

Table 21. Characteristics of Drugs Commonly Used for the Treatment of Heart Failure During Pregnancy and Lactation

Drug	Class	Pregnancy categories* ¹	Characteristics/ adverse effects	Teratogenicity* ¹	Breast feeding	Package insert* ²	
						Pregnancy	Lactation
Furosemide	Diuretic	C (D)	Decreased uteroplacental circulation, fetal dehydration	Absent	Probably compatible	2	1
Spironolactone	Diuretic	C (D)	Possible feminization	Absent	Probably compatible	2	1
Chlorothiazide	Diuretic	C (D)	Thrombocytopenia, hemolytic anemia	Absent	Compatible	2	1
Digoxin	Digitalis	C	Bradycardia, low birth weight infants	Absent	Compatible	2	
Nitroglycerin	Nitrate	B	Few reports	Absent	Probably compatible	2	1
Isosorbide dinitrate	Nitrate	C	Few reports	Absent	Probably compatible	2	1
Carvedilol	β -blocker	C→D	IUGR, bradycardia, hypoglycemia	Absent	Potential toxicity	1	1
Metoprolol	β -blocker	C→D	IUGR, bradycardia, hypoglycemia	Absent	Potential toxicity	1	1
Hydralazine	Peripheral vasodilator	C	Headache, neonatal thrombocytopenia	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
Milrinone	PDE III inhibitor	C	Few reports	Absent	Probably compatible	2	1
Amrinone	PDE III inhibitor	C	Few reports	Absent	Probably compatible	1	1
Olprinone	PDE III inhibitor		Few reports			1	1
Carperitide	hANP		Few reports			2	1
Dopamine	Catecholamine	C	Few reports	Absent	Probably compatible	2	
Dobutamine	Catecholamine	B	Few reports	Absent	Probably compatible	2	
Isoproterenol	Catecholamine	C	Few reports	Absent	Probably compatible	2	

ACE, angiotensin converting enzyme; hANP, human atrial natriuretic peptide; IUGR, intrauterine growth retardation; 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).

*1C→D: Pregnancy category 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.

*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.

Table 22. Directions of Future Research on Pregnancy and Childbirth in Patients With Heart Disease

1. Counseling	Management of pregnancy and delivery, hereditary (risk of familial recurrence), maternal and fetal prognosis, support by family, and psychological approaches
2. Organization	Team-based practice, criteria for desirable hospitals, and cooperation with perinatal medical centers
3. Maternal management	Hemodynamics monitoring, management corresponding to types of heart disease, contractions, drug therapy, cardiac intervention (catheter intervention, cardiovascular surgery), and paternal management
4. Fetal management	Effects of maternal heart disease on the fetus, effects of drug therapy in the mother on the fetus, monitoring of fetal well-being, diagnosis of congenital anomalies of the fetus, and fetal treatment
5. Perinatal management	Perinatal monitoring, induction of delivery, anesthetic methods, delivery management, neonatal management (premature birth, low birth weight infants, and infants with congenital heart disease), excretion of drugs to the mother in the milk, effects of lactation on maternal heart disease, and caring for baby
6. Long-term management for child and mother	Assessment of maternal cardiac function, effects of pregnancy and delivery on the natural history of heart disease, growth and development of the children, and precautions for next pregnancy

V Types and Key Points of Treatment of the Mother

1. Antiarrhythmic Treatment (Table 20)^{110–112}

2. Heart Failure Treatment (Table 21)^{113–116}

3. Invasive Treatment

It has been reported that intervention using balloon catheters during pregnancy is effective for patients with pulmonary stenosis, aortic stenosis or mitral stenosis.^{117,118} Cardiovascular surgery during pregnancy is required in rare cases.^{2,71} The

appropriateness of cardiovascular surgery during pregnancy should be determined according to the progression of lesions in aortic stenosis; the worsening of valvular regurgitation or heart failure due to diseases associated with valvular regurgitation; the severity of aortic dissection or giant aneurysms in aortic dilatation, or the status of vegetation or worsening of heart failure in infective endocarditis, among other conditions.¹¹⁹ When surgery during pregnancy is unavoidable, those performed at 16 to 20 weeks of gestation or 24 to 28 weeks of gestation or thereafter are safer to the fetus than in other periods. When surgery may be waited to 28 to 30 weeks of gestation or thereafter, surgery after childbirth may be feasible.^{117,120}

VI Directions of Future Research (Table 22)

It is expected that team management of high-risk pregnant women will advance, the number of women with heart disease who become pregnant and have children will increase, and that patient registration systems will be operated more effi-

ciently. We hope that the directions for future research will be delineated more clearly and many of current problems will be solved by the time of the next revision of the present guidelines.

