Updated Guidance:
Prevention and Management of Perinatal Group B Streptococcus Infection

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- Group B Streptococcus (GBS) remains the most common cause of neonatal early-onset sepsis among term infants and a major cause of late-onset sepsis among both term and preterm infants.

- The American Academy of Pediatrics and the American College of Obstetricians and Gynecologists published separate but aligned guidelines in ٢٠١٩ and ٢٠٢٠ for the prevention and management of perinatal GBS disease. Together, these replace prior consensus guidelines provided by the Centers for Disease Control and Prevention.

- Maternal intrapartum antibiotic prophylaxis based on antenatal screening for GBS colonization remains the **primary recommended approach to prevent perinatal GBS disease**, though the optimal window for screening is changed to ٣٦ ٠/٧ to ٣٧ ٦/٧ weeks of gestation rather than beginning at ٣٥ ٠/٧ weeks' gestation.

- **Penicillin**, **ampicillin**, or **cefazolin** are recommended for prophylaxis, with clindamycin and vancomycin reserved for cases of significant materal penicillin allergy .

- Pregnant women with a history of penicillin allergy are now recommended to undergo skin testing, because confirmation of or delabeling from a penicillin allergy can provide both short and long-term health benefits.

- Aligned with the AAP recommendations for evaluating newborns for all causes of early onset sepsis, separate consideration should be given to infants born at less than ٣٥ weeks' and more than or equal to ٣٥ weeks' gestation when performing GBS risk assessment.

- **Empiric antibiotics are recommended for infants at high risk for GBS early-onset disease.**

- Although intrapartum antibiotic prophylaxis is effective in preventing GBS early-onset disease, currently there is **no approach for the prevention of GBS late-onset disease.**

- Streptococcus agalactiae, or group B Streptococcus (GBS), is a facultative gram-positive organism commonly found in the adult gastrointestinal and genitourinary microbiome.

- vaginal-rectal colonization rates varying by age, race, and geographic location.

- GBS continues to be identified as the most common cause of neonatal early-onset sepsis (EOS; blood or cerebrospinal fluid culture-confirmed infection occurring from birth to ۶ days of age) among infants born at term (>,= ۳۷ weeks') gestation. (۴۵%-۵۰%)

GBS is also isolated in approximately ۱۵% to ۲۵% of all culture-confirmed EOS cases in preterm infants.

- Approximately ۵۰% of all newborns of women colonized with GBS will themselves become colonized during birth in the absence of preventive measures, and of those, ۱% to ۲% will develop invasive disease.

- The incidence of GBS early-onset disease (EOD) has declined with the use of intrapartum antibiotic prophylaxis (IAP), from ١/٨ **cases per** ١’٠٠٠ live births in ١٩٩٠ to ٠/٢٥ **cases per** ١’٠٠٠ live births in ٢٠١٨.

- **CDC** first published consensus guidelines for the prevention of perinatal GBS disease in ١٩٩٦, recommending either :
- ١) universal screening of pregnant women for GBS colonization between ٣٥ and ٣٧weeks’ gestation and administration of IAP to women with positive GBS screening results.

Or

٢) the use of clinical risk factors for perinatal GBS disease to determine indication for IAP.

- The CDC revised these guidelines in ٢٠٠٢ based on active surveillance demonstrating that the antenatal screening approach was more effective in preventing GBS EOD compared to the risk factor–based approach.

- **The superiority of antenatal screening–based IAP was reaffirmed in the CDC’s revised ٢٠١٠ guidelines.**

In ٢٠١٧, CDC officials indicated a desire to transition further leadership in perinatal GBS prevention to the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP).

These professional organizations collaborated and released updated guidelines in June and July ٢٠١٩, with additional ACOG revisions in April ٢٠٢٠, reflecting changing practice standards based on evolving epidemiology and newly published evidence.

NEONATAL GBS DISEASE

- **GBS Early-onset Disease :**

GBS EOD is defined as isolation of GBS from blood, cerebrospinal fluid, or other normally sterile sites in a newborn infant **from birth to ۶** days of age.

