

## ON THE ISSUE OF PRECONCEPTION CARE IN PATIENTS WITH PATHOLOGY OF THE CARDIOVASCULAR SYSTEM

**N. Meskhi<sup>1</sup>, A. Zhidovinov<sup>3</sup>,  
O. Pitirimova<sup>2</sup>**

<sup>1</sup> O.M. Filatov City Clinical Hospital n. 15, Moscow

<sup>2</sup> A.N. Bakulev National Medical Research Center of cardiovascular surgery, Ministry of Health of the Russian Federation, Moscow, Russia

<sup>3</sup> Astrakhan State Medical University, Ministry of Health of the Russian Federation, Astrakhan Russia



**Nester T. Meskhi,**  
obstetrician



**Olga A. Pitirimova, MD**  
Obstetrician, Vice-Director



**Alexei Zhidovinov, professor,**  
Head of the Department of  
Pediatric Surgery

### ABSTRACT

**OBJECTIVE:** To assess the clinical efficacy of preconception care of women with cardiovascular pathology.

**MATERIAL AND METHODS:** 138 women with cardiovascular diseases were examined during pregnancy, 68 of whom underwent preconception preparation.

**RESULTS:** preconception care allowed to reduce the percentage of preterm birth and rate of caesarean section, and to improve perinatal outcomes.

**CONCLUSION:** the proposed scheme of preconception preparation in patients with cardiovascular pathology takes into account risk factors, severity of diseases, possible complications. This scheme of preconception care is proposed for women of reproductive age who plan a pregnancy or are already pregnant and are preparing for childbirth.

**KEYWORDS** — pathology of the cardiovascular system, pregnancy, preconception care, perinatal outcomes.

Cardiovascular system diseases in pregnant women and people of reproductive age are still one of the main causes of complications during pregnancy and childbirth [1–3]. In this case a great importance belongs to observations of hemodynamics in the process of preconception care. Ensuring hemodynamic stability guarantees reduced risk of hemodynamic disorders while providing clinical medication or surgical intervention in patients suffering from CVD [4, 5]. Normal pregnancy is always associated with significant hemodynamic overload, which is associated with fluid retention, increased volume of circulating blood and, as a consequence, cardiac output [6–8]. In conditions of altered hemodynamics associated with the presence

of any pathology of the cardiovascular system, the development of pregnancy can pose a threat to the mother's (especially during childbirth) and the child's health (throughout the gestation period, which is primarily due to the tendency to lack of uterine-placental blood flow) [9–12]. In conditions of physiological pregnancy on the background of increasing volume of circulating blood, hemodynamic changes occur, increasing the overall load on the cardiovascular system [13–15], which is especially important in patients with heart diseases. In women with heart disease, the frequency of operative delivery is higher due to indications regarding the cardiovascular system.

Newborns of mothers with heart diseases often have a lower Apgar score, lower growth-weight indicators, which may affect the further physical and mental development of the children.

Thus, the cardiovascular system pathology significantly reduces the reproductive potential of women of childbearing age. Timely adequate correction can compensate for the pathological process and help to choose the most correct individual tactics of pregnancy management [16]. Timely use of complex correction of cardiovascular pathology at the preconception stage can significantly improve the results of reproductive potential. That is why at the stage of preconception preparation, it is important to take into account the indicators of hemodynamics in order to predict the risks of possible complications during pregnancy. All methods of correction at the stage of preconception care can be divided into 2 stages: 1) diagnosis 2) choice of the most optimal methods of correction.

## MATERIAL AND METHODS OF THE RESEARCH

Preconception preparation was carried out in 68 women with CVS pathology planning pregnancy. The following parameters of hemodynamics were evaluated: the dynamics of the rhythm of cardiac contractions, stroke volume by ECHO-CG, arterial pressure. Parameters of hemostasis: D-dimer, thrombin-anti-thrombin complex (TAT), fragments of prothrombin 1 + 2 (F1 + 2), platelet activation by aggregatogram. The term of preconception care was 3 months. The comparison group consisted of 70 pregnant women with various cardiovascular diseases, who came under our observation already during pregnancy on terms from 8 to 24 weeks.