References

- Guidelines for the Diagnosis and Treatment of Cardiovascular Diseases (2003–2004 Joint Working Groups Report). Guidelines for Indication and Management of Pregnancy and Delivery in Women with Heart Disease (JCS 2005). *Circ J* 2005; **69**(Suppl IV): 1267–1328 (in Japanese).
- Child JS, Perloff JK, Koos B. Management of pregnancy and contraception in congenital heart disease. In: Perloff JK, Child JS, Aboulhosn J, editors. *Congenital heart disease in adults*, 3rd edn. Philadelphia: Saunders/Elsevier, 2009; 194–220.
- Hunter S, Robson S. Adaptation of the cardiovascular system to pregnancy. In: Oakley C, editor. *Heart disease in pregnancy*. London: BMJ Publishing Group, 1997; 5–18.
- Robson SC, Hunter S, Boys RJ, Dunlop W. Serial study of factors influencing changes in cardiac output during human pregnancy. *Am J Physiol* 1989; **256**: H1060–H1065.
- Mabie WC, DiSessa TG, Crocker LG, Sibai BM, Arheart KL. A longitudinal study of cardiac output in normal human pregnancy. *Am J Obstet Gynecol* 1994; **170**: 849–856.
- Poppas A, Shroff SG, Korcarz CE, Hibbard JU, Berger DS, Lindheimer MD, et al. Serial assessment of the cardiovascular system in normal pregnancy. *Circulation* 1997; **95**: 2407–2415.
- Clark SL, Cotton DB, Lee W, Bishop C, Hill T, Southwick J, et al. Central hemodynamic assessment of normal term pregnancy. *Am J Obstet Gynecol* 1989; **161**: 1439–1442.
- Easterling TR, Benedetti TJ, Schmucker BC, Carlson K, Millard SP. Maternal hemodynamics and aortic diameter in normal and hypertensive pregnancy. *Obstet Gynecol* 1991; **78**: 1073–1077.
- Katz NM, Collea JV, Moront MG, MacKenzie RD, Wallace RB. Aortic dissection during pregnancy. *Am J Cardiol* 1984; **54**: 699–701.
- Niwa K, Perloff JK, Bhuta SM, Laks H, Drinkwater DC, Child JS, et al. Structural abnormalities of great arterial walls in congenital heart disease: Light and electron microscopic analyses. *Circulation* 2001; **103**: 393–400.
- Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology. Expert consensus document on management of cardiovascular disease during pregnancy. *Eur Heart J* 2003; **24**: 761–781.
- Drenthen W, Pieper PG, Roos-Hesselink JW, van Lottum WA, Voors AA, Mulder BJ, et al; ZAHARA Investigators. Pregnancy and delivery in women after Fontan palliation. *Heart* 2006; **92**: 1290–1294.
- Canobbio MM, Perloff JK, Rapkin AJ. Gynecological health of