- Among term infants, the most common pathogenesis of GBS EOD **is vertical transmission from a colonized pregnant woman ,** primarily during labor or after rupture of membranes .(ROM)

- Vertical transmission occurs via ascending colonization of the uterine compartment, and subsequent colonization and infection of the fetus and/or fetal aspiration of infected amniotic fluid.

- The pathogenesis of GBS EOD and timing of transmission is less certain among preterm infants; although vertical transmission can occur in a similar fashion, maternal GBS colonization and intraamniotic infection may contribute to the pathogenesis of preterm delivery.

✓ Most GBS EOD presents clinically as bacteremia without a focus, with the organism isolated from blood in ٩٩% of cases.

✓ Clinical meningitis is identified in approximately ١٠% of cases, with bacteria isolated from the cerebrospinal fluid in approximately ٣% of affected newborns.

✓ Studies of human protective immunity to GBS infection have focused on the role of serotype-specific antibody directed to capsular polysaccharide; the risk of neonatal infection is decreased in the presence of maternally derived, transplacentally acquired, type-specific antibody.

- **GBS Late-onset Disease :**

GBS LOD is defined as isolation of group B Streptococcus from a normally sterile site ٧ to ٨٩ days after birth.

- The pathogenesis of GBS LOD is debated, but generally thought to be the invasion of normally sterile sites preceded by infant pharyngeal or gastrointestinal colonization.

- Neonatal colonization may result from maternal vertical and horizontal transmission as well as from horizontal transmission from nonmaternal sources.
- It remains unclear whether breast milk is a potential source of horizontal transmission to the infant or simply a marker for high levels of neonatal nasopharyngeal GBS colonization.

- GBS is isolated from blood cultures in ٩٣% of LOD cases but additional organ involvement is more frequently observed in LOD compared with EOD cases.
- Meningitis is diagnosed in ٣٠% of cases, with GBS isolated from cerebrospinal fluid in ٢٠% of LOD cases.
- In addition, GBS LOD may involve bone, joint, or soft tissue infection.
- **Serotypes Ia , Ib , and II-V account for ٩٩/٧% of GBS LOD in the United States, whereas serotype III alone accounts for ٥٦% of cases.**

Disparities in Neonatal GBS Disease

- Both GBS EOD and LOD disproportionately affect prematurely born infants and infants born to black women in the United States.

Among cases identified in CDC surveillance studies from ٢٠٠٦-٢٠١٥, a quarter of GBS EOD cases and ٤٠% of GBS LOD cases occurred in infants born at **less than ٣٧ weeks' gestation.**

- The absolute incidence per ١'٠٠٠ live births for **EOD** is roughly ٣ times higher among preterm versus term infants, and the incidence of **LOD** is ٦ times higher among preterm versus term infants.

- Mortality is also disproportionately greater among those born preterm.

(**EOD** case-fatality was **٢٫١%** among term infants and **١٩٫٢%** among preterm infants whereas **LOD** case-fatality was **٣٫٤% and ٧٫٨%** among term and preterm infants, respectively.)

- **Racial disparities in GBS EOD**, with rates being ١٫٥ to ٣ times higher among black versus nonblack infants, among both term and preterm infants born before ٣٧ weeks of gestation.

- These differences have not been explained by variations in antenatal screening or administration of IAP.

- GBS LOD rates were also roughly ٣ times higher among black versus nonblack infants in ٢٠٠٦-٢٠١٥ surveillance, but this finding was not adjusted for gestational age at birth.

UPDATED OBSTETRIC GUIDANCE

- Background :

- The administration of antibiotics to laboring women can decrease the occurrence of GBS EOD.

