

Factors Leading to Premature Birth and Modern Clinical Diagnostic Methods

Abduraximova Adiba Abdurashit qizi

Samarkand State Medical University, 1st year clinical resident of the Department of Obstetrics
and Gynecology No. 3

Yunusova Aziza

Samarkand State Medical University,
Assistant of the Department of Obstetrics and Gynecology No. 3

Abstract: Preterm labor (regular uterine contractions that result in cervical dilatation) is considered preterm. Risk factors include rupture of membranes, uterine anomalies, infection, history of preterm labor, multiple pregnancies, and fetal or placental abnormalities. The diagnosis is made on the basis of clinical findings. Causes are identified and, if possible, eliminated. Treatment usually includes bed rest, tocolytic therapy (if labor is ongoing), corticosteroids (e.g., if gestational age < 34 weeks [see below]), and possibly magnesium sulfate (if gestational age < 32 weeks). Antistreptococcal antibiotics are prescribed until vaginal and anal cultures are negative for group B streptococci.

Keywords: Diagnostics; Treatment; Premature birth can occur due to the following reasons; Preterm rupture of membranes; Chorioamnionitis.

Introduction: Premature birth may increase the risk of intraventricular hemorrhage in newborns; Intraventricular hemorrhage may lead to developmental defects in the nervous system (e.g., cerebral palsy).

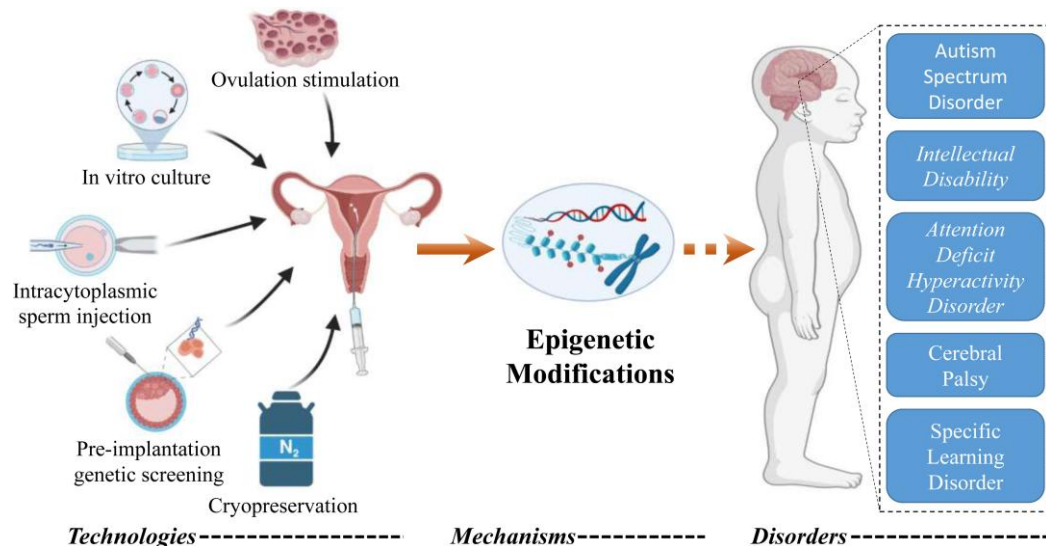
- a. Premature birth diagnosis
- b. History taking and physical examination
- c. The diagnosis of preterm birth is based on signs specific to the birth and duration of pregnancy.

Anovaginal cultures are performed for group B streptococci and antibiotic prophylaxis is initiated (if cultures are negative, then discontinued). Urinalysis and cultures are performed to diagnose cystitis and pyelonephritis. Cervical cultures are performed to detect STIs, if suggested by risk factors and if the patient has not been tested recently.

Many women with preterm labor do not go into labor, and some women diagnosed with preterm labor do not go into labor.

- a. Treatment of premature birth
- b. Antibiotics against group B streptococci
- c. Sometimes tocolytics
- d. Corticosteroids (e.g., 23 to 34 weeks)
- e. Magnesium sulfate for neuroprotection

Management of preterm labor includes antibiotics (if infection is diagnosed or suspected), tocolytics, and corticosteroids (1).



