

Prenatal Screening

Policy Number: AHS – G2035 – Prenatal Screening	Prior Policy Name and Number, as applicable:
Original Effective Date: 5/15/2022 Current Effective Date: 5/15/2022	

I. Policy Description

Prenatal screening refers to testing done to determine health status of the pregnant individual and/or fetus. Prenatal screening can consist of screening for infectious diseases and conditions that may complicate the pregnancy as well as testing to determine risk of fetal abnormalities, including genetic and developmental abnormalities. Any individual undergoing screening tests, especially genetic carrier screenings, needs to realize the limitations of screening tests and the difference between screening and diagnostic testing where screening refers to testing of asymptomatic or healthy individuals to search for a condition that may affect the pregnancy or individual. Diagnostic testing is used to either confirm or refute true abnormalities in an individual (Grant & Mohide, 1982; Lockwood & Magriples, 2020).

II. Related Policies

Policy Number	Policy Title
AHS-G2009	Preventive Screening in Adults
AHS-G2042	Pediatric Preventive Services

III. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual’s benefit coverage at the time of the request

1. The following routine prenatal screening **MEETS COVERAGE CRITERIA** for all pregnant women:
 - a. Screening for HIV infection
 - b. Screening for *Chlamydia trachomatis* infection
 - c. Screening for *Neisseria gonorrhoea* infection
 - d. Screening for hepatitis B

- e. Screening for syphilis
 - f. Screening for hepatitis C
 - g. Screening for bacteriuria
 - h. Screening for type 2 diabetes at the first prenatal visit
 - i. Screening for gestational diabetes during gestational weeks 24 – 28 and at the first prenatal visit if risk factors are present
 - j. Determination of blood type, Rh(D) status, and antibody status during the first prenatal visit, and repeated Rh (D) antibody testing for all unsensitized Rh (D)-negative women at 24 to 28 weeks' gestation, unless the biological father is known to be Rh (D)-negative
 - k. Screening for anemia meets coverage criteria with a CBC or hemoglobin and hematocrit with mean corpuscular volume
 - l. Screening for Group B strep once, recommended during gestational weeks 36 to 37 by American College of Obstetricians and Gynecologists (ACOG)
 - m. Urinalysis and urine culture
 - n. Rubella antibody testing
 - o. Testing for varicella immunity
 - p. Screening for tuberculosis in pregnant women deemed to be at high risk for TB (i.e. women with close contact with individuals with active pulmonary / respiratory tuberculosis or highly contagious active tuberculosis and women who are immunocompromised)
2. Third trimester re-screening of *Chlamydia trachomatis*, Neisseria gonorrhoea, syphilis, and/or HIV infections **MEETS COVERAGE CRITERIA** for pregnant women who meet ANY one of the following high-risk criteria:
- a. Sexually active young individuals under 25 years
 - b. New or multiple sexual partners
 - c. Past history of sexually transmitted diseases (Bacterial Vaginosis, Chancroid, Chlamydia, Gonorrhoea, Genital Herpes, Hepatitis B, Hepatitis C, HIV/AIDS, Human Papillomavirus, Lymphogranuloma Venereum, Syphilis, Trichomoniasis)
 - d. Current sex workers
 - e. Past or current injection drug use

3. Fetal Fibronectin (FFN) assays **MEET COVERAGE CRITERIA** for pregnant women who meet ALL of the following criteria:
 - a. Singleton or twin gestations,
 - b. Intact membranes,
 - c. Cervical dilation <3 cm, and
 - d. Patient experiencing symptoms suggestive of preterm labor between 24 and less than 35 weeks' gestation.
4. Testing pregnant women for thyroid dysfunction **MEETS COVERAGE CRITERIA** if they have any of the following:
 - a. Symptoms of thyroid disease
 - b. Personal history of thyroid disease
 - c. Personal history of other medical conditions associated with thyroid disease (e.g. diabetes mellitus, goiter, iodine deficiency)
5. Screening for Zika virus testing is covered in accordance with Avalon Policy AHS–G2133-Zika Virus Testing.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of a patient's illness.

6. All other applications of the FFN assay **DO NOT MEET COVERAGE CRITERIA**, including, but not limited to the following:
 - a. As part of routine pregnancy monitoring in asymptomatic women with singleton gestation and no risk factors for preterm birth.
 - b. As part of clinical monitoring of asymptomatic women at high risk for preterm birth, including but not limited to those with multiple gestations, history of preterm birth, uterine malformation, cervical incompetence, or history of two or more spontaneous second trimester abortions.
 - c. As part of clinical monitoring in women with triplet or higher-order gestations, intact membranes, cervical dilation <3 cm, and who are experiencing symptoms suggestive of preterm labor.
 - d. As a test to identify women at term being considered for induction who are likely to deliver within 24–48 hours and therefore, do not require induction.
7. Serial monitoring of salivary estriol levels as a technique of risk assessment for preterm labor or delivery **DOES NOT MEET COVERAGE CRITERIA**.

IV. Scientific Background

Prenatal screening is a part of overall prenatal care to promote optimal care of both mother and baby. Prenatal screening allows for assessment and monitoring of the fetus for the presence of congenital defects or disease. Various professional medical organizations provide guidelines for prenatal screening. “Screening is an offer on the initiative of the health system or society, rather than a medical intervention in answer to a patient’s complaint or health problem. Screening aims at obtaining population health gains through early detection that enables prevention or treatment (de Jong, Maya, & van Lith, 2015).”

Routine prenatal screening may include several laboratory tests. Hematocrit or hemoglobin testing can be performed to check for anemia and possible thalassemia, pending further diagnostic testing. Blood typing and antibody screening can be performed to prevent possible alloimmunization or hemolytic diseases. Glucose testing can screen for possible gestational diabetes mellitus. Screening for asymptomatic bacteriuria and proteinuria is recommended as well as screening for infectious disorders, such as HIV, syphilis, chlamydia, and gonorrhea (Lockwood & Magriples, 2020).

Additionally, genetic screening tests, including carrier screening for genetic mutations and fetal testing for chromosomal aneuploidy, can be a part of prenatal screening. Aneuploidy screening may be performed on cell-free DNA in maternal circulation or maternal serum levels of specific biochemical markers for trisomy (Lockwood & Magriples, 2020). These non-invasive prenatal testing (NIPT) can possibly decrease the number of more invasive procedures and the risks of unwanted side effects. A chromosomal microarray (CMA) can screen all chromosomes in a single test and “can detect many very small variants that cannot be detected by traditional karyotyping” (de Jong et al., 2015). In fact, the American College of Obstetricians and Gynecologists (ACOG) recommends CMA for instances where the ultrasound of a fetus shows a major structural abnormality (ACOG, 2016a). CMA in this situation should be performed on DNA from amniotic fluid, chorionic villus cells, or cord blood, however, rather than on maternal serum cell-free DNA since the process does not include an amplification step and the maternal DNA signal would be many times higher than the fetal DNA (Miller, 2020).

Several companies, such as LabCorp, have developed panels to test for potential genetic mutations in pregnant women, or in women planning to become pregnant. This includes the Inheritest® Carrier Screening which encompasses six different panels to identify potential genetic mutations. These six panels include the Inheritest® 500 PLUS Panel (which screens 525 genes for several clinically relevant genetic disorders), the Inheritest® Comprehensive Panel (which screens for more than 110 disorders), the Inheritest® Ashkenazi Jewish Panel (which screens for more than 40 Ashkenazi Jewish related disorders), the Inheritest® Society-Guided Panel (which screens for more than 13 disorders highlighted in the American College of Medical Genetics and Genomics and the American Congress of Obstetricians and Gynecologists guidelines), the Inheritest® Core Panel (which screens for cystic fibrosis, fragile X syndrome, and spinal muscular atrophy), and the Inheritest® CF/SMA Panel (which screens only for cystic fibrosis and spinal muscular atrophy) (LabCorp, 2020).

Red blood cell antigen discrepancy between a mother and fetus may also occur during pregnancy. This is known as hemolytic disease of the fetus and newborn (HDFN), and causes maternal antibodies to destroy the red blood cells of the neonate or fetus (Calhoun, 2020). Alloimmunization is the immune response which occurs in the mother due to foreign antigens after exposure to genetically foreign cells. This disease may arise in the ABO blood group, occurring almost exclusively in mothers with type O blood; ABO incompatibility is identified in almost 15% of pregnancies, but only results in HDFN in approximately 4% of pregnancies (Calhoun, 2020). Another important inherited antigen sometimes found on the surface of red blood cells is known as the Rhesus (Rh)D antigen. During pregnancy and delivery, women who are RhD negative may be exposed to RhD positive fetal cells, which can lead to the development of anti-RhD antibodies. This exposure typically happens during delivery and affects subsequent pregnancies; infants with RhD incompatibility tend to experience a more severe form of HDFN than those with ABO incompatibility (Calhoun, 2020). The clinical presentation of HDFN may be mild (such as hyperbilirubinemia with mild to moderate anemia) to severe and life-threatening anemia (such as hydrops fetalis) (Calhoun, 2020). Less severely affected infants may develop hyperbilirubinemia within the first day of life; infants with RhD HDFN may also present with symptomatic anemia requiring a blood transfusion. In more severe cases, infants with severe life-threatening anemia, such as hydrops fetalis, may exhibit shock at delivery requiring an emergent blood transfusion (Calhoun, 2020).

