Table 1. Baseline Demographic and Obstetric Characteristics of Patients With PAH

	Mild PAH (n=14)	Severe PAH (n=28)	P value
Maternal age (years)	29.5±3.5	30.1±4.0	NS
Nulli/multiparous	8/6	15/13	NS
Miscarriage/delivered	4/10	14/14	NS
Week of delivery*	36.4±4.0	31.4±2.8	<0.005
Birth weight (g)*	2543±350	1464±290	<0.005
SGA*	0	8	<0.05
Delivery mode*			<0.05
Vaginal	6	2	
Cesarean section	4	12	
Regional/general anesthesia	0/4	0/12	NS
BMI	21.2±1.5	22.1±1.8	NS
DM	1	3	NS
Hypertension	2	3	NS
Smoking	1	2	NS

*Only for delivery cases: mild group (n=10), severe group (n=14).
P<0.05 indicates a significant difference. Maternal age, week of delivery, birth weight, and BMI are shown as mean± SD and were analyzed by Student's t-test. Other data were analyzed by chi-square test and Fisher exact test.
PAH, pulmonary arterial hypertension; NS, not significant; SGA, small for gestational age; BMI, body mass index; DM, diabetes mellitus.

Table 2. Underlying Diseases In Patients With Mild and Severe PAH

Category	Mild PAH (n=14)		Severe PAH (n=28)	
	Miscarriage (n=4)	Delivered (n=10)	Miscarriage (n=14)	Delivered (n=14)
IPAH	2	–	2	3
Congenital heart disease	2	8	1	6
ASD (pre/post-op)	1 (0/1)	3 (1/2)	1 (0/1)	1 (0/1)
VSD (pre/post-op)	0	3 (1/2)	0	3 (2/1)
PDA (pre/post-op)	1 (0/1)	1 (1/0)	0	2 (0/2)
ECD (pre/post-op)	0	1 (0/1)	0	0
Eisenmenger syndrome	–	–	10*	4*
ASD			3	0
VSD	–	–	5	3
PDA			2	1
Collagen disease	–	2	–	–
Other	–	–	1	1

Data were analyzed by chi-square test and Fisher's exact test. *P<0.05.
PAH, pulmonary arterial hypertension; IPAH, idiopathic PAH; ASD, atrial septal defect; pre/post-op, pre/post operation; VSD, ventricular septal defect; PDA, patent ductus arteriosus; ECD, endocardial cushion defect.

Association (NYHA) classification or PABP during pregnancy or postpartum. Furthermore, there are no reports of the effects of PABP and maternal cardiac performance in pregnant Japanese women, and fetal growth has not been well studied. Therefore, we investigated the relationship of PABP before and during pregnancy to subsequent maternal cardiac function and neonatal outcome.

Methods

To study mortality and morbidity in maternal outcomes following PAH, we examined the charts of 42 pregnant women with PAH from January 1982 to December 2007. Cardiac function was evaluated using right-sided pulmonary catheterization and echocardiography, although in some cases of mild PAH only echocardiography was used. In the middle of the pregnancy, echocardiography was mainly used for the evaluation of PAH. The patients were divided into mild cases (systolic PABP ≥30 and <50 mmHg on echocardiography[32] or mean PABP ≥25 and <40 mmHg by catheterization[33]) and severe cases (systolic PABP ≥50 mmHg on echocardiography or mean PABP ≥40 mmHg by catheterization). Cardiac function was evaluated during pregnancy and after delivery. Some women chose early termination of pregnancy to avoid risk. Vaginal delivery was attempted for women with spontaneous labor, whereas cesarean section was selected for those with a need for early delivery because of an immature cervix. The NYHA classification was used to evaluate cardiac status.[34]

Data Collection

Data were collected for family history (sudden death, PAH), maternal age, height, body weight, parity, presence of hypertension, diabetes mellitus, change in PABP during and after pregnancy, right and left ventricular function, delivery mode (cesarean section or vaginal delivery), time of delivery (gestational week), and birth weight.

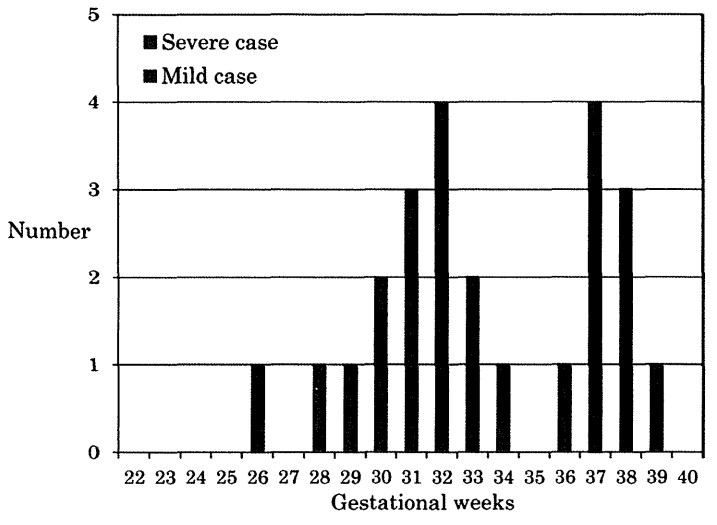

Figure 1. Week of delivery in pregnancies complicated with pulmonary arterial hypertension (PAH). Patients with mild PAH mostly delivered at term, whereas those with severe PAH had earlier deliveries.

Statistical Analysis

For continuous variables, a Student t-test was performed for analysis of normally distributed data, otherwise a Wilcoxon test was used. Chi-square test and Fisher's exact test were performed to compare categorical variables between the mild and severe cases. All statistical analyses were performed using JMP 7 (SAS Institute, Cary, NC, USA). $P<0.05$ was considered statistically significant.

Results

The baseline clinical and obstetrical characteristics of the 42 subjects are shown in **Table 1**. Overall, 42 cases of pregnancy complicated with PAH were analyzed, including 14 mild cases and 28 severe cases. Of the 42 patients, 18 (mild 4, severe 14) selected termination of pregnancy, and 24 (mild 10, severe 14) selected to continue after counseling. The number of patients in each PAH category is shown in **Table 2**.

Idiopathic PAH

There were 3 cases of severe idiopathic PAH. The maternal ages were 30, 38, and 20 years. All were referred because of exacerbated exertional fatigue, dyspnea, and pretibial edema at 25–30 weeks gestational age. On admission, the patients' respective PaO_2 level was 75, 66, and 86 mmHg; PABP was 72/30, 61/31, and 82/42 mmHg; and NYHA class was IV, IV, and III. Delivery by cesarean section was performed at 32, 28, and 32 weeks' gestation under general anesthesia with continuous Swan-Ganz catheter and systemic BP (via a radial arterial line) monitoring. Percutaneous cardiopulmonary support (PCPS) was ready in each case for use in an emergency. In the first case (in 1985), the mother died intraoperatively. Emergency cesarean section had been planned because of an abnormal fetal heart rate pattern, but the mother died of hypotension soon after intubation, despite attempts at resuscitation including PCPS. In the other two cases, which occurred in 2000 and 2003, the women survived to leave hospital. We attribute these outcomes to improved management using continuous infusion of epoprostenol. In the 2003 case, postpartum right-sided pulmonary catheterization showed PABP of 68/32. Dobutamine hydrochloride was started at $1\,\mu g \cdot kg^{-1} \cdot min^{-1}$ for severely low cardiac function, after which subjective symptoms such as shortness of breath during walking disappeared. Epoprostenol infusion therapy was then started at $0.5\,ng \cdot kg^{-1} \cdot min^{-1}$ and gradually increased in increments of $0.5\,ng \cdot kg^{-1} \cdot min^{-1}$ twice weekly until reaching a dose of $7\,ng \cdot kg^{-1} \cdot min^{-1}$. During the course the patient felt lower jaw pain as a side effect, but this gradually disappeared. Pretibial pitting edema and PAH evaluated by echocardiography and right-heart catheterization both improved and the patient was discharged from hospital on the 12th postpartum day.

Pregnancy Outcomes for Mild and Severe Cases of PAH

Gestational length at delivery showed a bimodal distribution (**Figure 1**). Patients with mild PAH mostly delivered at term, whereas those with severe PAH delivered earlier. The indications for delivery in patients with severe PAH were acute dyspnea (3 cases), fatigue and cough (3 cases), elevation of PABP (6 cases), and 2 women went into labor spontaneously. The gestational age at delivery and birth weights were significantly higher in the patients with mild PAH compared with those having severe PAH: 35.4 vs. 31.5 weeks, $P<0.05$; 2,543±350 vs. 1,464±290 g, $P<0.05$; respectively. More cases of fetal restricted growth were observed among the patients with severe PAH than among the mild PAH group: 0/10 vs. 8/15, $P<0.05$. Amniotic volume was adequate in all cases examined in both groups during pregnancy.

Echocardiographic and Cardiac Catheter Data

Among the patients with severe PAH, the average PABP increased as pregnancy progressed, based on the mean PABP pre-pregnancy and in the later stage of pregnancy measured by cardiac catheter (53.5±12.3 vs. 72.8±13.3 mmHg, $P<0.05$) and echocardiography (68.2±11.1 vs. 95.8±18.5 mmHg, $P<0.05$) (**Figure 2**). In the women with mild cases, PABP increased as pregnancy progressed, but did not reach statistical significance (**Table 3**).

NYHA Class

In 7 of the 10 women with mild PAH, NYHA class I was maintained throughout pregnancy (**Figure 3**). In these patients, elevation of PABP was not significant during pregnancy. The remaining 3 women were already NYHA class II in the pre-pregnancy period and 2 remained in NYHA class II until the postpartum period and 1 changed to NYHA class III. Of the 14

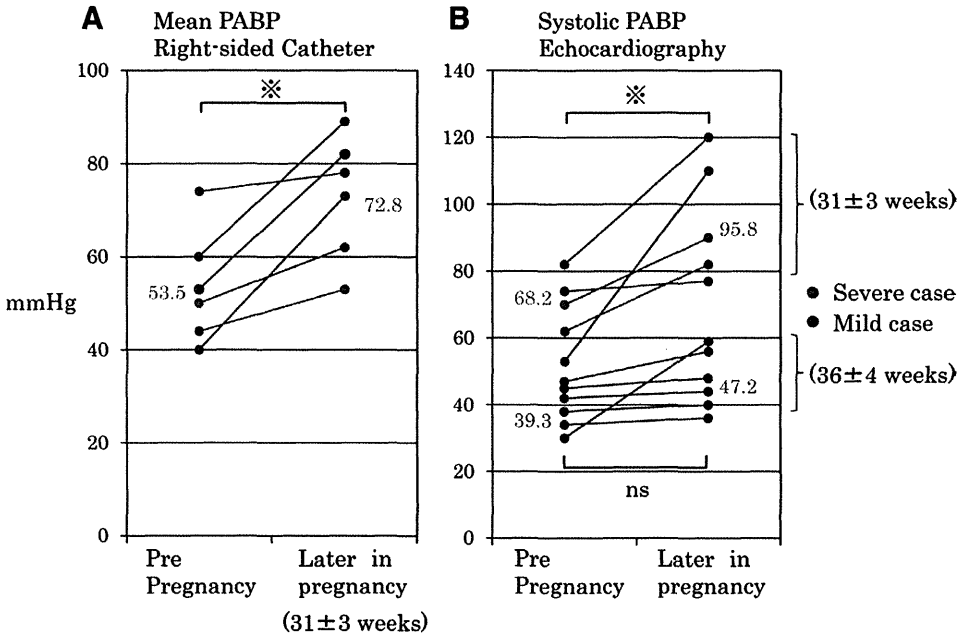

Figure 2. Changes in PABP during pregnancy. (**A**) Change in the mean PABP measured by a pulmonary cardiac catheter. (**B**) Change in the systolic PABP measured by echocardiography. Patients with severe PAH showed a significant increase in PABP later in pregnancy. PABP, pulmonary arterial blood pressure; PAH, pulmonary arterial hypertension.