Modern preconception preparation of patients with CVS pathology should provide for multi-stage and dynamic indicators [17–19]. The program of preconception preparation for patients with cardiovascular diseases we developed provides for a set of preventive measures aimed at minimizing the risks of cardiovascular system dysfunction during pregnancy management and childbirth. The main task of such preparation is to correct the existing disorders of the mother's health before pregnancy, so that she comes to the gestational period in the best state of health and full psychological preparedness. The algorithm of preventive and diagnostic measures consists in the complex approach of patient management taking into account the risk of possible complications both cardiovascular ones and the course of pregnancy on the whole (Fig. 1).

- folic acid 1 mg per day (4 mg per day for hyperhomocysteinemia and/or MTHFR C677T mutation)
- Dipyridamole (75 mg/day)
- Natural micronized progesterone
- Group B vitamins, antioxidants (omega-3 polyunsaturated fatty acids)
- LMWH when thrombotic readiness is detected (D-dimer, TAT, dopplerography of the main vessels, presence of a personal or family thrombotic anamnesis)

Later, during pregnancy, natural progesterone and dipyridamole, multivitamins and LMWH were used under the control of D-dimer and TAT complex. Data on the developed treatment program are given in Table 1.

In the course of pregnancy management in the patients of the study groups, we evaluated the following parameters of hemodynamics:

- 1) The presence of regurgitation with the measurement of the volume of regurgitation in %
- 2) Dynamics of changes in blood pressure
- 3) Heart rate
- 4) Intensity of heart chambers dilatation
- 5) Ejection fraction

The registration of these parameters in all the groups was carried out three times: in the period of 18–22 weeks, then in the period of 26–30 weeks and before delivery in the period of 34–38 weeks; but only in the 1<sup>st</sup> group the above parameters were evaluated before pregnancy as well [20].

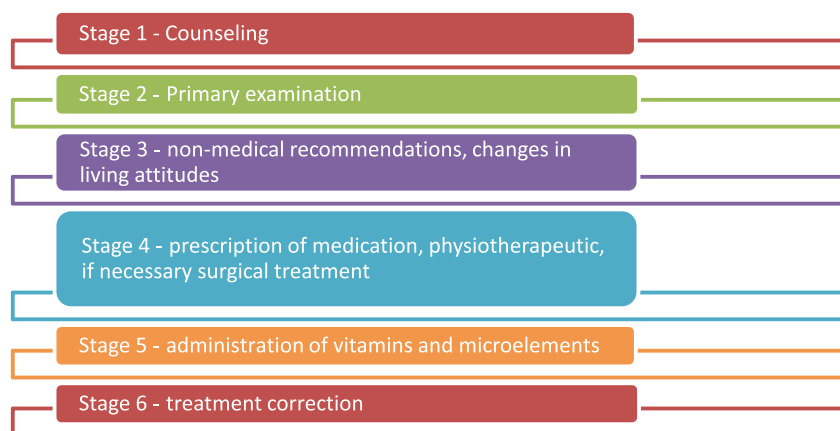


Fig. 1. Stages of preconception care

For correcting the pathological changes identified at the stage of the examination, the following prescriptions were made at the 4<sup>th</sup> stage of preconception preparation:

## RESULTS OF THE STUDY

At the stage of the preconception examination, various changes in hemodynamics were detected in 41 patients (60,3%), while only 22 patients (32.4%)

**Table 1.** *Methods of prevention and therapy in patients with CVD*

Fertile cycle	1 <sup>st</sup> trimester	2 <sup>nd</sup> –3 <sup>rd</sup> trimesters	Postpartum period
Dipyridamole (75 mg) B group vitamins Folic acid (400 mcg/day – 4 mg/day with hyperhomocysteinemia, MTHFR C677T mutations LMWH with elevated thrombophilia markers (D-dimer, TAT, F1 + 2) Omega-3 Natural progesterone	LMWH under the control of D-dimer Folic acid Natural progesterone Multivitamins for pregnant women Magne B6 (from 12–14 weeks) Dipyridamole 75 mg LMWH in the presence of a pre-thrombotic state	LMWH Folic acid Natural progesterone (up to 28–30 weeks) Multivitamins for pregnant women	LMWH for at least 10 days postpartum Switch to Warfarin according to indications Multivitamins for pregnant women and lactating mothers

had subcompensated changes and required correction.

