MINISTRY OF HEALTH PROTECTION OF UKRAINE

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Faculty of Medicine No. 1

Department of Obstetrics and Gynecology No. 1

METHODOLOGICAL INSTRUCTIONS ON THE DISCIPLINE "OBSTETRICS AND GYNECOLOGY"

by specialty 222 "MEDICINE"
according to the training plan of specialists of the second (MASTER'S)
level of field of knowledge 22 "Health care" in higher educational institutions
IV level of accreditation

On the topic "Pregnancy and extragenital pathology»

FOR STUDENTS OF THE V, VI COURSE
THE FACULTY OF TRAINING OF FOREIGN CITIZENS

"Approved"
At the methodological meeting of the department
of obstetrics and gynecology #1
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Head of Department
obstetrics and gynecology No. 1,
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"Approved"
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Head of the Central Methodological Commission
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Methodical instruction for students of the 5, 6 th year of the Faculty of Training of Foreign Citizens in obstetrics and gynecology

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Extragenital pathology and pregnancy

I. Relevance of the topic. Extragenital pathology (EGP) combines diseases, pathological syndromes in pregnant women that do not belong to gynecological diseases or obstetric complications. Extragenital pathology occurs in 60-80% of pregnant women.

In the structure of the EGP, chronic extragenital diseases are observed in approximately 60% of cases. At the same time, approximately 50% have chronic diseases of internal organs, and 10% - other organs and systems (surgical pathology, pathology of the organs of vision, nervous system, etc.). Obesity, pathology of the cardiovascular system, endocrine pathology and pyelonephritis prevail among chronic diseases. Among the acute - anemia, acute respiratory diseases and pathology of the urinary system (cystitis, pyelonephritis).

EGP burdens the course of pregnancy, delivery and the postpartum period. It negatively affects the condition of the fetus. It is a significant cause of placental dysfunction, fetal growth restriction and fetal distress. EGP increases the frequency of miscarriage, preterm labor and is the cause of perinatal losses.

In view of the above, a multidisciplinary approach is necessary in the management of pregnant women with EGP, that is, supervision of pregnant women by an obstetrician-gynecologist and related specialists. Patients with EGP should undergo prepregnancy counseling by a multidisciplinary pregnancy team to determine a delivery plan and define postpartum care. Careful examination of pregnant women with EGP, prevention and treatment of pregnancy complications, rational choice of the term and method of delivery, and specialized care for newborns are also important.

In the early stages of pregnancy, one of the difficult issues is identifying contraindications to the pregnancy.

II. Learning objectives

To form knowledge, the student *should familiarize* himself (α=1) with the topic of extragenital pathology and pregnancy.

The student *must learn* (α=2):

1. General principles of management of pregnant women with extragenital pathology.
2. Peculiarities of the course and management of pregnancy in women with diseases of the cardiovascular system.
3. Peculiarities of the course and management of pregnancy in women with diseases of the kidneys and urinary tract.
4. Peculiarities of the course and management of pregnancy in women with diseases of the endocrine system.
5. Peculiarities of the course and management of pregnancy in women with diabetes mellitus.
6. Peculiarities of the course and management of pregnancy in women with diseases of the liver and biliary system.
7. Peculiarities of the course and management of pregnancy in women with blood diseases.

The student *must be able* to (α=3):

1. Prescribe and evaluate the results of examination of pregnant women with extragenital pathology.
2. Assess the risks and predict possible complications of pregnancy and delivery in women with extragenital pathology, the impact on the condition of the fetus.
3. Determine the term and method of delivery of a pregnant woman with extragenital pathology.
4. Timely detection of contraindications to pregnancy in women with extragenital pathology.
5. Be able to properly provide the pregnant woman and, with her consent, relatives with the necessary information about the state of health of the pregnant woman and the risks to their child. Help them understand the risks and possible treatment options to make the best decision for their family together.

III. Educational objectives

- To teach and develop in students, as future doctors, obstetrician, an understanding of responsibility and consistency in work, sensitivity towards pregnant women, women in labor, postpartum women.
- To teach students logical clinical thinking, based on modern methods of diagnosis and treatment.

IV. Interdisciplinary integration: an integrative, interdisciplinary approach is necessary in the management and treatment of pregnant women with extragenital pathology. Therefore, the supervision of such pregnant women and decision-making regarding delivery is carried out by an obstetrician-gynecologist in conjunction with related specialists. Neonatologists, neonatologists-intensivists, a perinatal psychologist, and a member of the hospital's ethics committee are also usually included in the composition of the perinatal council.

V. Content of educational material

CARDIOVASCULAR DISEASES IN PREGNANCY

Cardiovascular diseases (CVD) during pregnancy remains the leading cause of maternal morbidity and mortality and has been on the rise over recent decades.

Novel messages of the new European Society of Cardiology (ESC) guidelines for the management of cardiovascular diseases during pregnancy :

- ✓ The use of the mWHO classification of maternal risk is recommended (see below table 1).
- ✓ The pregnancy heart team is introduced.
- ✓ Assisted reproductive therapy is defined.
- ✓ Bromocriptine is recommended for the treatment for peripartum cardiomyopathy (PPCM).
- ✓ Advice is given on contraception and the termination of pregnancy in women with cardiac diseases.
- ✓ Vaginal delivery is the preferred mode of birth in the majority of pregnancies.

- ✓ Beta blockers are recommended during and after pregnancy for congenital long QT syndrome and cat-echolaminergic polymorphic ventricular tachycardia.
- ✓ Low molecular weight heparin is the ideal substance for prophylaxis and treatment of venous thromboembolism in pregnancy under weekly monitoring of antifactor Xa activity.

The mWHO classification of maternal risk. It is recommended to perform risk assessment in all women of childbearing age with cardiac diseases and before conception, using the mWHO classification of maternal risk in pregnancy (class of recommendation I, evidence level C), (table 1).

It is recommended that ***patients with modified World Health Organization (mWHO) class IV risk are counselled against pregnancy***.

Fertility treatment is contraindicated in women with mWHO class IV. Fertility treatment requires a careful risk-benefit ratio assessment in women with mWHO class III disease, and in women who need anticoagulation.

Table 1. Modified World Health Organization (mWHO) classification of maternal cardiovascular risk (mod. from ESC, 2018).

	mWHO 1	mWHO II	mWHO II-III	mWHO III	mWHO IV
Diagnosis (if otherwise well and uncompli-cated)	Small or mild – pulmonary stenosis – patent ductus arteriosus – mitral valve prolapse	Unoperated atrial or ventricular septal defect	Mild left ventricular impairment (EF >45%)	Moderate left ventricular impairment (EF 30–50%)	Pulmonary arterial hyperten-sion
			Hypertrophic cardiomy-opathy	Previous peripartum cardiomyopathy without any residual left ventricular impairment	Previous peripartum cardiomyopathy with any residual left ventricular impairment
	Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage)	Repaired tetral-ogy of Fallot	Native or tissue valve disease not considered WHO I or IV (mild mitral stenosis, moderate aortic stenosis)	Mechanical valve	
	Atrial or ventricular ectopic beats, isolated	Most arrhythmias (supraventricular arrhythmias)	Marfan or other HTAD syndrome without aortic dilatation	Systemic right ventricle with good or mildly decreased ventricular function	Severe systemic ventricular dysfunction (EF <30% or NYHA classes III–IV)
		Turner syndrome without aortic dilatation	Aorta < 45 mm in bicuspid aortic valve pathology	Fontan circulation	A patient with Fontan circula-tion experiencing any medical complication
					Severe mitral stenosis
					Severe symptomatic aortic stenosis
					Systemic right ventricle with moderate or severely decreased ventricular function
			Repaired coarctation	Unrepaired cyanotic heart disease	
			Atrioventricular septal defect		
				Other complex heart disease	
				Moderate mitral stenosis	Severe aortic dilatation (>45 mm in Marfan syndrome or other HTAD, >50 mm in bicuspid aortic valve. Turner syndrome ASI >25 mm/m^2, tetralogy of Fallot >50 mm)
				Severe asymptomatic aortic stenosis	
				Moderate aortic dilatation (40–45 mm in Marfan syndrome or other HTAD; 45–50 mm in bicuspid aortic valve. Turner syndrome ASI 20–25 mm/m^2, tetralogy of Fallot <50 mm)	Vascular Ehlers–Danlos syn-drome
					Severe (re)coarctation
				Ventricular tachycardia	

ASI aortic size index, *EF* ejection fraction, *HTAD* hereditary thoracic aortic disease, *NYHA* New York Heart Association

Indications for exclusion of the II stage of labor with the help of obstetric forceps:

- septic endocarditis;
- endocarditis;
- heart failure (HF) IIA (class II);
- arrhythmias.
- **Indications for cesarean section:**
- chronic HF IIB -III stage;
- rheumatic carditis II-III degree of activity;
- coarctation of the aorta in the presence of hypertension or signs of aortic dissection;
- tachyarrhythmic form of atrial fibrillation with a large pulse deficit.

Pregnant women with CVD receive complex pharmacotherapy. It is important to remember that the following groups of drugs are contraindicated during pregnancy:

✓ angiotensin-converting enzyme inhibitors;

✓ angiotensin II receptor blockers (ARBs).

Heart failure

Heart failure (HF) remains the most common major cardiovascular complication arising in pregnancy and the postpartum period among women with preexisting heart disease regardless of the cause, whether related to cardiomyopathy (new or preexisting), pulmonary hypertension (PH), or valvular, ischemic, or congenital heart disease (CHD). Mothers who develop HF have been shown to experience an increased risk of death as well as a variety of adverse cardiac and obstetric outcomes. Risk to neonates is significant, with increased risks in perinatal morbidity and mortality, low Apgar scores, and prolonged neonatal intensive care unit stays.

Maternal Cardiovascular Physiology

During pregnancy, anatomic and physiologic hemodynamic changes within the maternal cardiovascular system are orchestrated to support the health and safety of the mother and her fetus. Increases in plasma volume (leading to physiologic anemia) and maternal heart rate occur, and arterial blood pressure and systemic vascular resistance decrease. Cardiac output (CO) increases, beginning in early pregnancy because of an increase in stroke volume, and is maintained further by way of tachycardia. Twin pregnancies exhibit an additional 15% higher CO throughout pregnancy. Increased left ventricular dimensions, aortocaval compression, and hypercoagulability also play a role in the dynamic alterations observed.

As labor begins, additional factors amplify the divergence from nonpregnant cardiovascular physiology; uterine contractions force a large volume of blood away from the uterus into general circulation, raising preload and CO in turn, and pain and anxiety increase sympathetic tone, raising blood pressure, heart rate, and CO as well. Within an hour of delivery, heart rate and CO return to prelabor levels, although still elevated above baseline nonpregnant levels. Stroke volume, heart rate, and cardiac output decrease dramatically over the first 2 weeks postpartum. Within the first 6 weeks postpartum, there is a persistent shift in the balance of the autonomic nervous system and endothelial

reactions as they aim to reapproximate the non-pregnant state. Atrial natriuretic peptide

and B-type natriuretic peptide (BNP) levels further increase postpartum, mediating

diuresis after delivery. The physiologic stress that these continuous adaptions create can both reveal previously undiagnosed cardiovascular disease in some and lead to development of new cardiac conditions in others, ultimately putting mothers at an increased risk of developing HF throughout their pregnancy course.

Cause of HF (Figure 1).

Major adverse cardiovascular event (MACE) rates are higher in those with cardiomyopathy and PH and lower in those with CHD. The largest group of women who present with HF are related to cardiomyopathy, where the risk of adverse cardiovascular events during pregnancy approaches 50%.

PH is associated with the highest overall risk of complications, particularly when combined with cardiomyopathy or valvular disease.

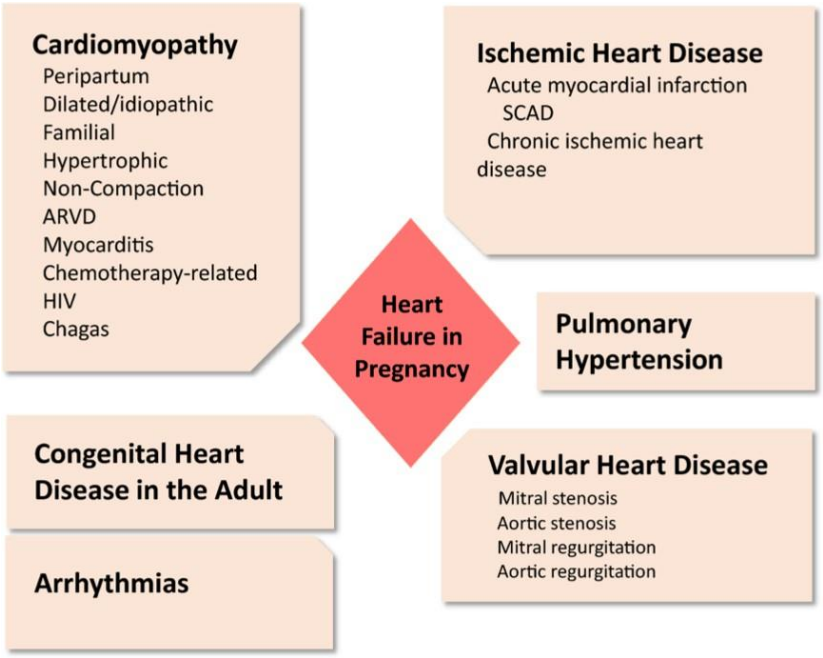

Figure 1. Major categories of potential etiologies of maternal heart failure (Rachel A. Bright, BS, Fabio V. Lima, MD, MPH, Cecilia Avila, MD, 2021).

→ Delineated are the major categorical etiologies that can result in mothers developing heart failure in pregnancy or the puerperium. ARVD indicates arrhythmogenic right ventricular dysplasia; and SCAD, spontaneous coronary artery dissection.

Timing of HF. Overall, 60% of HF cases occur in

the postpartum period, followed by 27% at delivery, and 13% during pregnancy. Timing of HF in mothers with known heart disease exhibits a bimodal distribution, with peaks at both 23 to 30 weeks and postpartum. Patients with underlying valvular heart disease develop HF throughout pregnancy, whereas those with cardiomyopathy primarily experienced onset in the weeks before and following delivery. However, PPCM has also been described as late as 5 to

12-months after delivery. Late onset was associated with a 2- to 3-fold increased risk of maternal mortality and MACE (Major Adverse Cardiovascular Events). Women with

shunt lesions experienced an earlier onset of HF at ≈25 weeks gestation.

Risk factors:

HF in pregnancy is more than twice as common in Black women compared with White women and is least common among Hispanic women.

Medical and obstetric risk factors play an important role in outcome.

- ✓ Mother may have cardiomyopathy and coexisting pulmonary hypertension (PH) or mitral stenosis and PH, placing her at an additional increased cardiac risk.
- ✓ Obstetric risk factors for HF include multiple gestation, gestational or chronic hypertension, preeclampsia/eclampsia, postpartum hemorrhage, placenta accreta/ abruptio/previa, and gestational diabetes mellitus. Additionally, hyperlipidemia, preexisting diabetes mellitus, obesity, chronic kidney disease, and anticoagulant use increase the risk for developing HF.
- ✓ Hypertensive disorders of pregnancy deserve special mention, consisting of a spectrum of disorders from exacerbation of preexisting hypertension, hypertension in

  pregnancy, preeclampsia, eclampsia, and postpartum hypertension. In women with preexisting heart disease, the added strain of preeclampsia precipitated HF in as many as 30% of patients.

Several studies have shown that the majority of **patients with PPCM** are Black, and incidence is highest among Black women and lowest among Hispanic women, as is true

for maternal HF overall. The association between PPCM and preeclampsia is well established (1\3 of women), whereas the other 2/3 occurred in other forms of heart disease.

Diagnosing heart failure may be more difficult because the physiological changes that occur during pregnancy may mimic cardiovascular disease, and thus mask an underlying disease condition. It is therefore necessary to take the condition of pregnancy into account, to perform in-depth analysis of the medical history, particularly the history of preceding pregnancies, and histories or family histories of hypertension or preeclampsia, and to perform a physical examination bearing in mind more subtle signs of disease. Dyspnea that is out of proportion to the pregnancy condition or a new heart murmur ne-

cessitate immediate transthoracic echocardiography. It is important to measure blood pressure in a standardized fashion, to search for proteinuria, and repeat those examinations throughout pregnancy.

Evaluation of heart failure during pregnancy

- ✓ Patients with a history of HF or cardiac disorders that put them at risk for HF should undergo a thorough initial evaluation prior to or in the early stage of pregnancy.
- ✓ Patients who develop signs or symptoms of HF during pregnancy should undergo an initial evaluation similar to that generally recommended for patients with suspected HF.
- ✓ Counseling – Management of a woman with HF (or at risk for HF) contemplating pregnancy includes counseling the patient regarding the expected prognosis and

  potential risks of pregnancy. The discussion should be based upon an individualized assessment of risk utilizing the modified World Health Organization classification of maternal cardiovascular risk. Counseling should ideally occur prior to pregnancy.

Symptoms and Detection of Heart Failure.