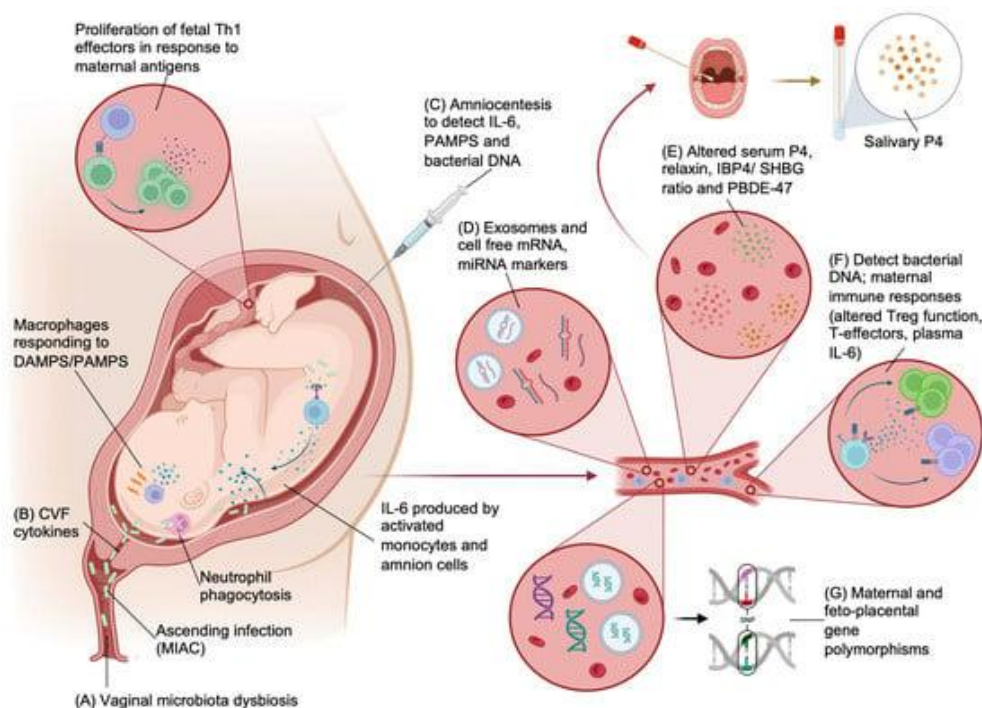
Antibiotics

Antibiotics effective against group B streptococci are prescribed while awaiting culture results (2). The following should be considered when choosing antibiotics:

If there is no allergy to penicillins: benzylpenicillin 5 million units intravenously, then 2.5 million units every 4 hours, or ampicillin 2 g intravenously, then 1 g every 4 hours.

If allergic to penicillin but low risk of anaphylaxis (e.g. urticaria with previous administration): cefazolin 2 g intravenously, then 1 g every 8 hours.

For allergies with a high risk of anaphylaxis (e.g., bronchospasm, angioedema, hypotension with previous administrations, especially within the first 30 minutes): clindamycin 900 mg intravenously every 8 hours if susceptibility to these antibiotics is confirmed; if culture results are resistant or results are not available - vancomycin 20 mg/kg intravenously every 8 hours (maximum dose 2 g)



Tocolytics

If the cervix is dilated, tocolytics (medications that can stop uterine contractions) may delay delivery for at least 48 hours to allow time for corticosteroids to be given to reduce the risk of complications for the fetus. Tocolytics include:

Calcium channel blocker

Prostaglandin synthesis inhibitors

No single tocolytic drug is preferred; the choice must be individualized to minimize side effects.

Prostaglandin inhibitors may cause transient oligohydramnios and fetal renal damage when used for more than 48 consecutive hours. They are contraindicated after 32 weeks of gestation due to the risk of premature narrowing or closure of the ductus arteriosus.

Magnesium sulfate

Intravenous magnesium sulfate should be administered for neuroprotection at <32 weeks of gestation. In utero exposure to the drug reduces the risk of severe neurological dysfunction (e.g., due to intraventricular hemorrhage), including cerebral palsy, in newborns.