The administration of anti-D immune globulin has been able to dramatically reduce, but not eliminate, the number of RhD alloimmunization cases. “Anti-D immune globulin is manufactured from pooled plasma selected for high titers of IgG antibodies to D-positive erythrocytes (Moise, 2020).” Before the development of this anti-D immune globulin, it has been reported that 16% of women with two deliveries of RhD positive ABO compatible infants became alloimmunized; however, after routine postpartum administration of anti-D immune globulin, and an additional administration in the third trimester of pregnancy, this statistic was reduced to 0.1-0.3% (Moise, 2020).

Fetal RhD genotyping using cell-free fetal DNA from maternal plasma can be performed to identify fetal blood type most accurately after 11 weeks of gestation. While the United States has not implemented fetal RhD genotyping for routine prophylaxis and fetal monitoring protocols, several European countries, such as Denmark, the Netherlands, England, Sweden, France and Finland, do utilize fetal RhD determination so that the administration of anti-D immune globulin can be avoided when an RhD-negative fetus is identified (Moise, 2020). Daniels, Finning, Martin, and Summers (2007) report that approximately 40% of RhD-negative pregnant women are carrying a RhD-negative fetus; genotypic screening would, therefore, be very valuable in preventing the unnecessary anti-D immune globulin to these women. Another article by Kent, Farrell, and Soothill (2014) suggest that the administration of anti-D immune globulin to the 1/3 of pregnant women who do not require this administration is unethical, and that the availability of RhD genotyping to all RhD-negative pregnant women would assist in more informed choices being made regarding anti-D immune globulin administration. Finning et al. (2008) agree with the previous statements, declaring that “High throughput RHD genotyping of fetuses in all RhD negative women is feasible and would substantially reduce unnecessary administration of anti-RhD immunoglobulin to RhD negative pregnant women with an RhD negative fetus.”

Clinical Utility and Validity

Biro, Rigo, and Nagy (2020) report on a noninvasive prenatal testing method for congenital heart disease via the measurement of cell-free nucleic acid and protein biomarkers in maternal blood. Congenital heart disease is considered the most common fetal malformation. Currently, prenatal ultrasonography is most commonly used to diagnose congenital heart disease, but it is not the most accurate method. After a large review completed with PubMed and Web of Sciences databases, the authors conclude that most fetal congenital heart disease related disorders can be diagnosed by noninvasive prenatal testing (NIPT) techniques. Further, cell-free RNAs and circulating proteins are potential biomarkers for fetal congenital heart disease, and may be able to improve the detection rate in early pregnancies (Biro et al., 2020).

Implementation of prenatal screening tests can positively affect pregnancies and pregnancy outcomes. The Centers for Disease Control and Prevention (CDC) reports that implementation of the 1996 guidelines concerning Group B Streptococcus (GBS) had a profound effect. Prior to screening and widespread use of intrapartum antibiotics, invasive neonatal GBS occurred in 2 - 3 cases per 1,000 live births; however, after prenatal screening implementation, the rate declined to 0.5 cases per 1,000 live births in 1999 (Schrag, Gorwitz, Fultz-Butts, & Schuchat, 2002). The CDC also reports in a multi-year study that screening for syphilis in all pregnant women at the first prenatal visit (and then rescreening in third trimester for women at risk) is very important in preventing congenital syphilis, which can cause spontaneous abortion, stillbirth, and early infant death. They show that 88.2% of cases of congenital syphilis was avoided when proper screening was applied; moreover, 30.9% of the cases of congenital syphilis that did occur were where the mother did not receive proper prenatal care (≥ 45 days before delivery) (Slutsker, Hennessy, & Schillinger, 2018).

A study by Persico et al. (2016) investigated the clinical implication of cell-free DNA (cfDNA) testing in high-risk pregnancies. In their cohort of 259 singleton pregnancies, cfDNA testing provided results in 249 (96.1%). Further, cfDNA testing is identified in 97.2% (35/36) of trisomy 21, 100% (13/13) of trisomy 18, 100% of trisomy 13 (5/5), and 75% of sex chromosome aneuploidies (3/4). The authors conclude that “a policy of performing an invasive test in women with a combined risk of ≥ 1 in 10 or NT ≥ 4 mm and offering cfDNA testing to the remaining cases would detect all cases of trisomy 21, 18 or 13, 80% of sex aneuploidies and 62.5% of other defects and would avoid an invasive procedure in 82.4% of euploid fetuses” (Persico et al., 2016). These data support the earlier meta-analysis that reported NIPT sensitivity of trisomy 21, trisomy 18, and trisomy 13 of 99%, 96.8%, and 92.1%, respectively and specificities of 99.92%, 99.85%, and 99.80%, respectively, for trisomies 21, 18, and 13 (Dondorp et al., 2015; Gil, Akolekar, Quezada, Bregant, & Nicolaidis, 2014).

A multi-year study of more than 5000 patients in public hospitals in Spain on the effect of NIPT on the number of invasive procedures performed shows that the introduction of NIPT drastically reduces the incidences of invasive procedures. The data shows that, even though a 60.5% reduction occurred in invasive procedures, the chromosomopathy detection rate was unaffected; moreover, the ratio of positive invasive procedures was improved to 50%, indicating that unwarranted invasive procedures had been avoided (Martinez-Payo, Bada-Bosch, Martinez-Moya, & Perez-Medina, 2018). The authors of the study concluded, “NIPT introduction has caused a significant reduction of 60.5% of IP [invasive procedures] in high

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chromosomopathy risk patients after combined screening without modifying detection rate” (Martinez-Payo et al., 2018).

A meta-analysis was completed by Mackie, Hemming, Allen, Morris, and Kilby (2017) which researched the accuracy of cell-free fetal DNA NIPT testing in singleton pregnancies. A total of 117 studies were included which analyzed 18 different conditions. For RHD testing, a sensitivity of 0.993 and specificity of 0.984 was identified, and for fetal sex identification, a sensitivity of 0.989 and a specificity of 0.996 was calculated (Mackie et al., 2017). With such high sensitivity and specificity calculations, NIPT testing for fetal sex and RHD status may be considered accurate diagnostic tools.

Clausen et al. (2014) completed a two-year evaluation of nationwide prenatal RhD screening in Denmark. A total of 12,668 pregnancies were analyzed, with blood samples drawn in week 25 of pregnancy. DNA was extracted from these blood samples and was analyzed for the *RHD* gene. Results were compared to the serological typing of the newborns after birth. “The sensitivity for the detection of fetal *RHD* was 99.9% (95% CI: 99.7-99.9%). Unnecessary recommendation of prenatal RhD prophylaxis was avoided in 97.3% of the women carrying an RhD-negative fetus. Fetuses that were seropositive for RhD were not detected in 11 pregnancies (0.087%) (Clausen et al., 2014).” This study shows high sensitivity of fetal *RHD* genotyping. These results were recently supported by another large scale meta-analysis completed by Yang et al. (2019) focusing on NIPT testing for fetal RhD status. A total of 3921 results confirmed that “High-throughput NIPT is sufficiently accurate to detect fetal RhD status in RhD-negative women and would considerably reduce unnecessary treatment with routine anti-D immunoglobulin (Yang et al., 2019).”

Darlington et al. (2018) completed an analysis of 11 French Obstetric Departments with a total of 949 patients to determine the effectiveness of RhD genotyping. The patients were separated into two groups (genotyping group: n=515, and control group: n=335). The authors concluded that “Early knowledge of the RHD status of the fetus using non-invasive fetal *RHD* genotyping significantly improved the management of *RHD* negative pregnancies with a small increase in cost (Darlington et al., 2018).”

A prospective cohort study by de Haas et al. (2016) completed a nationwide program in the Netherlands hoping to determine the sensitivity of fetal RhD screening for the safe guidance of targeted anti-immune globulin prophylaxis. A total of 25,789 RhD-negative pregnant woman participated in this study. Fetal testing for the *RHD* gene was assessed in the 27th week of pregnancy. Fetal *RHD* test results were compared to serological cord blood results after birth. “Sensitivity for detection of fetal *RHD* was 99.94% (95% confidence interval 99.89% to 99.97%) and specificity was 97.74% (97.43% to 98.02%). Nine false-negative results for fetal RHD testing were registered (0.03%, 95% confidence interval 0.01% to 0.06%) (de Haas et al., 2016).” Therefore, fetal RhD testing is a highly reliable testing method.

Manfroi et al. (2018) completed fetal *Rhd* genotyping with real-time polymerase chain reaction (qPCR) using cell-free fetal DNA extracted from maternal plasma. A commercial multiple-exon assay was used to determine fetal *RHD* genotypic accuracy. A total of 367 plasma samples obtained between the 24th and 28th weeks of pregnancy were used for this study. Neonatal results were available for 284 of the pregnancies. The sensitivity was reported

at 100% and specificity at 97.5%. The diagnostic accuracy was 96.1% with the inclusion of 9/284 inconclusive results (Manfroi et al., 2018). This is therefore an accurate and reliable tool for targeted prenatal immunoprophylaxis.