Table 3. Echocardiographic Findings in Patients With Mild and Severe PAH Measured Early in Pregnancy (Except Systolic PABP)

	Mild PAH (n=14)	Severe PAH (n=28)	P value
Systolic PABP			
Pre-pregnancy	39.3±6.6	68.2±11.1	<0.05
Late-stage pregnancy	47.2±9.2	95.8±18.5	<0.05
Tricuspid valve regurgitation			
None-mild	9	8	<0.05
Moderate-severe	5	20	
LVDs	31.1±4.7	30.1±4.6	NS
Pulmonary artery valve regurgitation	2	3	NS
%FS	36.5±5.6	37.5±4.6	NS
RA cavity enlarged	2	17	<0.05
RV cavity enlarged	2	18	<0.05

LVDd, LVDs, %FS, and systolic PABP were analyzed by Student's t-test and are shown as the mean±SD. Other data were analyzed by chi-square test and Fisher's exact test. P<0.05 indicates a significant difference.
PAH, pulmonary arterial hypertension; PABP, pulmonary arterial hypertension; LVDs, left ventricular end-systolic dimension; NS, not significant; %FS, fractional shortening; RA, right atrium; RV, right ventricle; LVDd, left ventricular end-diastolic dimension.

severe cases, 1 woman was in NYHA class I, 12 women were in class II, and 1 was in class III early in pregnancy. The NYHA class worsened in all but 2 patients as pregnancy progressed. In these women the elevation of PABP was significant during pregnancy. At delivery, 1 patient died soon after intubation in the operation room, 11 were in class III, and 2 were in class IV with severe heart failure.

Discussion

We believe this is the first study in which the change in PABP was monitored during pregnancies complicated by PAH. PABP increased in the later stage of pregnancy in comparison with pre-pregnancy in patients with severe PAH, but not in those with mild PAH. PABP increased in all cases of severe PAH, from a mean of 53.5 mmHg pre-pregnancy to 72.8 mmHg in the later stage of pregnancy. Because pulmonary vascular resistance is elevated in PAH patients, pregnancy continuation may lead to right-heart failure. Circulating blood volume gradually increases by approximately 50% up to around 30 weeks of gestation, and then reaches a plateau.[35] In severe cases, this early rise leads to decompensation and the need for delivery.

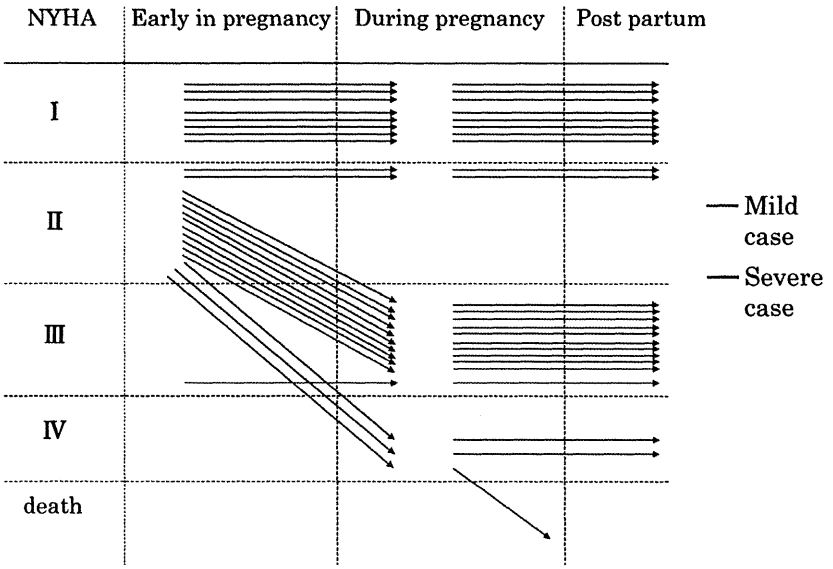

Figure 3. Changes in the New York Heart Association classification over the course of pregnancy.

The signs of decompensation are dyspnea, exertional fatigue, and pretibial edema. Perhaps surprisingly, signs and symptoms of right-heart failure, arrhythmia or angina (resulting from right ventricular ischemia) did not occur in the study subjects, although they might have done so if the pregnancies had been allowed to continue.

Although 70% of maternal deaths reported in the literature occur postpartum, there were no such deaths in our series and no deterioration of NYHA class postpartum. We attribute these improved results to 3 factors. The first is early termination of pregnancy around 30 weeks gestation in severe cases. Improvement of treatment in the NICU facilitated this decision, because all the preterm infants survived without neurological disorders, despite weighing only 1,000–1,500 g with prematurity of most organs. The second factor is the introduction of new drugs for the treatment of pulmonary hypertension, including beraprost, sildenafil, and epoprostenol; and the third is the improvement in anesthetic management. When PABP became higher than systemic BP during cesarean section, especially after removal of the placenta, the anesthetists were ready to reduce the blood volume by 100 ml in a few minutes from a Swan-Ganz catheter and use neosynesin (0.2 mg IV) to raise BP. The women with severe PAH had a higher rate of small-for-gestational-age babies compared with the women with mild cases, which was probably related to reduced cardiac output. However, some babies born to mothers with severe PAH grew adequately.

Patients with mild PAH mostly delivered at or near term, and tolerated the increased heart rate and circulating blood volume of pregnancy well. They were asymptomatic and showed no significant elevation of PABP. These findings indicate that PAH patients with mildly elevated PABP can be advised that pregnancy is appropriate. However, in 8 of 10 mild cases of PAH, the condition was associated with congenital heart disease. Thus, further studies are required to determine the safety of pregnancy for patients with mild idiopathic PAH, including analysis of the need for continuous treatment with epoprostenol (prostacyclin) or oral sildenafil. This study also indicates the significance of evaluating PAH before or in the early stage of pregnancy.

The NYHA class is used as the general standard for rating exercise tolerance in women with heart disease. One patient with severe PAH went from class I to class III during pregnancy and 15 patients with mild or severe PAH in class II pre-pregnancy went to class III during pregnancy (and 1 died), so special care has to be taken of patients who are already class II pre-pregnancy. In contrast, NYHA class I in a woman with mild PAH predicts continuation of pregnancy until term. The disease severity of the present patients may have been higher than that of general patients with PAH because the National Cerebral and Cardiovascular Center is a referral center for cardiovascular diseases. Many patients with severe PAH are referred for genetic analysis because of a family history of pulmonary hypertension. Because PAH is relatively rare, we were only able to include 42 patients in this study. The small number of subjects prevented correction of the results for the effects of potential confounding factors such as hypertension and previous obstetric history, performance of multifactorial analysis, and analysis of the effects of different etiologies of PAH (**Table 2**). However, measurements of the ventricles and atria, and the degree of tricuspid valve regurgitation, were better defined in the present study compared with other multicenter studies. In future work, we plan to investigate a larger cohort of patients to clarify the risk factors in female patients with PAH for cardiac dysfunction during pregnancy. The outcomes for these patients are improving because of the introduction of intravenous treatment with epoprostenol and/or oral sildenafil[36] during pregnancy. In some cases of severe PAH, use of this treatment results in PABP not increasing during pregnancy and appropriate birth weights for gestational age.

Study Limitations

The definition of PAH is a mean PABP ≥25 mmHg and diagnosis requires confirmation by right-sided catheterization. In

most cases in our study, right-heart catheterization was performed before pregnancy, but not during pregnancy provided the patient was not symptomatic, because this examination is invasive for both mother and fetus. For this reason, we are unable to show changes in PAH evaluated by right-sided catheterization, only the changes determined by echocardiography. Therefore, PABP may have been overestimated, because the mean pulmonary artery pressure has been shown to be significantly overestimated by echocardiography compared with catheterization.[37]

Conclusions

Among the cases of severe PAH in this study, PABP increased during pregnancy and there was 1 maternal death during cesarean delivery. The NYHA class in most cases of severe PAH was III or worse in later pregnancy. Early delivery was required and the rate of small-for-gestational age babies was significantly higher. Pregnancy may be safe for PAH patients with mildly elevated PABP. However, in 8 of 10 cases of mild PAH, the women had associated congenital heart disease, indicating that further studies are needed to determine the appropriateness of pregnancy in patients with idiopathic PAH, even if the condition is mild.

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Disclosure

None of the authors has a conflict of interest to disclose. Financial support was from institutional sources only.

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Guidelines for Indication and Management of Pregnancy and Delivery in Women With Heart Disease (JCS 2010)

– Digest Version –

JCS Joint Working Group

Table of Contents

(*Circ J* 2012; **76:** 240–260)

I Introduction to the Revised Guidelines

The latest version of the guidelines includes new findings of papers published after publication of the previous version[1] to reflect the current practice. Some sections regarding obstetrics and specific diseases were revised significantly, while other sections are kept almost unchanged because few reports have been published after publication of previous version. The current guidelines include new sections of "psychosocial issues" (subsection of the "Pre-Pregnancy Counseling"), "Hemodynamic Assessment During Pregnancy", "Drug Therapy During Pregnancy" and "Directions of Future Research".