Corticosteroids

If the gestational age is 24-34 weeks and delivery cannot be delayed, women are prescribed corticosteroids. An additional course of corticosteroids may be prescribed in the following cases:

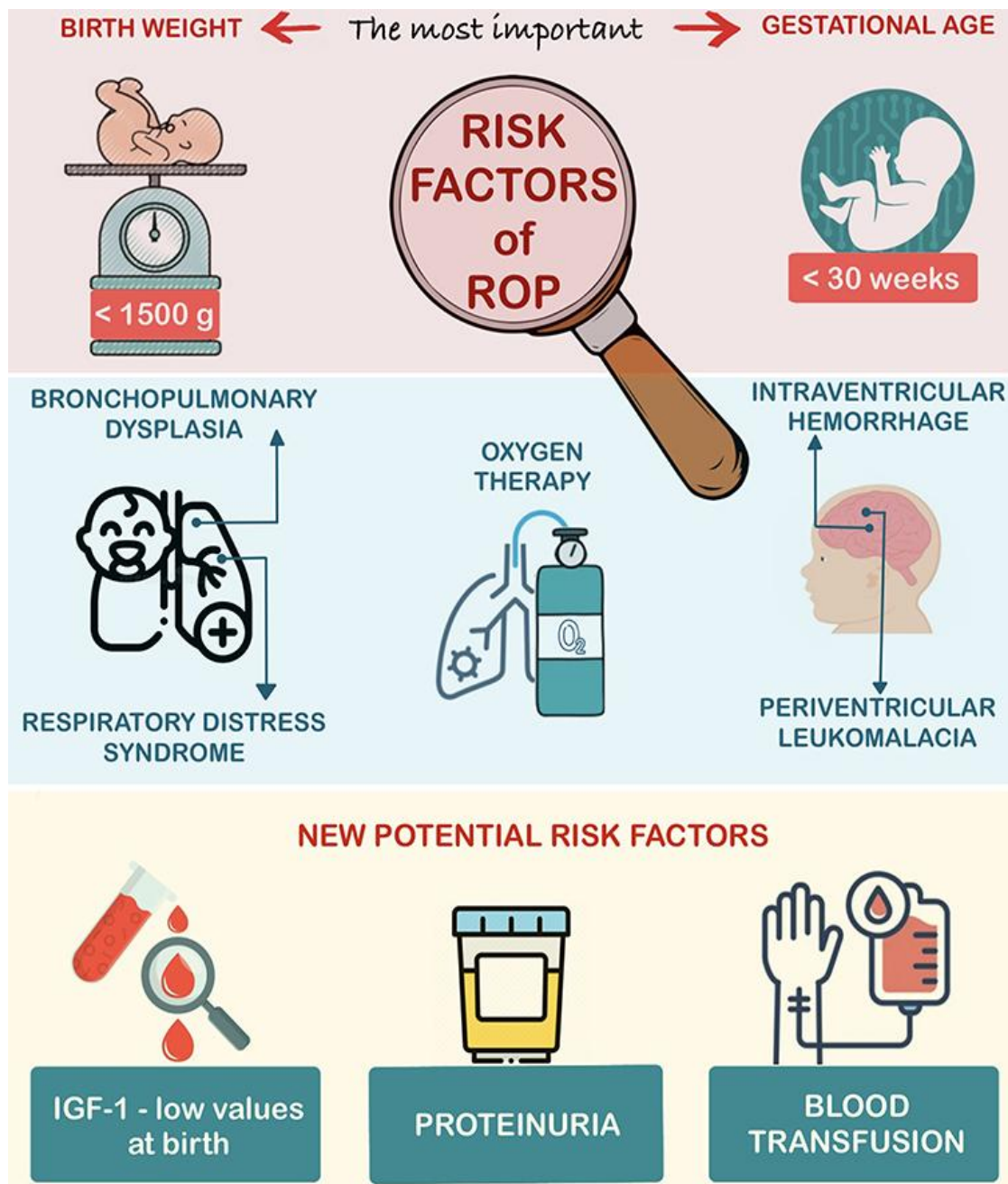
- a. Gestational age <34 weeks.
- b. The last course was administered more than 7 days ago (3 , 4).
- c. The use of corticosteroids should also be considered in the following cases:
- d. Between 34 0/7 weeks and 36 6/7 weeks of gestation, if the woman is at high risk of delivering within 7 days and has not previously been prescribed corticosteroids (2 , 3)
- e. Starting at 23 0/7 weeks of pregnancy, if there is a risk of preterm birth within the next 7 days (2 , 3).
- f. Between 22 0/7 weeks and 22 6/7 weeks of gestation, if neonatal resuscitation is planned and after appropriate parental counseling (4)