- females with congenital heart disease. *Int J Cardiol* 2005; **98**: 379–387.
14. Crossland DS, Jackson SP, Lyall R, Hamilton JR, Hasan A, Burn J, et al. Life insurance and mortgage application in adults with congenital heart disease. *Eur J Cardiothorac Surg* 2004; **25**: 931–934.
 15. Lane DA, Lip GY, Millane TA. Quality of life in adults with congenital heart disease. *Heart* 2002; **88**: 71–75.
 16. Celermajer DS, Deanfield JE. Employability and insurance for young adults with congenital heart disease. *Br Heart J* 1993; **69**: 539–543.
 17. Allen HD, Gersony WM, Taubert KA. Insurability of the adolescent and young adult with heart disease. Report from the fifth conference on insurability. *Circulation* 1992; **86**: 703–710.
 18. Mahoney LT, Skorton DJ. Insurability and employability. *J Am Coll Cardiol* 1991; **18**: 334–336.
 19. Guidelines for the Diagnosis and Treatment of Cardiovascular Diseases (2004–2005 Joint Working Groups Report). Guidelines for Genetic Test and Genetic Counselling in Cardiovascular Disease (JCS 2006). *Circ J* 2006; **70**(suppl IV): 1329–1375 (in Japanese).
 20. Nakazawa M, Seguchi M, Takao A. Prevalence of congenital heart disease in Japanese children. *The Journal of the Japan Pediatric Society* 1986; **90**: 2578–2587 (in Japanese).
 21. Matsuoka M. Epidemiology and genetic counseling for congenital heart disease. In: Yamagishi H, Shiraishi I, editors. Clinical cardiac embryology understanding for congenital heart disease. Tokyo: MEDICAL VIEW CO., LTD., 2007; 210–219 (in Japanese).
 22. Amino N, Matsunaga H, Kuma K. Changes in hormonal environment and mental function. *The Japanese Journal of Clinical Psychiatry* 2004; **33**: 1003–1010 (in Japanese).
 23. Mizuno Y. Practical mental support for women with congenital heart diseases during pregnancy and childbirth. *The Journal of the Japanese Society of Pediatric Cardiology and Cardiac Surgery* 2009; **25**: 4–6 (in Japanese).
 24. Tan J, de Swiet M. Cardiac disease in pregnancy. PACE review No. 98/02. London: Royal College of Obstetricians and Gynaecologists.
 25. Kamiya C, Nakatani S, Hashimoto S, Masuda Y, Neki R, Ikeda T. Role of echocardiography in assessing pregnant women with and without heart disease. *J Echocardiogr* 2008; **6**: 29–38.
 26. Colman JM, Silversides CK, Sermer M, Siu SC. Cardiac monitoring during pregnancy. In: Steer PJ, Gatzoulis MA, Baker P, editors. Heart disease and pregnancy. London: RCOG Press, 2006; 67–77.
 27. DeWilde JP, Rivers AW, Price DL. A review of the current use of magnetic resonance imaging in pregnancy and safety implications for fetus. *Prog Biophys Mol Biol* 2005; **87**: 335–353.
 28. Japan Radioisotope Association. ICRP Publication 84: Pregnancy and medical radiation. Tokyo: Maruzen, 2002; 11–16, 33–35 (in Japanese).
 29. Freeman RK, Garite TJ, Nageotte M, editors. Fetal heart rate monitoring, 2nd edn. Baltimore: Williams & Wilkins, 1991; 158–177.
 30. Matsuda Y. Assessment of fetal well-being. *The Journal of the Japanese Society of Pediatric Cardiology and Cardiac Surgery* 2001; **17**: 518–525 (in Japanese).
 31. Cunningham FG, MacDonald PC, Gant NF, Leveno KL, Gilstrap LC, Hankins GDV, et al, editors. Williams Obstetrics, 20th edn. Norwalk: Appleton & Lange, 1977; 1012–1013.
 32. Manning FA. Fetal biophysical profile scoring. In: Manning FA, editor. Fetal medicine: Principles and practice. Norwalk: Appleton & Lange, 1995; 262.
 33. Devoe LD. Antepartum fetal surveillance. In: Quilligan EJ, Zuspan FP, editors. Current therapy in obstetrics and gynecology, 5th edn. Philadelphia: W.B. Saunders Company, 2000; 372–375.
 34. Guidelines for the Diagnosis and Treatment of Cardiovascular Diseases (2007 Joint Working Groups Report). Guidelines for the Prevention and Treatment of Infective Endocarditis (JCS 2008). http://www.j-circ.or.jp/guideline/pdf/JCS2008_miyatake_h.pdf (available in May 2010) (in Japanese).
 35. Wilson WR, Karchmer AW, Dajani AS, Taubert KA, Bayer A, Kaye D, et al. Antibiotic treatment of adults with infective endocarditis due to streptococci, enterococci, staphylococci, and HECCK microorganisms. American Heart Association. *JAMA* 1995; **274**: 1706–1713.
 36. Warnes CA, Williams RG, Bashore TM, Child JS, Connolly HM, Dearani JA, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: A report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation* 2008; **118**: e714–e833.