II General Description

1. Cardiovascular Change During Pregnancy and Delivery

Hemodynamics during pregnancy and delivery is significantly affected by changes in fluid circulation, hematology, respiratory function, endocrinology and the autonomic nervous system.[2,3] Plasma volume begins to increase from 4 weeks of gestation, peaks at 32 weeks of gestation, and then is maintained at a similar level or increase gradually to the volume 40 to 50%

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This English language document is a revised digest version of Guidelines for Indication and Management of Pregnancy and Delivery in Women with Heart Disease reported at the Japanese Circulation Society Joint Working Groups performed in 2009. (website: http://www.j-circ.or.jp/guideline/pdf/JCS2010niwa.d.pdf)
Joint Working Groups: The Japanese Circulation Society, Japan Society of Obestetrics and Gynecology, Japanese Society of Pediatric Cardiology and Cardiac Surgery, The Japanese Society of Cardiovascular Surgery, Japanese College of Cardiology
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higher than that before pregnancy.[4–7] Heart rate peaks at around 32 weeks of gestation to about 20% higher than that before pregnancy. Cardiac output increases to 30 to 50% higher than that before pregnancy at 20 to 24 weeks of gestation, and is maintained at a similar level throughout the pregnancy.[6,7] Aortic pressure and systemic vascular resistance decrease during pregnancy. Uterine contraction and labor pain causes increases in circulatory volume by 300 to 500 ml, cardiac output by 15 to 25% and heart rate and blood pressure.[2,3] It is preferable that women in labor be kept in the left decubitus. Typical blood loss during vaginal delivery is about 500 ml, while that during cesarean section is about 1,000 ml. Immediately after delivery, venous return increases abruptly after the pressure on the inferior vena cava from the growing uterus was relieved. It takes about 4 to 6 weeks to return to a normal hemodynamic status after delivery.[2,3] During the first and second trimesters, hemoglobin and hematocrit levels decrease, which causes a relative anemia.[8–10] The risk of thromboembolism increases during pregnancy. Since aortic wall becomes fragile during pregnancy, aortic dissection may occur in susceptible patients such as Marfan syndrome associated with dilated aorta.

2. Cardiac Assessment Before Pregnancy

It is important for women with heart diseases to undergo appropriate assessment of pulmonary artery pressure, ventricular function, aortic diameter, cyanosis, New York Heart Association (NYHA) classification and other appropriate items to predict the risk of pregnancy-related complications in mother and fetus. Pre-pregnancy checkup for patients with underlying heart diseases includes history taking, physical examination, chest X-ray, electrocardiogram (ECG) and echocardiography. Cardiac catheterization, exercise stress test[11] and Holter monitoring may be also conducted whenever necessary.

3. Pre-Pregnancy Counseling

Women with heart diseases should receive pre-pregnancy counseling, including discussion about the risk to the mother, risk to the fetus, hereditary risk, possible course of pregnancy, and sexual activity and caring for baby. The prevalences of menstruation disorders and amenorrhea are high among women with a history of congenital heart disease especially those with a history of cyanotic congenital heart disease and those who underwent multiple surgeries. Frequent menstrual disorders and poor fertility are common findings among women with residual cyanosis following Fontan operation,[12,13] and women with cyanotic congenital heart disease. Recurrence rate of heart disease is higher in patients with congenital heart disease than in healthy parents, and the incidence is higher in children of mothers with congenital heart disease than those of fathers with it. It is likely that women with heart disease experience heart failure and/or arrhythmia after delivery, and encounter difficulties in caring for baby due to poor cardiac function.[14,15] Patients with heart disease often cannot have life insurances.[16–18] Although the NYHA classification is often used to consider whether pregnancy is contraindicated or not, physicians must not rely solely on it to predict the prognosis of pregnancy of their individual patients. **Table 1** lists patients with heart diseases and conditions that require careful monitoring during pregnancy or should be advised to avoid pregnancy.

Permanent sterilization procedures include tubal ligation, and temporal sterilization procedures include intrauterine devices, low-dose birth control pills, and the classic barrier method. Male contraceptive methods include permanent methods via vasoligation and temporary methods using condoms.

Table 1. Patients With Heart Diseases Requiring Careful Monitoring During Pregnancy or Strongly Recommended to Avoid Pregnancy

- Pulmonary hypertension (Eisenmenger syndrome)
- Outflow tract stenosis (severe aortic stenosis with a mean pressure gradient of >40 to 50 mmHg)
- Heart failure (NYHA Class III to IV, left ventricular ejection fraction <35 to 40%)
- Marfan syndrome (ascending aortic diameter at end-diastole >40 mm)
- Mechanical valves
- Cyanotic heart disease (arterial oxygen saturation <85%)

NYHA, New York Heart Association.

Patients with heart disease must be educated about genetics such as the risk of familial recurrence of heart disease. The Guidelines for Genetic Test and Genetic Counseling in Cardiovascular Disease proposed by the Japanese Circulation Society (JCS) in 2006 describe how to provide genetic counseling for patients with heart disease in detail.[19] Congenital cardiovascular diseases, which are known to occur in 1.06% among liveborn infants in Japan, are the most common congenital disorders to cause neonatal death.[20] They are reported to be accounted for genetic factors (about 12.9%) including chromosomal abnormalities (eg, Down syndrome, Turner syndrome, 22q11.2 deletion syndrome and Williams syndrome, 8.2%) and genetic disease (eg, Noonan syndrome, Holt-Oram syndrome, Marfan syndrome, Jervell-Lange-Nielsen syndrome, 4.7%); disorders involving environmental (external) factors (0.5%) such as those affected by mother's systemic disease, fetal infections and teratogens; and disorders of unknown cause involving multifactorial inheritance (86.7%) (eg, many of congenital heart diseases, idiopathic pulmonary hypertension and idiopathic cardiomyopathy) (**Table 2**).[21] Congenital heart diseases may be caused by not only genetic abnormalities but also environmental factors possibly affecting fetuses and mothers during pregnancy.

Psychosocial issues are also important during pregnancy and delivery. Anxiety and depression may worsen during the perinatal period.[22] Patients with heart disease have strong desire to experience pregnancy and having a baby, and often feel anxiety about the possible effect of pregnancy on their health and potential genetic risks to the child. In order to prevent depression and anxiety during the perinatal period, patients should be provided with correct information and education on heart disease, contraception, sexual activity and social support during the period of adolescence.[23]

4. Cardiac Monitoring of the Mother During Pregnancy

In women with heart disease, complications during pregnancy may often develop in the mother and fetus, and may sometimes be fatal. They must be continuously monitored by a team consisting of obstetricians, cardiologists, anesthesiologists, and nurses for arrhythmia, heart failure and thrombosis during pregnancy.[24] Periodic checkups for healthy pregnant women generally consist of 3 checkups by 11 weeks of gestation, every 4 week monitoring in 12 to 23 weeks of gestation, every other week monitoring in 24 to 35 weeks of gestation,

Table 2. Congenital Cardiovascular Diseases Due to Inherited Abnormalities or Chromosomal Aberrations

Diagnosis	Cardiovascular findings	Non-cardiovascular findings	Causative gene mutation or variant protein	Gene locus
Alagille syndrome	Peripheral pulmonary stenosis, pulmonary valve stenosis, tetralogy of Fallot, ventricular septal defect, atrial septal defect, aortic stenosis, coarctation of the aorta	Cholestasis, specific facial appearance, mental retardation, renal dysplasia, eye abnormalities, butterfly vertebrae	*JAG1(jagged-1)* *NOTCH2*	20p12 1p12
Barth syndrome	Dilated cardiomyopathy, left ventricular noncompaction	Neuromuscular disorders, leukopenia, mitochondrial metabolic disorders, mental retardation	*TAZ (Tafazzin)*	Xq28
Cat eye syndrome	Hypoplastic left heart, total anomalous pulmonary venous drainage, ventricular septal defect, atrial septal defect	Iris tear, anal atresia, malformed ears, small jaw, renal malformation	*DGCR*	Duplication 22q11.1
CHARGE association	Tetralogy of Fallot, atrioventricular septal defect, Ebstein's anomaly, complete transposition of the great arteries	Coloboma, choanal atresia, developmental retardation, renal malformation, genital hypoplasia, malformed ears, hearing loss, tracheoesophageal fistula	*CHD7* *SEMA3E*	8q12.1 7q21.11
Down syndrome	Atrioventricular septal defect, ventricular septal defect, atrial septal defect, aberrant subclavian artery	Specific facial appearance, growth/developmental retardation, duodenal atresia, anal atresia, tracheomalacia, hearing loss, hypothyroidism, muscular hypotonia, leukemia	Multiple	Trisomy 21
Duchenne muscular dystrophy	Cardiomyopathy, conduction disorder, mitral valve prolapse	Progressive skeletal muscle atrophy	*DMD (Dystrophin)*	Xp21.2
Edward syndrome	Ventricular septal defect, patent ductus arteriosus, bicuspid aortic valve, bicuspid pulmonary valve	Intrauterine growth retardation, polyhydramnios, umbilical vessel anomalies, specific facial appearance, psychomotor retardation, overlapping fingers, muscular hypotonia	Multiple	Trisomy 18
Ehlers-Danlos syndrome	Mitral valve prolapse, tricuspid valve prolapse, aortic dilatation, cerebral aneurysms, atrial septal defect	Fragile skin, joint/skin hyperextensibility, subcutaneous bleeding, blue sclera, pneumothorax	*COL5A1,A2* (Types I and II), *COL3A1* (Type IV), *PLOD* (Type IV)	9q34.2-q34.3 2q31 1p36.3
Ellis-van Creveld syndrome	Large atrial septal defect, atrioventricular septal defect	Short extremities, polydactyly, nail hypoplasia, pelvic dysplasia	*EVC*	4p16
Fabry disease	Myocardial ischemia, myocardial infarction, mitral regurgitation, left ventricular hypertrophy, cardiomyopathy, arrhythmia, congestive heart failure	Extremity pain, paresthesia, angiokeratoma, hypohidrosis, renal failure, cerebrovascular disorders, corneal opacity, cataract, constipation, esophageal achalasia, hearing loss	*GAL (Alpha-galactosidase)*	Xq22.1
Friedreich ataxia	Cardiomyopathy, conduction disorder	Progressive ataxia, muscular hypotonia	*FRDA (Frataxin)*	9q13
Goldenhar syndrome	Ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, coarctation of the aorta, atrial septal defect	Asymmetrical facial features, spinal anomalies, microtia, mandibular hypoplasia, hearing loss, conjunctival epidermoid carcinoma	Unknown	Unknown
Heterotaxy syndrome	Single atrium, single ventricle, common atrioventricular canal, pulmonary atresia, transposition of the great arteries, atrioventricular septal defect, conduction disorder	Kartagener syndrome: male infertility, heterotaxia, bronchoectasis, hearing loss Ivemark syndrome: asplenia/polysplenia	*ZIC3, LEFTY2, CFC1, ACVR2B*	Xq26.2 3p22-p21.3 1q42.1 2q21.1
Holt-Oram syndrome	Atrial septal defect, ventricular septal defect, conduction disorder (sinus bradycardia, atrioventricular block)	Radial anomaly (thumb anomalies, 2nd to 5th finger anomalies), upper limb hypoplasia	*TBX5*	12q24.1
Homocystineuria	Thromboembolism, aortic dilatation	Congenital metabolic disorders, mental retardation, skeletal anomalies (tall stature, extension of fingers and toes), ectopia lentis, psychiatric disorder, osteoporosis	*MTHFR*	1p36.3

(Table 2 continued next page.)