Similarly, Liang et al. (2019) used cell-free plasma DNA to assess the clinical utility of using an expanded noninvasive prenatal screening (“NIPS-Plus”) to detect aneuploidy and genome-wide microdeletion/microduplication syndromes (MMS). Of the 94,085 women with singleton pregnancies enrolled in the study, 1128 were suspected of having clinically significant fetal chromosome abnormalities. Follow-up testing in the study reported the positive predictive values (PPVs) of 95%, 82%, 46%, 29%, and 47% for T21, T18, T13, rare trisomies, and sex chromosome aneuploidies, respectively. For known MMS (n=32), PPVs were 93% (DiGeorge), 68% (22q11.22 microduplication), 75% (Prader-Willi/Angleman [sic]), and 50% (Cri du Chat). Thus, the researchers conclude that “the data have potential significance in demonstrating the usefulness of cfDNA profiling” and that “NIPS-Plus can be used as a first-tier pregnancy screening method to improve detection rates of clinically significant fetal chromosome abnormalities” (Liang et al., 2019).

Runkel et al. (2020) completed a systematic review to determine the benefit of NIPT for fetal RhD status in RhD-negative pregnant women because “All non-sensitized Rhesus D (RhD)-negative pregnant women in Germany receive antenatal anti-D prophylaxis without knowledge of fetal RhD status.” The meta-analysis included data from 60,000 participants, with the focus of the research on the impact of fetal and maternal morbidity. The researchers concluded that “NIPT for fetal RhD status is equivalent to conventional serologic testing using the newborn's blood. Studies investigating patient-relevant outcomes are still lacking” (Runkel et al., 2020).

However, the field continues to evolve, with potential shifts from one testing method to another in pursuit of optimality and comprehensiveness. A multicenter retrospective study of singleton high-risk pregnancies for chromosomal abnormalities was conducted by Zhu et al. (2020) to evaluate the utility of expanded noninvasive prenatal screening as compared with chromosomal microarray analysis (CMA). The analysis enrolled subjects who underwent expanded NIPS and CMA sequentially during pregnancy from 2015 through 2019. The study demonstrated that of the 943 high-risk pregnancies, 550 (58.3%) cases had positive NIPS results, while positive CMA results were detected in 308 (32.7%) cases, and the agreement rates between NIPS and CMA were 82.3%, 59.6% and 25.0% for trisomy 21, 18 and 13, respectively. Regarding rare aneuploidies and segmental imbalances, NIPS and CMA results were concordant in 7.5% and 33.3% of cases. However, copy number variants were better detected with CMA than with NIPS, and additional genetic aberrations were detected by CMA in 1 of 17 high-risk pregnancies that were otherwise passed over when processed with NIPS. The researchers then contend that “CMA should be offered for high-risk pregnancies” to provide comprehensive detection of chromosomal abnormalities in high-risk pregnancies (Zhu et al., 2020)

This policy focuses on laboratory testing performed during pre-conception and/or prenatal periods as part of a comprehensive prenatal care program.

V. Guidelines and Recommendations

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American College of Obstetricians and Gynecologists (ACOG) (2011, 2012, 2014, 2015, 2016, 2018, 2019, 2020)

ACOG has a number of practice guidelines related to prenatal care as well as both pre-conception and prenatal testing. ACOG recommendations and guidelines include the following:

- **Vitamin D Screening:** Concerning vitamin D screening, “there is insufficient evidence to support a recommendation for screening all pregnant women for vitamin D deficiency. For pregnant women thought to be at increased risk of vitamin D deficiency, maternal serum 25-hydroxyvitamin D levels can be considered and should be interpreted in the context of the individual clinical circumstance [reaffirmed in 2017] (ACOG, 2011).”
- **Lead Screening:** Concerning lead screening, they recommend risk assessment of lead exposure at earliest contact with blood lead testing if even one single risk factor is identified. This was reaffirmed in 2019 (ACOG, 2012).
- **Subclinical Hypothyroidism:** ACOG Committee Opinion on subclinical hypothyroidism in pregnancy does not recommend routine screening for subclinical hypothyroidism. It states that “thyroid testing in pregnancy should be performed on symptomatic women and those with a personal history of thyroid disease or other medical conditions associated with thyroid disease (e.g., diabetes mellitus) (ACOG, 2015a).”
- **Depression and Anxiety:** “All obstetrician-gynecologists and other obstetric care providers screen patients at least once during the perinatal period for depression and anxiety symptoms using a standardized, validated tool. [They should] complete a full assessment of mood and emotional well-being (including screening for postpartum depression and anxiety with a validated instrument) during the comprehensive postpartum visit for each patient (ACOG, 2018a).”
- **Listeria monocytogenes:** Concerning testing for *Listeria monocytogenes* (ACOG, 2014), “No testing, including blood and stool cultures, or treatment is indicated for an asymptomatic pregnant woman who reports consumption of a product that was recalled or implicated during an outbreak of listeria contamination. An asymptomatic patient should be instructed to return if she develops symptoms of listeriosis within 2 months of eating the recalled or implicated product.” If an exposed pregnant woman shows signs and symptoms consistent with infection, then blood culture testing is the standard of care. Stool culture testing is not recommended since it has not been validated as a screening tool. This position was reaffirmed in 2019.
- **HIV:** Concerning HIV, ACOG recommends that all women should be tested for HIV with the right to refuse testing. “Human immunodeficiency virus testing using the opt-out approach, which is currently permitted in every jurisdiction in the United States, should be a routine component of care for women during prepregnancy and as early in pregnancy as possible. Repeat HIV testing in the third trimester, preferably before 36 weeks of gestation, is recommended for pregnant women with initial negative HIV antibody tests who are known to be at high risk of acquiring HIV infection; who are

receiving care in facilities that have an HIV incidence in pregnant women of at least 1 per 1,000 per year; who are incarcerated; who reside in jurisdictions with elevated HIV incidence; or who have signs and symptoms consistent with acute HIV infection (eg, fever, lymphadenopathy, skin rash, myalgias, arthralgias, headache, oral ulcers, leukopenia, thrombocytopenia, or transaminase elevation). Rapid screening during labor and delivery or during the immediate postpartum period using the opt-out approach should be done for women who were not tested earlier in pregnancy or whose HIV status is otherwise unknown. Results should be available 24 hours a day and within 1 hour (Pollock, Cohan, Pecci, & Mittal, 2019).”

- For pregnant women who test positive for HIV, “Additional laboratory work, including CD4⁺ count; HIV viral load; testing for antiretroviral resistance; hepatitis C virus antibody; hepatitis B surface antigen and viral load; and hepatitis A using antibody testing for immunoglobulin G for women who have hepatitis B virus infection and who have not already received the hepatitis A virus vaccine series; complete blood count with platelet count; and baseline chemistries with comprehensive metabolic testing, will be useful before prescribing antiretroviral therapy (Pollock et al., 2019).”
- **Genetic Testing and Genetic Counseling:** Concerning genetic testing and genetic counseling, ACOG recommends:
 - “A hereditary cancer risk assessment is the key to identifying patients and families who may be at increased risk of developing certain types of cancer. This assessment should be performed by obstetrician–gynecologists or other obstetric–gynecologic providers and should be updated regularly. If a hereditary cancer risk assessment suggests an increased risk of a hereditary cancer syndrome, referral to a specialist in cancer genetics or a health care provider with expertise in genetics is recommended for expanded gathering of family history information, risk assessment, education, and counseling, which may lead to genetic testing [reaffirmed in 2020] (ACOG, 2015b).”
 - “The routine use of whole-genome or whole-exome sequencing for prenatal diagnosis is **not** recommended outside of the context of clinical trials until sufficient peer-reviewed data and validation studies are published.” This was reaffirmed in 2020 (ACOG, 2016a, 2020b).
 - Chromosomal microarray analysis (CMA) is recommended for patients with a fetus with at least one major structure abnormality identified via ultrasound. CMA can be considered for all pregnant women who undergo prenatal diagnostic testing; however, “In a patient with a structurally normal fetus who is undergoing invasive prenatal diagnostic testing, either fetal karyotyping or a chromosomal microarray analysis can be performed. Chromosomal microarray analysis of fetal tissue (ie, amniotic fluid, placenta, or products of conception) is recommended in the evaluation of intrauterine fetal death or stillbirth when further cytogenetic analysis is desired because of the test’s increased likelihood of obtaining results and improved detection of causative abnormalities [(ACOG, 2016a)”. This was reaffirmed in 2020.

- “All patients who are considering pregnancy or are already pregnant, regardless of screening strategy and ethnicity, should be offered carrier screening for cystic fibrosis and spinal muscular atrophy, as well as a complete blood count and screening for thalassemias and hemoglobinopathies. Fragile X premutation carrier screening is recommended for women with a family history of fragile X-related disorders or intellectual disability suggestive of fragile X syndrome, or women with a personal history of ovarian insufficiency. Additional screening also may be indicated based on family history or specific ethnicity (Romero, Rink, Biggio, Saller, & ACOG, 2017).” This was reaffirmed in 2020 (ACOG, 2020a).
- “Direct-to-consumer genetic testing should be discouraged because of the potential harm of a misinterpreted or inaccurate result (Rink, Biggio, Kamyar, & ACOG, 2017).”
- ACOG “recommends considering whole-exome sequencing when specific genetic tests available for a phenotype, including targeted sequencing tests, have failed to arrive at a diagnosis in a fetus with multiple congenital anomalies suggestive of a genetic disorder (Vora, Ralston, & ACOG, 2018)”; however, they note that “Cascade testing has been shown to be cost effective in part because testing for specific mutations (eg, those identified in the affected relative) is less expensive than whole-gene sequencing (Witkop & ACOG, 2018).”
- **Prenatal Diagnostic Testing for Genetic Disorders:** Concerning prenatal diagnostic testing for genetic disorders, ACOG has published the following recommendations (ACOG, 2016b, 2021a):
 - “An abnormal FISH result should not be considered diagnostic. Therefore, clinical decision making based on information from FISH should include at least one of the following additional results: confirmatory traditional metaphase chromosome analysis or chromosomal microarray, or consistent clinical information
 - Prenatal genetic testing cannot identify all abnormalities or problems in a fetus, and any testing should be focused on the individual patient’s risks, reproductive goals and preferences
 - Genetic testing should be discussed as early as possible in pregnancy, ideally at the first obstetric visit, so that first-trimester options are available (ACOG, 2016b).” This guideline was reaffirmed in 2021 (ACOG, 2021a).
- **Prevention of Rh D Alloimmunization:** Concerning the prevention of Rh D alloimmunization, ACOG has published the guidelines supporting the administration of anti-D immune globulin to women in various scenarios. However, these guidelines do not mention the use of cell-free fetal DNA for fetal RHD testing to determine if anti-D immune globulin is needed (ACOG, 2017b).