- **IAP is hypothesized to prevent GBS EOD by ٣ mechanisms:**

١) by temporarily decreasing the burden of maternal GBS colonization

٢) by preventing fetal or newborn colonization of surfaces and mucus membranes

٣) by reaching blood levels above minimum inhibitory concentration for GBS in newborns

The pharmacokinetics and pharmacodynamics of this observation have been addressed in a number of studies using **ampicillin and penicillin.**

Fewer studies have addressed the actions of **cefazolin, clindamycin, and vancomycin**.

IAP with all ٥ of these antibiotics can rapidly decrease maternal vaginal GBS colony counts.

- Ampicillin, penicillin, and cefazolin can quickly cross the placenta, and are subsequently excreted by the fetal kidney, resulting in antibiotic levels in amniotic fluid, cord blood, and neonatal blood above the minimal inhibitory concentration needed to kill GBS within ١ to ٢ hours after maternal administration.

- IAP is thus hypothesized to derive from a combination of decreased exposure to GBS during labor and delivery and decreased colonization of the fetus and newborn, as well as some potential efficacy in clearing low-level fetal bacteremia.

✓ Studies addressing the impact on neonatal surface colonization with GBS after birth, as well as epidemiologic analyses of efficacy, suggest that optimal benefit is achieved when penicillin, ampicillin, or cefazolin are administered at least ٤ hours before delivery.

- IAP is conceptualized as prophylaxis—interrupting the pathogenesis of GBS EOD— and should be differentiated from the administration of intrapartum antibiotics as maternal and fetal treatment when intra-amniotic infection is suspected or confirmed.

- Studies comparing the efficacy of administering GBS IAP based on antenatal culture results versus the administration of IAP only when risk factors for infection develop during labor, ***have established that antenatal screening–based IAP is the more effective strategy.***

- The prophylactic administration of IAP based on antenatal GBS vaginal-rectal culture results has formed the core of perinatal GBS prevention guidance since the CDC ٢٠٠٢ guidelines were published.
- This core recommendation is unchanged in the ACOG ٢٠٢٠ guidance.

Timing of Antenatal Culture

- GBS colonization of the maternal gastrointestinal and genitourinary flora is transient and changeable.
- The correlation between antenatal GBS vaginal-rectal culture results and colonization status at the time of presentation for delivery is better the closer the antenatal culture is performed relative to delivery.
- Further, regardless of the timing of antenatal culture, the correlation decreases with passing time such that negative culture results are considered **unreliable if performed more than ♢ weeks** before delivery.

- Because GBS IAP is recommended for all women with onset of preterm labor (before ٣٧ ٠/٧ weeks' gestation), the new ACOG recommendation is that routine antenatal screening is optimally timed **between ٣٦ ٠/٧ and ٣٧ ٦/٧** weeks of gestation rather than beginning at ٣٥ ٠/٧ weeks' gestation.

- This new time frame provides a ٥-week window for valid culture results that includes births occurring up to ٤١ ٠/٧ weeks' gestation.

- This change addresses the epidemiologic observation that in an era of good compliance with antenatal screening and administration of IAP, most cases of persistent GBS EOD are seen among term infants born to women with negative antenatal screening culture results.

- **Nucleic acid amplification tests (NAAT)** are currently available to detect GBS, and their performance is validated in numerous published studies.
- The performance of NAAT is equivalent to culture-based screening for GBS detection if the specimen has been incubated in an enrichment broth for ١٨ to ٢٤ hours.

- The sensitivity of NAAT without an enrichment broth step is suboptimal.

- Aligned with the CDC ٢٠١٠ recommendations, ACOG ٢٠٢٠ continues to endorse the use of NAAT on specimens that first undergo incubation in enrichment broth, to maximize detection as well as to allow for subsequent antibiotic susceptibility testing for penicillin-allergic women.
- When available, ACOG ٢٠٢٠ endorses the use of rapid, point-of- care NAAT for the care of women who present in labor with unknown GBS status.