 37. Stuart G. Maternal endocarditis. In: Steer PJ, Gatzoulis MA, Baker P, editors. Heart disease and pregnancy. London: RCOG Press, 2006; 267–282.
 38. Child JS, Pegues DA, Perloff JK. Infective endocarditis and congenital heart disease. In: Perloff JK, Child JS, Aboulhosn J, editors. Congenital heart disease in adults, 3rd edn. Philadelphia: Saunders/Elsevier, 2008; 168–193.
 39. Guidelines for the Diagnosis and Treatment of Cardiovascular Diseases (2001–2002 Joint Working Groups Report). Guidelines for the Prevention and Treatment of Infective Endocarditis (JCS 2003). *Circ J* 2003; **67**(suppl IV): 1039–1082 (in Japanese).
 40. Briggs GG, Freeman RK, Yaffe SJ, editors. Drugs in pregnancy and lactation, 8th edn. Philadelphia: Lippincott Williams & Wilkins, 2008.
 41. Buttar HS. An overview of the influence of ACE inhibitors on fetal-placental circulation and perinatal development. *Mol Cell Biochem* 1997; **176**: 61–71.
 42. Cooper WO, Hernandez-Diaz S, Arbogast PG, Dudley JA, Dyer S, Gideon PS, et al. Major congenital malformations after first-trimester exposure to ACE inhibitors. *N Engl J Med* 2006; **354**: 2443–2451.
 43. McFaul PB, Dornan JC, Lamki H, Boyle D. Pregnancy complicated by maternal heart disease: A review of 519 women. *Br J Obstet Gynaecol* 1988; **95**: 861–867.
 44. Yap SC, Drenthen W, Meijboom FJ, Moons P, Mulder BJ, Vliegen HW, et al. Comparison of pregnancy outcomes in women with repaired versus unrepaired atrial septal defect. *BJOG* 2009; **116**: 1593–1601.
 45. Zuber M, Gautschi N, Oechslin E, Follath F, Kiowski W. Outcome of pregnancy in women with congenital shunt lesions. *Heart* 1999; **81**: 861–867.
 46. Tzemos N, Silversides CK, Colman JM, Therrien J, Webb GD, Mason J, et al. Late pregnancy outcomes after pregnancy in women with congenital aortic stenosis. *Am Heart J* 2009; **157**: 474–480.
 47. Menderson MA. Pregnancy in patients with obstructive lesions: Aortic stenosis, coarctation of the aorta and mitral stenosis. *Progress in Pediatric Cardiology* 2004; **19**: 61–70.
 48. Bonow RO, Carabello BA, Kanu C, de Leon AC Jr, Faxon DP, Freed MD, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation* 2006; **114**: e84–e231.
 49. Hameed AB, Goodwin TM, Elkayam U. Effect of pulmonary stenosis on pregnancy outcomes: A case-control study. *Am Heart J* 2007; **154**: 852–854.
 50. Connolly HM, Warnes CA. Ebstein's anomaly: outcome of pregnancy. *J Am Coll Cardiol* 1994; **23**: 1194–1198.
 51. Connolly HM, Grogan M, Warnes CA. Pregnancy among women with congenitally corrected transposition of great arteries. *J Am Coll Cardiol* 1999; **33**: 1692–1695.
 52. Therrien J, Barnes I, Somerville J. Outcome of pregnancy in patients with congenitally corrected transposition of the great arteries. *Am J Cardiol* 1999; **84**: 820–824.
 53. Niwa K, Nakazawa M, Aomi S. Nationwide survey of management of pregnancy and delivery in women with cardiovascular disease. *Int J Cardiol* 2004 submitted.
 54. Whittemore R, Hobbins JC, Engle MA. Pregnancy and its outcome in woman with and without surgical treatment of congenital heart disease. *Am J Cardiol* 1982; **50**: 641–651.
 55. Nissenkorn A, Friedman S, Schonfeld A, Ovadia J. Fetomaternal outcome in pregnancies after total correction of the tetralogy of Fallot. *Int Surg* 1984; **69**: 125–128.
 56. Pedersen LM, Pedersen TA, Ravn HB, Hjortdal VE. Outcomes of pregnancy in women with tetralogy of Fallot. *Cardiol Young* 2008; **18**: 423–429.
 57. Akagi T, Niwa K, Nakazawa M, Ishizawa A, Chiba Y, Shinohara T, et al. Pregnancy related cardiovascular complications in women with post operative tetralogy of Fallot: Multiinstitutional survey in Japan. *Circulation* 2005; **108**(Suppl II): 682.
 58. Singh H, Bolton PJ, Oakley CM. Pregnancy after surgical correction of tetralogy of Fallot. *Br Med J Clin Res* 1982; **285**: 168–170.
 59. Veldtman GR, Connolly HM, Grogan M, Ammash NM, Warnes CA. Outcomes of pregnancy in women with tetralogy of Fallot. *J Am Coll Cardiol* 2004; **44**: 174–180.
 60. Meijer JM, Pieper PG, Drenthen W, Voors AA, Roos-Hesselink JW, van Dijk AP, et al. Pregnancy, fertility, and recurrence risk in corrected tetralogy of Fallot. *Heart* 2005; **91**: 801–805.
 61. Canobbio MM, Mair DD, Van der Velde M, Koos BJ. Pregnancy outcomes after the Fontan repair. *J Am Coll Cardiol* 1996; **28**:

- 763–767.
62. Hoarc JV, Radford D. Pregnancy after Fontan repair of complex congenital heart disease. *Aust N Z J Obstet Gynaecol* 2001; **41**: 464–468.
 63. Megerian G, Bell JG, Hunta JC, Bottalico JN, Weiner S. Pregnancy outcome following Mustard procedure for transposition of the great arteries: A report of five cases and review of the literature. *Obstet Gynecol* 1994; **83**: 512–516.
 64. Genoni M, Jenni R, Hoerstrup SP, Vogt P, Turina M. Pregnancy after atrial repair for transposition of the great arteries. *Heart* 1999; **81**: 276–277.
 65. Clarkson PM, Wilson NJ, Neutze JM, North RA, Calder AL, Barratt-Boyes BG. Outcome of pregnancy after the Mustard operation for transposition of the great arteries with intact ventricular septum. *J Am Coll Cardiol* 1994; **24**: 190–193.
 66. Lao TT, Sermer M, Colman JM. Pregnancy following surgical correction for transposition of the great arteries. *Obstet Gynecol* 1994; **83**: 665–668.
 67. Ploeg M, Drenthen W, van Dijk A, Pieper PG. Successful pregnancy after an arterial switch procedure for complete transposition of the great arteries. *BJOG* 2006; **113**: 243–244.
 68. Fukuda T, Oku H, Nakamoto S, Mukobayashi M, Koike E. Successful pregnancy in a patient with double outlet left ventricle after a Rastelli operation using a prosthetic valve. *Circ J* 2004; **68**: 501–503.
 69. Siu SC, Colman JM, Sorensen S, Smallhorn JF, Farine D, Amankwah KS, et al. Adverse neonatal and cardiac outcomes are more common in pregnant women with cardiac disease. *Circulation* 2002; **105**: 2179–2184.
 70. Weiss BM, Zemp L, Seifert B, Hess OM. Outcome of pulmonary vascular disease in pregnancy: A systematic overview from 1978 through 1996. *J Am Coll Cardiol* 1998; **31**: 1650–1657.
 71. Connolly HM, Warnes CA. Pregnancy and contraception. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and management of adult congenital heart disease*. London: Churchill Livingstone, 2003; 135–144.
 72. Niwa K, Perloff JK, Kaplan S, Child JS, Miner PD. Eisenmenger syndrome in adults; ventricular septal defect, truncus arteriosus and univentricular hearts. *J Am Coll Cardiol* 1999; **34**: 223–232.
 73. Niwa K, Tateno S, Akagi T, Himeno W, Kawasoe Y, Tatebe S, et al. Arrhythmia and reduced heart rate variability during pregnancy in women with congenital heart disease and previous reparative surgery. *Int J Cardiol* 2007; **122**: 143–148.
 74. Silversides CK, Dore A, Poirier N, Taylor D, Harris L, Greutmann M, et al. Canadian Cardiovascular Society 2009 Consensus Conference on the management of adults with congenital heart disease: Shunt lesions. *Can J Cardiol* 2010; **26**: e70–e79.
 75. Weiss BA, Atanassoff PG. Cyanotic congenital heart disease and pregnancy: Natural selection, pulmonary hypertension, and anesthesia. *J Clin Anesth* 1993; **5**: 332–341.
 76. McCaffrey R, Dunn L. Primary pulmonary hypertension in pregnancy. *Obstet Gynecol Surv* 1964; **19**: 567–591.
 77. Guidelines for the Diagnosis and Treatment of Cardiovascular Diseases (2002–2003 Joint Working Groups Report). Guidelines for Management of Anticoagulant and Antiplatelet Therapy in Cardiovascular Disease (JCS 2004). *Circ J* 2004; **68**(Suppl IV): 1153–1219 (in Japanese).
 78. Ginsberg JS, Kowalchuk G, Hirsh J, Brill-Edwards P, Burrows R. Heparin therapy during pregnancy: Risks to the fetus and mother. *Arch Intern Med* 1989; **149**: 2233–2236.
 79. de Swiet M, Ward PD, Fidler J, Horsman A, Katz D, Letsky E, et al. Prolonged heparin therapy in pregnancy causes bone demineralization. *Br J Obstet Gynaecol* 1983; **90**: 1129–1134.
 80. Stevenson RE, Burton M, Ferlauto GJ, Taylor HA. Hazards of oral anticoagulants during pregnancy. *JAMA* 1980; **243**: 1549–1551.
 81. Chong MK, Harvey D, de Swiet M. Follow-up study of children whose mothers were treated with warfarin during pregnancy. *Br J Obstet Gynaecol* 1984; **91**: 1070–1073.
 82. Gott VL, Greene PS, Alejo DE, Cameron DE, Naftel DC, Miller DC, et al. Replacement of the aortic root in patients of Marfan's syndrome. *N Engl J Med* 1999; **340**: 1307–1313.
 83. Gott VL, Cameron DE, Alejo DE, Greene PS, Shake JG, Caparelli DJ, et al. Aortic root replacement in 271 Marfan patients: A 24-year experience. *Ann of Thorac Surg* 2002; **73**: 438–443.
 84. Sharma BK, Jain S, Vasishtha K. Outcome of pregnancy in Takayasu arteritis. *Int J Cardiol* 2000; **75**(Suppl 1): S159–S162.
 85. Bloechle M, Bollmann R, Chaoui R, Birnbaum M, Bartho S. Pregnancy in Takayasu arteritis. *Z Geburtshilfe Neonatol* 1995; **199**: 116–119.
 86. Thaman R, Varnava A, Hamid MS, Firoozi S, Sachdev B, Condon M, et al. Pregnancy related complications in women with hypertrophic cardiomyopathy. *Heart* 2003; **89**: 752–756.