- **Newborn Screening Panel:** ACOG issued the recommended uniform newborn screening panel of core conditions in 2019. The table is listed below (ACOG, 2019a):

Table 1. Recommended Uniform Newborn Screening Panel of Core Conditions	
Disease Categories	Diseases
Inborn errors of organic acid metabolism	Isovaleric acidemia Glutaric acidemia type I 3-Hydroxy-3-methylglutaric aciduria Holocarboxylase synthase deficiency Methylmalonic acidemia (methylmalonyl-CoA mutase) 3-Methylcrotonyl-CoA carboxylase deficiency Methylmalonic acidemia (cobalamin disorders) Propionic acidemia β -ketothiolase deficiency
Inborn errors of fatty acid metabolism	Medium-chain acyl-CoA dehydrogenase deficiency Very long-chain acyl-CoA dehydrogenase deficiency Long-chain L-3 hydroxyacyl-CoA dehydrogenase deficiency Trifunctional protein deficiency Carnitine uptake defect/transport defect
Inborn errors of amino acid metabolism	Classic phenylketonuria Maple syrup urine disease Homocystinuria Citrullinemia, type I Argininosuccinic aciduria Tyrosinemia, type I
Hemoglobinopathies	S,S disease (Sickle cell anemia) S, β -thalassemia S,C disease
Miscellaneous multisystem diseases	Primary congenital hypothyroidism Biotinidase deficiency Congenital adrenal hyperplasia Classic galactosemia Cystic fibrosis

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	<p>Glycogen Storage Disease Type II (Pompe)</p> <p>Mucopolysaccharidosis type 1</p> <p>Spinal Muscular Atrophy</p> <p>X-linked adrenoleukodystrophy</p> <p>Severe combined immunodeficiency</p>
Newborn screening by methods other than by heel stick	<p>Hearing loss</p> <p>Critical congenital heart disease</p>

- **Genetic Carrier Screening:** Concerning genetic carrier screening, including testing for specific conditions, ACOG recommends [(Rink, Romero, et al., 2017) reaffirmed 2020]:
 - “Carrier screening and counseling ideally should be performed before pregnancy.
 - If an individual is found to be a carrier for a specific condition, the individual’s reproductive partner should be offered testing in order to receive informed genetic counseling about potential reproductive outcomes. Concurrent screening of the patient and her partner is suggested if there are time constraints for decisions about prenatal diagnostic evaluation.
 - Carrier screening for a particular condition generally should be performed only once in a person’s lifetime, and the results should be documented in the patient’s health record. Because of the rapid evolution of genetic testing, additional mutations may be included in newer screening panels. The decision to rescreen a patient should be undertaken only with the guidance of a genetics professional who can best assess the incremental benefit of repeat testing for additional mutations.
 - Prenatal carrier screening does not replace newborn screening, nor does newborn screening replace the potential value of prenatal carrier screening.
 - The cost of carrier screening for an individual condition may be higher than the cost of testing through commercially available expanded carrier screening panels. When selecting a carrier screening approach, the cost of each option to the patient and the health care system should be considered.
 - Screening for spinal muscular atrophy should be offered to all women who are considering pregnancy or are currently pregnant. In patients with a family history of spinal muscular atrophy, molecular testing reports of the affected individual and carrier testing of the related parent should be reviewed, if possible, before testing. If the reports are not available, *SMN1* deletion testing should be recommended for the low-risk partner.
 - Cystic fibrosis carrier screening should be offered to all women who are considering pregnancy or are currently pregnant. Complete analysis of

the *CFTR* gene by DNA sequencing is not appropriate for routine carrier screening.

- A complete blood count with red blood cell indices should be performed in all women who are currently pregnant to assess not only their risk of anemia but also to allow assessment for risk of a hemoglobinopathy. Ideally, this testing also should be offered to women before pregnancy. A hemoglobin electrophoresis should be performed in addition to a complete blood count if there is suspicion of hemoglobinopathy based on ethnicity (African, Mediterranean, Middle Eastern, Southeast Asian, or West Indian descent). If red blood cell indices indicate a low mean corpuscular hemoglobin or mean corpuscular volume, hemoglobin electrophoresis also should be performed.
- Fragile X premutation carrier screening is recommended for women with a family history of fragile X-related disorders or intellectual disability suggestive of fragile X syndrome and who are considering pregnancy or are currently pregnant.
- If a woman has unexplained ovarian insufficiency or failure or an elevated follicle-stimulating hormone level before age 40 years, fragile X carrier screening is recommended to determine whether she has an *FMR1* premutation.
- All identified individuals with intermediate results and carriers of a fragile X premutation or full mutation should be provided follow-up genetic counseling to discuss the risk to their offspring of inheriting an expanded full-mutation fragile X allele and to discuss fragile X-associated disorders (premature ovarian insufficiency and fragile X tremor/ataxia syndrome).
- Prenatal diagnostic testing for fragile X syndrome should be offered to known carriers of the fragile X premutation or full mutation.
- DNA-based molecular analysis (eg, Southern blot analysis and polymerase chain reaction) is the preferred method of diagnosis of fragile X syndrome and of determining *FMR1* triplet repeat number (eg, premutations). In rare cases, the size of the triplet repeat and the methylation status do not correlate, which makes it difficult to predict the clinical phenotype. In cases of this discordance, the patient should be referred to a genetics professional.
- When only one partner is of Ashkenazi Jewish descent, that individual should be offered screening first. If it is determined that this individual is a carrier, the other partner should be offered screening. However, the couple should be informed that the carrier frequency and the detection rate in non-Jewish individuals are unknown for most of these disorders, except for Tay–Sachs disease and cystic fibrosis. Therefore, it is difficult to accurately predict the couple’s risk of having a child with the disorder.
- Screening for Tay–Sachs disease should be offered when considering pregnancy or during pregnancy if either member of a couple is of Ashkenazi Jewish, French–Canadian, or Cajun descent. Those with a family history consistent with Tay–Sachs disease also should be offered screening. When one

member of a couple is at high risk (ie, of Ashkenazi Jewish, French–Canadian, or Cajun descent or has a family history consistent with Tay–Sachs disease) but the other partner is not, the high-risk partner should be offered screening. If the high-risk partner is found to be a carrier, the other partner also should be offered screening. Enzyme testing in pregnant women and women taking oral contraceptives should be performed using leukocyte testing because serum testing is associated with an increased false-positive rate in these populations. If Tay–Sachs disease screening is performed as part of pan-ethnic expanded carrier screening, it is important to recognize the limitations of the mutations screened in detecting carriers in the general population. In the presence of a family history of Tay–Sachs disease, expanded carrier screening panels are not the best approach to screening unless the familial mutation is included on the panel (Rink, Romero, et al., 2017).”

- Regarding expanded carrier screening panels, ACOG recommends that “the disorders selected for inclusion should meet several of the following consensus-determined criteria: have a carrier frequency of 1 in 100 or greater, have a well-defined phenotype, have a detrimental effect on quality of life, cause cognitive or physical impairment, require surgical or medical intervention, or have an onset early in life.” ACOG further states that “screened conditions should be able to be diagnosed prenatally and may afford opportunities for antenatal intervention to improve perinatal outcomes, changes to delivery management to optimize newborn and infant outcomes, and education of the parents about special care needs after birth (Romero et al., 2017).”
- **Carrier Screening in the Age of Genomic Medicine:** Concerning carrier screening in the age of genomic medicine, the ACOG has published the following guidelines (ACOG, 2017a, 2020a):
 - “Ethnic-specific, panethnic and expanded carrier screening are acceptable strategies for prepregnancy and prenatal carrier screening
 - If a patient requests a screening strategy other than the one used by the obstetrician-gynecologist or other health care provider, the requested test should be made available to her after counseling on its limitations, benefits, and alternatives
 - All patients who are considering pregnancy or already pregnant, regardless of screening strategy and ethnicity, should be offered carrier screening for cystic fibrosis and spinal muscular atrophy, as well as a complete blood count and screening for thalassemias and hemoglobinopathies. Fragile X premutation carrier screening is also recommended for women with a family history of fragile x-related disorders or intellectual disability suggestive of fragile X syndrome, or women with a personal history of ovarian insufficiency. Additional screening also may be indicated based on family history or specific ethnicity
 - If a woman is found to be a carrier for a specific condition, her reproductive partner should be offered screening to provide accurate genetic counseling for

the couple with regard to the risk of having an affected child. Additional genetic counseling should be provided to discuss the specific condition, residual risk, and options for prenatal testing.