- ✓ **Signs that warrant further investigation for cardiac disease** are cyanosis, clubbing, resting tachycardia, any type of arrhythmia, hypertension or hypotension,

  hypoxia, tachypnea, elevated jugular venous pressure, diastolic murmur, murmur radiating beyond the left sternal edge, murmur associated with a thrill, marked peripheral edema, or evidence of pulmonary edema; symptoms such as shortness of breath and orthopnea also indicate a need for further consideration. Most patients with HF presented with bibasal crepitations.
- ✓ A pure clinical evaluation of pregnant patients with suspected HF often does not suffice in steering physicians to a diagnosis of HF; ECG, BNP (B-type Natriuretic peptide), and echocardiogram, with the possible addition of chest X-ray in the setting of pulmonary complaints, are needed.

- ✓ The utility of **BNP in diagnosing HF** in pregnant populations has been elucidated. Median BNP levels in normal pregnancies rest at 19 to 20 pg/mL which is increased from nonpregnancy levels (median 10 pg/mL) but still lower than levels correlating to congestive HF in the general population. For mothers with preeclampsia this level is elevated even further. BNP level of ≤100 pg/mL has a 100% negative predictive value for identifying cardiac events during pregnancy.

A threshold of 111 pg/mL as an "elevated" BNP level to predict HF in pregnant or postpartum women exhibited 95% sensitivity.

- ✓ Echocardiography serves the same utility in pregnant women as in the general population and can detect structural or physiologic changes to the heart, which may be because of either expected pregnancy-related alterations or cardiovascular disease.

The Interdisciplinary Cardio-Obstetrics Team: Maternal Care Reimagined.

In order to provide moderate and high-risk mothers with effective care aimed at preventing HF and other associated adverse maternal and fetal outcomes, a distinct multidisciplinary approach coordinated among experts from cardiology, obstetrics, maternal fetal medicine, obstetric anesthesiology, neonatology, nursing departments, pharmacists, and social workers must be in place; *this forms the cardio-obstetrics team*.

This should occur before pregnancy, at the precontemplative stage or within routine cardiology or gynecologic visits, to prepare patients for the considerations that are in their future. Discussing pregnancy within the context of routine visits years ahead of an actual pregnancy would help set the stage for pregnancy contemplation and allow for family planning.

This cardio-obstetrics team should be used at multiple points, starting with prenatal counseling through labor and delivery planning as well as close postpartum follow-up and long-term longitudinal care.

Key prenatal visit elements include:

- ✓ assessment of symptoms,
- ✓ medication review,
- ✓ preconception health evaluation,
- ✓ maternal cardiovascular risk screening with the mWHO scoring system and patient education that would include advising against pregnancy for those women falling under mWHO class IV.

If a woman requires more advanced specialty care, transfer to a center in which a HF specialist, PH specialist, interventional cardiologist, cardiac surgeon, adult congenital specialist, or electrophysiology specialist can be available depending on the needs of the patient.

For women experiencing HF, as well as those with significant cardiomyopathy, PH, arrhythmia, significant valve disease, aortopathy, or recent myocardial infarction, postpartum care will require that they continue with monitoring until stability is achieved.

Consideration of breast feeding and contraceptive care planning should begin before delivery and should take into account the mother's preferences as well as medical factors. **Therapeutics and Principles of Management**

Pregnant or postpartum woman presents in acute HF:

- ✓ Initial goals should be to stabilize the patient, confirm the diagnosis, assess the severity of HF, assess fetal status and viability, and contact members of an interdisciplinary cardio-obstetrics care team.
- ✓ Any reversible factors that may have contributed to the patient's presentation, such as anemia, thyroid dysfunction, pulmonary embolism, preeclampsia/eclampsia, or infection, should be addressed.

- ✓ The last initial step is to assess fetal viability as well as stability.
- ✓ Steroids can be considered if there is concern for poor fetal lung maturity.

Treatment will vary depending on whether a woman is pregnant or postpartum, as once mothers have delivered there is no longer a concern about fetal stability/maturity or teratogenicity of medications and more standard HF therapies can be initiated (Figure 2). **In patients with stable HF:**

- ✓ Medical treatment approach parallels that of nonpregnant patients; however, there is a need to avoid teratogenic drugs (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, angiotensin receptor neprilysin inhibitors, mineralocorticoid receptor antagonists, atenolol, direct factor Xa inhibitors).
- ✓ Mainstays of treatment include hydralazine, nitrates, and β-blockers.
- ✓ Diuretics should be used in those patients with signs or symptoms of pulmonary edema; however, caution must be exercised as they have the potential to reduce placental perfusion.
- ✓ *In patients who have already delivered*, treatment with standard HF therapy should be the highest priority, focusing on angiotensin-converting enzyme inhibitors,

  angiotensin II receptor blockers, angiotensin receptor neprilysin inhibitors, β-blockers, and aldosterone antagonists, as they are known to provide a mortality and treatment benefit to HF patients.

For patients with cardiogenic shock or severe HF:

- ✓ Transfer to a tertiary center where mechanical support can be provided should be pursued immediately.
- ✓ Treatment in these patients must aim to optimize preload (consider diuretics) and oxygenation, use inotropes/vasopressors, consider adding PPCM-specific therapies,

  and if the patient is pregnant plan for urgent cesarean section.

If the mother's condition is complicated by the presence of hypertensive disease:

- ✓ The best pharmacologic options include intravenous labetalol or hydralazine or oral nifedipine for severe hypertension (persistent blood pressure of ≥160/110 mm Hg),

  and in cases of less severe hypertension labetalol, nifedipine, and methyldopa are first-line choices. Intravenous nitroglycerin is preferred for patients who present with evidence of pulmonary edema .

Patients with newly diagnosed PPCM or other dilated cardiomyopathies:

- ✓ Have a favorable response rate to medical HF management;
- ✓ Therefore, implantation of implantable cardioverter-defibrillators should be deferred.
- ✓ A more appropriate option is a wearable cardioverter-defibrillator for the first 3 to 6 months after diagnosis in those with severe left ventricular impairment (ejection fraction <35%).

Delivery Considerations

In women with severe HF or persistent hemodynamic instability despite treatment - urgent delivery by cesarean section should be considered irrespective of gestational duration.

For women with stable HF - vaginal delivery with epidural anesthesia is the preferred route.

If vaginal delivery is pursued - instrumentation is often used to shorten the second stage of labor. Invasive hemodynamic monitoring by way of intra-arterial line may be used to monitor stability in labor and delivery. Epidural is the preferred anesthetic technique. Postpartum cardiorespiratory monitoring is often required in these patients in an intensive care unit or stepdown setting.

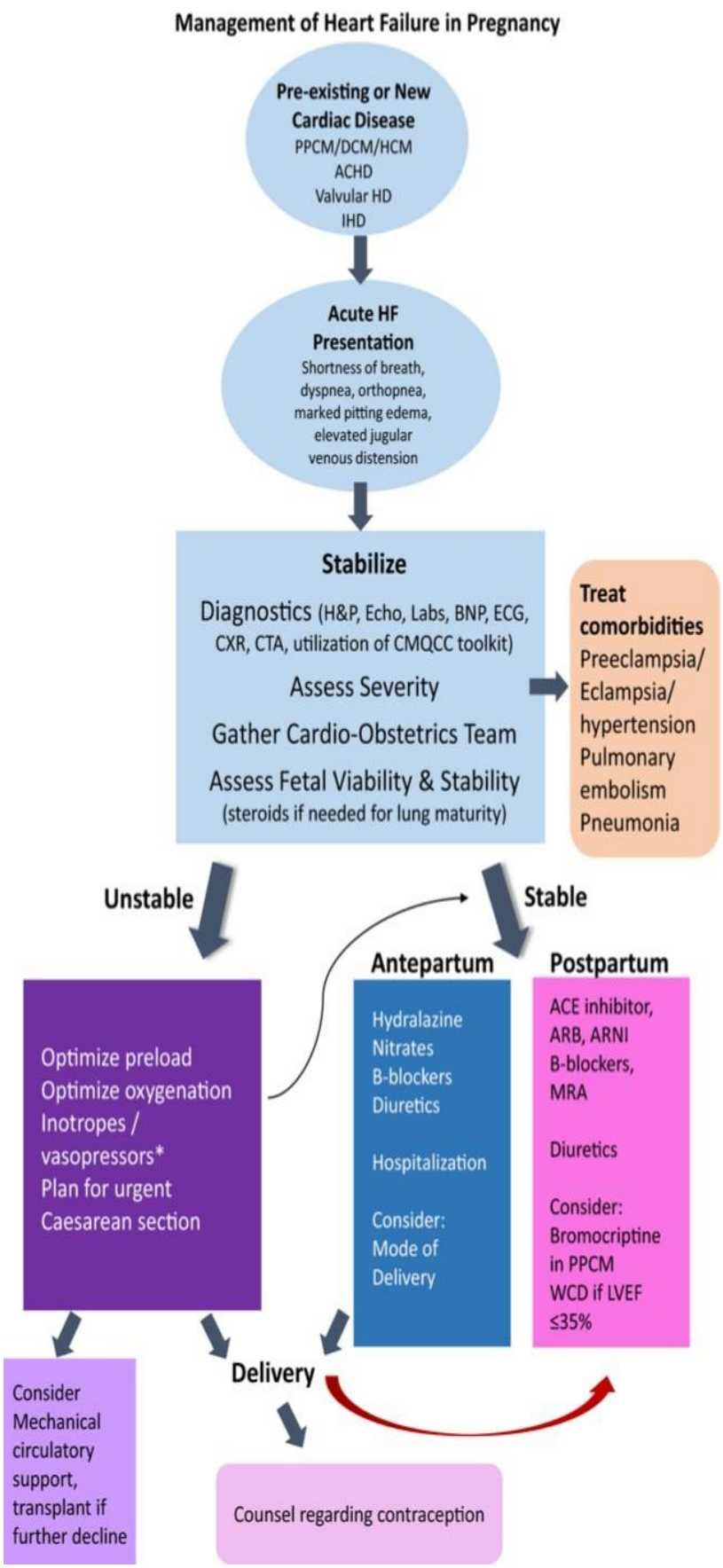

Figure 2. Management of heart failure in pregnancy (Rachel A. Bright, BS, Fabio V. Lima, MD, MPH, Cecilia Avila, MD, 2021).

Overall scheme for approaching a pregnant or postpartum patient in acute heart failure. Importantly, management will be determined by pregnancy status and severity of disease.

ACE indicates angiotensin-converting enzyme; ACHD, adult congenital heart disease; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitors; BNP, B-type natriuretic peptide; CM, cardiomyopathy; CMQCC, California Maternal Quality Care Collaborative; CTA, computed tomography angiography; CXR, chest X-ray; DCM, dilated cardiomyopathy; H&P, history and physical exam; HCM, hypertrophic cardiomyopathy; HD, heart disease; HF, heart failure; IHD, ischemic heart disease; LVEF, left ventricleejection fraction; MRA, mineralocorticoid receptor antagonists; PPCM, peripartum cardiomyopathy; and WCD, wearable cardioverter-defibrillator.

In the past, rheumatic heart disease was the most common form of cardiac disease in pregnant people; it still predominates in developing countries.

Today, congenital heart disease is the most common form of heart disease complicating pregnancy in high-income, industrialized countries, including in the United States. In part because advances in the treatment of congenital heart disease have made it possible for more affected children to reach adulthood and attempt pregnancy.

This pattern differs greatly from the experience of low- and middle-income countries, where 88% to 90% of antenatal heart disease is attributable to rheumatic heart disease.

Rheumatic heart disease in pregnancy

Rheumatic heart disease (RHD) is by far the most important form of acquired heart disease in resource-limited nations, although the prevalence of RHD has declined sharply in industrialized countries during the last century. RHD is also called the disease of poverty.

Today, acute rheumatic fever and chronic rheumatic heart disease are distinguished.

Acute rheumatic fever (ARF) - causes a pancarditis, affecting the valve leaflets, pericardium, epicardium, myocardium, and endocardium. Mitral regurgitation (MR; with or without aortic regurgitation) is the most common valve lesion. The revised Jones criteria incorporating epidemiology and Doppler echocardiography should be applied.

Patients with suspected or confirmed ARF or a new murmur should undergo echocardiography to determine if valve abnormalities are present.

Rheumatic heart disease is defined as permanent heart valve damage subsequent to ARF.

The transition from rheumatic carditis (ARF) to RHD with chronic valvular lesions develops over many years after one or more episodes of ARF.

RHD should be suspected in patients with past history of ARF and/or suspected pathologic cardiac murmur. The diagnosis is confirmed by the presence of echocardiographic morphologic and Doppler criteria. While RHD occurs only as a sequela of ARF, most patients with RHD lack a history of past ARF, suggesting that the diagnosis of ARF is frequently missed.

Prevention of the initial development of acute rheumatic fever (ARF) involves prompt diagnosis and antibiotic treatment of group A streptococcal (GAS).

Management

Pre-pregnancy care

A woman's journey with RHD often starts well before pregnancy. Decisions during childhood about treatment interventions for RHD, such as surgery and anticoagulation, may be required. These decisions will have lifelong consequences. Conversations about treatment and pregnancy planning with the adolescent/woman, other family and partner as appropriate to age and circumstance should begin in adolescence and continue through reproductive years.

In high-risk women who are planning pregnancy or pregnant, multi-disciplinary care is required, including obstetric/obstetric physician, cardiac, neonatology, fetal and anaesthetic specialisations.

Preconception care - the overall aim is to improve health status and optimise pregnancy outcome through identifying and reducing risk before conception occurs.

Pre-conception diagnosis of RHD allows optimisation of management including surgical management, before pregnancy.

Contraception. In high-risk women who may need future cardiac intervention or surgery, the use of long-acting reversible contraception (intra-uterine contraceptive device including Mirena or etonogestrel implant such as Nexplanon). Oestrogen-containing contraceptives are associated with elevated risk of thrombosis and should be avoided.

Pregnancy planning and risk. If a woman is already symptomatic with moderate or severe RHD, or has asymptomatic clinically significant mitral stenosis (MS), interventional therapy such as Percutaneous Balloon Mitral Valvuloplasty (PBMV) or surgery prior to pregnancy is likely to be required, to avoid the risk of life-threatening complications. Consider and discuss the risks and benefits of options for all surgical interventions, including mechanical prostheses, bioprostheses and repair. Some women with severe RHD may be advised against becoming pregnant. A left ventricular ejection

fraction of <30% or reduced systolic function with New York Heart Association (NYHA) class III/IV symptoms is associated with high risk of maternal morbidity or mortality, and pregnancy is strongly discouraged.They need to beable to discuss and make choices

about risks associated with pregnancy. Final decision-making lies with women and must be respected, even if it differs from medical advice.

Termination of pregnancy. Termination of pregnancy may occur according to a woman's preference or if medically indicated such Level III or IV RHD in pregnancy severity.

During pregnancy

The first presentation of RHD may be during pregnancy or in the early post-partum period. A high index of suspicion and early diagnosis, along with appropriate follow-up, are key elements to a successful outcome for mother and child.

The modified World Health Organization classification of maternal cardiovascular risk (mWHO) provides reliable risk assessment and associated recommendations of level of specialist care management required for the pregnancy (table 1).

Any degree of reduced left ventricular systolic function in the presence of severe MR carries a high risk of maternal heart failure, morbidity and possible mortality. Similarly, in combined aortic regurgitation AR/MR, the combination of the moderate lesions may be associated with a higher risk of heart failure.

Women with severe RHD or otherwise assessed as high risk require ongoing review at a tertiary centre with intensive care, obstetric/cardiology and anaesthetic services.

Further risk stratification can be performed with baseline and serial B-type natriuretic peptide (BNP) levels. BNP levels <100 pg/mL at 20 weeks' gestation, or on serial assessment, have been associated with a high negative predictive value for maternal cardiac events.

A pregnant or post-partum woman at higher risk of or diagnosed with RHD who presents with breathlessness, orthopnoea, wheeze or worsening fatigue should be investigated with an echocardiogram

Anticoagulation is needed for all women with mechanical prosthetic valves to prevent stroke and other thromboembolic disease and may be needed for atrial fibrillation depending on thromboembolic risk assessment. All anticoagulants pose risks in pregnancy. Risks to the mother include both antepartum and post-partum haemorrhage. Risks to the fetus include teratogenicity and stillbirth (warfarin).

Women with valve lesions posing problems in pregnancy (moderate or greater mitral stenosis, severe mitral or aortic regurgitation, severe aortic stenosis, pulmonary hypertension or heart failure) are at high risk with elevated chance of cardiac events during pregnancy and adverse fetal outcomes. They require specialist care and close monitoring.

When low molecular weight heparin is used in pregnancy to replace warfarin, monitoring of anti-Xa levels and appropriate dose adjustment is essential.