 87. Autore C, Conte MR, Piccininno M, Bernabò P, Bonfiglio G, Bruzzi P, et al. Risk associated with pregnancy in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002; **40**: 1864–1869.
 88. Felker GM, Jaeger CJ, Klodas E, Thiemann DR, Hare JM, Hruban RH, et al. Myocarditis and long-term survival in peripartum cardiomyopathy. *Am Heart J* 2000; **140**: 785–791.
 89. Nishi I, Ishimitsu T, Ishizu T, Ueno Y, Suzuki A, Seo Y, et al. Peripartum cardiomyopathy and biventricular thrombi. *Circ J* 2002; **66**: 863–865.
 90. Elkayam U. Pregnant again after peripartum cardiomyopathy: to be or not to be? *Eur Heart J* 2002; **23**: 753–756.
 91. Shotan A, Ostrzege E, Mehra A, Johnson JV, Elkayam U. Incidence of arrhythmias in normal pregnancy and in relation to palpitations, dizziness, and syncope. *Am J Cardiol* 1997; **79**: 1061–1064.
 92. Tawam M, Levine J, Mendelson M, Goldberger J, Dyer A, Kadish A. Effect of pregnancy on paroxysmal supraventricular tachycardia. *Am J Cardiol* 1993; **72**: 838–840.
 93. Tateno S, Niwa K, Nakazawa M, Akagi T, Shinohara T, Yasuda T; Study Group for Arrhythmia Late after Surgery for Congenital Heart Disease (ALTAS-CHD). Arrhythmia and conduction disturbances in patients with congenital heart disease during pregnancy: Multicenter study. *Circ J* 2003; **67**: 992–997.
 94. Elkayam U. Pregnancy and cardiovascular disease. In: Braunwald E, Zipes DP, Libby P, editors. *Heart disease*, 6th edn. Philadelphia: W.B. Saunders Company, 2001.
 95. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. *Ann Intern Med* 1996; **125**: 751–762.
 96. Acute myocardial infarction and combined oral contraceptives: Results of an international multicenter casecontrol study. WHO collaborative study of cardiovascular disease and steroid hormone contraception. *Lancet* 1997; **349**: 1202–1209.
 97. Schumacher B, Belfort MA, Card RJ. Successful treatment of acute myocardial infarction during pregnancy with tissue plasminogen activator. *Am J Obstet Gynecol* 1997; **176**: 716–719.
 98. Weber MD, Halligan RE, Schumacher JA. Acute infarction, intracoronary thrombolysis, and primary PTCA in pregnancy. *Cathet Cardiovasc Diagn* 1997; **42**: 38–43.
 99. Ascarelli MH, Grider AR, Hsu HW. Acute myocardial infarction during pregnancy managed with immediate percutaneous transluminal coronary angioplasty. *Obstet Gynecol* 1996; **88**: 655–657.
 100. Nolan TE, Savage RW. Peripartum myocardial infarction from presumed Kawasaki's disease. *South Med J* 1990; **83**: 1360–1361.
 101. McAndrew P, Hughes D, Adams P. Pregnancy and Kawasaki disease. *Int J Obstet Anesth* 2000; **9**: 279–281.
 102. Elkayam U, Tummala PP, Rao K, Akhter MW, Karaalp IS, Wani OR, et al. Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy. *N Engl J Med* 2001; **344**: 1567–1571.
 103. Itoh M, Kusanagi Y. A standard for medical care and clinical practice: Pregnancy induced hypertension. *Acta Obstetrica et Gynaecologica Japonica* 2006; **58**: N61–N70 (in Japanese).
 104. Cunningham FG, MacDonald PC, Gant NF, Leveno KJ, Gilstrap LC, editors. *Williams Obstetrics*, 21st edn. Norwalk: Appleton & Lange, 2001; 569.
 105. Ferrer RL, Sibai BM, Mulrow CD, Chiquette E, Stevens KR, Cornell J. Management of mild chronic hypertension during pregnancy: A review. *Obstet Gynecol* 2000; **96**: 849–860.
 106. Japan Society of Obstetrics and Gynecology. Guidelines for the use of low-dose contraceptive pills: Second edition, 2006 (in Japanese).
 107. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician-Gynecologists: Number 38, September 2002. Perinatal care at the threshold of viability. *Obstet Gynecol* 2002; **100**: 617–624.
 108. Iams JD. Prevention and management of preterm birth. In: Zuspan FP, Quilligan EJ, editors. *Current therapy in obstetrics and gynecology*, 4th edn. Philadelphia: W.B. Saunders, 1994; 283.
 109. Matsuda Y, Yamamichi G. Induction of delivery. In: Chiba Y, editor. *The new encyclopedia of gynecology and obstetrics*, Volume 33. Tokyo: Nakayama Shoten, 2000; 142–146 (in Japanese).
 110. Page RL. Treatment of arrhythmias during pregnancy. *Am Heart J* 1995; **130**: 871–876.
 111. Joglar JA, Page RL. Antiarrhythmic drugs in pregnancy. *Curr Opin Cardiol* 2001; **16**: 40–45.
 112. Schroeder JS, Harrison DC. Repeated cardioversion during pregnancy: Treatment of refractory paroxysmal atrial tachycardia during three successive pregnancies. *Am J Cardiol* 1971; **27**: 445–446.
 113. Rodoriguez SU, Leikin SL, Hiller MC. Neonatal thrombocytopenia associated with antepartum administration of thiazide drugs. *N*