One of the following corticosteroids may be used:

Betamethasone 12 mg intramuscularly every 24 hours, for a total of 2 doses

Dexamethasone 6 mg intramuscularly every 12 hours for a total of 4 doses

These corticosteroids accelerate fetal lung maturation and reduce the risk of neonatal respiratory distress syndrome, intracranial hemorrhage, and fetal death.



Progestins

To reduce the risk of recurrence, progestin injections are no longer recommended for women with a history of preterm birth. The previously recommended supporting evidence has been rejected, and the U.S. Food and Drug Administration (FDA) withdrew approval of 17-alpha hydroxyprogesterone caproate (17-OHPC) for this indication in April 2023 (5).

The Society for Maternal-Fetal Medicine (SMFM) also recommends continued use of 17-OHPC, including through compounding (6). However, the IOM believes that it is appropriate to offer cerclage or vaginal progesterone to patients with a history of preterm birth and a diagnosis of a short cervix (<25 mm) before 24 weeks of gestation. The SMFM encourages a shared decision-making process for the use of vaginal progesterone for primary prevention of recurrent preterm birth if the cervix is ≥ 25 mm long, especially for patients who have been treated with progesterone to prevent preterm birth in a previous pregnancy. Furthermore, the SMFM does not recommend changing the indications for cerclage or recommendations for activity restriction.

Research methods and materials: Patients are given cultures of vaginal and anal mucosa for group B streptococci, as well as cultures for any infections suspected based on symptoms (e.g., pyelonephritis, STIs) that may lead to preterm labor.

While waiting for the culture results, treatment is with antibiotics effective against group B streptococci.

Consider tocolysis with a prostaglandin inhibitor if the cervix is dilated, a calcium channel blocker, or if the fetus is <32 weeks.

Corticosteroids are prescribed for gestational ages ≥ 24 weeks and < 34 weeks (in some cases < 37 weeks).

If there is a risk of preterm birth within 7 days, corticosteroids should be considered from 23 weeks of gestation.