Labor and birth

- ***Individual management approaches are determined by the multi-disciplinary team taking account of cardiovascular and obstetric issues.***
- ***For nearly all gravidas with cardiac disease, vaginal delivery is preferred to cesarean delivery since vaginal delivery generally poses less cardiac risk.***
  Vaginal
  birth is associated with less blood loss, lower risk of infection, less venous thromboembolic complications and is advised for most women with RHD.
- ***In most patients with heart failure controlled with medication, vaginal delivery is recommended*** if obstetric factors are favourable, with adequate heart rate control and
  analgesia.
- A caesarean section is usually recommended for women on oral anticoagulant therapy presenting in pre-term labour, or those with high-risk aortopathies, severe heart failure or severe pulmonary hypertension.
- Maternal deterioration with failure to respond to medical therapies may require

premature delivery for maternal safety.

- ✓ During labour, cardiac output increases as heart rate and blood pressure rise. An inability to increase cardiac output secondary to moderate/ severe RHD (particularly

  obstructive left sided lesions) may lead to pulmonary oedema. ***Early epidural administration will help*** - after appropriately-timed short-term cessation of anticoagulation – may be indicated to reduce tachycardia and hypertension that can precipitate acute heart failure during delivery.
- ✓ The increased systemic vascular resistance and venous return with labour and birth often necessitate the use of diuretic therapy in women with significant valvular disease.
- ✓ Peri-delivery and post-partum care in an intensive-care setting may be required for high-risk women.
- ✓ Routine antibiotic prophylaxis for bacterial endocarditis not recommended and antibiotics should be given as per local obstetric indications.

Management of vaginal labor

- ✓ Spontaneous onset of labor is preferred to induced labor for most women with heart disease. Pregnant people with cardiac disease who are considered functionally normal

  or well-controlled should be allowed to go into labor spontaneously.
- ✓ If there are any concerns about the functional adequacy of the heart and circulation,

  induction of labor under controlled conditions is suggested.
  - A planned daytime induction is the most practical.
  - The timing of induction is individualized, taking into account the gravida's cardiac status, inducibility of the cervix, and fetal lung maturity.
  - A long induction in a woman with an unfavorable cervix should be avoided.
  - From a practical point of view, it may be useful to plan the induction so that

delivery occurs during the working day when all hospital services are readily available.

- Induction of labor in a gravida with a **favorable cervix** usually requires only **oxytocin administration and artificial rupture of the membranes (amniotomy)**.
- An **unfavorable cervix** should be ripened with a **prostaglandin E analogue**.
- Prostaglandin analogues are absorbed into the systemic circulation and can lower systemic vascular resistance, lower systemic pressure, and increase heart rate. These effects are more frequent with E2 than E1 and when the drugs are used in the higher doses required for termination of pregnancy.
- Laminaria or a Foley catheter balloon can also be used for cervical ripening.
- Once in labor, the woman should be placed in a lateral decubitus position to attenuate the hemodynamic fluctuations associated with major uterine contractions and the supine position. The obstetrician should allow uterine contraction to descend the fetal head to the perineum, unassisted by maternal pushing, to avoid the undesirable circulatory effects of the Valsalva maneuver.
- Delivery may then be assisted by low forceps or vacuum extraction, as needed.

Medications to treat and prevent post-partum haemorrhage

Oxytocin: administer slowly by infusion in third stage of labour. Avoid ergometrine in severe RHD, unless life- threatening bleeding.

✓ Oxytocin and carbetocin can cause vasodilatation, resulting in hypotension and reflex tachycardia and has been associated with coronary vasoconstriction. Cautious use
including limiting boluses and using a continuous slow infusion is generally tolerated.

✓ Ergometrine, an α-adrenergic receptor agonist, may cause coronary vasospasm, pulmonary vasoconstriction and hypertension. Depending on the severity of RHD, it
should be avoided, particularly if the woman has pulmonary hypertension.

✓ Carboprost, a smooth muscle contractor, should be avoided. It may cause hypertension, increased pulmonary vascular resistance and

severe bronchospasm in asthmatics.

✓ Misoprostol, a prostaglandin E1 analogue, is better tolerated.

Management strategies must be balanced against maternal risk and life-threatening bleeding.

Post-partum and post-discharge

Post-partum

Consider need for diuretic therapy to assist with haemodynamic shifts post-partum. 2C

Follow anticoagulation protocol where relevant. 1A

Investigate post-partum/ post-discharge dyspnoea or new-onset cough promptly. 1A

Encourage breastfeeding and review safety of cardiac medications with lactation. 1C

Discuss family planning and contraception. 2C

Post-discharge

Follow-up cardiac review according to priority. 1C

Clinical communication follow-up with primary health services and other relevant services.

Maintain high degree of suspicion for presentation of dyspnoea.

Specific cardiac valve lesions and complications

Mitral/aortic regurgitation

✓ Single lesion mild/MR and AR are generally well tolerated during pregnancy. The increase in blood volume and cardiac output in pregnancy increases left ventricular (LV) volume overload but the decrease in systemic vascular resistance partly compensates for this.

✓ However, combined rheumatic aortic and mitral disease as well as mixed valve disease may be under-represented in studies, and an individual approach to pregnancy risk must always be considered.

Mitral stenosis

"Isolated" mitral stenosis, as well as mixed moderate to severe regurgitation and stenosis (with predominance of MS), is the most unfavorable heart disease.

There are very high rates of heart failure (up to 50%) in women with severe MS which can persist post-partum, with significant risks of acute pulmonary oedema, atrial arrhythmias, stroke or need for intervention during pregnancy, as well as fetal risks.

MS that is asymptomatic before pregnancy may be poorly tolerated in pregnancy because the fixed stenotic mitral valve limits the required increase in cardiac output of advancing pregnancy.

- ✓ Rates of HF in moderate MS (based on guidelines as 1.0–1.5 cm^2) - 31.8%.
- ✓ Mild MS may be well tolerated but a decline in functional class and development of HF has been reported in up to 15% of women.
- ✓ Women diagnosed or presenting late in pregnancy have an increased risk of complications.
- ✓ A pre-pregnancy functional status of NYHA >1 is an independent predictor for adverse events but women with MS are often asymptomatic until faced with the increased

  cardiac work of pregnancy.
- ✓ A reduction in functional state is often gradual so the first diagnosis of MS in pregnancy may be with severe symptoms including acute heart failure.
- ✓ Mitral valve area (MVA) by accurate planimetry is used as the reference value in determining severity, as it is independent of cardiac output, which increases in

  pregnancy along with increased mitral valve gradient.
- ✓ In patients with mild or moderate symptoms during pregnancy, medical therapy with beta blockers and diuretics may be sufficient. The development of atrial fibrillation (AF) with rapid ventricular rates may precipitate acute heart failure, requiring emergency treatment, including use of beta blockers for rate control. Digoxin can be added to beta-blocker therapy for rate control in AF if required.

- ✓ In patients with severe MS, the prophylactic use of beta blockers should be considered to reduce the risk of rapid ventricular rates if AF develop.
- ✓ Consider PBMV prior to pregnancy for women with moderate-severe MS (orifice area <1.5 cm2), even if asymptomatic or mildly symptomatic.
- ✓ There are very high rates of heart failure (up to 50%) in women with severe MS which can persist post-partum, with significant risks of acute pulmonary oedema, atrial arrhythmias, stroke or need for intervention during pregnancy, as well as fetal risks.

Indications for PBMV during pregnancy include:

- NYHA class III or IV symptoms (despite medical therapy),
- MVA <1–1.5 cm^2,
- suitable valve characteristics,
- no atrial thrombus.

The exact timing of the procedure requires a multi-disciplinary team consultation.

Aortic stenosis

- ✓ Isolated severe rheumatic aortic stenosis (AS) is rare. It may be seen with bioprosthetic valve degeneration and is associated with a significant risk of adverse maternal and fetal outcomes. Heart failure can occur during pregnancy in initially asymptomatic women but is more common in those with pre-pregnancy symptoms. Severe AS is associated with low birth weight and higher rates of caesarean sections.
- ✓ In asymptomatic women with AS, exercise testing is recommended to assess functional status and haemodynamic response preferably before pregnancy, or in early pregnancy. An abnormal blood pressure response to stress is associated with an increase in cardiac events and poor prognosis.
- ✓ Aortic valve area is the preferred measure of AS grade in combination with aortic valve gradient, as the increased cardiac output that occurs during pregnancy

is

associated with increased aortic gradients.

Tricuspid regurgitation

Tricuspid regurgitation (TR) is usually secondary to left heart valvular disease in RHD and may be associated with pulmonary hypertension.

Severe TR with right ventricular dysfunction may be associated with heart failure and atrial arrhythmias in pregnancy. It can usually be managed with diuretic therapy alone, with management directed as appropriate for left heart disease, and surgery performed at the time of aortic or mitral surgery pre- or postpartum.

Left ventricular systolic dysfunction

- ✓ In RHD, the impact of impaired left ventricular (LV) function is variable according to the valve lesion.
- ✓ In women with severe MR, hyperdynamic systolic function (high ejection fraction (EF)) is expected.
- ✓ An LVEF <60% in these patients is a sign of LV decompensation and may be poorly tolerated.
- ✓ **In general, an LVEF <30% or reduced systolic function with NYHA class III/IV symptoms is associated with a high risk of maternal morbidity and possible**

  mortality, and pregnancy is strongly discouraged.
- ✓ In contrast, mild LV systolic dysfunction has a better prognosis.

Pulmonary hypertension

Idiopathic pulmonary arterial hypertension is known to be associated with high rates of morbidity and mortality in pregnancy.

- ✓ Heart failure often occurs late in the second trimester, early third trimester

or in the post-partum period due to the changing haemodynamic demands.

- ✓ Outcomes with mild pulmonary hypertension (pulmonary artery systolic pressure

<45-50 mmHg) are better than those with moderate, or severe (pulmonary artery

systolic pressure >50 mmHg). Morbidity increases with worsening symptoms and severity of pulmonary hypertension.

✓ Ergometrine and prostaglandin F analogues are contraindicated in pulmonary hypertension due to the effects of pulmonary vasoconstriction.

Congenital heart disease

Improved medical and surgical options have resulted in most women with congenital heart disease surviving to bear children. Despite these advances, congenital heart disease remains an important cause of maternal mortality and morbidity.

Maternal risk assessment – Modified World Health Organization (WHO) risk classification for maternal risk assessment (table 1).

High risk conditions – The following maternal conditions pose very high maternal and/or fetal risk during pregnancy:

- significant pulmonary arterial hypertension of any cause,
- severe mitral stenosis,
- severe symptomatic aortic stenosis,
- bicuspid aortic valve with aorta diameter >50 mm,
- Marfan syndrome with aorta dilated >45 mm,
- severe systemic ventricular systolic dysfunction (left ventricular ejection fraction <30 percent, New York Heart Association III to IV),
- native severe coarctation. (See table 1 above.)

Natriuretic peptide level – Some experts recommend obtaining baseline and serial brain type natriuretic peptide levels during pregnancy in women with congenital heart disease deemed at risk for developing heart failure (See 'Natriuretic peptide levels' above.) **Option of termination** – The option of pregnancy termination should be discussed with women in whom gestation represents a major maternal or fetal risk.

Fetal risk – Impaired maternal functional class, maternal cyanosis, and maternal

medications expose the fetus to risks that threaten normal intrauterine growth and development.

Risk in offspring – Offspring of women with congenital heart disease are at increased risk of congenital heart defects.

Hypercoagulability – This is a particular concern in women at risk for thrombosis related to prosthetic heart valves, atrial fibrillation, previous thromboembolic events, or intracardiac shunts. Such patients are candidates for anticoagulation. Considerations in choosing an anticoagulation regimen should include adverse fetal effects (eg, warfarin embryopathy) in the first trimester, bleeding risk, and the risk of thrombosis on the prosthetic valve.

Role of cesarean delivery – For women with congenital heart disease, cesarean delivery should be reserved for obstetrical indications, such as cephalopelvic disproportion, placenta previa, or preterm labor in a gravida on oral anticoagulants.

Chronic hypertension in pregnancy

Blood pressure criteria for hypertension in pregnancy are systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or both. Hypertension should be confirmed by at least two measurements at least four hours apart before beginning treatment, except for blood pressures in the severe range, which should be repeated sooner and promptly treated.

Hypertensive disorders that occur in pregnant women are (table 2):

- Preeclampsia (and related disorders: eclampsia and HELLP [hemolysis, elevated liver enzymes, low platelets] syndrome)
- Gestational hypertension
- Chronic hypertension
- Preeclampsia superimposed on chronic hypertension

Table 2. Definitions/diagnostic criteria for the hypertensive disorders in pregnancy

Gestational hypertension	• New onset of systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on at least 2 occasions 4 hours apart after 20 weeks of gestation in a previously normotensive individual **And:** • No proteinuria • No signs/symptoms of preeclampsia-related end-organ dysfunction (eg, thrombocytopenia, acute kidney injury, elevated liver transaminases, pulmonary edema, cerebral or visual symptoms)
Preeclampsia	• New onset of systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on at least 2 occasions at least 4 hours apart after 20 weeks of gestation in a previously normotensive individual. Patients with systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg should have blood pressure confirmed within a short interval (minutes) to facilitate timely administration of antihypertensive therapy. **And:** • Proteinuria (≥300 mg per 24-hour urine collection [or this amount extrapolated from a timed collection], or protein:creatinine ratio ≥0.3, or urine dipstick reading ≥2+ [if other quantitative methods are not available]). **In a patient with new-onset hypertension without proteinuria, the diagnosis of preeclampsia can still be made if any features of severe disease are present.**
Preeclampsia with severe features	**In a patient with preeclampsia, presence of any of the following findings are features of severe disease**: • Systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg on 2 occasions at least 4 hours apart (unless antihypertensive therapy is initiated before this time) • Thrombocytopenia (platelet count <100,000/microL) Impaired liver function as indicated by liver transaminase levels at least • twice the normal concentration or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both • Acute kidney injury (serum creatinine concentration >1.1 mg/dL [97

	• micromol/L] or doubling of the serum creatinine concentration in the absence of other kidney disease) • Pulmonary edema • Persistent cerebral or visual disturbances
Eclampsia	• A generalized seizure in a patient with preeclampsia that cannot be attributed to other causes
HELLP syndrome	• **H**emolysis, **E**levated **L**iver enzymes, and **L**ow **P**latelets. Hypertension may be present (HELLP in such cases is often considered a variant of preeclampsia)
Chronic (preexisting) hypertension	**Hypertension diagnosed or present before pregnancy or on at least two occasions before 20 weeks of gestation. Hypertension that is first diagnosed during pregnancy and persists for at least 12 weeks postpartum is also considered chronic hypertension.** Blood pressure criteria during pregnancy are: - Systolic ≥140 mmHg and/or diastolic ≥90 mmHg Prepregnancy and 12 weeks postpartum blood pressure criteria are: - Stage 1 – Systolic 130 to 139 mmHg or diastolic 80 to 89 mmHg - Stage 2 – Systolic ≥140 mmHg or diastolic ≥90 mmHg
Chronic hypertension with superimposed preeclampsia	**Any of these findings in a patient with chronic hypertension:** • A sudden increase in blood pressure that was previously well-controlled or an escalation of antihypertensive therapy to control blood pressure • New onset of proteinuria or a sudden increase in proteinuria in a patient with known proteinuria before or early in pregnancy • Significant new end-organ dysfunction consistent with preeclampsia after 20 weeks of gestation or postpartum

Chronic hypertension with superimposed preeclampsia with severe features	**Any of these findings in a patient with chronic hypertension and superimposed preeclampsia:** • Systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg despite escalation of antihypertensive therapy • Thrombocytopenia (platelet count <100,000/microL) • Impaired liver function as indicated by liver transaminase levels at least twice the normal concentration or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both • New-onset or worsening renal insufficiency Pulmonary edema Persistent cerebral or visual disturbances

Adapted from: Gestational hypertension and preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol, 2020; 135:e237.; Phyllis August, MD et al., 2024.

In pregnant patients, chronic hypertension (also called preexisting hypertension) can be defined as hypertension known to be present before conception or first recognized before 20 weeks of gestation. In patients with a previous pregnancy complicated by gestational hypertension, hypertension that persists 12 or more weeks after giving birth is also classified as chronic.

Patients with chronic hypertension are at risk for a variety of adverse maternal and fetal/ neonatal outcomes, some of which can be mitigated by appropriate pregnancy management.

***Maternal risk*:** severe hypertension, superimposed preeclampsia, placental abruption, postpartum hemorrhage, renal insufficiency/failure, stroke, myocardial infarction, pulmonary edema, in-hospital mortality.

Fetal/neonatal risk: fetal growth restriction/small for gestational age infant, preterm delivery, congenital anomalies, stillbirth, neonatal death.

Management

Preconception – Ideally, patients with chronic hypertension are assessed prior to conception, in addition to routine preconception assessments. Patients are informed about the anticipated course of pregnancy, need for heightened maternal and fetal

surveillance, and likely need for more frequent obstetric visits and possibly hospitalization (eg, if superimposed preeclampsia develops) compared with a low- risk population.

Early pregnancy evaluations – Baseline laboratory and cardiac evaluation is repeated at the first prenatal visit, if not recently performed. In addition, accurate gestational dating is important since these pregnancies are at increased risk for developing fetal growth restriction (FGR) and undergoing obstetrically indicated preterm birth.