- Individuals with a family history of a genetic disorder may benefit from the identification of the specific familial mutation or mutations rather than carrier screening. Knowledge of the specific familial mutation may allow for more specific and rapid prenatal diagnosis.
 - Given the multitude of conditions that can be included in expanded carrier screening panels, the disorders selected for inclusion should meet several of the following consensus-determined criteria: have a carrier frequency of 1 in 100 or greater, have a well-defined phenotype, have a detrimental effect on quality of life, cause cognitive or physical impairment, require surgical or medical intervention, or have an onset early in life. Additionally, screened conditions should be able to be diagnosed prenatally and may afford opportunities for antenatal intervention to improve perinatal outcomes, changes to delivery management to optimize newborn and infant outcomes, and education of the parents about special care needs after birth.
 - Carrier screening panels should not include conditions primarily associated with a disease of adult onset (ACOG, 2017a).” This guideline was reaffirmed in 2020 (ACOG, 2020a).
- **Group B Streptococcal (GBS) Disease:** “all pregnant women should undergo antepartum screening for GBS at 36 0/7–37 6/7 weeks of gestation, unless intrapartum antibiotic prophylaxis for GBS is indicated because of GBS bacteriuria during the pregnancy or because of a history of a previous GBS-infected newborn. This new recommended timing for screening provides a 5-week window for valid culture results that includes births that occur up to a gestational age of at least 41 0/7 weeks” (ACOG, 2020c)
 - **Lab Tests:** ACOG lists the following lab tests to be performed early in pregnancy: complete blood count (CBC), blood type, urinalysis, urine culture, rubella, hepatitis B, hepatitis C, HIV, sexually transmitted infection (STI) testing, and tuberculosis. Concerning STIs, all pregnant women should be tested for syphilis and chlamydia with proof-of-cure testing for women who are treated for either infection. Women who are at high-risk for gonorrhea should be tested (ACOG, 2017c).
 - ACOG lists the following lab tests to be performed later in pregnancy: repeat CBC, Rh antibody test, glucose screening test, and Group B streptococci (GBS) (ACOG, 2017c).
 - **ZIKA Virus:** The April 2019 update concerning Zika, ACOG states the following (ACOG, 2018b, 2019b):
 - “Symptomatic pregnant women with possible Zika virus exposure or women who are pregnant with a fetus showing abnormalities consistent with congenital Zika virus syndrome should be tested as soon as possible. Asymptomatic pregnant women with ongoing possible exposure can be offered nucleic acid testing during pregnancy as (ACOG, 2020c)Asymptomatic pregnant women

with possible Zika virus exposure but without ongoing possible exposure are not recommended routinely to have Zika virus testing, but testing can be considered as part of a shared patient–provider decision-making model (ACOG, 2019b).”

Finally, ACOG published a guideline on “Direct-to-Consumer” Testing. In it, they recommend that testing revolving around single nucleotide polymorphism analysis should be considered investigational at time of writing (ACOG, 2021b).

United States Preventive Services Task Force (USPSTF) (2005, 2006, 2008, 2009, 2013, 2014, 2015, 2016, 2018, 2020)

The United States Preventive Services Task Force (USPSTF) recommends the following testing for pregnant women:

- Screening for hepatitis B virus (HBV) infection at the first prenatal visit (Grade A) (Owens, Davidson, Krist, Barry, Cabana, Caughey, Doubeni, Epling, Kemper, et al., 2019; USPSTF, 2009, 2019)
- Screening for asymptomatic bacteriuria with urine culture is recommended in pregnant persons (Grade B) (Owens, Davidson, Krist, Barry, Cabana, Caughey, Doubeni, Epling, Kubik, et al., 2019; USPSTF, 2008a)
- Screening for gestational diabetes mellitus after 24 weeks of gestation (Grade B) (V. A. Moyer, 2014)
- Screening for HIV is recommended in all pregnant persons, including those in labor or whose HIV status is unknown at delivery (Grade A) (V. A. Moyer & USPSTF, 2013b; Owens, Davidson, Krist, Barry, Cabana, Caughey, Curry, et al., 2019)
- Rh (D) blood typing and antibody testing during the first prenatal visit (Grade A) (USPSTF, 2005)
- Repeated Rh (D) antibody testing for all unsensitized Rh (D)-negative women at 24-28 weeks' gestation, unless the biological father is known to be Rh (D)-negative (Grade B) (USPSTF, 2005)
- Screening early for syphilis infection in all pregnant women (Grade A) (USPSTF, 2018)

Additional recommendations from the USPSTF that may be relevant during pregnancy include:

- Screening for chlamydia in sexually active women aged 24 years or younger and in older women who are at increased risk for infection (Grade B) (LeFevre & USPSTF, 2014)
- Screening for gonorrhea in sexually active women aged 24 years or younger and in older women who are at increased risk for infection (Grade B) (LeFevre & USPSTF, 2014)

- Screening for depression in general population, including pregnant and post-partum women (Grade B) (Siu & USPSTF, 2016)
- Screening for hepatitis C virus (HCV) infection is recommended in all adults aged 18 to 79 years (Grade B) (Chou et al., 2020; V. A. Moyer & USPSTF, 2013a)
- Concerning screening adults for drug use, Krist et al. (2020) state that “The USPSTF recommends screening by asking questions about unhealthy drug use in adults age 18 years or older. Screening should be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred. (Screening refers to asking questions about unhealthy drug use, not testing biological specimens.)” The USPSTF also states that “This new evidence supports the current recommendation that primary care clinicians offer screening to adults 18 years or older, including those who are pregnant or postpartum, when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred.”
- However, the USPSTF recommends against the following tests during pregnancy:
 - Screening for bacterial vaginosis in pregnant women who are not at risk for preterm delivery (grade D); further, current evidence is insufficient for screening pregnant persons who are at increased risk for preterm delivery (Owens et al., 2020; USPSTF, 2008b)
 - Serological screening for herpes simplex virus (HSV) in asymptomatic pregnant women (USPSTF, 2016)
 - Screening for elevated blood lead levels in asymptomatic pregnant women has been given an I recommendation as current evidence is insufficient to determine if this testing is beneficial or not (Curry et al., 2019; USPSTF, 2006)
 - “The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes (Siu, 2015).”

American Diabetes Association (ADA) (ADA, 2018, 2020)

The American Diabetes Association in the 2018 *Standards of Medicare Care in Diabetes* make the following recommendations (ADA, 2018, 2020):

- “Test for undiagnosed prediabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria. [Grade] **B**
- Test for gestational diabetes mellitus at 24–28 weeks of gestation in pregnant women not previously found to have diabetes. [Grade] **A**
- Test women with gestational diabetes mellitus for prediabetes at 4–12 weeks postpartum, using the 75-g oral glucose tolerance test and clinically appropriate nonpregnancy diagnostic criteria. [Grade] **E**
- Women with a history of gestational diabetes mellitus should have lifelong screening for the development of diabetes or prediabetes at least every 3 years. [Grade] **B**

- Women with a history of gestational diabetes mellitus found to have prediabetes should receive intensive lifestyle interventions or metformin to prevent diabetes. [Grade] A”

Centers for Disease Control and Prevention (CDC) (CDC, 2015b, 2019a, 2019b, 2020a)

The Centers for Disease Control and Prevention (CDC) recommends:

- All pregnant women get testing for HIV, hepatitis B virus (HBV) and syphilis during each pregnancy (CDC, 2019b). Additional CDC (2019b) recommendations can be found in the table below:

	First Prenatal Visit	Third Trimester	At Delivery
Syphilis	All pregnant women	Certain groups of pregnant women ^v at 28-32 weeks	Select group of pregnant women, ^v pregnant women with no previously established status, or pregnant women who deliver a stillborn infant
HIV	All pregnant women ⁱ	Certain groups of pregnant women ^{vi} before 36 weeks	Pregnant women not screened during pregnancy
HBV	All pregnant women ⁱⁱ	N/A	Pregnant women not screened during pregnancy, ^{vii} who are at high risk, ^{viii} or with signs or symptoms of hepatitis
Chlamydia	All pregnant women <25 years of age and older pregnant women at increased risk ⁱⁱⁱ	Pregnant women <25 years of age or continued high risk ⁱⁱⁱ	N/A
Gonorrhea	All pregnant women <25 years of age and older pregnant women at increased risk ⁱⁱⁱ	Pregnant women at continued high risk ⁱⁱⁱ	N/A

“Endnotes:

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1. To promote informed and timely therapeutic decisions, health care providers should test women for HIV as early as possible during each pregnancy.¹
2. All pregnant women should be tested for hepatitis B surface antigen (HBsAg) during an early prenatal visit (e.g., first trimester) in each pregnancy, even if they have been vaccinated or tested previously.²
3. “Increased risk” means new or multiple sex partners, sex partner with concurrent partners, sex partners who have a sexually transmitted disease (STD).^{3,4}
4. “At increased risk” means injection-drug use (IDU), had a blood transfusion before July 1992, receipt of an unregulated tattoo, long-term hemodialysis, intranasal drug use, and other percutaneous exposures.³
5. “Certain groups” includes women who are at high risk for syphilis or live in areas of high syphilis morbidity.³
6. “Certain groups” includes women who receive health care in areas with an elevated incidence of HIV or AIDS among women aged 15–45 years, who receive health care in facilities in which prenatal screening identifies at least one HIV-infected woman per 1,000 women screened, known to be at high risk for HIV (i.e., injection-drug user and their sex partners, exchange sex for money or drugs, sex partner of HIV-infected persons, have had a new or >1 sex partner during this pregnancy), or have signs or symptoms consistent with acute HIV infection.¹
7. Women admitted for delivery at a health care facility without documentation of HBsAg test results should have blood drawn and tested as soon as possible after admission.²
8. Having had more than one sex partner during the previous 6 months, an HBsAg-positive sex partner, evaluation or treatment for a STD, or IDU² (CDC, 2019b).²

Further, in 2020, the CDC recommended “Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is less than 0.1%” (CDC, 2020a)

- Repeat HIV screening in the third trimester for women at high-risk of STDs—“Women who use illicit drugs, have STDs during pregnancy, have multiple sex partners during pregnancy, live in areas with high HIV prevalence, or have partners with HIV infection (CDC, 2015b).”
- Screening of all pregnant women for HBsAg (Hepatitis B Surface Antigen Test) during each pregnancy regardless of prior testing with a retest at time of deliver for those at high risk, including persons born in regions of high endemicity ($\geq 2\%$ prevalence) and HIV positive individuals (CDC, 2015b).
- Testing of all pregnant women for syphilis during the first prenatal visit and, for individuals at high risk, retest early in the third semester as well as time of delivery (CDC, 2015b).
- Chlamydia trachomatis screening at the first prenatal visit and repeat testing during the third trimester for women under 25 years or at high risk for acquisition. “Pregnant women with chlamydial infection should have a test-of-cure 3-4 weeks after treatment and be retested within 3 months (CDC, 2015b).”

- N. gonorrhea testing of all pregnant women under 25 years of age and older women at risk for infection or living in an area of high prevalence of N. gonorrhea. For pregnant women who receive treatment for gonorrhea, they should be retested 3 months after treatment (CDC, 2015b).
- Screening for hepatitis C is recommended in pregnant women at high risk for infection and pregnant women born between 1945 – 1965 (CDC, 2015b). It is not recommended for pregnant women who have no risk factors (CDC, 2015c).
- Zika virus testing for symptomatic pregnant persons:
 - “For symptomatic pregnant women who had recent travel to areas with active dengue transmission and a risk of Zika, specimens should be collected as soon as possible after the onset of symptoms up to 12 weeks after symptom onset.
 - The following diagnostic testing should be performed at the same time:
 - Dengue and Zika virus NAAT testing on a serum specimen, and Zika virus NAAT on a urine specimen, and
 - IgM testing for dengue only.
 - Zika virus IgM testing is NOT recommended for symptomatic pregnant women.
 - Zika IgM antibodies can persist for months to years following infection. Therefore, detecting Zika IgM antibodies might not indicate a recent infection.
 - There is notable cross-reactivity between dengue IgM and Zika IgM antibodies in serologic tests. Antibodies generated by a recent dengue virus infection can cause the Zika IgM to be falsely positive.
 - If the Zika NAAT is positive on a single specimen, the Zika NAAT should be repeated on newly extracted RNA from the same specimen to rule out false-positive NAAT results. If the dengue NAAT is positive, this provides adequate evidence of a dengue infection and no further testing is indicated.
 - If the IgM antibody test for dengue is positive, this is adequate evidence of a dengue infection and no further testing is indicated (CDC, 2019a).”
 - ZIKA virus testing in asymptomatic pregnant women is not recommended.
- Cervical cancer screening intervals in pregnant women should be the same as for nonpregnant women (CDC, 2015b).
- “Evidence does not support routine HSV-2 serologic screening among asymptomatic pregnant women. However, type-specific serologic tests might be useful for identifying pregnant women at risk for HSV infection and guiding counseling regarding the risk for acquiring genital herpes during pregnancy (CDC, 2015b, 2019a).”
- “Evidence is insufficient to recommend routine screening for BV in asymptomatic pregnant women at high or low risk for preterm delivery for the prevention of preterm birth (CDC, 2015a).”

American College of Medical Genetics and Genomics (ACMG) (2004, 2005, 2008, 2013, 2014, 2016)

The American College of Medical Genetics and Genomics (ACMG) recommends that the following (Gregg et al., 2016):

- “Allowing patients to select *diagnostic* or *screening* approaches for the detection of fetal aneuploidy and/or genomic changes that are consistent with their personal goals and preferences.”
- “Informing all pregnant women that *diagnostic* testing (CVS or amniocentesis) is an option for the detection of chromosome abnormalities and clinically significant CNVs [copy-number variants].”
- “Informing all pregnant women that NIPS [non-invasive prenatal screening] is the most sensitive screening option for traditionally screened aneuploidies (i.e., Patau, Edwards, and Down syndromes).”
- “Offering *diagnostic* testing when a positive screening test result is reported after NIPS.”
- The ACMG does NOT recommend “NIPS to screen for autosomal aneuploidies other than those involving chromosomes 13, 18, and 21.”
- “Offering *diagnostic* testing for a no-call NIPS result due to low fetal fraction if maternal blood for NIPS was drawn at an appropriate gestational age. A repeat blood draw is NOT appropriate.”
- “Offering aneuploidy screening other than NIPS in cases of significant obesity.”
- “Offering *diagnostic* testing when a positive screening test result is reported after screening for sex chromosome aneuploidies.”
- “Offering *diagnostic* testing (CVS or amniocentesis) with CMA when NIPS identifies a CNV.”
- ACMG does NOT recommend “NIPS to screen for *genome-wide* CNVs. If this level of information is desired, then diagnostic testing (e.g., chorionic villous sampling or amniocentesis) followed by CMA is recommended.”
- “Offering aneuploidy screening other than NIPS for patients with a history of bone marrow or organ transplantation from a male donor or donor of uncertain biologic sex.”

In the ACMG practice guidelines concerning carrier screening in individuals of Ashkenazi Jewish descent, they “recommend that carrier screening for cystic fibrosis, Canavan disease, familial dysautonomia, and Tay-Sachs disease be offered to all Ashkenazi Jews who are pregnant or considering pregnancy, according to current American College of Medical Genetics and/or the American College of Obstetricians and Gynecologists (ACOG) guidelines. In addition, we recommend that carrier screening be offered for Fanconi anemia (Group C), Niemann-Pick (Type A), Bloom syndrome, mucopolipidosis IV, and Gaucher disease (Gross, Pletcher, & Monaghan, 2008).”

Concerning carrier screening for spinal muscular atrophy, ACMG recommends, “Because SMA is present in all populations, carrier testing should be offered to all couples regardless of race or ethnicity. Ideally, the testing should be offered before conception or early in pregnancy (Prior, 2008).” They also recommend carrier screening for Fragile X syndrome for pregnant women and those considering pregnancy who have a family history of Fragile X syndrome or undefined mental retardation (Sherman, Pletcher, & Driscoll, 2005). Cystic fibrosis carrier screening for all pregnant women and those considering pregnancy is recommended; moreover, the ACMG released the mutation frequency data of various ethnic groups within their 2004 revision of the cystic fibrosis screening guidelines (Watson et al., 2004).

In 2014, the American College of Medical Genetics and Genomics issued the following guidelines for the clinical evaluation and diagnosis of hearing loss. For individuals lacking physical findings suggestive of a known syndrome and having medical and birth histories that do not suggest an environmental cause of hearing loss, ACMG recommends that a tiered diagnostic approach should be implemented (Alford et al., 2014):

- “Single-gene testing may be warranted in cases in which the medical or family history, or presentation of the hearing loss, suggests a specific etiology.”
- “In the absence of any specific clinical indications and for singleton cases and cases with apparent autosomal recessive inheritance, the next step should be testing for DFNB1-related hearing loss (due to mutations in GJB2 and adjacent deletions in GJB6).”
- “If initial genetic testing is negative, genetic testing using gene panel tests, NGS technologies such as large sequencing panels targeted toward hearing loss–related genes, WES, or WGS may be considered.”

Also, in 2014, the ACMG released guidelines concerning the diagnosis and management of phenylalanine hydroxylase (PAH) deficiency. They recommend PAH testing be part of newborn screening and that quantitative blood amino acids testing should be performed for diagnostic testing following a positive newborn screen of PAH deficiency. “Additional testing is needed to define the cause of elevated PHE and should include analysis of pterin metabolism; PAH genotypic is indicated for improved therapy planning (Vockley et al., 2014).”

In 2013, the ACMG released guidelines concerning prenatal/preconception expanded carrier screening. These guidelines provide the following recommendations:

- “When adult-onset disorders (disorders that could affect the offspring of the individual undergoing carrier screening once the offspring reaches adult life) are included in screening panels, patients must provide consent to screening for these conditions, especially when there may be implications for the health of the individual being screened or other family members
- For each disorder, the causative gene(s), mutations, and mutation frequencies should be known in the population being tested, so that meaningful residual risk in individuals who test negative can be assessed

- There must be validated clinical association between the mutation(s) detected and the severity of the disorder (Grody et al., 2013).”