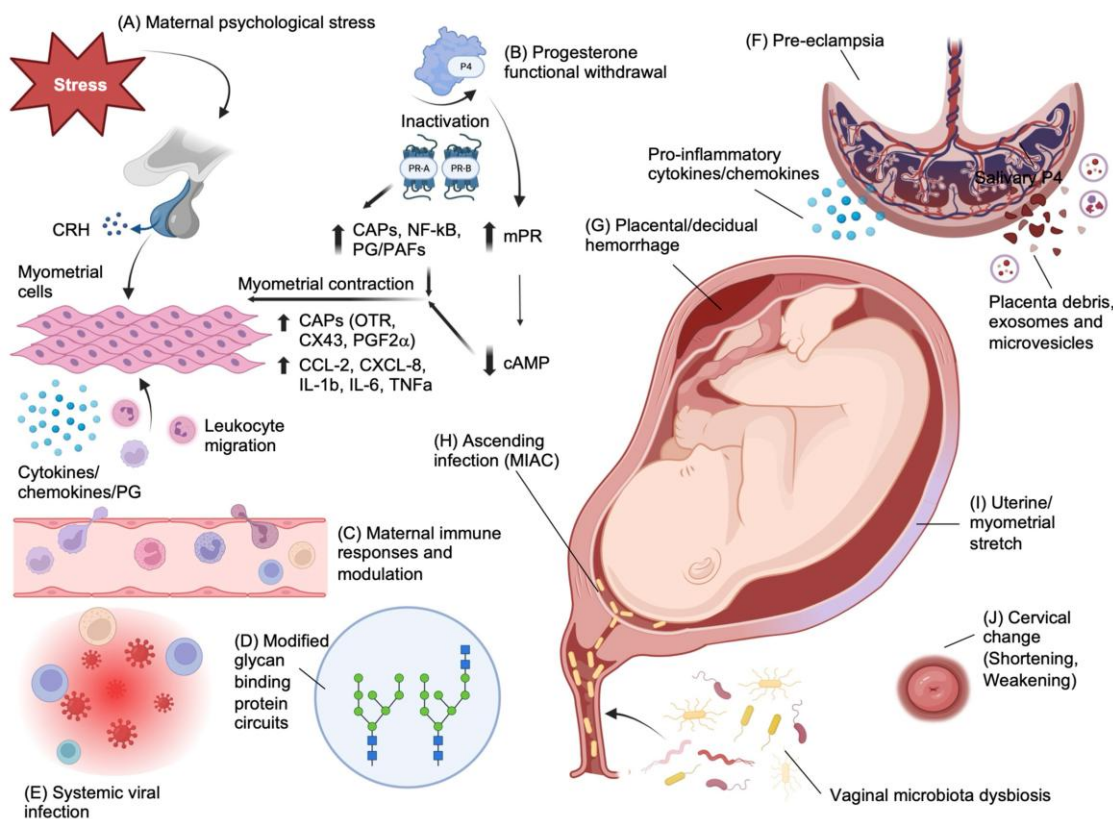
If the fetal age is less than 32 weeks, the use of magnesium sulfate should be considered.

Stillbirth is the death of a fetus (fetal death) at ≥ 20 weeks of gestation (in some definitions > 28 weeks). Management of such a patient includes labor and postpartum care. The mother and fetus should be evaluated to determine the cause.

Stillbirth is defined as the death of a fetus. In the United States, stillbirth is defined as the death of a fetus before or during birth at ≥ 20 weeks of gestation. The World Health Organization defines stillbirth as the death of a fetus after 28 weeks of gestation. There are approximately 2 million stillbirths worldwide each year (1). A previous stillbirth increases the risk of fetal death in a subsequent pregnancy.

Research results: World Health Organization: stillbirth. As of March 2024

Fetal death in late pregnancy can occur due to anatomical or genetic abnormalities of the mother, fetus, or placenta (see table: "The most common causes of stillbirth. If the fetus dies in late pregnancy, but remains in the uterine cavity for several weeks, consumptive coagulopathy or even disseminated intravascular coagulation (DIC) may develop.



Stillbirth diagnosis

- History taking and physical examination
- Tests to determine the cause

- c. The diagnosis of stillbirth is made based on clinical presentation.
- d. Tests to determine the cause of a stillbirth may include:
- e. General examination of the stillborn fetus (e.g., appearance, weight, length, head circumference [1])
- f. Fetal autopsy, karyotype examination, and microarray analysis
- g. Placenta examination
- h. Complete blood count (CBC) to detect anemia or leukocytosis.
- i. Kleihauer-Betke test

Targeted screening for acquired thrombotic diseases, including antiphospholipid antibodies (lupus anticoagulant, anticardiolipin [IgG and IgM], anti-beta2 glycoprotein I [IgG and IgM])

Determination of thyroid-stimulating hormone (TSH) levels and, if abnormal, free T4 (thyroxine) levels.

Diabetes test (HbA1C)

TORCH infection test (toxoplasmosis [with IgG and IgM detection], other pathogens [e.g., human parvovirus B19, herpes zoster virus], rubella virus, cytomegalovirus, herpes simplex virus)

Detection of reagin antibodies in blood serum

Drug test

Testing for hereditary thrombophilia is controversial and not generally recommended. The association between stillbirth and hereditary thrombophilia is unclear, but not strong, except for the factor V Leiden mutation. Testing (e.g., for factor V Leiden) may be considered if severe placental abnormalities are identified, intrauterine growth retardation occurs, or if the woman has a personal or family history of thromboembolic disease (1).