Low-dose aspirin prophylaxis – Low-dose aspirin is recommended after 12 weeks of gestation for prevention of preeclampsia as these patients are at high risk of developing the disease.

Diet and gestational weight gain — Patients should be encouraged to meet gestational weight gain targets that are appropriate for their body mass index. In particular, excessive gestational weight gain should be avoided because increased adiposity is strongly associated with higher blood pressure. Excessive gestational weight gain can also lead to significant postpartum weight retention.

Monitoring for FGR and evaluation of fetal wellbeing – It is recommended to conduct monitor for FGR beginning at 28 to 32 weeks and initiate twice weekly (or other mode according local guideline) nonstress tests or biophysical profiles at 32 weeks.

Timing of delivery – For patients with well-controlled blood pressures off of medication, we generally deliver at 39+0 to 39+6 weeks of gestation, in the absence of standard indications for earlier delivery. For patients with well-controlled blood pressures on medication, we tend to deliver close to or at 39+0 weeks.

ACOG (2019) suggested the following approach for delivery of patients with chronic hypertension:

- ≥38+0 to 39+6 weeks of gestation for patients not requiring medication
- ≥37+0 to 39+0 weeks for patients with hypertension controlled with medication
- 34+0 to 36+6 weeks for patients with severe hypertension that is difficult to control .

The Society of Obstetricians and Gynaecologists of Canada (2017) also states that patients with uncomplicated preexisting hypertension who are otherwise well should be

considered for delivery at 38+0 to 39+6 weeks of gestation

Cesarean birth should be reserved for standard obstetric indications.

Use of intrapartum magnesium sulfate for seizure prophylaxis is not indicated in the absence of superimposed preeclampsia.

Treatment of hypertension (table 3)

- ✓ Antihypertensive medication regimens started prior to labor should be continued intrapartum, and severe hypertension should be treated promptly
- ✓ Angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and direct renin inhibitors are **contraindicated** at all stages of pregnancy

  because of the potential for teratogenesis.

Table 3. Drug doses for oral treatment of hypertension in pregnancy.

Drug	Class	Initial dose	Usual effective dose range	Max suggested total daily dose	Comments
Labetalol	Combined alpha and beta blocker	100 mg 2 times daily, increase by 100 mg twice daily every 2 to 3 days as needed	200 to 800 mg in 2 divided doses	2400 mg	Can cause bronchoconstriction. Avoid in patients with asthma, chronic obstructive lung disease, heart failure, bradycardia (heart rate <60 beats per minute), or greater than first degree heart block. The dosing interval can be increased to 3 times daily if BP is increased

					prior to the next
Hydralazine	Peripheral vasodilator	Begin with 10 mg 4 times per day, increase by 10 to 25 mg/ dose every 2 to 5 days	50 to 100 mg in 2 to 4 divided doses	200 mg	**NOTE:** Due to reflex tachycardia, monotherapy with oral hydralazine is not recommended; hydralazine may be combined with methyldopa or labetalol if needed as add-on therapy
Drug	**Class**	**Initial dose**	**Usual effective dose range**	**Max suggested total daily dose**	**Comments**

Nifedipine extended release (ER)	Calcium channel blocker	30 to 60 mg once daily as an extended release tablet, increase at 7 to 14 day intervals	30 to 90 mg once daily	120 mg	Do not administer sublingually. Based upon clinical experience of UpToDate contributors, some patients better tolerate nifedipine ER administered in divided doses, whic may serve to minimize its peak t trough effects (eg, instead of increasing the dose to 60 mg once daily, it may be desirable in some patients to increase to 30
Methyldopa	Centrally acting alpha agonist	250 mg 2 to 3 times daily, increase every 2 days as needed Δ	250 to 1000 mg in 2 to 3 divided doses	3000 mg	Sedation is a common side effect

Δ The full hypotensive effect of an initial dose or adjustment of methyldopa may not occur until after 2 to 3 days of continuous use

Postpartum monitoring

Blood pressure control in women with chronic hypertension after delivery:

- ✓ daily during the first two days after childbirth;
- ✓ at least once between the 3rd and 5th days after childbirth;
- ✓ according to clinical indications, if hypotensive therapy is changed after delivery;
- ✓ In women with chronic hypertension after childbirth, blood pressure should be kept below 140/90 mm Hg.

- ✓ Continue treatment with antihypertensive drugs that were prescribed before delivery, except for methyldopa. Discontinue the appointment of this drug within 2 days after

  delivery and prescribe captopril or enalapril until the end of breastfeeding. Further, the treatment is carried out in accordance with current clinical guidelines for the treatment of hypertension.

Long-term prognosis – Patients with pregnancy-associated hypertension are at increased risk for developing chronic hypertension and other manifestations of cardiovascular disease and should undergo at least annual lifelong blood pressure measurement. Traditional cardiovascular risk factors, including hyperlipidemia, diabetes, obesity, and sedentary lifestyle, should also be addressed.

KIDNEY DISEASE AND PREGNANCY

Diseases of the kidneys and urinary tract in pregnant women are common and pose a serious threat to the physiological course of pregnancy and the condition of the fetus. Therefore, the management of pregnancy with this pathology requires a multidisciplinary approach, often the combined efforts of an obstetrician-gynecologist, a therapist, and in many cases a urologist or a nephrologist are needed.

Renal Changes During Pregnancy

The urinary system undergoes significant yet predictable physiologic and anatomic changes during normal pregnancy. It is essential to understand these changes to appropriately interpret common laboratory and diagnostic studies when evaluating kidney disease in women during pregnancy.

Anatomic changes

Kidney size increases by about 1-1.5 cm, primarily in the collecting system. Dilatation of the ureters and pelvis occurs and is presumed to be secondary to the smooth muscle–relaxing effect of progesterone. These changes may persist for up to 12 weeks postpartum and should not be misinterpreted as hydronephrosis if ultrasound of the kidneys is performed.

Hemodynamic and physiologic changes

- ✓ The glomerular filtration rate (GFR) increases immediately after conception to about 50% above baseline in the second trimester and then falls about 20% in the last trimester, resulting in significant hyperfiltration.
- ✓ Renal plasma flow also increases significantly in early pregnancy, causing the filtration fraction to fall in mid-pregnancy.
- ✓ As a result the normal serum creatinine level falls, so any value greater than 0.87 mg/ dL should be considered abnormal.
- ✓ Similarly the value for blood urea nitrogen (BUN) falls.
- ✓ Renal plasma flow increases up to 85% in the second trimester due to an increase in cardiac output and increased renal vasodilation of the afferent and arteriole arterioles.

These changes are particularly important, as a normal serum creatinine or BUN level in a pregnant woman may represent kidney disease.

- ✓ Blood pressure falls shortly after conception due to peripheral vasodilation, mediated by nitric oxide synthesis and relaxin, and a resistance to the action of angiotensin II specific to normal pregnancy.
- ✓ There is a compensatory increase in heart rate and activation of the renin-angiotensin- aldosterone axis. Blood volume increases by 20%, and sodium retention of up to 900 mEq occurs. Although edema may therefore be benign in pregnancy, blood pressure greater than 139/89 mm Hg is not normal.
- ✓ The osmotic threshold for arginine vasopressin resets downward, leading to lower serum sodium values.
- ✓ The higher GFR increases urate clearance, lowering serum uric acid values, and the filter load of glucose increases, which may result in renal glycosuria.
- ✓ Increased ventilation in pregnancy also causes a chronic respiratory alkalosis and

an appropriate fall in the serum HCO3 value.

Chronic kidney disease (CKD)

Chronic kidney disease (CKD) is defined by the presence of kidney damage or reduced glomerular filtration rate (GFR) for three or more months, irrespective of the cause.

Acute kidney disease or injury (AKI) informally refers to any decline in kidney function that evolves over more than 48 hours but less than three months. AKI is defined by a rise in the serum creatinine level that has developed within hours to days.

CKD is estimated to affect 3% of pregnant women in high-income countries. The prevalence of CKD in pregnancy is predicted to rise in the future due to increasing maternal age and obesity.

Clinical presentation

- ✓ Patients with CKD may present with symptoms and signs resulting directly from diminished kidney function, such as edema or hypertension.
- ✓ However, many have no clinical symptoms, and kidney disease is often detected in these patients when an elevated serum creatinine, reduced estimated GFR (eGFR), or

  an abnormal urinalysis is discovered incidentally (when such tests are obtained as part of routine evaluation or for a possibly unrelated disorder).
- ✓ In addition, multiple bilateral kidney cysts with enlarged kidneys suggestive of polycystic kidney disease etc. may be observed on imaging.

Even mild CKD is associated with a high risk of adverse maternal and fetal outcomes. Pregnancy rarely occurs in women with severe CKD.

The risk of adverse pregnancy outcomes is increased in women with CKD including: pre-eclampsia, fetal growth restriction, preterm delivery, stillbirth, neonatal mortality and accelerated loss of maternal renal function.

It is recommended **multidisciplinary teams (including a consultant obstetrician, consultant nephrologist/expert physician)** are established to offer advice and care for women with CKD who are pregnant or planning a pregnancy.

Pre-pregnancy care

Contraception

- ✓ It is recommended safe and effective contraception is offered to women of reproductive age who are taking teratogenic medication, have active glomerulonephritis, are within one year of renal transplantation or acute graft rejection, and for any woman who does not wish to conceive (1D).
- ✓ It is recommended that the progesterone only-pill, a progesterone subdermal implant, and the progesterone intra-uterine system are safe and effective for women with CKD (1C).

Fertility

- ✓ It is suggested that fertility preservation is considered for women of reproductive age who require treatment with cyclophosphamide (2C).
- ✓ It is recommended that single-embryo transfer is performed to reduce risk of complications associated with multifetal pregnancies in women with CKD (1C).

Pre-pregnancy counseling by a multidisciplinary team (MDT) for the optimisation of maternal and neonatal outcomes in women with CKD, which may include:

- ✓ stabilising disease activity in advance of pregnancy on minimised doses of pregnancy- appropriate medications (1B);
- ✓ optimising blood pressure control (< 140/90 mmHg) on pregnancy-appropriate medications (1B);
- ✓ optimising glycaemic control in women with diabetes mellitus (1A);
- ✓ minimising risk of exposure to teratogenic medications (1C).

Pregnancy care

It is suggested that pregnant women with CKD who have not had pre-pregnancy counselling by the MDT are referred to the MDT and receive the same counselling and optimisation as for women attending pre-pregnancy (2D).

Assessment of renal function in pregnancy

- ✓ It is recommended that renal function in pregnancy is assessed using serum creatinine concentrations as eGFR is not valid for use in pregnancy (1C).
- ✓ It is recommended that women with CKD have formal quantification of proteinuria in pregnancy (1D).
- ✓ It is recommended to undertake quantification of proteinuria by protein:creatinine ratio (uPCR) or albumin:creatinine ratio (uACR). Twenty-four hour urine collection for quantification of protein is not required (1B).

Pre-eclampsia prophylaxis

It is recommended that women with CKD are offered low-dose aspirin (75-150 mg) in pregnancy to reduce the risk of pre-eclampsia (1B).

It is suggested that kidney donors are offered low dose aspirin (75mg–150mg) to reduce the risk of pre-eclampsia (2D).

Blood pressure management

- ✓ It is recommended that the target blood pressure during pregnancy for women with CKD is 135/ 85 mmHg or less.
- ✓ It is recommended that labetalol, nifedipine and methyldopa can be used to treat hypertension in pregnancy (1B).
- ✓ It is suggested to consider a role for angiogenic markers (PlGF±sFlt-1) as an adjunct to diagnose superimposed pre-eclampsia, dependent upon on-going research in women with CKD (2C).

Bone health

- ✓ It is also necessary to remember the syndrome of mineral and bone disorders associated with CKD. In which there is a violation of the metabolism of calcium (hypo- or hypercalcemia), phosphorus (hyperphosphatemia), vitamin D deficiency and parathyroid hormone secretion disorders (secondary or tertiary

hyperparathyroidism), which lead to disorders of bone tissue metabolism (renal osteodystrophy) and calcification of vessels and other m what fabrics

- ✓ It is recommended women with CKD who are vitamin D deficient to give vitamin D supplementation in pregnancy (1B).

It is recommended that **fluid balance is managed** with the aim of maintaining normal fluid volume, avoiding dehydration and pulmonary oedema, with input from clinicians with expertise in fluid balance and renal disease (1D).

It is recommended to consider **prevention of venous thromboembolism** in pregnant women with CKD.

Delivery

- ✓ In women with CKD mode and timing of birth is usually determined by obstetric factors. Where maternal complications arise, clinicians must balance the competing risks of preterm delivery and maternal wellbeing.
- ✓ There is no evidence that mode of delivery affects maternal renal function. Mode of delivery should therefore be based on obstetric indications and maternal preference according to guidance in women without CKD.
- ✓ It is recommended that the **timing of birth for women with CKD** is determined by obstetric indications, with consideration of renal factors including deteriorating renal function, symptomatic hypoalbuminaemia, pulmonary oedema, and refractory hypertension (1D).
- ✓ It is suggested to plan delivery at 39-40 weeks of pregnancy, if the mother or fetus has no indications for earlier delivery.
- ✓ If labor has not occurred by the expected date of delivery, induced labor is indicated for most women.
- ✓ Caesarean section is performed according to standard obstetric indications.

It is recommended that **concentrations of calcineurin inhibitors (tacrolimus, ciclosporin)** are checked throughout pregnancy and immediately postpartum, as blood concentrations may change (1C).

Postnatal care

- ✓ It is recommended that non-steroidal anti-inflammatories should not be given (1C).
- ✓ It is recommended that women with CKD have a planned early postpartum renal review (1D).
- ✓ It is recommended that women with CKD are offered safe and effective contraception postpartum and receive updated pre-pregnancy counselling before future pregnancies (1D).

Dialysis

Women receiving maintenance dialysis before pregnancy :

- ✓ It is recommended that women established on dialysis prior to pregnancy receive pre-pregnancy counselling including the options of postponing pregnancy until transplantation (when feasible) and the need for long frequent dialysis prior to and during pregnancy (1C).
- ✓ It is recommended that women established on haemodialysis prior to pregnancy receive long, frequent haemodialysis to improve pregnancy out- comes(1C).
- ✓ It is suggested that women receiving haemodialysis during pregnancy have dialysis dose prescribed accounting for residual renal function, aiming for a pre-dialysis urea < 12.5 mmol/l (2C).
- ✓ It is recommended that women established on peritoneal dialysis prior to pregnancy should convert to haemodialysis during pregnancy (1D).

Initiating dialysis during pregnancy

- ✓ It is suggested that haemodialysis should be initiated in pregnancy when the maternal urea concentration is 17-20 mmol/L and the risks of preterm delivery outweigh those of dialysis initiation.
- ✓ Gestation, renal function trajectory, fluid balance, biochemical parameters, blood pressure and uraemic symptoms should be considered in addition to maternal urea concentration (2D).

Urinary tract infection

Urinary tract infection (UTI) is one of the more common perinatal complications, affecting approximately 8% of pregnancies. These infections represent a spectrum, from asymptomatic bacteriuria (ASB), to symptomatic acute cystitis, to the most serious, pyelonephritis.

Overall, Escherichia coli is the most common bacterial pathogen isolated in urine samples from pregnant individuals.

The presence of UTIs has been associated with adverse pregnancy outcomes, including increased rates of preterm delivery and low birth weight, neonatal infections. Furthermore, serious maternal complications of pyelonephritis include sepsis, disseminated intravascular coagulation, and acute respiratory distress syndrome (ARDS).

Epidemiology

Urinary tract infections are classified based on the site of infection: lower urinary tract (ASB or cystitis) or upper urinary tract (pyelonephritis).

Progesterone-induced ureteral dilation, combined with mechanical compression of the ureter by the gravid uterus, leads to increased residual volume in the bladder and urinary stasis, resulting in vesicoureteral reflex. As a result, these changes increase the risk of bacterial colonization and ascending infection.

ASYMPTOMATIC BACTERIURIA - the presence of significant bacterial counts in the urine ($\geq 10^5$ CFU/mL) on urine culture in the absence of symptoms consistent with

UTI. ASB is identified in 2–10% of pregnant patients

Screening — Clinicians should screen for ASB with a midstream urine for culture once at a visit early in prenatal care. There is insufficient evidence to recommend for or against repeat screening during pregnancy after a negative initial culture result.

Specimen collection — The diagnosis of asymptomatic bacteriuria should be based on culture of a urine specimen collected in a manner that minimizes contamination. Instructing women to spread their labia and collect a **midstream urine** (the second portion of the voided urine after discarding the initial stream) without requiring a clean-catch (local cleansing of the urethral meatus and surrounding mucosa) seems most reasonable. Routine catheterization to screen for bacteriuria is not warranted due to the risk of introducing infection.

Several studies suggest that local cleansing is of little value, as it does not reduce contamination when a midstream urine is collected.