World Health Organization (WHO) (WHO, 2016)

In 2016, the WHO released their publication titled, *WHO recommendations on antenatal care for a positive pregnancy experience*, which had the following recommendations (WHO, 2016):

- Anemia (Context-specific recommendation)—“Full blood count testing is the recommended method for diagnosing anaemia in pregnancy.”
- Asymptomatic bacteriuria (Context-specific recommendation)—“Midstream urine culture is the recommended method for diagnosing asymptomatic bacteriuria (ASB) in pregnancy. In settings where urine culture is not available, on-site midstream urine Gram-staining is recommended over the use of dipstick tests as the method for diagnosing ASB in pregnancy.”
- Gestational diabetes mellitus (Recommended)—“Hyperglycaemia first detected at any time during pregnancy should be classified as either gestational diabetes mellitus (GDM) or diabetes mellitus in pregnancy, according to WHO criteria.”
- HIV and syphilis (Recommended)—“In high-prevalence settings, provider-initiated testing and counselling (PITC) for HIV should be considered a routine component of the package of care for pregnant women in all antenatal care settings. In low-prevalence settings, PITC can be considered for pregnant women in antenatal care settings as a key component of the effort to eliminate mother-to-child transmission of HIV, and to integrate HIV testing with syphilis, viral or other key tests, as relevant to the setting, and to strengthen the underlying maternal and child health systems.”
- Tuberculosis (Context-specific recommendation)—“In settings where the tuberculosis (TB) prevalence in the general population is 100/100 000 population or higher, systematic screening for active TB should be considered for pregnant women as part of antenatal care (WHO, 2016).”

To help circumvent prenatal transmission, the CDC also “recommends that all pregnant women get tested for HIV, hepatitis B virus (HBV), hepatitis C virus (HCV), and syphilis during each pregnancy” for all women during pregnancy, as “Screening is necessary to access medical services for HCV and treatment to prevent transmission of HIV, HBV, and syphilis to the infant” (CDC, 2020b).

International Society for Prenatal Diagnosis (ISPD), the Society for Maternal Fetal Medicine (SMFM), and the Perinatal Quality Foundation (PQF) (ISPD, 2018)

The ISPD, SMFM and PQF published the following guidelines on the use of genome-wide sequencing for fetal diagnosis:

- “The use of diagnostic sequencing is currently being introduced for evaluation of fetuses for whom standard diagnostic genetic testing, such as chromosomal microarray

analysis (CMA), has already been performed and is uninformative or is offered concurrently according to accepted practice guidelines, or for whom expert genetic opinion determines that standard genetic testing is less optimal than sequencing for the presenting fetal phenotype.

- The routine use of prenatal sequencing as a diagnostic test cannot currently be supported due to insufficient validation data and knowledge about its benefits and pitfalls (ISPD, 2018).”

The Canadian National Rh Working Group and the Society of Obstetricians and Gynaecologists of Canada (SOGC) Genetics Committee (Fung & Eason, 2018; Johnson, MacDonald, Clarke, & Skoll, 2017)

Guidelines were published by a consensus meeting of the Canadian National Rh Working Group in collaboration with the SOGC Genetics committee. The following recommendations were provided:

- “The current optimal management of the D-negative pregnant woman is based on the prediction of the fetal D-blood group by cell-free DNA in maternal plasma with targeted antenatal anti-D prophylaxis. This approach should be adopted in Canada (II-2A).
- While various algorithms of implementation of fetal RHD genotyping have been described, a model positioned in the first trimester appears to be most in alignment with the existing Canadian antenatal anti-D prophylaxis program and should be endorsed (II-2A).
- While the risk of a false-negative result with RHD genotyping is very small and the benefits of knowing the fetal RHD status in terms of compliance with prophylaxis seem to outweigh the risks, the chance of immunization is not zero. Quality control at a laboratory and clinical level should be of utmost priority in program planning (II-3A) (Johnson et al., 2017).”

College of American Pathologists (CAP) Transfusion Medicine Resource Committee (TMRC) Work Group (Sandler et al., 2015)

The following recommendations were given by the CAP RMRC work group:

- “The Work Group recommends that *RHD* genotyping be performed whenever a discordant RhD typing result and/or a serological weak D phenotype is detected in patients, including pregnant women, newborns and potential transfusion recipients. It is anticipated that the immediate benefit will be fewer unnecessary injections of RhIG and increased availability of RhD-negative RBCs for transfusion
- For women with a serological weak D phenotype associated with *RHD* genotypes other than weak D type 1, 2 or 3, the Work Group recommends that these women receive conventional prophylaxis with RhIG, including postpartum RhIG if the newborn is RhD-positive or has a serological weak D phenotype (Sandler et al., 2015).”

The National Institute for Health and Care Excellence (NICE) (NICE, 2016, 2020)

The NICE published the following guideline in November 2016 regarding fetal *RHD* genotyping: “High-throughput non-invasive prenatal testing (NIPT) for fetal *RHD* genotype is recommended as a cost-effective option to guide antenatal prophylaxis with anti-D immunoglobulin, provided that the overall cost of testing is £24 or less. This will help reduce unnecessary use of a blood product in pregnant women, and conserve supplies by only using anti-D immunoglobulin for those who need it (NICE, 2016).”

In 2020, the NICE published a document through their Pathways program, synthesizing its recommendations on screening for antenatal care for uncomplicated pregnancies. The recommendation for each condition is reported below (NICE, 2020).

Condition	Screening recommended?	Indications
Anaemia	Yes	<p>“Screening should take place early in pregnancy (at the booking appointment) and at 28 weeks when other blood screening tests are being performed. This allows enough time for treatment if anaemia is detected.</p> <p>Haemoglobin levels outside the normal UK range for pregnancy (that is, 11 g/100 ml at first contact and 10.5 g/100 ml at 28 weeks) should be investigated and iron supplementation considered if indicated.”</p>
Down’s Syndrome	Yes	<p>“Screening for Down's syndrome should be performed by the end of the first trimester (13 weeks 6 days), but provision should be made to allow later screening (which could be as late as 20 weeks) for women booking later in pregnancy.</p> <p>The 'combined test' (nuchal translucency, beta-human chorionic gonadotrophin,</p>

Condition	Screening recommended?	Indications
		<p>pregnancy-associated plasma protein-A) should be offered to screen for Down's syndrome between 11 weeks and 13 weeks 6 days. For women who book later in pregnancy the most clinically and cost-effective serum screening test (triple or quadruple test) should be offered between 15 weeks and 20 weeks.</p> <p>When it is not possible to measure nuchal translucency, owing to fetal position or raised BMI, women should be offered serum screening (triple or quadruple test) between 15 weeks and 20 weeks.”</p> <p>“The presence of an isolated soft marker, with the exception of increased nuchal fold, on the routine anomaly scan, should not be used to adjust the a priori risk for Down's syndrome.</p> <p>The presence of an increased nuchal fold (6 millimetres or above) or two or more soft markers on the routine anomaly scan should prompt the offer of a referral to a fetal medicine specialist or an appropriate healthcare professional with a special interest in fetal medicine.”</p>
Sickle cell diseases and thalassaemias	Yes	“Screening for sickle cell diseases and thalassaemias should be offered to all women as early as possible in pregnancy (ideally by 10 weeks). The type of screening

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Condition	Screening recommended?	Indications
		depends upon the prevalence and can be carried out in either primary or secondary care.”
Asymptomatic bacteriuria	Yes	“Women should be offered routine screening for asymptomatic bacteriuria by midstream urine culture early in pregnancy. Identification and treatment of asymptomatic bacteriuria reduces the risk of pyelonephritis.”
Asymptomatic bacterial vaginosis	No	“Pregnant women should not be offered routine screening for bacterial vaginosis because the evidence suggests that the identification and treatment of asymptomatic bacterial vaginosis does not lower the risk of preterm birth and other adverse reproductive outcomes.”
Chlamydia trachomatis	No	“Chlamydia screening should not be offered as part of routine antenatal care.”
Cytomegalovirus	No	“The available evidence does not support routine cytomegalovirus screening in pregnant women and it should not be offered.”
Hepatitis B virus	Yes	“Serological screening for hepatitis B virus should be offered to pregnant women so that effective postnatal interventions can be offered to infected women to decrease the risk of mother-to-child transmission.”
Hepatitis C virus	No	“Pregnant women should not be offered routine screening for

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Condition	Screening recommended?	Indications
		hepatitis C virus because there is insufficient evidence to support its clinical and cost effectiveness.”
HIV	Yes	“Pregnant women should be offered screening for HIV infection early in antenatal care because appropriate antenatal interventions can reduce mother-to-child transmission of HIV infection.”
Group B streptococcus	No	“Pregnant women should not be offered routine antenatal screening for group B streptococcus because evidence of its clinical and cost effectiveness remains uncertain.”
Syphilis	Yes	“Screening for syphilis should be offered to all pregnant women at an early stage in antenatal care because treatment of syphilis is beneficial to the mother and baby.”
Toxoplasmosis	No	“Routine antenatal serological screening for toxoplasmosis should not be offered because the risks of screening may outweigh the potential benefits.”
Pre-eclampsia	Yes	“Blood pressure measurement and urinalysis for protein should be carried out at each antenatal visit to screen for pre-eclampsia.”
Preterm labour	No	“Routine screening for preterm labour should not be offered.”