Evaluation of the parameters of the dynamics of the state of the cardiovascular system was significantly different in the examined groups. However, even in spite of the measures taken at the preconception stage, as well as corrective measures during pregnancy, the state of the cardiovascular system worsened as pregnancy progressed, and by the end of the third trimester, 40% of the patients in the study group had severe pathological changes.

In the comparison group, in women who did not undergo preconception preparation but only treatment and corrective measures during pregnancy, already in the second trimester in 40% of cases there was a significant functional stress of the cardiovascular system that reached a peak at the gestational age of 34–38 weeks, when pathological changes were detected already in 60–65% of all patients.

In the process of pregnancy progression, the patients of the 1<sup>st</sup> group had an increase in the regurgitation degree from 5–10% in the second trimester to 15–25% at the term of 26–30 weeks, and before the birth regurgitation reached 20–30%. In the comparison group, the rates of regurgitation were more diverse within the group, and already in the 2<sup>nd</sup> trimester it was within a wide range of 10% to 30%. At the period of 26–30 weeks, the median of regurgitation was already within 25%, but in some cases, it reached 40%. When analyzing the degree of regurgitation before delivery, the spread of the scores within the group was even more significant; in the presence of pathological changes the median was around 30%, but in some patients it reached critical values up to 50% or more.

In both groups, there was no pattern in the dynamics of heart rate during pregnancy, but it was found that as the gestation period increased, we noted a decrease in the number of patients with normal heart rate.

So, in the 1<sup>st</sup> group in the 2<sup>nd</sup> trimester, there were 16% of patients with bradycardia and 22% of patients

with tachycardia. In the 3<sup>rd</sup> trimester, there were 10% of patients with bradycardia and 35% with tachycardia. Before delivery — already 4,5% with bradycardia and 38% with tachycardia. In the same time, only 2 patients had a bradycardia with heart rate less than 55 beats per minute, and the maximum heart rate exceeded 105 beats per minute in only 3 patients with tachycardia.

In the 2<sup>nd</sup> group, the variability of the heart rate was even more significant in the group as a whole. In the 2<sup>nd</sup> trimester, bradycardia was noted in 16% of patients, and tachycardia in 30%. In the 3<sup>rd</sup> trimester, these patients were 13% with bradycardia and 36% with tachycardia. Before delivery there were already 7% with bradycardia and 37% with tachycardia. At the same time, the peak values of bradycardia in some patients reached 47 beats per minute, the median of bradycardia was at the level of 50–55 beats/min. In the presence of tachycardia, the median was 95–100 beats/min, and in 6 patients it exceeded 105 beats/min.

When assessing ECHO-CG parameters in the 1<sup>st</sup> group, beginning from the 2<sup>nd</sup> trimester, the ejection fraction decreased in the dynamics, while at the term of 34–38 weeks the median was below the norm, and there was considerable variation in the whole group. Signs of dilatation of various parts of the heart also increased in the course of pregnancy progression; at the examination at the period of 26–30 weeks, pathological changes of the heart were observed in 32% of patients, and already at the term of 34–38 they were observed in 50% of all patients of the study group (Table 2).

In the 2<sup>nd</sup> group, the changes in ECHO-CG parameters were more pronounced, and already in the 2<sup>nd</sup> trimester, 27% of the patients had pathological changes. The ejection fraction was reduced in 31% of patients in the 2<sup>nd</sup> trimester; then, with the progression of pregnancy there was a further decrease in the ejection fraction in 47% of patients at the term of 26–30