Diagnostic criteria — For asymptomatic women, bacteriuria is formally defined as two consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts of ≥105 colony-forming units (cfu)/mL or a single catheterized urine specimen with one bacterial species isolated in a quantitative count of ≥102 cfu/mL. In clinical practice, however, only one voided urine specimen is typically obtained, and diagnosis (and treatment initiation) is made in women with ≥105 cfu/mL without obtaining a confirmatory repeat culture.

Rapid screening tests, such as dipstick, enzymatic screen, reagent strip, or interleukin-8 testing, do not come close to urine culture in terms of sensitivity and specificity for detecting asymptomatic bacteriuria in pregnant women and should not be used.

Management

- ✓ Asymptomatic bacteriuria during pregnancy increases the risk of pyelonephritis and has been associated with adverse pregnancy outcomes, such as preterm birth and low

  birth weight infants.

- ✓ Antimicrobial treatment reduces the risk of subsequent development of

pyelonephritis and is associated with improved pregnancy outcomes.

Antimicrobial treatment — Asymptomatic bacteriuria is treated with an antibiotic tailored to the susceptibility pattern of the isolated organism, which is generally available at the time of diagnosis.

- ✓ Potential options include beta-lactams, nitrofurantoin, and fosfomycin (table 4).
- ✓ Although nitrofurantoin is generally avoided during the first trimester, it is an appropriate alternative when other options cannot be used.
- ✓ The optimal duration of antibiotics for asymptomatic bacteruria is uncertain. Clinicians should prescribe a 5–7-day course of targeted antibiotics to treat ASB with

  colony counts of 10^5 CFU/mL or higher (ACOG, 2023).
- ✓ An exception is single-dose fosfomycin, which successfully treats bacteriuria.

Uncertain role of follow-up testing — Up to 30 percent of women fail to clear asymptomatic bacteriuria following a short course of therapy. However, given the paucity of data, it is not clear that there is any clinical benefit to performing a follow-up culture after an initial episode of asymptomatic bacteriuria or retreating recurrent asymptomatic bacteriuria.

Statements from expert groups (IDSA etc.) highlight the uncertain value of repeat screening for asymptomatic bacteriuria.

The ACOG guidelines (2023) state that follow-up urine culture after treatment of asymptomatic bacteriuria is recommended but indicate that more data are needed to determine the effectiveness of this strategy .

The diagnosis (and treatment) of asymptomatic bacteriuria due to group B streptococcus during pregnancy:

Asymptomatic GBS bacteriuria in pregnancy is a marker for heavy genital colonization with GBS and, as such, is associated with increased risk of upper genital tract infection and postpartum endometritis, neonatal infection.

However, whether asymptomatic GBS bacteriuria during pregnancy warrants treatment at the time of identification depends on the quantification of bacteria (in colony-forming units [CFU] per mL) in the urine:

✓ **Bacteriuria ≥10^5 CFU/mL** – warrants antimicrobial treatment in addition to later intrapartum chemoprophylaxis. This is based on the cutoff for reporting bacteriuria that is recommended by the IDSA and ACOG guidelines.

✓ Antibiotic therapy is typically with amoxicillin, penicillin, or cephalexin. For patients with a history of penicillin allergy, ACOG recommends formal allergy testing to determine if they have true penicillin allergy. Clindamycin should not be used for bacteriuria because it is poorly concentrated in the urine.

✓ The optimal duration of therapy for asymptomatic bacteriuria in pregnancy is uncertain -generally beta-lactam antibiotics for 5 to 7 days.

✓ **Bacteriuria <10^5 CFU/mL** – The utility of treating GBS bacteriuria at colony counts <105 prior to 35 weeks of gestation is controversial.

✓ Genital colonization with GBS persists despite adequate therapy for GBS bacteriuria. Documented GBS bacteriuria during pregnancy is an indication for intrapartum chemoprophylaxis at the time of delivery.

Table 4. Antibiotics for asymptomatic bacteriuria and cystitis in pregnancy (Mod. from ACOG, 2023).

Antibiotic	Dose	Duration	Notes
Nitrofurantoin	100 mg orally every 12 hours	5 to 7 days	Does not achieve therapeutic levels in the kidneys, so should not be used if pyelonephritis is suspected. Typically avoided during the first trimester and at term; however, it is an appropriate alternative during these periods when other options cannot

			be used.
Amoxicillin	500 mg orally every 8 hours or 875 mg orally every 12 hours	5 to 7 days	Resistance may limit its utility among gram negative pathogens.
Antibiotic	**Dose**	**Duration**	**Notes**
Amoxicillin-clavulanate	500 mg orally every 8 hours or 875 mg orally every 12 hours	5 to 7 days	
Cephalexin	250 to 500 mg orally 5 to 7 days every 6 hours	5 to 7 days	
Cefpodoxime	100 mg orally every 12 hours	5 to 7 days	
Fosfomycin	3 g orally as single dose		Does not achieve therapeutic levels in the kidneys so should not be used if pyelonephritis is suspected.
Trimethoprim-sulfamethoxazole	800/160 mg (1 double- strength tablet) every 12 hours	3 days	Typically avoided during the first trimester and at term; however, it is an appropriate alternative during these periods when other options cannot be used.

Cystitis (bladder infection) – Acute cystitis should be suspected in pregnant women who complain about new onset dysuria, frequency, or urgency. Hematuria and pyuria are also frequently seen on urinalysis.

Pyuria, defined as more than 5 white blood cells/high-power field.

The presence of fever and chills, flank pain, or costovertebral angle tenderness should

raise suspicion for pyelonephritis.

Acute cystitis is estimated to occur in 1–2% of pregnant patients

The diagnosis of acute cystitis is confirmed by finding of bacterial growth on urine culture.

✓ Clinicians should evaluate patients with symptoms of acute cystitis with a urine culture.

✓ UTI should be suspected based on the presence of symptoms, may be supported by a positive urinalysis result, and is confirmed by urine culture.

✓ Ideally, a urine culture should be obtained to confirm the diagnosis and allow tailoring of antibiotic therapy by sensitivities.

✓ The threshold colony count to confirm UTI is 100,000 (10^5) CFU/mL. However, in the presence of symptoms, in direct contrast to treatment for ASB, some authors suggest that

treatment for colony counts as low as 100 (10^2)CFU/mL of a single organism may be appropriate.

Management

✓ Antibiotic treatment of acute cystitis in pregnant women is often empiric, initiated at the time of complaints of dysuria, and then tailored to the susceptibility pattern of the

isolated organism once urine cultures return.

✓ Potential options for empiric and directed therapy include beta-lactams, nitrofurantoin, and fosfomycin (table 4).

✓ Clinicians should treat acute cystitis in pregnant individuals with a 5–7-day course of a targeted antibiotic. If empiric therapy is started before culture and sensitivity results are

available, **amoxicillin or ampicillin** regimens should be avoided due to high rates of resistance in E coli to these antibiotics in most areas. Antibiotic treatment then is modified as needed based on urinary culture results for targeted therapy.

✓ **Nitrofurantoin and sulfonamides** are reasonable in the first trimester if no appropriate alternatives are available.There are some data regarding possible findings of congenital

anomalies associated with nitrofurantoin and sulfamethoxazole-trimethoprim if used in the first trimester. Additionally, use of nitrofurantoin in patients with glucose-6-phosphate dehydrogenate deficiency has been associated with rare findings, including pulmonary toxicity and hemolytic anemia, and should be avoided in these patients Nitrofurantoin and sulfonamides in the second and third trimesters can continue as first-line treatment for UTI.

✓ **Nitrofurantoin and fosfomycin** should be avoided in the setting of uncertainty regarding a diagnosis of cystitis compared with pyelonephritis, given the inability of

these agents to reach adequate tissue levels within the kidney.

✓ The optimal duration of treatment for acute cystitis during pregnancy is uncertain. As with asymptomatic bacteriuria, short courses of antibiotics are preferred, to minimize the

antimicrobial exposure to the fetus.

✓ Routine follow-up cultures to confirm urine sterilization are not recommended.

There is insufficient evidence to guide management after recurrent UTI in

pregnancy.

✓ After treating a recurrent acute infection, clinicians may consider initiating antimicrobial urinary suppression for the remainder of the pregnancy, preferably using a

lower single daily dose of an antibacterial drug to which the bacterium isolated was susceptible. Recurrent UTI is defined as having two or more UTIs diagnosed during pregnancy and occurs in 4–5% of pregnancies.

✓ If prophylaxis is initiated, there are **two common strategies available: postcoital or continuous prophylaxis for the remainder of the pregnancy**. For patients for whom

the postcoital option is selected, antibiotics are taken before or after vaginal intercourse. This strategy has been associated with a decrease in adverse events related to antibiotic use. With continuous prophylaxis, antimicrobials are taken once daily.

✓ Common suppressive regimens include nitrofurantoin 100 mg orally daily or cephalexin 250–500 mg orally daily

Pyelonephritis – Acute pyelonephritis during pregnancy should be suspected in the presence of fever of 38.0° C or higher and urine studies suggesting UTI, with additional symptoms of upper genitourinary tract infection, such as flank pain or costovertebral angle tenderness, supporting the diagnosis.Pregnant women may become quite ill and are at risk for both medical (eg, sepsis, respiratory failure) and obstetrical complications from pyelonephritis.

Pyelonephritis presents with signs of infection, such as fever, nausea, and vomiting. Systemic symptoms are accompanied by physical examination findings localizing to the upper urinary tract, such as flank pain, costovertebral angle (CVA) tenderness, or abnormalities on renal ultrasonography.

Complete blood count may show leukocytosis, bandemia, thrombocytopenia, or anemia. Pregnant patients suspected of having pyelonephritis should have a midstream or catheterized urine specimen collected for urinalysis, urine microscopy, and culture. This specimen should be obtained before antibiotics are initiated, but treatment should not be delayed while awaiting culture results.

Management

✓ Clinicians initially should manage pyelonephritis in pregnancy in the inpatient setting. Initial management includes fluid hydration and initiation of intravenous antibiotics.

✓ Empiric antibiotic therapy should have adequate renal tissue penetration and be targeted against the most likely pathogens. Antibiotic therapy should be adjusted as

needed based on urine culture and sensitivity. Parenteral antibiotics should be continued until the patient is clinically improving. Patients should complete a total of 14 days of

antibiotic therapy.

✓ First-line antimicrobial management includes broad spectrum b-lactams with consideration of addition of aminoglycosides, including ampicillin plus gentamicin, or

single-dose cephalosporins, such as ceftriaxone or cefepime (table 5).

✓ For patients with a b-lactam allergy, further investigation regarding the severity of allergic reaction is essential. In patients who are at low risk for anaphylaxis from penicillins, treatment with cephalosporins would be appropriate; however, individuals at high risk for anaphylaxis would need to be treated with an alternative regimen such as aztreonam. In such situations, consultation with an infectious disease specialist is recommended.

✓ Nitrofurantoin and fosfomycin are not appropriate oral agents to complete treatment for pyelonephritis, because they work within the lower urinary tract only and do not

penetrate to reach therapeutic levels in the renal parenchyma, where the foci of infection reside. Urine culture should be obtained after completion of antibiotics to ensure no residual infection.

✓ Antibiotic therapy can be converted to an oral regimen tailored to the susceptibility profile of the isolated organism following clinical improvement. Oral options are generally limited to beta-lactams or, if in the second trimester, trimethoprim-sulfamethoxazole.

✓ There is insufficient evidence to guide management after treatment of pyelonephritis in pregnancy. Clinicians may consider suppressive therapy for the remainder of the

pregnancy, as for recurrent UTI.

Recurrent pyelonephritis - occurs in up to 25% of pregnant patients before delivery.

✓ Following the treatment course, preventive antibiotics are a reasonable strategy for the remainder of the pregnancy to prevent recurrence.

✓ A small number of studies support use of daily suppressive therapy after treatment of

pyelonephritis for reduction of recurrence rates, yet their generalizability is limited due to

small sample size and older data.

✓ If suppression is initiated, nitrofurantoin 100 mg or cephalexin 250–500 mg orally every day for the remainder of pregnancy and continuing until 4–6 weeks postpartum is

recommended.

✓ Still, as a rule, the sup-pressive agent selected should be matched against the susceptibility profile of the pathogen isolated with diagnosis of pyelonephritis.

✓ Additionally, routine monthly urine culture to screen for recurrence should be considered for the duration of the pregnancy.

Table 5. Antibiotic Regimens for Treatment of Pyelonephritis (ACOG, 2024).

Antimicrobial	Regimen
Ampicillin + gentamicin	2 g IV every 6 h 1.5 mg/kg IV every 8 h 5 mg/kg IV every 24 h
Ceftriaxone 1 g IV every 8–12	1 g IV every 24 h
Cefepime	1 g IV every 12 h
Aztreonam (appropriate in patients with b-lactam allergy)	1 g IV every 8–12

→ Aminoglycosides have been associated with fetal ototoxicity; this regimen should be used only if intolerance precludes the use of less toxic agents.

THYROID DISEASE AND PREGNANCY

Thyroid physiology — To meet the increased metabolic needs during a normal pregnancy, there are changes in thyroid physiology that are reflected in altered thyroid function tests. The major changes in thyroid function during pregnancy are:

- An increase in serum thyroxine-binding globulin (TBG) concentrations (estrogen)
- Stimulation of the thyrotropin (thyroid-stimulating hormone [TSH]) receptor by

human chorionic gonadotropin (hCG).

- Together, these changes lead to an increase in both serum total (but not free) thyroxine (T4) and triiodothyronine (T3) concentrations and a reduction in serum TSH.

Human chorionic gonadotropin (hCG) is one of a family of glycoprotein hormones, including TSH, with a common alpha subunit and a unique beta subunit. However, there is considerable homology between the beta subunits of hCG and TSH. As a result, hCG has weak thyroid-stimulating activity.

Serum hCG concentrations increase soon after fertilization and peak at 10 to 12 weeks. During this peak, total serum T4 and T3 concentrations increase. Serum free T4 (fT4) and T3(fT3) concentrations increase slightly, usually within the normal range, and serum TSH concentrations are appropriately reduced. However, in 10 to 20 percent of normal women, serum TSH concentrations are transiently low or undetectable. Very high levels of hCG can be seen in multiple pregnancies (ie, twins, triplets, etc) and in hyperemesis gravidarum.

This transient, usually subclinical, hyperthyroidism should be considered a normal physiologic finding. It is not known if this action of hCG benefits the mother or fetus. Later in pregnancy, as hCG secretion declines, serum free T4 and T3 concentrations decline and serum TSH concentrations rise slightly to or within the normal range.

Trimester-specific reference ranges – Because of the changes in thyroid physiology during normal pregnancy, thyroid function tests should, whenever possible, be interpreted using population and trimester-specific TSH and T4 reference ranges for pregnant women. If the laboratory does not provide trimester-specific reference ranges for TSH (mU/L), a TSH reference range of approximately 0.1 to 4 mU/L can be used. Total T4 and total T3 levels during pregnancy are 1.5-fold higher than in nonpregnant women. Reference ranges for fT4 are assay method-specific, and trimester-specific reference ranges should be provided with the assay kits.

Assessment of thyroid function – When evaluating thyroid tests during pregnancy, we typically measure TSH and fT4 (if there is a trimester-specific) and/or total T4. In such settings where fT4 measurements appear discordant with TSH measurements, total T4 should also be measured. For patients whose initial thyroid tests show subclinical

thyroid disease or isolated changes in fT4, it is recommended to repeat the thyroid tests in a couple of weeks to confirm the abnormality.

It is necessary to additionally determine antibodies to thyroperoxidase (ATPO), if:

- there is another concomitant autoimmune disease (type I diabetes) or such a disease occurs in the family;
- TSH level is >2.5 mIU/l;
- suspicion of autoimmune thyroid disease according to ultrasound;
- presence of postpartum thyroiditis in the anamnesis;
- history of infertility, spontaneous abortions, premature labor.

Hyperthyroidism

Clinical manifestations – Many of the nonspecific symptoms associated with pregnancy are similar to those associated with hyperthyroidism, including tachycardia, heat intolerance, and increased perspiration. Additional symptoms may include anxiety, hand tremor, and weight loss despite a normal or increased appetite. Specific findings such as goiter and ophthalmopathy suggest **Graves' hyperthyroidism**.

Diagnosis – The diagnosis of hyperthyroidism during pregnancy should be based primarily upon a finding of a suppressed (<0.1 mU/L) or undetectable (<0.01) serum TSH value and elevated thyroid hormone levels (serum fT4 and/or fT3 or total T4 and/or total T3) that exceed the normal range for pregnancy.

Establishing the cause – Once the diagnosis of hyperthyroidism is established, the cause of hyperthyroidism should be determined. Although hyperthyroidism from any cause can complicate pregnancy, Graves' (occurring in 0.1-1% of all pregnancies) and hCG- mediated hyperthyroidism (1-3% of pregnancies) are the most common causes of hyperthyroidism.

hCG-mediated hyperthyroidism may occur transiently in the first half of gestation and is typically less severe than Graves' disease.

Graves' disease usually becomes less severe during the later stages of pregnancy due to a reduction in TSH receptor antibody (TRAb) concentrations.

