second World Congress of Pediatric Cardiology and Cardiac Surgery*. Futura, New York, 1998: 618–19.

35 Satomi G. Fetal cardiology. In: Takao A (ed). *Clinical and Developmental Cardiology*, 3rd edn. Chugai Igaku-sha, Tokyo, 2001: 65–76 (in Japanese).

36 Satomi G. Prenatal diagnosis of congenital heart disease. *Shonika* 2001; 41: 634–42 (in Japanese).

37 Satomi G. Diagnostic methods of fetal arrhythmias. In: Satomi G (ed). *Atlas of Echocardiography*. In *Children and Fetuses*. Vectorcore, Tokyo, 1999: 218–22 (in Japanese).

38 Simpson J. Fetal arrhythmias. In: Allan L, Horneriker LK, Sharland G (eds). *Textbook of Fetal Cardiology*. Greenwich Medical Media, London, 2000; 423–37.

39 Maeno Y. Diagnosis and therapy of fetal arrhythmias. In: Kato H (ed). *Pediatric Echocardiography*. From *Basics to Current Clinical Applications*. Kanahara Press, Tokyo, 1993: 54–9 (in Japanese).

40 Wakai RT, Strasburger JF, Li Z et al. Magneto-cardiacographic rhythm patterns at initiation and termination of fetal supraventricular tachycardia. *Circulation* 2003; 107: 307–12.

41 Reinf AJJT, O’Donnell C, Geva T et al. Use of tissue velocity imaging in the diagnosis of fetal cardiac arrhythmias. *Circulation* 2002; 106: 1827–33.

42 Rosenthal R. Fetal heart block. In: Allan L, Horneriker LK, Sharland G (eds). *Textbook of Fetal Cardiology*. Greenwich Medical Media, London, 2000; 438–52.

43 Maeno Y, Rikitake N, Toyoda O et al. Prenatal diagnosis of sustained bradycardia with 1:1 atrioventricular conduction. *Ultrasound Obstet. Gynecol.* 2003; 21: 234–8.

44 Schmidt KG, Ulmer HE, Silverman NH et al. Pernatal outcome of fetal complete atrioventricular block: A multicenter experience. *J. Am. Coll. Cardiol.* 1991; 17: 1360–66.

45 Buyon JP, Hiebert R, Copel J et al. Autoimmune-associated congenital heart block: Demographics, mortality, morbidity and recurrence rates obtained from a national neonatal lupus registry. *J. Am. Coll. Cardiol.* 1998; 31: 1658–66.

46 Frohn-Mulder IM, Meilof JF, Szatmari A et al. Clinical significance of maternal anti-Ro/SS-A antibodies in children with isolated heart block. *J. Am. Coll. Cardiol.* 1994; 23: 1677–81.

47 Groves AM, Allan LD, Rosenthal E. Outcome of isolated congenital complete heart block diagnosed in utero. *Heart* 1996; 75: 190–94.

48 Jaeggi ET, Hamilton RM, Silverman ED et al. Outcome of children with fetal, neonatal or childhood diagnosis of isolated congenital atrioventricular block. A single institution’s experience of 30 years. *J. Am. Coll. Cardiol.* 2002; 39: 130–37.
et al.

Shinohara K, Miyagawa S, Fujita T et al., Neonatal lupus erythematosus: Results of maternal corticosteroid therapy. Obstet. Gynecol. 1999; 93: 952–7.

Carpenter RJ, Strasburger JF, Garson A et al. Fetal ventricular pacing for hydrops secondary to complete atrioventricular block. J. Am. Coll. Cardiol. 1986; 8: 1434–6.

Groves AMM, Allan LD, Rosenthal E. Therapeutic trial of sympathectomies in three cases of complete heart block in the fetus. Circulation 1995; 92: 3394–6.

Copel JA, Buyon JP, Kleinman CS. Successful in utero therapy of fetal heart block. Am. J. Obstet. Gynecol. 1995; 173: 1384–90.

Rosenthal D, Druzin M, Chin C et al. A new therapeutic approach to the fetus with congenital complete heart block: Preemptive, targeted therapy with dexamethasone. Obstet. Gynecol. 1998; 92: 689–91.

Moak JP, Barron KS, Hougen TH et al. Congenital heart block: Development of late-onset cardiomyopathy, a previously underappreciated sequela. J. Am. Coll. Cardiol. 2001; 37: 238–42.