**Table 2.** Dynamics of ECHO-CG parameters in patients of the study group

Measured parameter	18–22 weeks	26–30 weeks	34–38 weeks
Ejection fraction (%)	62±13,9	57±11,2	48±23,4
EDV of the right atrium (ml)	84±17,3	87±12,1	95±11,0
Diameter of the right ventricle (mm)	18±7,1	21±9,9	26±10,9
Size of the left atrium (mm)	29±4,2	34±5,1	38±5,7
End-systolic dimension of the left ventricle (mm)	31±3,9	35±4,7	39±6,1
End-diastolic dimension of the left ventricle (mm)	46±10,3	50±8,2	56±9,8

weeks and in 61% at the term of 34–38 weeks. Also, there was an even larger spread in the group as a whole if compared with the 1<sup>st</sup> group. Signs of dilatation of various parts of the heart also increased in the process of pregnancy progression; during examination in the 2<sup>nd</sup> trimester there were noted in 24% of, at 26–30 weeks — in 39% of patients, and at the term of 34–38 they were observed in 61% of all patients of the comparison group (Table 3).

was 5,8±0,3–7,1±0,3 points. In 47 patients (67,1%) of the 2<sup>nd</sup> group, the current pregnancy ended in premature birth. 36 (76,6%) had a cesarean section, 11 (23,4%) delivered through natural birth canal at 32–36 weeks of gestation. The average weight of newborns was 2250±430 g, the height — 40.3±3.6 cm, the average value of the Apgar score for the group was 4,2±0,7–6,1±0,4 points (Table 4).

**Table 3.** Dynamics of ECHO-CG parameters in patients of the comparison group

Measured parameter	18–22 weeks	26–30 weeks	34–38 weeks
Ejection fraction (%)	52±16,7	48±13,4	44±18,1
EDV of the right atrium (ml)	88±22,5	98±26,7	101±27,3
Diameter of the right ventricle (mm)	23±7,8	27±14,9	30±9,8
Size of the left atrium (mm)	32±5,5	36±7,6	41±7,2
End-systolic dimension of the left ventricle (mm)	38±4,7	41±7,0	44±6,5
End-diastolic dimension of the left ventricle (mm)	52±13,4	61±10,1	63±16,1

In the 1<sup>st</sup> group of pregnant women, 32 women (47%) had births in time out of 68. Of these, 21 patients (65,6%) had a cesarean section, 11 (34,4%) delivered through natural birth canal. The average weight of newborns in this group was 3110 ± 187g, the height — 48.5±2.5 cm; the average Apgar score for the group was 6,2± 0,5–7,5±0,5 points. In 36 patients (53%), the current pregnancy ended with premature birth. 23 of 36 patients (64%) had a cesarean section, 13 (36%) delivered through natural birth canal at 32–36 weeks of gestation. The average weight of newborns was 2400±256 g, the height — 42.5±2.4 cm, the average Apgar score for the group was 4,8± 0,6–5,4±0,6 points.

In the 2<sup>nd</sup> group, 23 women (32,9%) had birth in time. Of these, 18 patients (78,3%) were had a cesarean section, and 5 (21,7%) had a delivery through the natural birth canal. The average weight of newborns was 2950 ± 360 g, the height — 44,5±3,5 cm, the average value of the Apgar score for the group

## CONCLUSION

It was noted that some patients are relatively easy to tolerate the physiological stresses associated with pregnancy, in the presence of CVP, and others are experiencing a strong overstrain, which leads to severe complications, decompensation, and in some cases, to death [21–23]. A similar trend was demonstrated in the framework of our study, especially in the comparison group among women who did not pass the stage of the preconception care. In the process of examination, there were significant differences within the group in the change in hemodynamic parameters as pregnancy progressed. In the study group, among women who have completed the stage of preconception preparation, the differences within the group are also present, however, they are not so pronounced.