In situations where the clinical diagnosis is uncertain, it is recommended to measure

TSH receptor antibodies (TRAbs), using a third-generation thyrotropin-binding inhibitory immunoglobulin (TBII) assay or a thyrotropin-stimulating immunoglobulin (TSI) assay. TRAbs are positive in 95% with Graves' disease, and therefore, the presence of TRAbs confirms the diagnosis of Graves' disease. If antibodies are negative, thyroid ultrasound with Doppler flow may be useful to distinguish Graves' disease (high blood flow) from painless or postpartum thyroiditis (low blood flow).

Treatment

Indications for treatment

- Women with **symptomatic and/or moderate to severe, overt hyperthyroidism due to Graves' disease, toxic adenoma, toxic multinodular goiter, or gestational trophoblastic disease** require therapy for the treatment of hyperthyroidism.
- Pregnant women with **subclinical hyperthyroidism** (low TSH, normal fT4) or total T4 and tT3 <1.5 times the upper limit of normal for nonpregnant adults) and pregnant women with **asymptomatic and/or mild, overt hyperthyroidism** may be followed with no treatment. In women who are being monitored without therapy, it is recommended to measure TSH, fT4 (if there is a trimester-specific reference range), and/or total T4 or total T3 every four to six weeks.

Beta blocker – Assuming there are no contraindications to its use, it is suggested to use a beta blocker for pregnant women with moderate to severe hyperthyroidism and hyperadrenergic symptoms (Grade 2B) - typically start with metoprolol 25 to 50 mg daily or propranolol 20 mg three to four times daily.

In general, long-term treatment with beta blockers (longer than two to six weeks) should be avoided in pregnant women because of concerns regarding neonatal growth restriction, hypoglycemia, respiratory depression, and bradycardia, especially with atenolol.

Thionamide – For pregnant women with moderate to severe hyperthyroidism due to Graves' disease, toxic adenoma, or toxic multinodular goiter, it is suggested that a thionamide as our first choice of treatment (Grade 2B).

It is suggested to use **propylthiouracil** (PTU) rather than **methimazole** in the first

trimester and using methimazole for women who present in the second or third trimester (Grade 2C). Patients taking PTU during the first trimester can either switch to methimazole after 16 weeks or continue PTU throughout pregnancy.

Surgical treatment is carried out in the II trimester, but if necessary (for example, in the development of severe side effects of pharmacotherapy).

Monitoring and dose adjustments – Thyroid function tests (TSH and fT4 or total T4 if a trimester-specific reference range is not available for fT4) should be obtained every four weeks throughout pregnancy. If thionamides are discontinued in early pregnancy, thyroid tests should be checked weekly throughout the first trimester, then monthly.

The thionamide dose should be adjusted based on the results of the thyroid function tests to maintain serum fT4 concentrations at or just above the upper limit of normal, using a trimester-specific reference range, or total T4 and T3 (if trimester- specific normal ranges are not available) at approximately 1.5-fold above the upper limit of normal for nonpregnant patients. Serum TSH concentrations should be maintained below the

reference range for pregnancy.

Postpartum care

- **Breastfeeding** – Given the concerns about potential PTU-associated hepatotoxicity, it is suggested that methimazole rather than PTU for nursing mothers (Grade 2C).

  Radioiodine therapy for the treatment of hyperthyroidism is absolutely contraindicated during breastfeeding.

- **Monitoring for relapse** – Women with Graves' disease who have been treated before or during pregnancy need careful monitoring during the postpartum period as they may

  experience an exacerbation.

Hypothyroidism

Clinical features – The range of clinical manifestations of hypothyroidism during pregnancy is similar to those that occur in nonpregnant patients and may include fatigue,

cold intolerance, constipation, and weight gain. Symptoms may be overlooked or attributed to the pregnancy itself. Many patients are asymptomatic.

Diagnosis – The diagnosis of overt primary hypothyroidism during pregnancy is based upon the finding of an elevated population and trimester-specific TSH concentration (or above 4.0 mU/L when local reference range is not available) in conjunction with a decreased fT4 concentration (below assay normal using reference range for pregnant women).

Subclinical hypothyroidism is defined as an elevated population and trimester-specific serum TSH concentration and a normal fT4 concentration.

Pregnancy complications – Hypothyroidism can have adverse effects on the pregnancy, depending upon the biochemical severity of the hypothyroidism.

Treatment

Indications for treatment:

- All pregnant women with **newly diagnosed, overt hypothyroidism** (TSH above population and trimester-specific normal reference range [or above 4.0 mU/L when local reference range is not available] with low free T4) should be treated with **thyroid hormone (levothyroxine, T4).**
- In addition, it is suggested to initiate T4 replacement in pregnant women with newly diagnosed **subclinical hypothyroidism** (TSH above population and trimester-specific normal reference range [or above 4.0 mU/L] with normal f T4) (Grade 2C).
- For pregnant women with a **TSH between 2.6 and 4 mU/L,** it is recommended to **individualize the decision** to treat based upon patient characteristics, values, and preferences.
  - Some experts offer T4 treatment (50 mcg daily) to patients with TPO

antibodies who have a history of miscarriage and who prefer this intervention.

- In the absence of a history of recurrent miscarriage, some experts also offer T4 (50 mcg daily) to TPO-positive women who prefer this intervention.
- Other experts, including the other editor of this topic, do not treat TPO-positive, euthyroid (TSH ≤4 mU/L) pregnant women.

In pregnant women who are not treated with thyroid hormone and who are at particularly high risk for developing hypothyroidism during pregnancy (TPO antibody-positive, post-radioiodine treatment, post-hemithyroidectomy, history of exposure to high-dose irradiation of the head or neck region), is is recommended to reassess TSH during pregnancy (eg, approximately every four weeks during the first trimester, and then once during each of the second and third trimesters). If TSH rises above the population and trimester-specific upper limit of normal (approximately 4 mU/L), it is recommended to treat with T4.

Dosing, monitoring, and dose adjustments

- √ Patients with overt hypothyroidism should be started on close to full replacement doses (1.6 mcg/kg body weight per day), while patients with subclinical hypothyroidism may become euthyroid with lower doses and can therefore be started on approximately 1 mcg/kg daily.
- √ TSH should be measured every four weeks during the first half of pregnancy because dose adjustments are often required.
- √ The goal of treatment is to maintain TSH in the lower half of the trimester-specific reference range (or approximately <2.5 mU/L).

Goiter

Goiter during pregnancy is common in regions where iodine intake is low, occurring in 16 to 70 percent of women in iodine-deficient regions of Western Europe.

Thyroid nodules

Thyroid nodules – A pregnant woman found to have a thyroid nodule should be evaluated in the same way as if she were not pregnant, except that thyroid radionuclide

scanning is contraindicated.

Thyroid cancer

Given the typically indolent nature of differentiated thyroid cancer, most women with newly diagnosed differentiated thyroid cancer can delay thyroidectomy until the postpartum period to minimize maternal and fetal complications.

Surgery during pregnancy is sometimes indicated for rare patients with larger, more aggressive or rapidly growing cancers, or in the presence of extensive nodal or distant metastasis. The safest time for any type of surgery during pregnancy is the second trimester.

When surgery for thyroid cancer is deferred, the patient should be monitored during pregnancy with thyroid ultrasound performed during each trimester. In such cases where thyroid surgery is deferred, it is suggested thyroid hormone suppressive therapy (Grade 2C). The goal is to maintain the TSH in the range of 0.3 to 2.0 mU/L.

Postpartum thyroiditis

Postpartum thyroiditis occurs in 5 to 10 percent of women. It may occur after pregnancy loss (miscarriage, abortion, ectopic pregnancy), as well as after normal delivery.

DIABETES IN PREGNANCY

Classification of diabetes in pregnancy

In pregnancy, pregestational (also called preexisting) diabetes, gestational diabetes and other forms of diabetes are distinguished (table 6).

Table 6. The classification of diabetes in pregnancy

Type 1 diabetes (autoimmune beta cell destruction, usually leading to absolute insulin deficiency): • Without vascular complications • With vascular complications (eg, nephropathy, retinopathy, hypertension, atherosclerotic cardiovascular disease, etc)
Type 2 diabetes (progressive loss of insulin secretion, often in the setting of insulin resistance): • Without vascular complications • With vascular complications (eg, nephropathy, retinopathy, hypertension, atherosclerotic cardiovascular disease, etc)

Gestational diabetes (diabetes diagnosed during pregnancy and not clearly overt [eg, not type 1 or type 2 diabetes])
Other diabetes (eg, genetic defects of beta cell function or insulin action, drug- or chemical-induced, pancreatic disease, endocrinopathy)

Traditionally, the severity of pregestational diabetes was categorized according to the White classification (table 7). Because the White classes are not mutually exclusive, the presence/absence of vascular complications, as described above, is a better predictor of adverse outcome than the specific White class.

Table 7. Modified White's classification of diabetes in pregnancy

Class	Description
A	Abnormal GTT before pregnancy at any age or of any duration treated only by diet therapy
B	Onset at age 20 years or older and duration of less than 10 years
C	Onset at age 10 to 19 years or duration of 10 to 19 years
D	Onset before 10 years of age, duration over 20 years, benign retinopathy, or hypertension (not preeclampsia)
R	Proliferative retinopathy or vitreous hemorrhage
F	Nephropathy with over 500 mg/day proteinuria
RF	Criteria for both classes R and F
H	Evidence of arteriosclerotic heart disease
T	Prior renal transplantation
Gestational diabetes	
A1	Diet-controlled gestational diabetes
A2	Insulin-treated gestational diabetes

Classes B through T require insulin treatment.

GTT: glucose tolerance test.

Adapted from: Hare JW, White P. Gestational Diabetes and White Classification. Diabetes Care 1980; 3:394.

Pregestational (preexisting) diabetes mellitus

The terms "pregestational diabetes" and "preexisting diabetes" refer primarily to type 1 or type 2 diabetes mellitus diagnosed prior to pregnancy. Pregestational diabetes complicates approximately 1 to 2 percent of all pregnancies and accounts for 13 to 21 percent of diabetes in pregnancy, with the remainder due to gestational diabetes.

Pregnancy risks

- ✓ The risk of adverse pregnancy outcome is increased in pregnant people with diabetes but appears to be similar for type 1 versus type 2 diabetes.
- ✓ Pregnant people with type 1 diabetes are more likely to have microvascular-disease-related complications than those with type 2 diabetes, and they are at higher risk of developing severe hypo- and hyperglycemia.
- ✓ Adverse pregnancy outcomes include miscarriage, congenital anomaly, macrosomia, preeclampsia, preterm birth, cesarean birth, and perinatal mortality. Short- and long-term morbidity in offspring are also concerns.
- ✓ Maternal medical risks include progression of retinopathy and nephropathy, diabetic ketoacidosis, serious hypoglycemia, and complications related to gastroparesis.

It is important to know that:

Type 1 diabetes

- ✓ Women with type 1 diabetes have an increased risk of developing hypoglycemia in the 1st trimester, which requires additional attention.
- ✓ Type I diabetes is often complicated by diabetic ketoacidosis, which is accompanied by a high risk of stillbirth. In order to prevent and detect ketoacidosis, pregnant women should be recommended to use ketone strips.
- ✓ In addition, type 1 diabetes is characterized by accompanying retinopathy, which is of particular concern during pregnancy.

Type 2 diabetes

- ✓ Type 2 diabetes is often associated with an increased risk of obesity. The recommended weight gain during pregnancy is 6.8–11.34 kg for overweight women and 4.54–9.07 kg
  for obese women.

Glucose management – Hyperglycemia is the primary driver of these risks, and studies repeatedly show that tight glucose management in the periconceptional period and during pregnancy is associated with improved outcomes.

The clinician should emphasize the importance of meticulous blood glucose monitoring (BGM) and attention to good glucose management throughout pregnancy to reduce the risks of adverse pregnancy outcomes.

Patients with type 1 diabetes should use **continuous glucose monitoring** (CGM) because it reduces the risk of neonatal complications. Data are lacking on CGM in other forms of diabetes in pregnancy.

Glucose targets are:

- Fasting, preprandial, and nocturnal glucose 70 to 95 mg/dL (3.9 to 5.3 mmol/L) **and**
- One-hour postprandial glucose 110 to 140 mg/dL (6.1 to 7.8 mmol/L) **or**
- Two-hour postprandial glucose 100 to 120 mg/dL (5.6 to 6.7 mmol/L)
- For patients with type 1 diabetes using continuous glucose monitoring (CGM), the target glucose range is 63 to 140 mg/dL (3.5 to 7.8 mmol/L), and the time in range goal is >70 percent. The CGM time-in-range goal for type 2 diabetes has not been established and likely needs to be higher to optimize pregnancy outcomes.

Pharmacotherapy

- ✓ ***Insulin is the preferred pharmacotherapy for hyperglycemia***.
- ✓ ***Metformin is an option for some patients with type 2 diabetes***.
- ✓ ***Other commonly used noninsulin glucose-lowering medications such as GLP-1 agonists, SGLT-2 inhibitors, and DPP-4 inhibitors should be avoided until and***

unless appropriate human data demonstrating safety are obtained, given that animal studies have reported fetal damage. For example, in animals, SGLT-2 inhibitors have caused kidney toxicity at developmental periods equivalent to the second and third trimesters in humans and GLP- 1 agonists have caused vascular (heart, blood vessels) and skeletal (cranial bones, vertebra, ribs) abnormalities at maternal exposures below the maximum recommended human dose. Data in humans are very limited.

Insulin requirements across pregnancy – While glucose targets are the same throughout pregnancy, insulin requirements may decrease in the first trimester so the risk for hypoglycemia increases. After 18 weeks of gestation, insulin requirements increase quickly until plateauing near 37 weeks of gestation. An unexpected ≥15 percent decline in insulin requirements should prompt an assessment of fetal well-being.

Hypoglycemia - Patients with frequent hypoglycemia often lose typical adrenergic symptoms (sweating, shaking, palpitations) that serve as warning signs before the glucose drops to a dangerous level, which is called hypoglycemia unawareness. Patients experiencing frequent hypoglycemia can benefit from relaxing glucose targets, which will restore hypoglycemia awareness and thus prevent serious hypoglycemia. Acute episodes of hypoglycemia are managed using standard approaches, with the exception that during pregnancy we do not intervene for asymptomatic glucose levels in the upper 60s mg/dL.

First trimester. Management

- ✓ **Nausea and vomiting** – treatment of nausea and vomiting of pregnancy - it facilitates insulin management and relieves maternal discomfort. Clinicians should also consider whether the nausea and vomiting may be manifestations of gastroparesis; metoclopramide is often used to treat these cases.
- ✓ **Maternal evaluation** (table 8).

Table 8. Initial maternal evaluation of pregnant patients with pregestational diabetes

All patients

- Routine prenatal laboratory tests and evaluation, including measurement of blood pressure and body mass index, and urine culture
- Glycated hemoglobin (hemoglobin A1C), which may be repeated periodically during pregnancy
- Serum creatinine
- 24-hour urine collection for protein (urinary protein-to-creatinine ratio is an acceptable alternative)
- Dilated eye examination, which may be repeated every trimester and for one year postpartum, as indicated by degree of retinopathy and as recommended by the eye care provider
- Clinical evaluation for atherosclerotic vascular disease, neuropathy, and gastroparesis

Select patients

- Electrocardiogram (in patients with symptoms of cardiovascular disease)
- Thyroid-stimulating hormone (in patients with type 1 diabetes). If elevated, thyroid peroxidase status is also checked.

→ *In the absence of significant red blood cell abnormalities, Hb A1C reflects the patient's average glucose level over the prior few weeks to months and thus assists in counseling about the risks of early pregnancy loss, congenital anomalies, preeclampsia, and other complications.*

√ **Noninsulin pharmacotherapy**

- Folic acid (at least 400 mg orally daily) is begun prior to pregnancy or as soon as pregnancy is diagnosed for prevention of neural tube defects (NTDs).
- Aspirin 81 to 162 mg is begun at 12 weeks of gestation for preeclampsia prophylaxis (patients with diabetes are at increased risk for preeclampsia).
- In patients with hypertension, the goal blood pressure is <140/90 mmHg. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers should be avoided.

√ **Fetal evaluation** – First-trimester obstetric ultrasound is useful to confirm cardiac activity and gestational age, and provide preliminary evaluation for major congenital

anomalies because pregestational diabetes is associated with increased risks for pregnancy loss, congenital anomalies, and preterm birth.

Second and third trimesters. Management

- **Glucose management** — ***Glucose targets are the same throughout pregnancy, though insulin requirements vary considerably.*** Close follow-up of glucose management is especially important after 18 weeks of gestation, as insulin resistance resulting from rising levels of placental hormones increases rapidly and, consequently, insulin requirements can rise quickly after this point.
- **Preeclampsia** – Monitoring for preeclampsia is a routine component of prenatal care.
- **Fetal anatomic survey** – Detailed ultrasound examination of fetal anatomy is performed between 18 and 22 weeks of gestation.
- **Antepartum fetal surveillance** – Patients with pregestational diabetes are at increased risk of stillbirth. Twice-weekly antepartum fetal surveillance (nonstress test, biophysical profile) is begun at 32 weeks of gestation.
- **Assessment of fetal growth and amniotic fluid** – ultrasound examination at 28 to 32 weeks of gestation to assess for normal, accelerated, or restricted fetal growth, and repeat the examination every four weeks.
- **Antenatal corticosteroids** – If a course of antenatal corticosteroids is administered to patients at high risk for preterm birth, blood glucose levels are checked frequently and hyperglycemia, which may become severe, is managed with increased insulin.
- **Tocolysis** – preferences for tocolytic therapy are nifedipine or indomethacin (for pregnancies less than 32 weeks of gestation). It is recommended to avoid beta-adrenergic receptor agonists as they can cause severe hyperglycemia in patients with diabetes.