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Condition	Screening recommended?	Indications
Placenta praevia	No	“Because most low-lying placentas detected at the routine anomaly scan will have resolved by the time the baby is born, only a woman whose placenta extends over the internal cervical os should be offered another transabdominal scan at 32 weeks. If the transabdominal scan is unclear, a transvaginal scan should be offered.”
Structural fetal anomalies	Yes	“Ultrasound screening for fetal anomalies should be routinely offered, normally between 18 weeks and 20 weeks 6 days.”

Department of Veterans Affairs/Department of Defense (VA/DoD) (VA & DOD, 2018)

In the 3rd edition of the VA/DoD *Clinical Practice Guideline for the Management of Pregnancy* (VA & DOD, 2018), they list the following lab tests as routine for all pregnancies in the first prenatal visit: HIV, CBC, ABO Rh blood typing, Antibody screen, anemia/hemoglobinopathies screen, rapid plasma reagin, gonorrhea, chlamydia, hepatitis B surface antigen test, rubella IgG, Urinalysis and culture, and varicella IgG (if status is unknown). They also list the following among their recommendations (VA & DOD, 2018):

- “We recommend screening for use of tobacco, alcohol, illicit drugs, and unauthorized use of prescription medication because their use is common and can result in adverse outcomes. For women who screen positive, we recommend additional evaluation and treatment.” [Strong]
- “We recommend screening for depression using a standardized tool such as the Edinburgh Postnatal Depression Scale or the 9- item Patient Health Questionnaire periodically during pregnancy and postpartum.” [Strong]
- “We suggest making prenatal diagnostic testing for aneuploidy available to all pregnant women.” [Weak]
- “We recommend offering prenatal screening for aneuploidy and the most common clinically significant genetic disorders to all pregnant women. When aneuploidy screening is desired, cellfree fetal DNA screening should be considered; however, screening test selection should be individualized and take into account the patient’s age, baseline aneuploidy risk, and test performance for a given condition.” [Strong]

- “We suggest the two-step process (one-hour oral glucose challenge test followed by three-hour oral glucose tolerance test) to screen for gestational diabetes mellitus at 24-28 weeks gestation for all pregnant women.” [Weak]
- “We suggest that pregnant women with an unexplained elevation of maternal serum alpha-fetoprotein be evaluated and counseled by a qualified obstetric provider due to increased risk for adverse perinatal outcomes.” [Weak]
- “We recommend **against** routine screening for preterm delivery using the fetal fibronectin test in asymptomatic women.” [Strong, against]
- “We recommend considering the use of fetal fibronectin testing as a part of the evaluation strategy in women between 24 and 34 6/7 weeks gestation with signs and symptoms of preterm labor, particularly in facilities where the result might affect management of delivery.” [Strong]
- “We suggest that women who have undergone bariatric surgery should be evaluated for nutritional deficiencies and need for nutritional supplementation where indicated (e.g., vitamin B12, folate, iron, calcium).” [Weak]

Health Resources & Services Administration (HRSA) (HRSA, 2017, 2019)

The HRSA-supported Women’s Preventive Services Initiative (HRSA, 2017) recommends the following:

- Screening pregnant women for gestational diabetes mellitus after 24 weeks of gestation (preferably between 24 and 28 weeks of gestation)
- Women with risk factors for diabetes mellitus be screened for preexisting diabetes before 24 weeks of gestation—ideally at the first prenatal visit

Royal College of Obstetricians and Gynaecologists (RCOG) (RCOG, 2014)

The RCOG have given the following recommendation for prenatal and fetal genotyping: “Non-invasive fetal genotyping using maternal blood is now possible for D, C, c, E, e and K antigens. This should be performed in the first instance for the relevant antigen when maternal red cell antibodies are present” (C recommendation) (RCOG, 2014).

VI. State and Federal Regulations, as applicable

The FDA has approved many tests for conditions that can be included in a prenatal screening, such as HSV, chlamydia, gonorrhea, syphilis, and diabetes. A search of the FDA Devices database of “HSV” on 02/01/2021 yielded 108 results. Likewise, a search of “chlamydia” and “syphilis” had 143 and 37 records, respectively. “Neisseria” and “gonorrhea” yielded a combined 59 records of approved FDA devices as of 02/01/2021. “Diabetes” returned 165 records of FDA-approved devices as of the same date.

Additionally, many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

VII. Applicable CPT/HCPCS Procedure Codes

Code Number	Code Description
80081	Obstetric panel (includes HIV testing)
80055	Obstetric panel (must include CBC, HbSAg, Rubella antibody, RBC antibody screen, qualitative non-treponemal antibody syphilis test, ABO blood typing and Rh D typing)
81001	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; automated, with microscopy
81002	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; non-automated, without microscopy
81003	Urinalysis, automated, without microscopy
81007	Urinalysis, bacteriuria screen, except by culture or dipstick
81015	Urinalysis; microscopic only
81253	known familial variants
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)
81420	Fetal chromosomal aneuploidy (eg, trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21
81507	Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy
82677	Estriol
82731	Fetal fibronectin, cervicovaginal secretions, semi quantitative

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Code Number	Code Description
82947	Glucose; quantitative, blood (except reagent strip)
82950	Glucose; post glucose dose (includes glucose)
82951	Glucose; tolerance test (GTT), 3 specimens (includes glucose)
82962	Glucose, blood by glucose monitoring device(s) cleared by the FDA specifically for home use
83020	Hemoglobin fractionation and quantitation; electrophoresis (eg, A2, S, C, and/or F)
83021	Hemoglobin fractionation and quantitation; chromatography (eg, A2, S, C, and/or F)
83036	Hemoglobin, glycosylated (A1C)
84443	Thyroid stimulating hormone (TSH)
85004	Blood count; automated differential WBC count
85007	Blood smear, microscopic examination with manual differential WBC count
85009	Blood Count
85014	Hematocrit (Hct)
85018	Hemoglobin (Hgb)
85025	Complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count) and automated differential WBC count
85027	Complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count)
85032	Blood count; manual cell count (erythrocyte, leukocyte, or platelet) each
85041	Blood count; red blood cell (RBC), automated
85048	Blood count; leukocyte (WBC), automated
86480	Tuberculosis test, cell mediated immunity antigen response measurement; gamma interferon
86580	Skin test; tuberculosis, intradermal

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Code Number	Code Description
86592	Syphilis test, non-treponemal antibody; qualitative (eg, VDRL, RPR, ART)
86593	Syphilis test, non-treponemal antibody; quantitative
86631	Antibody; Chlamydia
86632	Antibody; Chlamydia, IgM
86701	Antibody, HIV-1
86702	Antibody, HIV-2
86703	Antibody, HIV-1 and HIV-2, single result
86762	Rubella Antibody
86787	Antibody; varicella-zoster
86780	Antibody; Treponema pallidum
86803	Hepatitis C antibody
86804	Hepatitis C antibody; confirmatory test (eg, immunoblot)
86850	Antibody screen, RBC, each serum technique
86900	Blood typing; ABO
86901	Blood typing; Rh (D)
87077	Culture, bacterial; aerobic isolate, additional methods required for definitive identification, each isolate
87081	Culture, presumptive, pathogenic organisms, screening only
87086	Culture, bacterial; quantitative colony count, urine
87088	Culture, bacterial; with isolation and presumptive identification of each isolate, urine
87110	Culture, chlamydia, any source
87270	Infectious agent antigen detection by immunofluorescent technique; Chlamydia trachomatis
87320	Infectious agent antigen detection by immunoassay technique, (eg, enzyme

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Code Number	Code Description
	immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; hepatitis B surface antigen (HBsAg)
87340	Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; hepatitis B surface antigen (HBsAg)
87341	Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; hepatitis B surface antigen (HBsAg) neutralization
87490	Chlamydia trachomatis, direct probe technique
87491	Chlamydia trachomatis, amplified probe technique
87590	Neisseria gonorrhoea, direct probe technique
87591	Neisseria gonorrhoea, amplified probe technique
87592	Neisseria gonorrhoea, quantification
87653	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group B, amplified probe technique
87800	Infectious agent detection by nucleic acid (DNA or RNA), multiple organisms; direct probe(s) technique
87802	Infectious agent antigen detection by immunoassay with direct optical (ie, visual) observation; Streptococcus, group B
87810	Infectious agent antigen detection by immunoassay with direct optical (ie, visual) observation; Chlamydia trachomatis
87850	Infectious agent antigen detection by immunoassay with direct optical (ie, visual) observation; Neisseria gonorrhoeae
G0306	Complete CBC, automated (Hgb, HCT, RBC, WBC, without platelet count) and automated WBC differential count

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Code Number	Code Description
G0307	Complete (CBC), automated (Hgb, HCT, RBC, WBC; without platelet count)
G0432	Infectious agent antibody detection by enzyme immunoassay (EIA) technique, HIV-1 and/or HIV-2, screening
G0433	Infectious agent antibody detection by enzyme-linked immunosorbent assay (ELISA) technique, HIV-1 and/or HIV-2, screening
G0435	Infectious agent antigen detection by rapid antibody test of oral mucosa transudate, HIV-1 or HIV-2, screening
G0472	Hepatitis C antibody screening, for individual at high risk and other covered indication(s)
S3652	Saliva test, hormone level; to assess preterm labor risk

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Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

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IX. Review/Revision History

Effective Date	Summary
05/15/2022	Initial Policy Implementation