Diagnosis	Cardiovascular findings	Non-cardiovascular findings	Causative gene mutation or variant protein	Gene locus
Hurler syndrome	Cardiomyopathy, atrioventricular and semilunar valve insufficiency	Congenital metabolic disorders, specific facial appearance, progressive osteodysplasty, developmental retardation, corneal opacity, hearing loss, growth disorder, scoliosis, hypertrichosis, splenohepatomegaly	*IDUA (Alpha-L-Iduronidase)*	4p16.3
Jacobsen syndrome	Hypoplastic left heart, atrial septal defect, ventricular septal defect	Psychomotor retardation, specific facial appearance, deformed toe joints (hammer toe syndrome)	*BARX2*	Deletion 11q25
Jervell-Lange-Nielsen syndrome	Long QT syndrome	Hearing loss	*KCNQ1* *KCNE1*	11p15.5 21q22.1-q22.2
Kabuki make up syndrome	Coarctation of the aorta, bicuspid aortic valve, mitral valve prolapse, ventricular septal defect, pulmonary artery stenosis, aortic stenosis, mitral stenosis, tetralogy of Fallot, single ventricle, double outlet right ventricle, malposition of the great arteries	Specific facial appearance, psychomotor retardation, dermatoglyphic abnormalities, skeletal anomalies (scoliosis, hip dysplasia, shortened 5th finger), hearing loss	Unknown	Sporadic
LEOPARD syndrome	Pulmonary artery stenosis, atrioventricular block, hypertrophic cardiomyopathy	Multiple lentiginosis, ocular hypertelorism, external genitalia abnormalities, mental retardation, developmental disorder, hearing loss	*PTPN11, KRAS, SOS1, RAF1*	12q24.1 12p12.1 2p22-p21 3p25
Marfan syndrome	Aortic dilatation, atrioventricular valve regurgitation, mitral valve prolapse, annuloaortic ectasia, dissecting aortic aneurysm, pulmonary artery dilatation, pulmonary regurgitation	Tall stature, lens dislocation, myopia, blue sclera, scoliosis, funnel chest, spider-like fingers, joint hyperextensibility, long extremities	*FBN1 (Fibrillin)* *TGFBR1,2*	15q21.1 9q33-q34 3p24.1
Leigh encephalopathy, NARP syndrome	Hypertrophic cardiomyopathy	Progressive psychomotor developmental disorder, convulsions, cerebellar ataxia, feeding and swallowing disorder, muscular hypotonia, optic atrophy	*Mitochondrial loci*	Mitochondrial DNA
MERRF syndrome	Cardiomyopathy	Myoclonus, epilepsy, cerebellar ataxia, muscular hypotonia, intellectual deterioration, short stature	*MTTK*	Mitochondrial DNA
Myotonic dystrophy	Conduction disorder, cardiomyopathy, mitral regurgitation	Myotonia, muscle degeneration, cataract, blepharoptosis	*DMPK , ZNF9*	19q13.2 3q13.3
Noonan syndrome	Pulmonary artery stenosis, hypertrophic cardiomyopathy, atrial septal defect	Webbed neck, short stature, developmental retardation, pectus carinatum, funnel chest, blepharoptosis, bleeding tendency, abnormal platelet function	*PTPN11, KRAS, SOS1, RAF1*	12q24.1 12p12.1 2p22-p21 3p25
Osteogenesis imperfecta	Mitral valve prolapse, aortic regurgitation, aortic dilatation	Fragile bones, frequent bone fractures, hearing loss, blue sclera, short bowing legs, growth disorder, specific facial appearance	*COL1A1* *COL1A2*	17q21.33 7q21.3
Trisomy 13	Ventricular septal defect, patent ductus arteriosus, atrial septal defect	Mental retardation, holoprosencephaly, microcephaly, sloping forehead, hearing loss, malformed ears, rocker bottom feet, polydactyly	Multiple	Trisomy 13
Pompe disease	Myocardial hypertrophy due to glycogen storage	Congenital metabolic disorder, muscular weakness, hepatomegaly, macroglossia	*GAA (Lysosomal Alpha-Glucosidase)*	17q25
Rubinstein-Taybi syndrome	Various congenital heart diseases, hypoplastic left heart	Developmental disorder, specific facial appearance, hypertrichosis, drooping eyelid, ocular hypertelorism, maxillary hypoplasia, forehead enlargement, short stature, broad thumb-hallux	*CREBBP (CREB binding protein)*	16p13.3
Treacher-Collins syndrome	Ventricular septal defect, patent ductus arteriosus, atrial septal defect	Malformed ears, hearing loss, mandibular hypoplasia, cheek bone hypoplasia, choroidal coloboma, bilateral lower eyelid coloboma, cleft palate, choanal atresia	*TCOF1 (Treacle protein)*	5q32

(Table 2 continued next page.)

Diagnosis	Cardiovascular findings	Non-cardiovascular findings	Causative gene mutation or variant protein	Gene locus
Tuberous sclerosis	Cardiac tumor (rhabdomyoma), arrhythmia	Tumors, convulsions, facial angiofibromas, leukoderma, cafe-au-lait spots, osteosclerosis, renal hypoplasia, mental retardation, autism	*TSC1 (Hamartin), TSC2 (Tuberin)*	9q34 16p13.3
Turner syndrome	Coarctation of the aorta, bicuspid aortic valve, hypoplastic left heart, atrial septal defect, ventricular septal defect	Short stature, webbed neck, shield chest, low hairline, ovarian hypoplasia, renal hypoplasia, hearing loss	Multiple	Monosomy X (45, X)
VACTERL syndrome	Ventricular septal defect, atrial septal defect, patent ductus arteriosus	Spinal anomalies, anal atresia, tracheo-oesophageal fistula, radial dysplasia, limb anomalies, renal/urinary anomalies	*Numerous loci*	Unknown
22q11.2 deletion syndrome	Interruption of the aorta, persistent truncus arteriosus, tetralogy of Fallot with pulmonary atresia, right aortic arch, aberrant subclavian artery, ventricular septal defect	Conotruncal anomaly face, cleft palate with nasopharyngeal insufficiency, thymus hypoplasia, hypoparathyroidism, hypocalcemia, increased infection susceptibility, anal atresia, mental retardation, psychiatric disorders, thrombocytopenia	*TBX1 , UFD1L*	del 22q11.2
Williams syndrome	Supraaortic stenosis, supra-valvular pulmonary stenosis, peripheral pulmonary artery stenosis, aortic stenosis, pulmonary artery stenosis, cardiomyopathy	Mental retardation, elfin face, stellate pattern in iris, hypercalcemia, malocclusion, visuospatial cognitive disorders, joint contracture, hypertonia, learning disorder, cognitive visual impairment	*ELN (Elastin)*	7q11.23

and weekly thereafter to the end of the 40th week. For women with heart disease, an appropriate monitoring schedule should be designed on the basis of healthy pregnant women according to the risk during pregnancy. When women with heart disease become pregnant, attending cardiologists must explain the condition of heart disease to obstetricians, and provide information on important points to be monitored during pregnancy and the perinatal period.

5. Hemodynamic Assessment During Pregnancy

It is preferable that patients with heart disease be assessed for hemodynamic status several times during pregnancy and the puerperal period. Echocardiography, a noninvasive method providing detailed information, is very useful in evaluating hemodynamics during pregnancy.[25] The first assessment should be conducted immediately before pregnancy or during the first trimester when changes in hemodynamics are still slight. Patients with mild to moderate risk should be evaluated for hemodynamics again during the late second trimester (26 to 28 weeks of gestation).[26] Patients with severe risk require more frequent hemodynamics assessment. During the peripartum period, hemodynamics should be reassessed. Since child care including breast feeding may increase cardiac load, patients with severe heart disease must be followed up for at least 6 months after childbirth for clinical course including hemodynamics. Although cardiac MRI is believed useful for assessing right heart function and patients with complex congenital heart disease, this technique must be limited for necessary cases since the risk to the fetus remains unclear.[27] Cardiac catheterization and cardiac CT should be limited to patients who may benefit from the examination as these techniques cause radiation exposure. Since no increases in the risks of developmental retardation, central nervous system disorders and developmental disorders have been observed in children exposed to less than 100 mGy, exposure to radiation at this level is not considered to a valid reason for artificial termination of pregnancy.[28]

6. Fetal Examination

The fetal well-being can be assessed using fetal heart rate monitoring[29–31] and ultrasonic methods such as ultrasonic tomography and Doppler sonography.[32,33] Fetal heart rate monitoring is performed using nonstress tests (NST) or contraction stress tests (CST) to evaluate the fetal well-being and the fetal reserve. In the ultrasonic tomography, the biophysical profile (BPP) and a modified BPP combining a NST and an amniotic fluid index are used. Doppler sonographic assessment of fetal hemodynamics is performed on the basis of the systolic to diastolic (S/D) ratio, resistance index, and/or pulsatility index, which represent the vascular resistance in the peripheral vascular beds. The false positive rate is high in fetal assessment methods: The incidences of fetal death among fetuses determined to be in good condition in the NST, CST and BPP have been reported to be 1.9 to 6.45%, 0.3% and 0.65%, respectively.[32]

The presence of heart disease in either parent should be considered to represent a high risk for congenital heart disease in the fetus, and screening using fetal echocardiography should be indicated. In Japan, artificial termination of pregnancy is allowed by 22 weeks of gestation. Since assessment for fetal heart disease to be conducted by 22 weeks of gestation may provide important information for whether the pregnancy should be continued or not, physicians must fully explain the meaning of the assessment to the parents and obtain their informed consent. Fetal heart screening is possible at 18 weeks of gestation and thereafter, and fetal heart condition is best assessed in 20 to 24 weeks of gestation. Since heart anomaly may be first found in the third trimester, it is preferable that the fetal heart condition be assessed again in 30 weeks of gestation or thereafter.