Udink ten Cate FEA, Breur JMPJ, Cohen MI et al. Dilated cardiomyopathy in isolated congenital complete atrioventricular block: Early and long-term risk in children. J. Am. Coll. Cardiol. 2001; 37: 1129–34.

Nield LE, Silverman ED, Taylor GP et al. Maternal anti-Ro and anti-La antibody-associated endocardial fibroelastosis. Circulation 2002; 105: 843–8.

Gregoratos G, Abrams J, Epstein AE et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: Summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee to Update the 1998 Pacemaker Guidelines). Circulation 2002; 106: 2145–61.

Kasanuki H, Aizawa Y, Ohe T et al. Guideline for non-pharmacological treatment of arrhythmias. Jpn Circ. J. 2001; 65 (Suppl.): 1127–60 (in Japanese).

Naheed ZJ, Strasburger JF, Deal BJ et al. Fetal tachycardia: Mechanisms and predictors of hydrops fetalis. J. Am. Coll. Cardiol. 1996; 27: 1736–40.

Simpson JM, Milburn A, Yates RW et al. Outcome of intermittent tachyarrhythmias in the fetus. Pediatr. Cardiol. 1997; 18: 78–82.

Kropp M, Gembuch U, Baumann P. Venous blood flow pattern suggesting tachycardia-induced 'cardiomyopathy' in the fetus. Ultrasound Obstet. Gynecol. 1997; 10: 32–30.

Simpson JM, Sharland GK. Fetal tachycardias: Management and outcome of 127 consecutive cases. Heart 1998; 79: 576–81.

Gembuch U, Redel DA, Bald R et al. Longitudinal study in 18 cases of fetal supraventricular tachycardia: Doppler echocardiographic findings and pathophysiologic implications. Am. Heart J. 1993; 125: 1290–301.

Jaeggi E, Fournier JC, Fournier A et al. Ventriculo-atrial time interval measured on M mode echocardiography: A determining element in diagnosis, treatment, and prognosis of fetal supraventricular tachycardia. Heart 1998; 79: 582–7.

Fournier JC, Fournier A, Proulx F et al. Management of fetal tachyarrhythmia based on superior vena cava/aorta Doppler flow recordings. Heart 2003; 89: 1211–16.

Jaeggi E, Fournier JC, Driblik SP. Fetal atrial flutter: Diagnosis, clinical features, treatment, and outcome. J. Pediatr. 1998; 132: 335–9.

Lisowski LA, Verheijen PM, Benatar AA et al. Atrial flutter in the perinatal age group: Diagnosis, management and outcome. J. Am. Coll. Cardiol. 2000; 35: 771–7.

Allan LD. Fetal arrhythmias. In: Long WA (ed). Fetal and Neonatal Cardiology, WB Saunders, Philadelphia, PA, 1990; 180–96.

Maeno Y. Pharmacological treatment of fetal arrhythmias. In: Sugishita Y, Momma K, Yazak Y et al (eds). Annual Review in Cardiology 2002. Chugai Igaku-sha, Tokyo, 2002; 176–81 (in Japanese).

Blanch G, Walkinshaw SA, Walsh K. Cardioversion of fetal tachyarrhythmia with adenosine. Lancet 1994; 344: 1646.

Cuneo BF, Strasburger JF. Management strategy for fetal tachycardia. Obstet. Gynecol. 2000; 96: 575–81.

De Wolf D, De Schepper J, Verhaaren H et al. Congenital hypothyroid goiter and amiodarone. Acta Paediatr. Scand. 1988; 77: 616–18.

Ebenroth ES, Cordes TM, Darragh RK. Second-line treatment of fetal supraventricular tachycardia using flecainide acetate. Pediatr. Cardiol. 2001; 22: 483–7.

Oudijk MA, Michon MM, Kleinman CS et al. Sotalol in the treatment of fetal dysrhythmias. Circulation 2000; 101: 2721–6.

van Engelen AD, Weijtens O, Brenner JI et al. Management outcome and follow-up of fetal tachycardia. J. Am. Coll. Cardiol. 1994; 24: 1371–5.

Strasburger JF, Cuneo BF, Michon MM et al. Amiodarone therapy for drug-refractory fetal tachycardia. Circulation 2004; 109: 375–9.

Respondek M, Wloch S, Kaczmarek P et al. Diagnostic and perinatal management of fetal extrastoles. Pediatr. Cardiol. 1997; 18: 361–6.

Fetal echocardiography. In: Feigenbaum H (ed). Echocardiography (Chapter 7. Congenital Heart Disease), 5th edn. Lea & Febiger, PA, 1994; 431–2.