As a result of preconception care, there was a significant improvement in hemodynamic parameters during pregnancy in patients of the 1<sup>st</sup> group compared



Table 4. Outcomes of delivery in study groups

Term of delivery	Way of delivery	1 <sup>st</sup> group (n=68)		2 <sup>nd</sup> group (n=70)	
		Number	%	Number	%
Birth in time	Total	32	47,06%	23	32,86%
	Natural childbirth	11	34,38%	5	21,74%
	Cesarean section	21	65,63%	18	78,26%
Premature birth	Total	36	52,94%	47	67,14%
	Natural childbirth	13	36,11%	11	23,40%
	Cesarean section	23	63,89%	36	76,60%

with pregnant women of the 2<sup>nd</sup> group. Given that both the spectrum and severity of CVP in patients of the 1<sup>st</sup> and 2<sup>nd</sup> groups were comparable, these data show the effectiveness of the measures on the stage of preconception preparation. Thus, the implementation of the preconception preparation can generally reduce the severity of regurgitation and largely prevents the occurrence of sub- and decompensated degrees of impairment. We were able to demonstrate a decrease in the percentage of premature births and the percentage of cesarean section in the 1<sup>st</sup> group compared with patients of the 2<sup>nd</sup> group. There was also an improvement in perinatal outcomes in patients of the 1<sup>st</sup> group, especially those who gave birth on time.

The concept of implementing preconception preparation we proposed in patients of reproductive age in the presence of cardiovascular pathology takes into account risk factors, severity of diseases, and possible complications. During the examination, one should take into account: indicators of the hemostasis system, parameters of hemodynamics, parameters of metabolic and endocrine homeostasis, genetic research data. The purpose of correction is to compile a possible prognosis of CVD development in the near future in preparation for pregnancy.

Based on the conducted research, we proposed a scheme for preconception preparation of patients with CVD (Fig. 2).

From the perspective of modern concepts for the implementation of preconception preparation of patients of reproductive age in the presence of cardiovascular pathology, it is required to: identify risk factors for complications of the underlying disease and complications of pregnancy. Examination and detection of hypercoagulation state, violations of hemodynamic parameters, lipid spectrum of blood, genetic and acquired thrombophilia in the fertile cycle allow to assign effective corrective and preventive therapy of the revealed disorders.

Thus, the proposed technique of preconception care can help in identifying existing CVP in patients.

This scheme of preconception preparation is proposed for women of reproductive age who plan a pregnancy or are already pregnant and are preparing for childbirth.

## REFERENCES

1. **BAKALOV S.A., BUNIN Y.A., BUKHONKINA Y.M.** Diagnosis and treatment of cardiovascular diseases in pregnancy. – Moscow: All-Russian Scientific Society of Cardiology, CVD Section in Pregnant Women, – 2015
2. **SOSNOVA E.A.** Pregnancy and childbirth in patients with heart defects. – Moscow: SBEI HPE "Sechenov First Moscow State Medical University" – 2015. – P. 5
3. **RUYS T.P.E., CORNETTE J., ROOS-HESSELINK J.W.** Pregnancy and delivery in cardiac disease // J. Cardiol. – 2013. – Vol. 61. – P. 107–112.
4. **BALCI A, SOLLIE-SZARYNSKA KM, VAN DER BIJL AG, RUYS TP, MULDER BJ, ROOS- HESSELINK JW, VAN DIJK AP, WAJON EM, VLIENEN HW, DRENTHEN W, HILLEGEL HL, AARNOUDSE JG, VAN VELDHUISEN DJ, PIEPER PG, INVESTIGATORS Z-I.** Prospective validation and assessment of cardiovascular and offspring risk models for pregnant women with congenital heart disease. *Heart* 2014;100:1373–1381
5. **BERGER JS, JORDAN CO, LLOYD-JONES D, BLUMENTHAL RS.** Screening for cardiovascular risk in asymptomatic patients. *J Am Coll Cardiol* 2010;55:1169–1177
6. **BANDIK V.F.** Features of blood circulation in pregnant women. V.F. Bandik, N.M. Savinov, A.I. Novokhatsky // Medical work. – 1987. – No. 12. – P. 36–37;
7. **BALINT OH, SIU SC, MASON J, GREWAL J, WALD R, OECHSLIN EN, KOVACS B, SERMER M, COLMAN JM, SILVERSIDES CK.** Cardiac outcomes after pregnancy in women with congenital heart disease. *Heart* 2010;96:1656–1661.
8. **BOWATER SE, SELMAN TJ, HUDSMITH LE, CLIFT PF, THOMPSON PJ, THORNE SA.** Long-term outcome following pregnancy in women with a systemic right ventricle: is the deterioration due to pregnancy or a consequence of time? *Congenit Heart Dis* 2013;8: 302–307.