7. Infective Endocarditis

The Guidelines for the Prevention and Treatment of Infective Endocarditis published by the JCS in 2008[34] recommend that the prevention of infective endocarditis be considered for most patients with congenital heart diseases. The most common sources of bacteremia are urogenital infection, delivery, childbirth, indwelling catheter and surgeries. Bacteremia may develop after spontaneous abortion, vaginal delivery assisted by episiotomy or cesarean section, among others. Antibiotic treatment of infective endocarditis should be performed in a fashion similar to that for non-pregnant patients according to the susceptibility of causative agents.[35]

Preventive administration of antimicrobial agents during delivery is recommended for patients with a high risk for infective endocarditis (Table 3).[36–38] Although preventive administration of antimicrobial agents is not recommended for patients in whom the risk for infective endocarditis is not high because of its low incidence, the benefits of preventive antimicrobial treatment are not denied considering the risk-benefit balance. There are no currently available guidelines for the preventive administration of antimicrobial agents during delivery. Table 4 lists common measures to prevent infective endocarditis associated with urogenital or gastrointestinal surgeries/procedures.[39]

Table 3. Patients With Heart Diseases Recommended to Receive Preventive Antimicrobial Treatment During Obstetric Operations/Procedures and Delivery

- Patients with a history of infective endocarditis
- Patients with congenital heart disease
  - Patients with cyanotic heart disease
  - Patients who underwent complete repair using artificial patches and devices within the last 6 months
  - Patients who underwent repair and have remaining shunts around the implanted artificial patches and devices
- Patients using artificial valves
- Patients after heart transplant (receiving immunosuppressants or having valvular heart disease)

8. Drug Therapy During Pregnancy

Drugs used for pregnant women must be selected after careful consideration of the risk-benefit balance in the mother and fetus. The adverse effects of drugs on fetuses are classified into teratogenic effects and fetal toxicity. Since many drugs are not substantially excreted in the breast milk of nursing mothers, the blood concentration of a drug given to the nursing mother is substantially lower than the therapeutic range of the drug in the neonate. The pregnancy category proposed by the Food and Drug Administration (FDA) of the United States is often referred to as important information on the risk of drugs to the fetus or neonate.[40] When drugs contraindicated for pregnant women in the package inserts or drugs not accepted by the National Health Insurance (NHI) are used, the physicians must fully explain the risks and benefits of such drugs to the patients and their families and obtain informed consent.

Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers are contraindicated for women in the second and third trimester since they may directly affect the kidney of the fetus and neonate to cause renal failure, abortion or stillbirth.[41,42] Amiodarone is basically contraindicated for pregnant women since it may cause abnormal thyroid function in the fetus. Bosentan is absolutely contraindicated for pregnant women in the FDA's recommendation. Warfarin is teratogenic when given during the first trimester, and increases the risk for bleeding disorders in the fetus and neonate. Heparin does not have fetal toxicity because it does not cross the placenta, while the incidence of thrombosis among patients receiving heparin is higher than those receiving warfarin. Low-dose aspirin therapy is rated pregnancy category C by the FDA's recommendation and believed relatively safe. However, "aspirin is contraindicated for women in the last 12 weeks of gestation (regardless of the dose)" in the package insert; physicians must fully explain the risks and benefits of aspirin therapy during the second and third trimester of pregnancy to obtain consent from the patient.

9. Care Facility for Pregnancy

Women with heart disease in whom pregnancy poses a risk must be carefully monitored and planned for safer pregnancy and childbirth. High-risk pregnancy should be monitored in tertiary care facility in which team approach by obstetricians, heart disease specialists (eg, cardiologists, pediatric cardiologists, specialists of congenital heart disease in adults, and cardiovascular surgeons), anesthesiologists and neonatologists who have knowledge and experience in the management of high-risk pregnancy has been established. Every tertiary care

Table 4. Prevention of Infective Endocarditis In Patients Receiving Urogenital or Gastrointestinal Surgery/Procedures

Patients	Treatment
• For patients with heart disease in whom serious endocarditis may occur	
Patients who are not allergic to ampicillin/amoxicillin	Administer ampicillin 2.0 g and gentamycin 1.5 mg/kg (maximum dose 120 mg) intramuscularly or intravenously ≤30 minutes before delivery. Administer intravenous ampicillin 1.0 g or oral amoxicillin 1.0 g 6 hrs after delivery.
Patients who are allergic to ampicillin/amoxicillin	Administer intravenous vancomycin 1.0 g (infuse over 1 to 2 hrs) and intramuscular or intravenous gentamycin 1.5 mg/kg (maximum dose 120 mg) to conclude administration ≤30 minutes before delivery
• For other patients	
Patients who can take drugs orally	Administer oral amoxicillin 2.0 g (at lower doses for small patients) 1 hour before delivery
Patients who cannot take drugs orally	Administer intravenous or intramuscular ampicillin 2.0 g ≤30 minutes before delivery
Patients who are allergic to ampicillin/amoxicillin	Administer intravenous vancomycin 1.0 g (infuse over 1 to 2 hrs) to conclude administration ≤30 minutes before delivery

Cited from *Circ J* 2003; **67**(Suppl IV): 1039–1082.[39]

facility in which pregnancy and childbirth in patients with heart disease are managed should establish such a specialist team. Hospitals where such team cannot be established within the institutions should build a system to facilitate consultation with heart disease specialists in other hospitals.

III Specific Maternal Conditions

1. Congenital Heart Disease

Patients with atrial septal defect do not have a high risk for cardiac complications during pregnancy and childbirth, but do has a higher risk for fetal/neonatal complications.[43,44] Patients with ventricular septal defect who had not had signs/symptoms of heart failure during childhood but have only a small left-to-right shunt in adulthood may well tolerate pregnancy and childbirth well. Patients with endocardial cushion defect (atrioventricular septal defect) may often go through the process of pregnancy and childbirth without significant problems, but management of atrial arrhythmia may become necessary in some cases. Patients with patent ductus arteriosus may go through the process of pregnancy and childbirth without significant problems if the shunt volume is small and pulmonary arterial pressure is normal.[45] Patients with mild to moderate congenital aortic stenosis will be free from complications throughout pregnancy. However, in patients with severe aortic stenosis the aortic pressure gradient may increase as the pregnancy progresses, and may pose a risk to the mother. It is recommended that patients with severe aortic stenosis undergo aortic valve replacement or balloon aortic valvuloplasty to treat aortic stenosis before pregnancy.[46–48] Since mechanical valve replacement will require anticoagulation therapy which may pose a risk for the mother and fetus (See the section of "Valvular Heart Diseases"), having bioprosthetic valve replacement or Ross operation other than mechanical valve are recommended for women who want to become pregnant in future. Bicuspid aortic stenosis may lead to aortic dissection. The prognosis of pregnancy in patients with pulmonary stenosis is generally preferable, but percutaneous balloon pulmonic valvuloplasty should be considered for symptomatic patients with severe stenosis.[49] Although patients with a mild case of Ebstein's anomaly will rarely experience pregnancy complications, patients with a severe case of it may experience right heart failure, paradoxical thromboembolism, infective endocarditis, hypoxemia or other complications.[50] The risk of complications in the mother and fetus is small among patients with corrected transposition of the great arteries when their intracardiac abnormalities are mild, although the progression of systemic right ventricular dysfunction and tricuspid regurgitation (systemic atrioventricular valve regurgitation) may occur in some cases.[51,52]

Table 5. Possible Maternal and Fetal Complications During Pregnancy in Women Following Fontan Procedure

- Systemic venous congestion
- Worsening of systemic ventricular function
- Worsening of atrioventricular valve regurgitation
- Supraventricular tachycardia
- Thromboembolism
- Paradoxical thromboembolism (in patients following fenestrated Fontan procedure in which a fenestration was created in the atrial septum)
- Abortion and premature delivery
- Low birth weight infants
- Infertility, amenorrhea

In patients with acyanotic heart disease after repair with mild residua and sequelae, pregnancy, childbirth and vaginal delivery are feasible.[45,53,54] It is recommended that patients who have moderate to severe residua and sequelae which may worsen during pregnancy be treated with re-operation, catheter intervention or other appropriate measures to repair that before pregnancy.

Since repair is successful in many patients with tetralogy of Fallot, the risks for pregnancy and childbirth in them are similar to those observed in healthy pregnant women.[55] The presence of right ventricular dysfunction due to severe pulmonary regurgitation, left ventricular dysfunction or pulmonary hypertension increase the risk during pregnancy and childbirth, and may worsen heart failure or cause tachyarrhythmia. The risk to the fetus is relatively high, and the incidence of spontaneous abortion is higher in patients with tetralogy of Fallot after repair than in healthy pregnant women.[56–60] It is recommended that patients with severe right ventricular outflow tract stenosis undergo reoperation before pregnancy.

Patients following Fontan operation with a NYHA classification of I to II, favorable cardiac function, and sinus rhythm may tolerate cardiac load during pregnancy and can thus complete pregnancy and childbirth, but the number of such patients is not large (**Table 5**).[12,61,62]

The risk during pregnancy is not high among patients with complete transposition of the great arteries who underwent atrial switch operation (eg, Mustard operation or Senning operation), have favorable systemic ventricular function and only mild residua. The incidences of spontaneous abortion and obstetric complications are high. The prevalences of premature birth and low birth weight infants are high. Heart failure, right ventricular dysfunction, worsening of tricuspid regurgitation or supraventricular tachycardia including atrial fibrillation may also occur.[63–66] Although cardiac function is generally good and the incidence of arrhythmia is relatively low in patients following arterial switch operation (Jatene procedure), the presence of pulmonary stenosis, pulmonary regurgitation, aortic regurgitation or ischemic lesions due to coronary stenosis/occlusion increases the risk of complications in these patients.[67] Although few cases have been reported on pregnancy and childbirth in patients following Rastelli operation, the risk during pregnancy and childbirth is not high among patients with good cardiac function and without severe stenosis of right ventricular outflow tract.[68] Since patients with severe stenosis of right ventricular outflow tract are highly likely to have right ventricular dysfunction, ventricular tachycardia or supraventricular tachycardia including atrial fibrillation, it is recommended that they undergo reoperation to treat the stenosis before pregnancy.[69]

Patients who have cyanosis and patients with Eisenmenger syndrome have an extremely high risk to the mother and fetus during pregnancy and childbirth. The risk is especially high to the fetus among the former patients with cyanosis and to the mother among the latter patients with Eisenmenger syndrome.

Table 6. Characteristics of Drugs for the Treatment of Pulmonary Hypertension During Pregnancy and Lactation

Drug	Class	Pregnancy categories	Characteristics/ adverse effects	Teratogenicity	Breast feeding	Package insert*1	
						Pregnancy	Lactation
Beraprost	Prostacyclin	B	Oral	Absent	Probably compatible	1	1
Epoprostenol	Prostacyclin	B	Drip infusion	Absent	Probably compatible	2	1
Bosentan	Endothelin receptor antagonist	X	Oral, Hepatic disorder	Unknown*2	Potential toxicity	1	2
Sildenafil	PDE III inhibitor		Oral, Visual disorder			2	1

PDE III, phosphodiesterase III.

Note) The above information is based on "Drugs in pregnancy and lactation, 8th edition (2008)"[40] (Blank columns represent no information in the source material).

*1Information on the use during pregnancy and lactation in the package insert.

1. Contraindication: This drug should not be administered to women who are or may be pregnant. Treatment should be discontinued without delay when pregnancy is detected. The drug should not be given to lactating women, and, when treatment is necessary, should be given after lactation is stopped.
2. Relative contraindication: The drug should be used when the benefits of use outweigh the risks. It is desirable that the treatment be avoided in women who are or may be pregnant. The safety in pregnant women has not been established.

*2Bosentan has been reported teratogenic in animals, but the risk for teratogenicity is unclear in humans.