Evacuation of the products of conception may occur spontaneously. If this does not occur, evacuation must be performed, depending on the gestational age, either medically (e.g., oxytocin) or surgically (e.g., dilation and evacuation [D&E] procedure, with prior administration of osmotic dilators to prepare the cervix, with or without misoprostol).

After the products of conception have been expelled, curettage may be required to remove any remaining pieces of the placenta. Fragments are often left behind in stillbirths that occur very early in pregnancy.

If DIC develops, coagulopathy should be treated promptly and aggressively, with blood or blood product replacement if necessary.

The postpartum period is managed in the same way as after the birth of a live fetus.

Parents often experience feelings of grief and need emotional support and sometimes specialized counseling. The risks of subsequent pregnancies associated with the suspected cause of the miscarriage should be discussed with patients.

Stillbirth is the death of a fetus (fetal death) at ≥ 20 weeks (in some definitions > 28 weeks) of gestation.

There are many causes of stillbirth (maternal, fetal, or placental).

If evacuation of the uterine contents is delayed, disseminated intravascular coagulation may develop secondary to this.

Tests are performed to determine the cause; however, it is often not possible to determine it.

Evacuation of the uterine contents by medical induction or surgical evacuation and emotional support for the parents.

Differential diagnosis

Other diseases that cause vomiting should be ruled out; these include gastroenteritis, hepatitis, appendicitis, cholecystitis, other biliary tract diseases, peptic ulcer disease, intestinal obstruction, hyperthyroidism not caused by hyperthyroidism (e.g., due to Graves' disease), gestational trophoblastic disease, nephrolithiasis, benign gastritis, transcranial hypertension, and migraine.

1. Severe symptoms accompanied by vomiting indicate other causes of the disease.
2. Alternative diagnoses are considered based on laboratory, clinical, or ultrasound findings.
3. Treatment of excessive vomiting of pregnancy
4. Temporarily stop oral feeding, then gradually restart
5. Administer fluids, multivitamins, thiamine, electrolytes
6. Antiemetics
7. In rare cases, total parenteral nutrition

First, nothing can be prescribed orally. Intravenous fluids are started with 2 liters of lactated Ringer's solution over 3 hours to maintain urine output above 100 mL/hour (1). If dextrose is prescribed, 100 mg of thiamine should be given intravenously to prevent Wernicke's encephalopathy. This dose of thiamine should be given daily for 3 days.

Summary: Hyperemesis gravidarum is severe nausea and vomiting during pregnancy, leading to dehydration, weight loss, and ketosis. Diagnosis is made clinically and by measuring urine ketone levels, serum electrolytes, and renal function. Treatment consists of temporary parenteral nutrition, antiemetics, vitamins, and electrolytes. Pregnancy often causes nausea and vomiting; this is thought to be due to the rapid rise in estrogen levels or the beta subunit of hCG (beta-hCG). Vomiting usually develops around the 5th week of pregnancy, peaks at 9 weeks, and resolves by 16–18 weeks. It is often referred to as morning sickness, but it can occur at any time of the day. Women who experience mild nausea and vomiting during pregnancy usually continue to gain weight and are not dehydrated. Hyperemesis gravidarum is an extreme form of mild nausea and vomiting during pregnancy. This can be separated because it leads to:

Uncontrolled vomiting can cause mild, transient hyperthyroidism. Intractable vomiting lasting more than 16-18 weeks is rare, but can lead to serious liver damage, including centrilobular necrosis or fatty degeneration, as well as Wernicke's encephalopathy or esophageal rupture.

Clinicians suspect hyperemia gravidarum based on symptoms (e.g., onset, duration, and frequency of vomiting; aggravating and mitigating factors; type and volume of vomiting). Periodic weight measurements may support the diagnosis.

If hyperemesis gravidarum is suspected, urine ketones, thyroid-stimulating hormone, serum electrolytes, blood urea nitrogen (BUN), creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), magnesium, and phosphorus are measured. Obstetric ultrasound is required to rule out hydatidiform mole and to check for multiple gestation.

List of used literature:

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