- Engl J Med* 1964; **270**: 881–884.
114. Harley JD, Robin H, Robertson SE. Thiazide-induced neonatal haemolysis? *Br Med J* 1964; **1**: 696–697.
 115. Senior B, Slone D, Shapiro S, Mitchell AA, Heinonen OP. Letter: Benzothiadiazides and neonatal hypoglycaemia. *Lancet* 1976; **2**: 377.
 116. Anderson GG, Hanson TM. Chronic fetal bradycardia: Possible association with hypokalemia. *Obstet Gynecol* 1974; **44**: 896–898.
 117. Presbitero P, Prever SB, Brusca A. Interventional cardiology in pregnancy. *Eur Heart J* 1996; **17**: 182–188.
 118. Wloch A, Respondek-Liberska M, Sysa A, Moll J, Goc B, Krzysztofik-Ladzińska J, et al. Significant aortic and pulmonary valve stenosis in the prenatal period: Diagnosis, treatment and outcome: A two-centre study. *Acta Cardiol* 2004; **59**: 242–243.
 119. Parry AJ, Westaby S. Cardiopulmonary bypass during pregnancy. *Ann Thorac Surg* 1996; **61**: 1865–1869.
 120. Colman JM, Sermer M, Seaward PG, Siu SC. Congenital heart disease in pregnancy. *Cardiol Rev* 2000; **8**: 166–173.