[Precautions]

1) Indications and contraindications should be confirmed when considering the use during pregnancy.
2) When drugs contraindicated or not indicated for pregnant women in the package inserts, the physicians must fully explain the use of such drugs to the patients and their families and obtain informed consent.

Table 7. Classification of Valvular Heart Diseases by Maternal and Fetal Risks

	Low maternal/fetal risk factors	High maternal/fetal risk factors
Aortic stenosis	Asymptomatic; Normal left ventricular function; Mean pressure gradient <25 mmHg; Orifice area >1.5 cm^2	Severe stenosis; Complicated with severe pulmonary hypertension; Left ventricular dysfunction
Aortic regurgitation	NYHA Class I to II; Normal left ventricular function	NYHA Class III to IV; Complicated with severe pulmonary hypertension; Left ventricular dysfunction
Mitral stenosis	No severe pulmonary hypertension; Orifice area >1.5 cm^2; Mean pressure gradient <5 mmHg	NYHA Class II to IV; Complicated with severe pulmonary hypertension; Left ventricular dysfunction
Mitral regurgitation	NYHA Class I to II; Normal left ventricular function	NYHA Class III to IV; Complicated with severe pulmonary hypertension; Left ventricular dysfunction
Mitral valve prolapse	No mitral regurgitation, or Mild to moderate mitral regurgitation but normal left ventricular function	
Pulmonary stenosis	Mild to moderate stenosis	

- High maternal/fetal risk factors
  - Complicated with severe pulmonary hypertension (pulmonary artery pressure is ≥75% of systemic blood pressure)
  - Left ventricular dysfunction (LVEF<40%)
  - Using mechanical valves requiring anticoagulation therapy
  - Marfan syndrome
- Low maternal/fetal risk factors
  - Normal left ventricular function (LVEF>50%)

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

2. Pulmonary Hypertension (Table 6)

In women with pulmonary hypertension, pregnancy will increase pulmonary artery pressure, worsen right heart failure, and worsen ventilation-perfusion ratio mismatch. The risk during pregnancy and childbirth in patients with pulmonary hypertension is extremely high. It is strongly recommended that women with pulmonary hypertension avoid pregnancy by using reliable contraception, and prompt artificial termination of pregnancy, if occurs, should be considered whenever necessary.[70–72] If a patient decided to continue pregnancy after understanding the risk, she must be hospitalized at an appropriate timing to monitor the progress and perform childbirth under careful management by a special team.[73–75] Since death immediately after childbirth may often occur, the mother must be monitored for about 1 week in the intensive care unit. The outcome does not differ by delivery method (cesarean section vs. vaginal delivery) and anesthesia (general anesthesia vs. local anesthesia).[76]

3. Valvular Heart Diseases

Table 7 describes the guidelines for pregnancy and childbirth in patients with valvular heart diseases[48] and Table 8 lists anticoagulation and antiplatelet therapies during pregnancy.

Figure shows a flow chart of anticoagulation therapy during pregnancy in patients using mechanical valves that is commonly practiced in Japan empirically rather than based on scientific data.[77] During the first trimester of pregnancy, patients should receive unfractionated heparin or low molecular weight heparin[78,79] rather than warfarin[80,81] which may cause malformation in the fetus. At 14 weeks of gestation or thereafter, either subcutaneous heparin or oral warfarin should be selected. Since heparin is not highly reliable in terms of the prevention of thrombosis, oral warfarin therapy is a preferable method for the mother. At 36 weeks of gestation, oral warfarin should be replaced by continuous intravenous administration of heparin. Cesarean section is preferable since staff members and instrument can be scheduled in advance.

Table 8. Characteristics of Anticoagulation/Antiplatelet Drugs Used During Pregnancy and Lactation

Drug	Class	Pregnancy categories	Characteristics/ adverse effects	Teratogenicity	Breast feeding	Package insert*	
						Pregnancy	Lactation
Warfarin	Coumarin delivative	D	- Teratogenic (osteogenesis/ chondrogenesis, cerebral nervous system) - Bleeding complication in the fetus	Present	Compatible	1	1
Heparin	Unfractionated heparin	C	- Promote decal cification during long-term treatment (bone fracture in the mother) - Higher incidence of thrombosis than warfarin	Absent	Compatible	1	
Enoxaparin	Low molecular weight heparin	B	- Heparin-induced thrombocytopenia has been reported - Not indicated for the prevention of thrombosis in patients with cardiovascular disease	Absent	Compatible	2	2
Dalteparin		B		Absent	Compatible	1	1
Aspirin (low-dose)	Antiplatelet effect	C	- Considered relatively safe - Contraindicated in 28 weeks of gestation or thereafter regardless of the dose	Absent	Potential toxicity	2	1
Dipyridamole	Antiplatelet effect	B	Hypotension, worsening of anginal symptoms	Absent	Probably compatible	2	1
Ticlopidine	Antiplatelet effect	B	Bleeding, liver disorder	Absent	Potential toxicity	2	1

Note) The above information is based on "Drugs in pregnancy and lactation, 8th edition (2008)".[40]
*Information on the use during pregnancy and lactation in the package insert (Blank columns represent no information in the source material).
1 Contraindication: This drug should not be administered to women who are or may be pregnant. Treatment should be discontinued without delay when pregnancy is confirmed. The drug should not be given to lactating women, and, when treatment is necessary, should be given after lactation is stopped.
2 Relative contraindication: The drug should be used when the benefits of use outweigh the risks. It is desirable that the treatment be avoided in women who are or may be pregnant. The safety in pregnant women has not been established. It is desirable that the drug be given after lactation is stopped.
[Precautions]
1) Indications and contraindications should be confirmed when considering the use during pregnancy.
2) When drugs contraindicated or not indicated for pregnant women in the package inserts, the physicians must fully explain the use of such drugs to the patients and their families and obtain informed consent.

4. Aortic Diseases

See **Table 9** for recommendations for patients with Marfan syndrome.[82,83]

See **Table 10** for recommendations for patients with Takayasu disease.[84,85]

Patients with unrepaired congenital coarctation of the aorta may experience severe complications such as hypertension, left heart failure, aortic aneurysm formation and aortic dissection during pregnancy. When the patient shows aortic dilatation and develop hypertension during pregnancy, management with bed rest and β-blockers are required. Periodic blood pressure monitoring is necessary since a decrease in blood pressure reduces blood flow in the placenta. It is preferable that the patient undergo surgery or catheter intervention to repair coarctation of the aorta before pregnancy. The risk during pregnancy to the mother and fetus is low in patients following repair of coarctation of the aorta. However, patients with hypertension or aortic dilatation should be managed with β-blockers.

5. Cardiomyopathy

Women with hypertrophic cardiomyopathy, even those with chest pain, exertional dyspnea and/or syncope before pregnancy, will rarely experience worsening of signs/symptoms during pregnancy, and may tolerate pregnancy in most cases. The risk is believed high in those with a maximum wall thickness of $\geq$ 30 mm, those with a history of cardiac arrest or sustained ventricular tachycardia, those with recurrent syncope, and those with a family history of sudden death: The risk of pregnancy/childbirth should be carefully evaluated for these patients.[86,87]

Fatal heart failure is rare in women with dilated cardiomyopathy when heart failure is compensated and remained in NYHA Class I, and drug therapy may be discontinued during pregnancy. However, severe heart failure may develop in some cases during the third trimester, and careful consideration is required even for patients with mild heart failure.[88,89]

Peripartum cardiomyopathy develops most commonly in the first month after childbirth. Cardiac function returns to normal by 6 months after childbirth in about 50% of patients, but the prognosis of patients with persistent and progressive

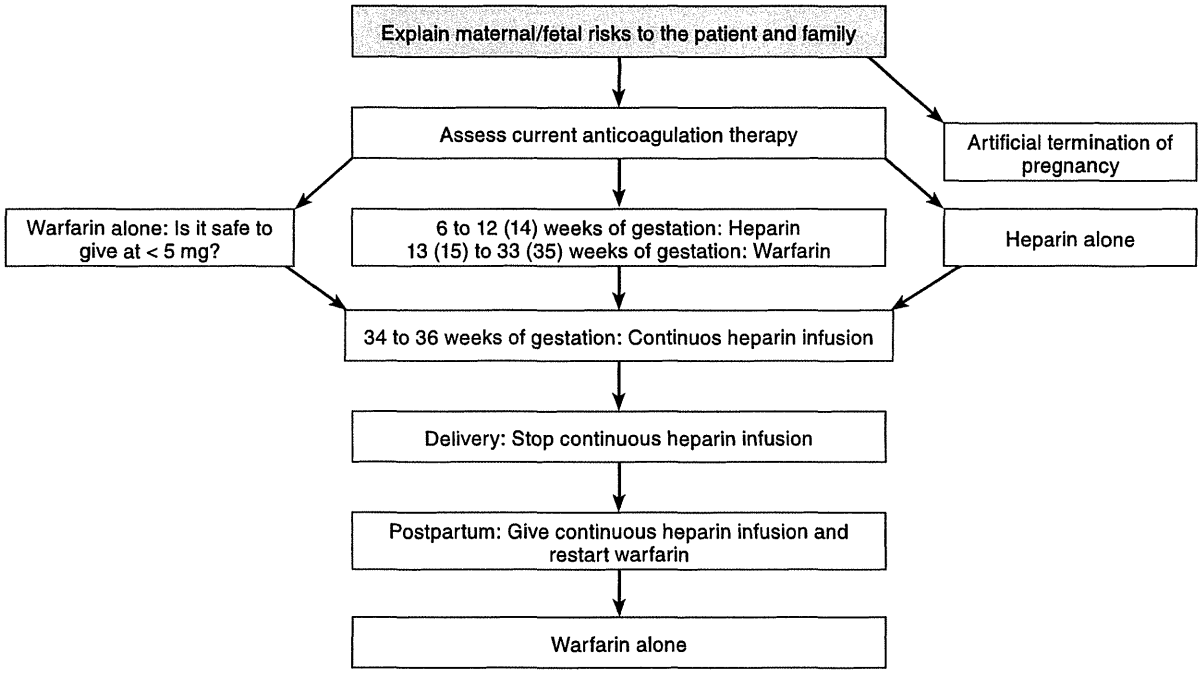

Figure. Flow chart of anticoagulation therapy in pregnant women with mechanical valves who have received Warfarin before pregnancy.

Table 9. Important Points of Management for Patients With Marfan Syndrome During Pregnancy and Childbirth

1. Explain that there is a 50% possibility of inheriting the disease.
2. Encourage the patient to undergo surgery before pregnancy, if indicated.
3. Instruct the patient to avoid pregnancy when the ascending aortic diameter (including Valsalva sinus) is 44 mm or larger or when aortic dissection is present. Patients with aortic diameter of 43 mm or smaller should be explained that they can become pregnant but may develop aortic dissection.
4. Patients with an ascending aortic diameter of <40 mm may have normal vaginal delivery.
5. Mitral regurgitation should be treated according to the guidelines for the treatment of valvular heart diseases.
6. β-blockers should be given whenever necessary with careful consideration of the potential effects on the mother and fetus.
7. Perform strict blood pressure control and pain management.