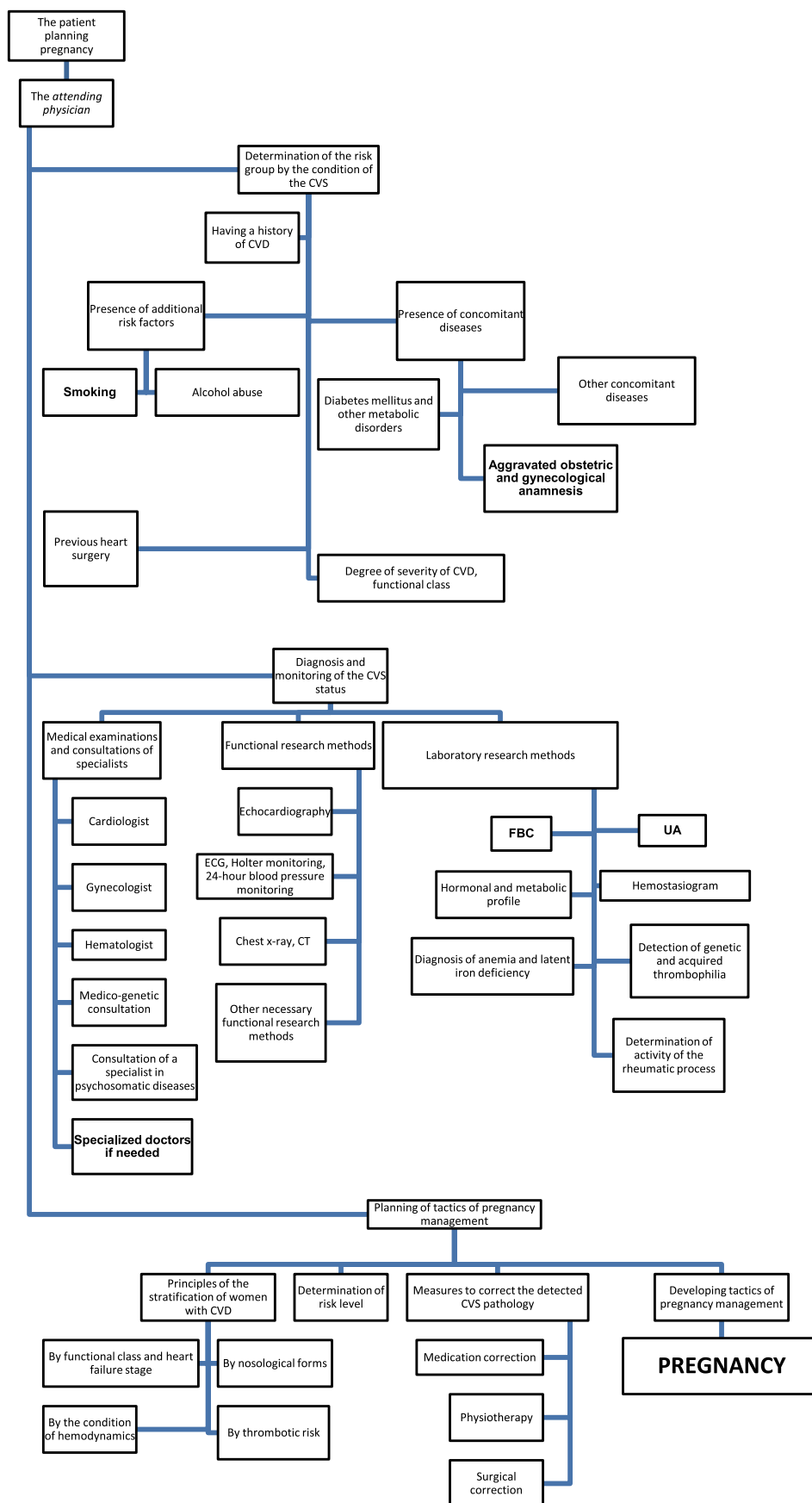


Fig. 2. Basic scheme of preconception preparation of patients with CVD

9. **BUKHONKINA, Y.M.** The course of pregnancy, child-birth and perinatal outcomes in women with congenital heart disease/Y.M. Bukhonkina, G.V. Chizhova, R.I. Struk // Far Eastern Medical Journal. - 2010. - №1. - P. 46–48;
10. **ABDEL-HADY ES, EL-SHAMY M, EL-RIFAI AA, GODA H, ABDEL-SAMAD A, MOUSSA S.** Maternal and perinatal outcome of pregnancies complicated by cardiac disease. *Int. J. Gynaecol. Obstet.* 90(1), 21–25 (2005)
11. **CURTIS SL, MARSDEN-WILLIAMS J, SULLIVAN C ET AL.** Current trends in the management of heart disease in pregnancy. *Int. J. Cardiol.* 133(1), 62–69 (2009).
12. **DRENTHE W., BOERSMA E., BALCIA., MOONS P., ROOS-HESELINK J.W., MULDERBJ.M. ET AL.** Predictors of pregnancy complications in women with congenital heart disease // *European Heart J.* — 2010. — Vol. 31. — P. 2124–2132.
13. **CORNETTE J, RUYS TP, ROSSI A, RIZOPOULOS D, TAKKENBERG JJ, KARAMERMER Y, OPIC P, VAN DEN BOSCH AE, GELEIJNSE ML, DUVEKOTJJ, STEEGERS EA, ROOS-HESELINK JW.** Hemodynamic adaptation to pregnancy in women with structural heart disease. *Int J Cardiol* 2013;168:825–831.
14. **THANAJIRAPRAPA T, PHUPONG V.** Pregnancy complications in women with heart disease. *J. Matern. Fetal Neonatal Med.* (2009)
15. **GELSON E, OGUEH O, JOHNSON M.** Cardiovascular Changes in Normal Pregnancy. RCOG Press, London, UK (2006).