Appendix

Chair:

- Koichiro Niwa, Department of Cardiology, St Luke's International Hospital

Members:

- Teiji Akagi, Cardiac Intensive Care Unit, Okayama University Hospital
- Shigeyuki Aomi, Department of Cardiovascular Surgery, Tokyo Women's Medical University
- Yoshihito Hata, Division of Cardiovascular Medicine, Adult Congenital Heart Disease Center, Jichi Medical University
- Tomoaki Ikeda, Department of Obstetrics and Gynecology, Mie University Graduate School of Medicine
- Yoshio Matsuda, Department of Obstetrics and Gynecology, Maternal and Perinatal Center, Maternal Division, Tokyo Women's Medical University
- Norifumi Nakanishi, Department of Cardiovascular Internal Medicine, National Cerebral and Cardiovascular Center

- Satoshi Nakatani, Division of Functional Diagnostics, Department of Health Sciences, Osaka University Graduate School of Medicine
- Isao Shiraishi, Department of Perinatal and Pediatric Cardiology, National Cerebral and Cardiovascular Center
- Katsuo Terui, Division of Obstetric Anesthesia, Saitama Medical Center, Saitama Medical University

Collaborators:

- Nobuhisa Hagiwara, Department of Cardiology, Tokyo Women's Medical University
- Tetsuko Ishii, Department of Pediatric Cardiology, Tokyo Women's Medical University
- Chizuko A. Kamiya, Department of Perinatology and Gynecology, National Cerebral and Cardiovascular Center
- Satoru Kawano, Department of Emergency and Critical Care Medicine, Graduate School of Comprehensive Human Sciences, University of Tsukuba
- Yasutaka Kawasoe, Department of Adult Congenital Heart Disease and Pediatric Cardiology, Chiba Cardiovascular Center
- Minoru Nomura, Department of Anesthesiology, Tokyo Women's Medical University
- Mayumi Ota, Medical Foundation, Gakufu-kai, Saito Clinic
- Tokuko Shinohara, Department of Pediatric Cardiology, Tokyo Women's Medical University
- Shigeru Tateno, Department of Adult Congenital Heart Disease and Pediatric Cardiology, Chiba Cardiovascular Center
- Yoshio Uetsuka, Department of Cardiology, Tokyo Women's Medical University

Independent Assessment Committee:

- Shigeyuki Echigo, Echigo Clinic
- Tsuyomu Ikenoue, University of Miyazaki Hospital
- Tohru Izumi, Department of Cardio-angiology, Kitasato University, School of Medicine
- Toshikatsu Yagihara, Department of Cardiovascular Surgery, National Cerebral and Cardiovascular Center

(The affiliations of the members are as of September 2011)