Table 10. Important Points of Management for Patients With Takayasu Disease During Pregnancy and Childbirth

1. It is reported that patients with untreated atypical coarctation of abdominal aorta may develop renal hypertension, which may lead to heart failure and renal failure. The prognosis of these patients is poor since sepsis and pregnancy-induced hypertensive nephropathy may develop.
2. Atypical coarctation of the aorta should be treated according to the recommendations for the treatment of coarctation of the aorta.
3. Aortic regurgitation should be treated according to the recommendations for the treatment of valvular heart diseases.
4. Aortic aneurysms (including annuloaortic ectasia) should be treated according to the recommendation for Marfan syndrome.
5. Ischemic heart disease (coronary ostial narrowing): Consider for surgery before pregnancy.
6. Hypertension should be treated with β-blockers. ACE inhibitors and angiotensin receptor blockers should be avoided.
7. Steroid therapy should be continued, but treatment at higher doses is rarely required.
8. Patients should be observed for autoimmune disorders and connective tissue diseases (collagen diseases).

ACE, angiotensin converting enzyme.

Table 11. Definition and Classification of Pregnancy Induced Hypertension: Proposed by Japan Society of Obstetrics and Gynecology, 2005

1. Term

Pregnancy toxemia should be referred to as pregnancy induced hypertension (PIH).

2. Definition

PIH is defined as hypertension with or without proteinuria developing during the period from 20 weeks of gestation to 12 weeks of postpartum. Hypertension due to other complications is not PIH.

3-1. Classification of PIH

(1) Preeclampsia
Preeclampsia is defined as hypertension with proteinuria that develops at 20 weeks of gestation or thereafter and subsided by 12 weeks of postpartum.

(2) Gestational hypertension
Gestational hypertension is defined as hypertension that developed 20 weeks of gestation or thereafter and subsided by 12 weeks of postpartum.

(3) Superimposed preeclampsia
Patients with superimposed preeclampsia include:
1) Women who have hypertension before pregnancy or by 20 weeks of gestation and develop proteinuria at 20 weeks of gestation or thereafter.
2) Women who have hypertension and proteinuria before pregnancy or by 20 weeks of gestation and experience worsening of hypertension and/or proteinuria at 20 weeks of gestation or thereafter.
3) Women who have proteinuria as the only sign of renal disease before pregnancy or by 20 weeks of gestation and develop hypertension at 20 weeks of gestation or thereafter.

(4) Eclampsia
Eclampsia is defined as the first onset of convulsions not related to epilepsy or secondary convulsions at 20 weeks of gestation or thereafter. Eclampsia is classified into antepartum eclampsia, intrapartum eclampsia and puerperal eclampsia according to the timing of onset.

3-2. Subclassification based on clinical findings

(1) Disease type by clinical findings

	Hypertension	Proteinuria
Mild	When one of the two criteria is met: 1. 140 mmHg≤ systolic blood pressure <160 mmHg 2. 90 mmHg≤ diastolic blood pressure <110 mmHg	Urinary protein excretion is at least 300 mg/day and less than 2 g/day in a 24-hour urine specimen
Severe	When one of the two criteria is met: 1. Systolic blood pressure is ≥160 mmHg 2. Diastolic blood pressure is ≥110 mmHg	Urinary protein excretion is ≥2 g/day, or spot urinary protein level is ≥300 mg/dl in more than 3 consecutive samples from fresh urine

(2) Disease type by timing of onset
Those developing by 32 weeks of gestation are referred to as early onset type, and those developing at 32 weeks of gestation or thereafter as late onset type.

[Remarks]

(1) Gestational proteinuria (proteinuria that is first detected at 20 weeks of gestation or thereafter and subsides by 12 weeks of postpartum) is not included in PIH typing.

(2) Chronic hypertension may often lead to superimposed preeclampsia, and should be managed carefully as in the case of PIH. Worsening of chronic hypertension is not included in PIH typing.

(3) Pulmonary edema, cerebral hemorrhage, premature separation of the normally implanted placenta, and HELLP syndrome* are not always caused by PIH, but are critical illness closely related to PIH. These findings are not included in PIH typing.

(4) The type of PIH is expressed using h and H for mild and severe hypertension, p and P for mild and severe proteinuria, EO for early onset type, LO for late onset type, S for superimposed type, and C for eclampsia.
For example, the type of preeclampsia may be expressed with Hp-EO and hP-LO, gestational hypertension with H-EO and h-LO, superimposed preeclampsia with Hp-EOS and hP-LOS, and eclampsia with HP-EOSC and hP-LOSC.

*HELLP syndrome is characterized by Hemolysis, Elevated Liver enzyme and Low Platelets, and develops during pregnancy (often at 27 weeks of gestation or thereafter) and the puerperal period.
Cited from *Acta Obstetrica et Gynaecologica Japonica* 2006; **58:** N61–N70.[103]

left ventricular dysfunction is poor.[88,89] In patients who continue to show a left ventricular ejection fraction (LVEF) of ≤ 50% after childbirth, cardiac function may often decrease to cause death during or after the next pregnancy. Contraception is strongly recommended for such patients.[90] Most effects on the fetus develop in the third trimester or after birth, and the incidences of low birth weight infants and stillbirth are slightly higher than in healthy women.

6. Arrhythmias

Patients with congenital heart disease associated with arrhythmia are often treated and monitored carefully for arrhythmia during pregnancy. In patients following repair of congenital heart disease, arrhythmia may newly develop or worsen during pregnancy and childbirth.[91,92] Since atrial flutter/fibrillation, atrial tachycardia, ventricular tachycardia, severe atrioventricular block, and other conditions may cause significant hemodynamic changes that highly affect the mother and fetus, appropriate diagnosis and emergency treatment are commonly required.[73,93] Pregnant women with risk factors for development of arrhythmia (eg, those with heart failure, those with pre-existing arrhythmia before pregnancy, and those with a history of tachyarrhythmia) should undergo regular checkups more frequently during pregnancy.

Table 12. Characteristics of Antihypertensive Drugs Commonly Used During Pregnancy and Lactation

Drug	Class	Pregnancy categories*1	Characteristics/ adverse effects	Teratogenicity*1	Breast feeding	Package insert*2	
						Pregnancy	Lactation
Methyldopa	Central antihypertensive	B	Lassitude, thirst Used in Europe and the United States	Absent	Probably compatible	2	1
Clonidine	Central antihypertensive	C	Few reports	Absent	Probably compatible	2	
Atenolol	β-blocker	D	IUGR, hypoglycemia, bradycardia	Absent	Potential toxicity	2	1
Propranolol	β-blocker	C→D	IUGR, hypoglycemia, bradycardia	Absent	Potential toxicity	2	1
Metoprolol	β-blocker	C→D	IUGR, hypoglycemia, bradycardia	Absent	Potential toxicity	1	1
Oxprenolol	β-blocker	C→D	IUGR, hypoglycemia, bradycardia	Absent	Potential toxicity	1	1
Labetalol	β-blocker	C	IUGR, hypoglycemia, bradycardia	Absent	Probably compatible	1	1
Sotalol	β-blocker	B→D	Bradycardia	Absent	Potential toxicity	2	1
Hydralazine	Peripheral vasodilator	C	Headache, neonatal thrombocytopenia	Absent	Probably compatible	2	1
Nifedipine Nicardipine	Calcium channel blocker	C	Headache, palpitation, hypotension	Absent	Probably compatible	1	1
Isosorbide dinitrate	Nitrate	C	Few reports	Absent	Probably compatible	2	1
Captopril*3	ACE inhibitor*3	C→D	Fetal renal dysplasia, renal failure, oligohydramnios	Present*3	Compatible	1	1
Enalapril*3	ACE inhibitor*3	C→D	Fetal renal dysplasia, renal failure, oligohydramnios	Present*3	Probably compatible	1	1
Candesartan*4 Losartan*4	Angiotensin receptor blocker*4	C→D	Fetal renal dysplasia, renal failure, oligohydramnios	Present*4	Probably compatible	1	1
Furosemide	Diuretic	C (D)	Disturbance of uteroplacental circulation, fetal dehydration	Absent	Probably compatible	2	1
Spironolactone	Diuretic	C (D)	Possible feminization	Absent	Probably compatible	2	1
Hydrochlorothiazide	Diuretic	C (D)	Thrombocytopenia, hemolytic anemia	Absent	Compatible	2	1

ACE, angiotensin converting enzyme; IUGR, intrauterine growth retardation.
Note) The above information is based on "Drugs in pregnancy and lactation, 8th edition (2008)".[40]
*1B→D/C→D: Pregnancy category B or C during the first trimester but pregnancy category D during the second and third trimesters. C (D): Pregnancy category C for patients without gestational hypertension, and pregnancy category D for patients with gestational hypertension. Teratogenicity: Since ACE inhibitors have been reported to be teratogenic, strict caution should be needed for the use of these drugs even in the first trimester.
*2Information on the use during pregnancy and lactation in the package insert (Blank columns represent no information in the source material).
1. Contraindication: This drug should not be administered to women who are or may be pregnant. Treatment should be discontinued without delay when pregnancy is detected. The drug should not be given to lactating women, and, when treatment is necessary, should be given after lactation is stopped.
2. Relative contraindication: The drug should be used when the benefits of use outweigh the risks. It is desirable that the treatment be avoided in women who are or may be pregnant. The safety in pregnant women has not been established.
*3Since ACE inhibitors have been reported to be teratogenic, strict caution should be needed for the use of these drugs even in the first trimester.
*4Strict caution in terms of teratogenicity should be needed for the use of angiotensin receptor blockers, which exert their effects in a way similar to ACE inhibitors.
[Precautions]
1) Indications and contraindications should be confirmed when considering the use during pregnancy.
2) When drugs contraindicated or not indicated for pregnant women in the package inserts, the physicians must fully explain the use of such drugs to the patients and their families and obtain informed consent.

7. Ischemic Heart Disease

Although the incidence of acute myocardial infarction (AMI) during the perinatal period is quite rare (1 in 10,000 cases), the incidence is expected to increase in the future.[94,95] Smoking and hypertension are the most significant risk factors for development of AMI during the perinatal period.[96] AMI is more common in women who have had children, and the most common lesion is the anterior wall. β-blockers are the first-line therapy to prevent myocardial infarction (MI). Low-dose aspirin is effective in preventing myocardial ischemic attacks during pregnancy. Many reports have described that thrombolytic therapy for the treatment of AMI is not teratogenic to the fetus and the prognosis of the mother and fetus is favorable.[97] Percutaneous coronary intervention and coronary artery bypass

grafting during pregnancy are also effective.[98,99]

Patients with coronary aneurysms in Kawasaki disease do not have significant problems during pregnancy and childbirth when coronary stenosis is absent and cardiac function is normal. Patients who have coronary stenosis, those after MI and those after coronary intervention may experience a progression of ischemic disease or a worsening of heart failure during pregnancy and childbirth.[100,101]

8. Heart Failure

Volume overload and tachycardia during pregnancy may worsen heart failure. The severer the heart failure during pregnancy, the higher the mortality of the mother and the incidences of premature birth, intrauterine growth retardation and abortion or stillbirth. Women with NYHA Class III or severer heart failure should be recommended to avoid pregnancy and terminate pregnancy promptly when they become pregnant.[94,102] There are no established data indicating the safety of pregnancy in patients in certain levels of ejection fraction.