Delivery

- **For patients meeting glycemic targets and without vascular complications or**

macrosomia, we suggest induction at 39+0 to 39+6 weeks of gestation (**Grade 2C**), in

the absence of standard obstetric or medical indications for earlier intervention or cesarean birth.

- **For patients not meeting glycemic targets, vascular complications, or history of stillbirth and without macrosomia,** we suggest induction at 36+0 to 38+6 weeks (Grade 2C), in the absence of standard obstetric or medical indications for earlier intervention or cesarean birth. The timing of birth within this range depends on patient-specific factors.
- **For patients with estimated fetal weight (EFW) >4500 grams, it is suggest planned cesarean rather than vaginal birth** (Grade 2B). The risk of shoulder dystocia is increased at birth weights >4000 grams and high at birth weights >4500 grams.

Since both diabetes and forceps- or vacuum-assisted vaginal birth are associated with an increased risk for shoulder dystocia, it is reasonable to perform a cesarean rather than an assisted vaginal birth in patients with diabetes and EFW >4000 grams.

- **Glycemic targets** — A reasonable target range for **intrapartum glucose levels** is 70 to 125 mg/dL (3.9 to 6.9 mmol/L). This target range encompasses recommendations of

the American College of Obstetricians and Gynecologists (ACOG, 2018; 70 to 110 mg/dL [3.9 to 6.1 mmol/L]).

Postpartum management

- **Glucose management** – Insulin requirements drop sharply after delivery and are transiently lower than requirements prior to pregnancy.
- **Breastfeeding** – Patients with diabetes are encouraged to breastfeed. Insulin and metformin are compatible with breastfeeding.
- **Contraception** – The United States Medical Eligibility Criteria for Contraceptive Use consider all hormonal methods acceptable for patients with diabetes and no

vascular

disease, but depot medroxyprogesterone may raise glucose levels so close self- monitoring is required.

In patients **with vascular disease**, combined hormonal contraceptives and depot medroxyprogesterone are avoided.

- **Surveillance for retinopathy** – Eye examinations are continued for one year postpartum, as indicated by the degree of retinopathy.

Gestational diabetes mellitus

Pregnancy is generally a state of both enhanced beta-cell function and insulin resistance, mediated primarily by placental secretion of diabetogenic hormones including growth hormone, corticotropin-releasing hormone, placental lactogen (chorionic somatomammotropin), prolactin, and progesterone. These and other metabolic changes, which are most prominent in the third trimester, ensure that the fetus has an ample supply of nutrients.

Gestational diabetes mellitus (GDM) develops in pregnant people whose pancreatic beta- cell function is insufficient to overcome the insulin resistance associated with the pregnant state.

Terminology

Gestational diabetes traditionally referred to any pregnant person in whom abnormal glucose tolerance was first recognized at any time during pregnancy.

A more contemporary definition, and that used by the American Diabetes Association (ADA), is diabetes diagnosed in the second or third trimester that was not clearly overt diabetes prior to conception (typically refers to diagnosis of diabetes at 24 to 28 weeks of gestation). Diagnosis of diabetes early in pregnancy (sometimes called **overt diabetes**) is more consistent with previously undiagnosed type 2 diabetes.

These ***two categories (gestational and overt diabetes) differ in the degree of hyperglycemia and the fact that in manifest diabetes, hyperglycemia does not disappear after the end of pregnancy, as in gestational diabetes***.

Significance - GDM has been associated with increased risks of several adverse outcomes. The association between hyperglycemia and adverse pregnancy outcomes is dose-dependent and continuous.

- Hypertensive disorders of pregnancy (preeclampsia, gestational hypertension)
- Large for gestational age (LGA) or macrosomic newborn
- Polyhydramnios
- Medically-indicated preterm birth
- Operative birth (cesarean, forceps- or vacuum-assisted vaginal)
- Shoulder dystocia
- Maternal and/or newborn birth trauma
- Fetal/neonatal cardiomyopathy
- Neonatal respiratory problems and metabolic complications (eg, hypoglycemia, hyperbilirubinemia, hypocalcemia, hypomagnesemia, polycythemia and hyperviscosity syndrome)
- Stillbirth
- Long-term risks
  - Maternal – Development of diabetes mellitus (primarily type 2), metabolic syndrome, and cardiovascular disease.
  - Adolescent and adult offspring – Obesity, abnormal glucose tolerance, hypertension, and metabolic syndrome.
- In contrast to diabetes that develops pregestationally, GDM is not generally associated with an increased risk for congenital anomalies since hyperglycemia develops after organ formation is complete.

There is no universally accepted standard regarding screening for or diagnosis of GDM. Practitioners tend to follow the guidance of their national medical organizations.

How to screen

Early pregnancy screening for previously undiagnosed type 2 diabetes (overt diabetes)

There is no standard approach to early pregnancy screening for undiagnosed type 2

diabetes.

The research approach - It is obtained an **A1C level at the initial prenatal visit** in all patients as part of the initial prenatal blood work:

- **A1C l ≥6.5 percent (≥48 mmol/mol)** is diagnostic of diabetes and the patient is managed accordingly.
- **A1C is <6.5 percent (<48 mmol/mol)** - it is performed standard screening for GDM at 24 to 28 weeks.

A1C <6.5 percent (<48 mmol/mol) is not sufficiently sensitive to detect mildly impaired glucose tolerance, especially if the A1C is ≥5.7 (which is above the upper limit of normal in nonpregnant individuals), but the overall value of detecting and treating mildly impaired glucose tolerance in early pregnancy has not been established in randomized trials

Targeted approach - alternatively, several national organizations have suggested a targeted approach that limits screening to patients at high risk.

The International Association of Diabetes and Pregnancy Study Groups (IADPSG, 2010), the American Diabetes Association (ADA, 2024), and the American College of Obstetricians and Gynecologists (ACOG, 2024) suggest **targeting early pregnancy screening to individuals at increased risk of undiagnosed type 2 diabetes**. However, the ADA also suggests that clinicians consider testing all individuals for undiagnosed diabetes at the first prenatal visit (or preconceptionally).

The ADA and ACOG define patients at increased risk of type 2 diabetes based on:

- First-degree relative with diabetes.
- High-risk race/ethnicity (eg, African American, Latino, Native American, Asian American, Pacific Islander).
- History of cardiovascular disease.
- Hypertension (≥130/80 mmHg prepregnancy) or on therapy for hypertension.
- High-density lipoprotein cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L).
- Polycystic ovary syndrome (PCOS).
- Physical inactivity.

- Other clinical condition associated with insulin resistance (eg, severe obesity, acanthosis nigricans).
- Glycated hemoglobin ≥5.7 percent (39 mmol/mol), impaired glucose tolerance (two- hour glucose level 140 to 199 mg/dL), or impaired fasting glucose (glucose level 100 to 125 mg/dL) on a previous 75-gram oral glucose tolerance test (GTT) in the nonpregnant state.
- HIV infection, exposure to high-risk medicines, history of pancreatitis.
- Age ≥35 years.

Choice of screening test — **No approach has been validated for diagnosis of diabetes in the first or early second trimester**. Clinical practice varies by institution and clinician preference. Screening practice varies from a hemoglobin A1C alone, fasting glucose alone, a two-hour 75-gram oral GTT, or two-step test (one-hour 50-gram GTT followed by a three- hour 100-gram GTT if the 50-gram GTT is positive).

1. If a one-step test is used ADA criteria for diabetes are shown in the table (table 9). These thresholds are the same as those used by the ADA for diagnosis of diabetes in nonpregnant people and were chosen because they correlate with development of adverse vascular events, such as retinopathy and coronary artery disease, in these individuals over time.

ADA criteria for "early abnormal glucose metabolism"

- fasting glucose 110 to 125 mg/dL (6.1 to 6.9 mmol/L) **or**
- A1C 5.9 to 6.4 percent (41 to 47 mmol/mol).

Table 9. American Diabetes Association criteria for the diagnosis of diabetes

1. A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
2. FPG ≥126 mg/dL (7 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.*
OR

3. 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 * g anhydrous glucose dissolved in water *. **OR**
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

A1C: glycated hemoglobin; DCCT: Diabetes Control and Complications Trial; FPG: fasting plasma glucose; NGSP: National Glycohemoglobin Standardization Program; OGTT: oral glucose tolerance test.

* In the absence of unequivocal hyperglycemia, diagnosis requires 2 abnormal test results from the same sample or in 2 separate test samples.

2. If a two-step test is used, ACOG criteria for diabetes are shown in the tables (table 10, 11). These criteria are the same as those used for diagnosis of gestational diabetes mellitus later in pregnancy.

Table 10. ACOG two-step approach for screening and diagnosis of gestational diabetes mellitus

Step one
1. Give 50 gram oral glucose solution without regard to time of day.
2. Measure venous plasma or serum glucose concentration at one hour after administration.
3. Glucose ≥135 mg/dL (7.5 mmol/L) or ≥140 mg/dL (7.8 mmol/L) is elevated and requires administration of a 100 gram oral glucose tolerance test.* The lower threshold provides greater sensitivity, but would result in more false positives and would require administering the full glucose tolerance test to more patients than the 140 mg/dL threshold. The lower threshold should be considered in populations with higher prevalence of gestational diabetes.
Step two
1. Measure fasting venous plasma or serum glucose concentration.
2. Give 100 gram oral glucose solution.
3. Measure venous plasma or serum glucose concentration at one, two, and three hours after administration.

4. A positive test is generally defined by elevated glucose concentrations at two or more time points (either Carpenter and Coustan thresholds or National Diabetes Data Group thresholds can be used)

ACOG: American College of Obstetricians and Gynecologists; GDM: gestational diabetes mellitus.

* Some experts use a threshold of 130 mg/dL (7.2 mmol/L).

Table 11. Diagnostic criteria for the three-hour 100 gram oral GTT for gestational diabetes mellitus

	Carpenter/Coustan	National Diabetes Data Group
	Plasma or serum: mg/dL (mmol/L)	**Plasma: mg/dL (mmol/L)**
Fasting	95 (5.3)	105 (5.8)
One hour	180 (10)	190 (10.6)
Two hours	155 (8.6)	165 (9.2)
Three hours	140 (7.8)	145 (8)

→ A 100 gram oral glucose load is given in the morning to a patient who has fasted overnight for at least eight hours. A positive test is generally defined as ≥2 glucose values at or above these thresholds.

Abnormal GTT – If a patient in early pregnancy (before significant insulin resistance) meets ADA (table) or IADPSG criteria for diagnosis of diabetes in the nonpregnant state, they are assumed to have had the disorder prior to the pregnancy and their **management is similar to those with documented preexisting diabetes mellitus in pregnancy**.

Normal GTT – Patients with normal 75- or 100-gram oral GTT in early pregnancy are screened for GDM at 24 to 28 weeks of gestation.

Screening for GDM at 24 to 28 weeks of gestation - all pregnant women at 24 to 28 weeks of gestation, except for women who have been diagnosed with any pre- gestational disorder of carbohydrate metabolism, are subject to an screening for GDM. **One- and two-step approaches** - Screening is performed at 24 to 28 weeks of gestation since 24 weeks is the gestational age when insulin resistance is significantly increasing, leading to hyperglycemia in those with insufficient insulin secretory capacity to maintain euglycemia. It can be performed as a one- or two-step process.

There is no consensus among national and international organizations for the optimal approach, and the choice generally depends on local customs.

One-step test — The one-step approach simplifies screening by performing only a diagnostic test, typically a fasting 75-gram oral glucose tolerance test (GTT), in all patients. The criteria for diagnosis of GDM are shown in the table (table 12). The International Association of Diabetes and Pregnancy Study Groups (IADPSG) prefers this approach, which has been widely adopted internationally, and the American Diabetes Association (ADA) considers it an acceptable alternative to the two-step approach [2]. The procedure is described below.

Table 12. IADPSG and ADA criteria for a positive two-hour 75-gram oral glucose tolerance test for the diagnosis of gestational diabetes.

Two-hour 75-gram oral glucose tolerance test thresholds	
Fasting	92 mg/dL (5.1 mmol/l)
OR	
One hour	180 mg/dL (10 mmol/L)
OR	
Two hour	153 mg/dL (8.5 mmol/mol)

→ The diagnosis of gestational diabetes mellitus is made at 24 to 28 weeks of gestation when ≥1 plasma glucose value is at or above these thresholds.

IADPSG: International Association of the Diabetes and Pregnancy Study Groups; ADA: American Diabetes Association.

Two-step test — In the United States, the two-step test is the most widely used approach for identifying pregnant people with GDM. It is endorsed by American College of Obstetricians and Gynecologists (ACOG), (2024) and the ADA (2024) considers it an acceptable option. Because fewer patients are diagnosed and managed as GDM, without incurring an increase in adverse outcome. The first step has the practical advantages that fasting is unnecessary and only one blood sample is required. A minority of patients need to undergo the second step (16 percent at the ≥140 mg/dL threshold in a large series

- **The first step** is a one-hour 50-gram oral GTT administered without regard to time

of day/previous meals (table 10 above).

- **The second step** is a three-hour 100-gram oral GTT performed after an overnight fast; the GTT is the diagnostic test for GDM (table 11 above).

Screening for and birth of the macrosomic fetus

✓ Ultrasound – We perform a single third-trimester ultrasound at 36 to 39 weeks to screen for macrosomia in all patients with gestational diabetes mellitus it is performed.

✓ Scheduled cesarean birth is typically offered at 39+0 weeks to patients with GDM (any class) and an estimated fetal weight ≥4500 grams.

Fetal surveillance and timing of birth in patients with A1 GDM well controlled with nutritional medical therapy alone – These patients are not at increased risk for stillbirth.

✓ Antenatal fetal surveillance – Usually not ordered antenatal fetal testing (nonstress test, biophysical profile) in these patients unless they have a standard obstetric indication

for fetal surveillance (eg, growth restriction).

✓ Timing of induction – For candidates for vaginal birth, we offer induction of labor at 39+0 weeks of gestation and suggest performing induction by 41+0 weeks of gestation

(Grade 2C), as with other late term pregnancies.

Fetal surveillance and timing of birth in patients with A2 GDM (ie, on pharmacologic therapy) or A1 GDM with suboptimal glucose control – These patients may be at increased risk for stillbirth.

✓ Antenatal fetal surveillance – The optimal testing regimen has not been established from rigorous studies. It is ordered twice weekly antenatal testing, using a nonstress test with an amniotic fluid index, starting at 32 weeks of gestation. Ideally, patients with suboptimal glucose control will be brought under better control with diet and/or medication.

✓ Timing of induction:

- For candidates for vaginal birth, it is suggested induction of labor at 39+0 weeks of

gestation (Grade 2C).

- If a concomitant medical condition (eg, hypertension) is present or glycemic control is suboptimal on pharmacologic therapy, birth should be undertaken as clinically indicated prior to 39+0 weeks of gestation.
- The American College of Obstetricians and Gynecologists suggests birth at 39+0 to 39+6 weeks of gestation for patients with A2 GDM that is well controlled with medication. For patients with suboptimal glycemic control on pharmacologic therapy, birth at 37+0 to 38+6 weeks may be reasonable, but that birth prior to 37+0 weeks should only be done when more aggressive efforts to control blood sugars, such as hospitalization, have failed.

Postpartum follow-up – Individuals with GDM should be screened for diabetes postpartum and periodically thereafter because they are at increased risk for developing type 2 diabetes mellitus.

LIVER DISEASES DURING PREGNANCY

The following liver pathology during pregnancy should be differentiated:

1. Chronic liver diseases that occurred before pregnancy.
2. New liver disease that occurred during pregnancy.
3. Liver disease caused by pregnancy. Example:
   - Preeclampsia or HELLP syndrome
   - Intrahepatic cholestasis of pregnancy
   - Acute fatty liver dystrophy during pregnancy

- Pregnancy has different effects on women with chronic liver disease (eg, cirrhosis and portal hypertension). There may be increased jaundice with progressive liver failure, ascites, and hepatic encephalopathy. The frequency of stillbirths and premature births may be increased. Some women with cirrhosis can carry a pregnancy without any deterioration in liver function.
- The increase in total circulating blood volume associated with pregnancy can worsen existing portal hypertension. One approach for women with cirrhosis who wish to become pregnant is to perform a diagnostic endoscopy to screen for esophageal

varices prior to pregnancy (or during the second trimester if not performed prior to pregnancy). Patients should be informed about the increased risk of upper gastrointestinal bleeding during pregnancy. Patients at high risk for variceal bleeding should receive primary prophylaxis with nonselective beta-blockers or endoscopic variceal ligation. Newborns whose mothers received beta-blockers should be monitored in the first days of life due to the risk of developing hypoglycemia and bradycardia.