16. **REGITZ-ZAGROSEK V., BLOOMSTROM LUNDQVIST C., BORCHI C. ET AL.** Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on Management of Cardiovascular Diseases during pregnancy of the European Society of Cardiology (ESC) // *Eur. Heart J.* — 2011. — Vol. 32, N. 24. — P. 3147–3197.
17. **KUZMINA T.E., PASHKOV V.M., KLINDUKHOV I.A.** Preconception preparation. Modern concepts. – M.: Library of the Sechenov First Moscow State Medical University. – 2016, – P. 3
18. Preconception preparation: clinical protocol//IARS (Interdisciplinary Association of Specialists in Reproductive Medicine). Approved by Protocol No. 4P-16 of the Presidium of the Board of the Interdisciplinary Association of Specialists in Reproductive Medicine (IARS) of June 28, 2016. – Moscow: Publishing house «StatusPraesens». – 2016, – P. 15
19. **UDOVKA N.A., SIEPURA V.V.** Observance of the principle of preconception preparation: what the doctor and future parents should know (part 2) – Lugansk: Library of LSMU, – 2015, – P. 37–38
20. **TSIARAS S., POPPAS A.** Cardiac disease in pregnancy: value of echocardiography // *Cun. Cardiol. Rep.* — 2010. — Vol. 12. — P. 250–256.
21. **DAYAN N, LASKIN CA, SPITZER K, MASON J, UDELL JA, WALD RM, SIU SC, ITEN-SCOTT T, SILVERSIDES CK** Pregnancy complications in women with heart disease conceiving with fertility therapy. *J Am Coll Cardiol* 2014;64:1862–1864.
22. **KHAIRY P, OUYANG DW, FERNANDES SM, LEE-PARRITZ A, ECONOMY KE, LANDZBERG MJ.** Pregnancy outcomes in women with congenital heart disease. *Circulation* 113, 517–524 (2006).
23. **MADAZLI R, SAL V, CIFT T, GURALP O, GOYMEN A.** Pregnancy outcomes in women with heart disease. *Arch. Gynecol. Obstet.* 281(1), 29–34 (2010).