9. Hypertension (Tables 11,[103] 12)

Patients with hypertension may prone to have premature birth, intrauterine growth retardation, perinatal death, and other perinatal disorders related to pregnancy-induced hypertension. The incidences of premature separation of the normally implanted placenta and perinatal death are high in patients with pregnancy-induced hypertension.[104,105] They are often prone to have such as malignant hypertension, cerebral hemorrhage, heart failure, and renal dysfunction.

IV Important Points in Obstetric Management

Table 13. Expected Annual Pregnancy Rates With Different Contraceptive Methods

Methods	General use	Optimal use
No contraception	85%	85%
Coitus interruptus (extravaginal ejaculation)	27%	4%
Tracking menstrual cycle, sexual abstinence	25%	1 to 9%
Condom	15%	2%
Pessary	16%	6%
Oral contraceptives	8%	0.3%
Intrauterine contraceptive device	0.1 to 0.8%	0.1 to 0.6%
Tubal ligation	0.5%	0.5%
Vasoligation	0.15%	0.1%

Cited with modification from "Guidelines for the use of low-dose contraceptive pills: second edition" in 2006[106] proposed by Japan Society of Obstetrics and Gynecology.

Table 14. Incidence of Neurological Sequelae in Liveborn Infants by Gestational Age at Birth

	Hospitalized	Dead (%)	Disability
≤24 weeks	20	12 (60)	1 (13)
24 to 27 weeks	158	19 (12)	30 (22)
28 to 31 weeks	311	18 (6)	37 (13)
≥32 weeks	3,478	87 (3)	30 (1)

Data in 1984 to 1997 from the Maternal and Perinatal Center, Tokyo Women's Medical University Hospital.

1. Contraception (Table 13)[106]

2. Effects of Hemodynamic Condition of the Mother on the Fetus

When progressive worsening of maternal health to a life-threatening condition is expected, physicians should consider for termination of pregnancy (artificial abortion or early delivery). When the growth in the fetal head circumference stops due to progressive worsening of maternal condition, pregnancy should be terminated (for early delivery).

3. Timing of Delivery

The timing of delivery should be determined by considering the survival and incidence of neurological sequelae by weeks of gestation at delivery. The prognoses of infants born with a body weight of <1,000 g and infants born earlier than 28 weeks of gestation are poor[107] (**Table 14**).

4. Controlling Uterine Contraction

Patients with impending abortion or premature labor are indicated for tocolytics (**Tables 15, 16**),[108] while patients who need

Table 15. Methods of Administration of and Contraindications to Tocolytics

Methods of administration	
Ritodrine (β-stimulant)	Start at 50 μg/min, and increase the dose by 50 μg/min in every 10 to 20 minutes.
Terbutaline (not indicated in Japan)	Start at 10 μg/min, and increase the dose by 5 μg/min in every 10 minutes.
Magnesium sulfate	Administer 4 g intravenously over 30 minutes, and continue infusion at 2 to 4 g/hr by monitoring blood magnesium concentration in the mother until uterine contraction subsides.
Indomethacin (not indicated in Japan)	Administer 25 to 50 mg intrarectally or orally every 6 hours for ≤48 hours.
Contraindications	
Ritodrine (β-stimulant)	Poorly controlled diabetes, pulmonary hypertension
Magnesium sulfate	Hypocalcemia, myasthenia gravis, renal failure
Indomethacin (not indicated in Japan)	Peptic ulcer, blood disorders, hepatic/renal insufficiency, asthma, pancreatitis, proctitis, obstetric bleeding

Table 16. Important Adverse Drug Reactions to Tocolytics

Ritodrine (β-stimulant)	
Significant ADRs:	Pulmonary edema, acute heart failure, agranulocytosis, hypokalemia, rhabdomyolysis
Neonates:	Ventricular septal thickening, intestinal obstruction
Others:	Tachycardia, arrhythmia (mother and fetus), hepatic dysfunction, thrombocytopenia, tremor, hyperglycemia, salivary gland swelling associated with hyperamylasemia, headache, erythema
Magnesium sulfate	
Significant ADRs:	Pulmonary edema, respiratory failure, heart block, cardiac arrest, tetany, muscular paralysis, hypoglycemia, facial flashing, hot flash, paralytic ileus, rhabdomyolysis
Neonates:	Abnormal bone findings (transverse radiolucent bands and thin skin proximal humeral diaphysis)
Indomethacin (not indicated in Japan)	
Significant ADRs:	Shock, hepatic dysfunction, renal failure, gastrointestinal bleeding, asthma, aplastic anemia, hemolytic anemia, mucocutaneous ocular syndrome (Stevens-Johnson syndrome), oligohydramnios
Fetuses:	Ductus contraction, renal failure, bowel perforation
Neonates:	Necrotizing enterocolitis

ADR, adverse drug reaction.

Table 17. Indications for Cesarean Section

General conditions

1) Maternal Indications

- Cephalopelvic disproportion
- Pelvic soft tissue stiffness
- Difficulty with vaginal delivery due to stenosis, scarring, or pelvic tumors
- When a risk of uterine rupture is present (women who had underwent cesarean section and women with a history of enucleatic myomectomy)
- When the mother is at a risk (eg, complicated with severe pregnancy-induced hypertension, eclampsia, placenta previa, premature separation of the normally implanted placenta, heart disease, lung disease, renal disease and liver disease)
- When vaginal delivery through trial labor, vacuum extraction and forceps delivery is not expected successful

2) Fetal Indications

- Non-reassuring fetal status
- Umbilical cord prolapse
- Unreduced transverse presentation, abnormal position, malpresentation or abnormal rotation of the fetus
- Pelvic presentation suggesting fetal immaturity

Maternal heart disease

- Cardiac dysfunction
- Patients at a risk of unstable hemodynamics induced by changes in blood pressure, for example patients with Marfan syndrome, significant coarctation of the aorta, aortic stenosis or severe pulmonary artery stenosis, and patients following Fontan operation (vaginal delivery is possible in only limited cases)
- Pulmonary hypertension
- Uncontrolled arrhythmia
- Patients using mechanical valves
- Patients with cyanosis

Table 18. Considerations in Selection of Anesthetic Methods During Cesarean Section in Patients With Heart Disease

	Spinal (subarachnoid) anesthesia	Epidural anesthesia	General anesthesia
Risk of aspiration pneumonitis	Almost absent	Almost absent	Present
Sympatholytic action	Rapid	Slow	Slight
Sympathetic stimulant	Absent	Absent	During intubation/extubation
Systemic vascular resistance	Decrease	Decrease	Increase during light anesthesia Decrease by anesthetic agents
Pulmonary vascular resistance	Difficult to control	Difficult to control	Controllable through mechanical ventilation
Intrathoracic pressure	Not changed	Not changed	Increase by controlled ventilation
Cardiac contraction	Not changed	Not changed	Possible inhibition
Transesophageal echocardiography monitoring	Painful	Painful	Easy
Communications with staff	Possible	Possible	Impossible
Use during anticoagulation therapy	Avoid	Avoid	Low risk

Table 19. Underlying Heart Disease and Anesthetic Methods

Diagnosis	Vaginal delivery				Cesarean section				
	No	Spinal	Epidural	Sedation	Spinal	Epidural	CSEA	General	Other
• Arrhythmias									
Tachyarrhythmia									
Tachycardia									
Supraventricular tachycardia	○		◎		●		●	◎	
Ventricular tachycardia	◎		◎		○			◎	
Congenital long QT syndrome			●	○	◎	●	◎	◎	
Arrhythmogenic right ventricular dysplasia	○		○			●			
Fibrillation and flutter									
Atrial fibrillation			◎					○	
Preexcitation syndrome									
WPW syndrome	◎	●	◎		●			●	
Bradyarrhythmia									
Sinus bradycardia/sinus arrest	●								
Complete atrioventricular block	◎		●		○			●	
Artificial pacemaker	◎		●		○	●		●	
• Ischemic heart disease									
Angina			○ CSEA					●	
Acute myocardial infarction	◎					○		●	
Old myocardial infarction			●			◎		●	
Coronary arterial lesions due to Kawasaki disease			○			◎		◎	
• Congenital heart disease									
Eisenmenger syndrome	●				◎ CSA	●	●	◎	
Pulmonary stenosis		● CSA							
Congenital right pulmonary artery absent					○				
Tricuspid atresia					● CSA				
Fontan operation	●	○	●		● CSA	●		◎	
Ebstein anomary	○		●			●		◎	
Complete transposition of the great arteries						●		○	
Mustard operation	●					●		○	
Coarctation of the aorta	●		●			●	●	●	
Pulmonary valve atresia + ventricular sepal defect						●			
Pulmonary valve atresia + intact ventricular septum						●		●	
Corrected transposition of the great arteries			●		●	●		◎	
Double outlet right ventricle						◎	●	●	
Truncus arteriosus								●	
Coronary artery anomaly						●		●	
Single ventricle			●			●		●	
• Acquired valvular heart disease									
Mitral stenosis			◎			◎		◎	
Mitral regurgitation	●				○	●		○	
Aortic stenosis			●			◎		●	
Aortic regurgitation						○		●	
Mitral stenosis+aortic stenosis			●			●			
Mitral stenosis+aortic regurgitation								●	
Mitral regurgitation+aortic regurgitation			●						
Infective endocarditis	●				○			◎	
• Myocardial disease									
Cardiomyopathy									
Hypertrophic cardiomyopathy		○	◎			◎	○	◎	
Dilated cardiomyopathy	○		○			○	○	◎	
Peripartum cardiomyopathy	○		●			●	●	◎	Local infiltration
• Aortic disease									
Aortitis syndrome (Takayasu arteritis)			●			●	◎	●	
• Vascular lesions associated with congenital connective tissue disease									
Marfan syndrome			◎		○	◎	●	◎	
• Pulmonary heart disease									
Pulmonary arterial hypertension	●		●			◎	●	◎	

Note) ○ : reported only in Japan, ● : reported only in foreign countries, ◎ : reported in and outside of Japan.
CSA, continuous spinal anesthesia; CSEA, combined spinal epidural anesthesia; WPW, Wolff-Parkinson-White.