- Women with chronic viral hepatitis C can carry a pregnancy without deterioration of liver function or other negative consequences for the mother or the fetus. Transmission of hepatitis C virus from mother to newborn occurs, but much less often than with hepatitis B virus infection.
- Liver transplant patients often regain fertility. It is recommended that conception be delayed until at least 24 months after transplantation to ensure stabilization of the immunosuppressive regimen and to ensure that the transplanted organ is functioning well. Pregnancy outcomes for both mother and newborn in liver transplant recipients are generally favorable. But there is an increased incidence of preterm birth, hypertension/preeclampsia, fetal growth retardation, and gestational diabetes. In addition, there may be an increased risk of teratogenicity with standard immunosuppressive regimens, but the magnitude of the risk is uncertain.
- Other liver diseases that can affect pregnancy include:
  - Autoimmune hepatitis
  - Primary biliary cholangitis
  - Primary sclerosing cholangitis
  - Wilson's disease
  - Hepatocellular adenoma
  - Familial hyperbilirubinemia
  - Familial intrahepatic cholestatic syndromes (Alagille syndrome and progressive familial intrahepatic cholestasis)
  - Porphyria
  - Budd-Chiari syndrome.

VI. Plan and organizational structure of the lesson

Organizational moment	2% of the study time
Motivation of the topic	3%
Control of the initial level of knowledge	20%
Independent work of students under the supervision of the teacher	35%
Control of the final level of knowledge	15%
Evaluation of students' knowledge	20%
Summary of the teacher, homework	5%

VII. Methodological support materials.

Place of the lesson: classroom, simulation class, department of pregnant pathology and extragenital pathology.

Equipment: phantom, doll, stethoscope, bone pelvis, obstetric forceps, vacuum extractor, tables, slides, medical history of pregnant women with extragenital pathology.

Control questions to assess the initial level of knowledge:

1. What are the maternal and fetal complications in pregnant women with cardiovascular diseases?
2. What are the features of management pregnant women with cardiovascular diseases?
3. What are the features of delivery in women with cardiovascular diseases (term and method of delivery)?
4. What are the contraindications to a pregnancy in case of cardiovascular diseases?
5. What are the features of the course and management of pregnancy and delivery in women with cardiac valve lesions?
6. What hypertensive disorders occur during pregnancy?
7. What are the peculiarities of management of arterial hypertension in pregnancy?
8. What are the peculiarities of delivery with arterial hypertension?
9. What are the maternal and fetal complications in women with arterial hypertension?
10. What are the features of hypertension therapy during pregnancy? What drugs

are contraindicated in the treatment of arterial hypertension in pregnant women?

11. How are the physiological changes of the kidneys and urinary tract during pregnancy?
12. What are the features of the course and management of pregnancy in women with asymptomatic bacteriuria?
13. What are the features of the course and management of pregnancy in women with acute cystitis?
14. What are the features of the course and management of pregnancy in women with acute pyelonephritis?
15. What are the features of the course and management of pregnancy in women with kidney and urinary tract stones?
16. What are the features of the course and management of pregnancy in women with chronic kidney disease?
17. What are the physiological changes of the thyroid gland during pregnancy?
18. What pathology of the thyroid gland is most common during pregnancy?
19. What are the features of thyroid function research during pregnancy?
20. What are the features of the course and management of pregnancy in women with hypothyroidism?
21. What are the features of the course and management of pregnancy in women with hyperthyroidism?
22. What types of diabetes should be distinguished in pregnant women?
23. What are the complications of pregnancy and delivery in women with diabetes?
24. What are the management of pregnancy in women with diabetes?
25. What are the plan of delivery and the management of postpartum period in women with diabetes?
26. What liver pathologies should be distinguished during pregnancy?

Tasks for independent work

1. Collect anamnesis, conduct a general and special obstetric examination of a pregnant woman with extragenital pathology.
2. Based on the received data and analysis of the examination results, establish a preliminary diagnosis.
3. Prescribe additional examination methods for pregnant women with extragenital pathology.
4. Determine contraindications to a pregnancy in women with extragenital pathology.
5. Determine the risks of maternal and fetal complications in a pregnant woman with extragenital pathology.
6. Make a plan of pregnancy management for women with extragenital pathology.
7. Establish a plan to delivery in case of extragenital pathology.
8. Inform the pregnant woman about the need for regular examination, self-monitoring, specifics of diet and lifestyle modification, regular using of medicines prescribed for this extragenital pathology.

Test to assess the final level of knowledge

1. A 28-year-old woman complains of constant aching pain, a feeling of heaviness in the right hypochondrium, sometimes sharp pain radiating to the back, nausea, bitterness in the mouth, heartburn that worsens closer to the evening. These complaints appeared from the 28th week of pregnancy. Objectively: tenderness during palpation in the right hypochondrium. What is the most likely diagnosis?

A. Cholelithiasis
B. Acute pancreatiti
C. Acute gastritis
D. Dyskinesia of biliary tract
E. Gastric ulcer disease

2. After hypothermia, a pregnant woman complains of painful, frequent urination, pain in the lower abdomen. The general condition is not disturbed. Body temperature is not

elevated. During physical examination - costovertebral angle is normal. In the general urine test: leukocytes - 80-100 in the field of vision, bacteriuria. What is the diagnosis?

A. Acute pyelonephritis

B. Acute cystitis

C. Acute glomerulonephritis

D. Acute urethritis

E. Urolithiasis

3. First-time pregnant woman, 19 years old, height 168 cm, weight 62 kg, pregnancy 36 weeks of gestation. During the physician consultation, she complains of palpitations, irritability, tearfulness, and weight loss. Objectively: skin and mucous membranes of normal color. Blood pressure - 115/70 mmHg, pulse - 108 bpm, systolic murmur is heard. The borders of the heart have not changed, ECG: vertical position of the EOS, sinus tachycardia, slight hypertrophy of the left ventricular myocardium. Clinical tests of blood and urine without pathological changes. Diagnosis?

A. Acquired heart disease

B. Adaptation to pregnancy

C. Rheumatic heart disease

D. Congenital heart disease

E. Thyroid disease

4. Maternity age of 35, second timely labor. Complaints of headache, dizziness. From the anamnesis: 2 years ago, an increase in blood pressure to 150/90 mmHg was noted. During this pregnancy, blood pressure is constantly 140/90 mmHg. Objectively: BPr – 150/90 mmHg, BPL 155/90 mmHg. The borders of the heart are expanded to the left, the accent of the second tone over the aorta. There are no swellings. On the fundus, the papillae of the optic nerve are pale, the arteries are narrowed, the veins are unchanged. Urinalysis: no protein, specific gravity 1.018, leukocytes 2–5 in the field of vision. What is the diagnosis?

A. Chronic hypertension with superimposed preeclampsia

B. Gestational hypertension

C. Chronic hypertension
D. Preeclampsia moderate
E. Severe preeclampsia

5. A 28-year-old pregnant woman complains of periodic, spastic, intense lower back pain. Urine is brown color. Ultrasound revealed a large number of small hyperechoic inclusions in the kidney bowls. Complete blood count: erythrocytes - $4.6x10^{12}$ /l, leukocytes - $6.6x10^{9}$ /l. General urine test: specific gravity - 1016, protein - 0.099 g/l, unchanged erythrocytes - the entire field of vision, a large number of uric acid crystals. State the most likely diagnosis?
A. Kidney amyloidosis
B. Acute glomerulonephritis
C. Chronic glomerulonephritis
D. Chronic pyelonephritis
E. Urolithiasis

6. During a routine visit to obstetrician, a 32-week pregnant woman complains of rapid fatigue, constipation, weight gain, and excessive hair loss. During the examination: the skin is pale pink in color, there is no swelling. According to the results of laboratory examinations: Hb 120 g/l, ferritin 45 µg/l. The level of Vitamin D in the blood is 45 ng/ml. TSH 5 IU/l. Blood glucose 4.4 g/l. What is the likely diagnosis?
A. Iron deficiency anemia
B. Vegetative dysfunction
C. Hypothyroidism
D. Vitamin D deficiency
E. Physiological course of pregnancy

7. A pregnant woman, 39 weeks of gestation, complains of aching pain in the right lower back, an increase in body temperature to 38^{0}C, general weakness, nausea. Conclusion of the ultrasound scan - there is an expansion of the right kidney bowl. In the general urine test - leukocytes cover the entire field of vision, bacteriuria. What are the doctor's

tactics?

A. Installation of a catheter-stent

B. Conservative treatment (antibacterial and detoxification therapy)

C. Knee-elbow position

D. Operative intervention and nephrectomy

E. Puncture nephrostomy

8. In a pregnant woman, 30 weeks of gestation, with bronchial asthma after a stressful situation, shortness of breath, noisy "whistling" breathing, a feeling of tightness in the chest, cyanosis of the face suddenly appeared. Auscultatively: breathing is weakened, many dry "whistling" rales; with percussion - a box sound. After the attack, the woman produced a small amount of sputum. What is the likely diagnosis?

A. Thromboembolism of the pulmonary artery

B. Exacerbation of bronchial asthma

C. Obstructive bronchitis

D. Pulmonary edema

E. Acute pneumonia

9. A 25-year-old pregnant woman, 10 weeks pregnant, went to a women's consultation with a diagnosis of diabetes. Medical history: has been suffering from diabetes for 10 years. Diabetes with a predisposition to ketoacidosis, complicated by retinopathy. Both father and mother have diabetes. The woman applied for a solution to the issue of pregnancy management tactics. What is the most appropriate thing to offer the patient?

A. Prolongation of pregnancy, therapy and prevention of complications, delivery (term and method will be specified later)

B. Hospitalization of the pregnant woman to an endocrinological hospital for further examination

C. Clinical examination, clarification of the forms and degree of severity of diabetes mellitus

D. Continuation of pregnancy, correlation of the optimal dose of insulin

E. Terminate pregnancy before 12 weeks

10. Labor I, in term, lasts 8 hours. From the anamnesis: mitral stenosis III st. The woman in labor is sitting on the bed with her legs down. Complaints of shortness of breath, breathing with open mouth, face and upper body covered with drops of sweat, cyanosis. Wheezing can be heard in the distance, and frothy sputum mixed with blood and sputum is emitted from the mouth. Ps 130–150/min. What complication occurred during labor?

A. Heart failure
B. An attack of bronchial asthma
C. Paroxysmal tachycardia
D. Atrial fibrillation
E. Pulmonary edema

11. A 35-year-old pregnant woman, 20 weeks of gestation, was brought to the hospital without consciousness. A woman has been suffering from type 1 diabetes for 12 years. During the last week, she had gastroenteritis. Objectively: the skin is dry, hyperemia of the face, shallow breathing, sunken eyeballs, the smell of acetone is not felt. Blood pressure 80/40 mmHg. Pulse 115/min. What kind of coma is most likely in the patient?

A. Hyperosmolar (non-ketoacidotic)
B. Alcohol
C. Hyperlactacidemic
D. Ketoacidotic

12. A 27-week pregnant woman complained of a headache. During the consultation, it became clear that for a long time the pregnant woman has noticed increased fatigue, poor sleep, and muscle pain. On examination: pale pink skin. Blood pressure 115/75 mmHg. PS 76 bpm. ECG - no changes. According to the results of laboratory examinations: Hb 120 g/l, ferritin 45 μg/l. The level of Vitamin D in the blood is 15 ng/ml. TSH 2.9 IU/l. What is the cause of the pregnant woman's complaints?

A. Iron deficiency anemia
B. Vegetative dysfunction
C. Hypothyroidism
D. Vitamin D deficiency

E. Migraine

13. A 26-year-old pregnant woman, 22 weeks of gestation, who has been suffering from diabetes for 13 years, developed a hyperglycemic coma. What could be the cause of this complication?

A. Appointment of biguanides

B. Insufficient nutrition

C. Excessive dose of insulin

D. Insufficient fluid intake

E. Insufficient dose of insulin, lack of glycemic control

14. A 26-year-old woman, 25 weeks of gestation, has diabetes. After the introduction of insulin, a comatose state suddenly occurred. Pale skin, cold sweat. What is the tactic?

A. Administer a concentrated glucose solution intravenously

B. Let the patient drink sweet tea

C. Take an ECG

D. Administer insulin

E. Nitroglycerin under the tongue

Situational tasks

1. A 23-year-old pregnant woman, 16 weeks of gestation, complains of general weakness, fatigue, feeling cold, and dry skin. During the analysis of previous examinations before pregnancy, according to the results of ultrasound of the thyroid gland, signs of thyroiditis were found. What is the preliminary diagnosis? What are the management of this pregnancy?

2. A 37-year-old pregnant woman, 27 weeks of gestation, complained of sudden, extremely severe pain in the lower back, nausea, burning during urination. Urine is brown color. What is the preliminary diagnosis? What are the management?

3. A 42-year-old pregnant woman, 16 weeks of gestation, complained of a severe headache. During the examination, attention is drawn to an increase BP 160/100 mmHg, pulse 82 bpm, rhythmic. There are no peripheral edemas. Diuresis is sufficient. What is the preliminary diagnosis? What are the management?
4. A 28-year-old pregnant woman, 24 weeks of gestation, complained of general weakness, a sudden rise in body temperature to 38^0C, nausea, lower back pain, and frequent urges to urinate. From the anamnesis of the disease - dysuric disorders during the week, the body temperature rose suddenly today, she did not seek medical help. What is the preliminary diagnosis? What are the management?

5. Pregnant women 28 years old, 12-13 weeks of gestation. History of 2 miscarriage. According to the results of the examination, an increased level of antithyroid antibodies, a normal level of fT4 and an increased level of TSH in the blood serum attract attention. What is the preliminary diagnosis? What are the management?

6. Pregnant women 24 years old, pregnancy I, 34-35 weeks of gestation. The cephalic presentation of fetus. Prolonged asthma attack (from several hours) with short light intervals. The general condition of the patient is very serious. She is exhausted, sometimes excited. The skin is bluish, wet. Shortness of breath up to 60 per minute, shallow breathing, noisy at a distance and sharply weakened by auscultation, signs of "silent lung". Pulse - 120 beats/min., BP - 80/60 mmHg, hypoxemia and hypercapnia. What is the likely diagnosis?

7. Pregnant for 24 years old, pregnancy I, 34-35 weeks of gestation. The cephalic presentation of fetus. An attack of bronchial asthma occurred suddenly. The patient takes a forced position - sitting. Paroxysmal cough and "whistling" breath, suffocation. The pregnant woman takes a short breath, which is immediately followed by a difficult prolonged exhalation. Intercostal muscles, supraclavicular, jugular fossa participate in breathing; with percussion - a box sound, a decrease in cardiac dullness, hard breathing with prolonged exhalation, dry wheezes on exhalation, emphasis of the II tone over the pulmonary artery. What is the likely

diagnosis?

8. Pregnant for 23 years old, first pregnancy. She was not sick before pregnancy. In the period of 24-25 weeks of gestation after eating spicy food, she felt pain in the lower back, chills, a sudden increase in temperature to 380C. In the complete blood count: leukocytes - $15.5x10^9$ /l, rod-shaped neutrophils - 12%. ESR - 35 mm/h, in the general urine test: protein - 0.06 g/l, leukocytes cover the entire field, bacteriuria. What is the most likely diagnosis? What antibiotics are recommended during pregnancy in this case?

9. Pregnant for 20 years old, first pregnancy. In the period of 25-26 weeks of gestation, during a visit to the obstetrician, bacteriuria was diagnosed. The general condition is not disturbed, there are no dysuric disorders. What is the most likely diagnosis? What is the management?

10. Pregnant women, 40 weeks of gestation with gestational diabetes, she turned to a obstetrician. There are no complaints. Glucose level within the normal range after diet correction. What are the management?

11. A 12-week pregnant woman visited to an obstetrician. According to the results of the complete blood count: leukocytes - $10.5x10^9$ /l, erythrocytes - $2.9x10^9$ /l, Hb 98g/l,

    platelets - $234x10^{12}$/l, ESR - 9 mm/h. What is the most likely cause of the altered blood count? What is the management?

12. An 18-week pregnant woman visited to an obstetrician with complaints of a headache and an increase in BP 160/90 mmHg. For the first time (2 years before pregnancy), BP increased to 140/90 mmHg. What is the likely diagnosis, a differential diagnosis. What is the examination plan?

13. A 29-week pregnant woman complained of fatigue, swelling of the lower extremities. Blood pressure 160/90 mmHg. In the general urine test: protein 0.9g/l,

granular cylinders, hematuria. What is the likely diagnosis, a differential diagnosis. What is the examination plan?

14. A pregnant woman visited to a women's consultation with complaints of general weakness, rapid fatigue, shortness of breath, "unpleasant sensations" in the heart area and increased body temperature. From the anamnesis: a 1 week ago, the pregnant woman had flu. What is the likely diagnosis? What are the management?

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