Pregnant women should be screened for GBS colonization by vaginal-rectal culture

Pregnant women should be screened for GBS colonization by vaginal-rectal culture

- Between 36 0/7 and 37 6/7 weeks of gestation
- With onset of labor <37 0/7 weeks' gestation with or without preterm ROM
- With occurrence of preterm, prelabor ROM
- If they remain pregnant >5 weeks after a prior negative GBS culture

Indications for IAP

- ACOG ٢٠٢٠ endorses the same basic indications for GBS IAP with ١ addition.

- **ACOG ٢٠٢٠ recommends that IAP be considered for a woman who presents in labor with current unknown GBS status if she is known to have had GBS colonization in a previous pregnancy, before the development of intrapartum risk factors for infection.**

Pregnant women should be administered IAP in labor

Pregnant women should be administered IAP in labor
• If colonized with GBS as identified on antenatal culture
• With GBS bacteriuria during current pregnancy
• With history of a previous infant with GBS disease
• With positive intrapartum NAAT result
• At ≥37 0/7 weeks' gestation with unknown GBS status; or with negative GBS status obtained >5 weeks prior; or with negative intrapartum NAAT result ***if*** maternal temperature ≥100.4°F (≥38°C) ***or*** ROM ≥18 hours occurs during labor
• At ≥37 0/7 weeks' gestation with unknown GBS status, IAP may be considered if woman is known to have been GBS positive in prior pregnancy
• At <37 0/7 weeks' gestation with unknown GBS status
Notes: Standard obstetric antibiotic regimens for preterm, prelabor ROM should include coverage for GBS IAP if GBS status is unknown or positive. Women undergoing planned cesarean delivery before the onset of ROM or labor do not require GBS IAP regardless of GBS status

Penicillin Allergy Testing

- Up to ١٠% of pregnant women report an unconfirmed history of penicillin allergy, but true, Ig E-mediated hypersensitivity can be ruled out in more than ٩٠% of such persons if formal allergy skin testing is performed.

- The opportunity to “delabel” a pregnant woman with an unconfirmed history of penicillin allergy provides long-term health care management advantages beyond the opportunity to administer b-lactam–based IAP.

- ACOG ٢٠٢٠ confirms the safety of skin testing during pregnancy and endorses its use for all pregnant women with an unconfirmed allergy history.
- ACOG ٢٠٢٠ also provides new guidance for the history-based clinical determination of low- and high-risk for penicillin anaphylaxis as well as for identification of histories that suggest severe but rare non–IgE-mediated reactions (such as Stevens-Johnson syndrome).

Vancomycin Administration

- Vancomycin is the antibiotic of last resort for women with confirmed or unconfirmed high-risk penicillin allergy **if the woman is colonized with clindamycin-resistant GBS.**
- Vancomycin **is also recommended if the susceptibilities are unknown**, because up to ۴۷% of GBS cases in the United States are resistant to clindamycin.
- However, as summarized in ACOG ۲۰۲۰, the transplacental pharmacokinetics and pharmacodynamics of vancomycin have been informed by conflicting data.
- ACOG ۲۰۲۰ recommends changes to vancomycin administration to pregnant women, including the use of weight-based doses given at shorter intervals to optimize transplacental drug transfer.

GBS and Obstetric Procedures

- ACOG ٢٠٢٠ directly addresses GBS colonization and obstetric interventions such as membrane sweeping or mechanical cervical ripening to initiate labor ; artificial ROM to augment labor progression; vaginal examinations and intrauterine monitoring to assess labor progression; and water immersion during labor

- ACOG ٢٠٢٠ notes that overall, specific data to inform the relative risks of these procedures in GBS-positive (vs GBS-negative) women are limited, and counsels that they each be undertaken as otherwise clinically indicated, with administration of appropriate IAP.

IAP Regimens

- Penicillin G: Preferred
- Ampicillin: Acceptable alternative to penicillin G
- Cefazolin: Women with low-risk penicillin allergy[a]
- Clindamycin: Women with high-risk penicillin allergy[a] if colonizing isolate is susceptible to clindamycin
- Vancomycin: Women with high-risk penicillin allergy[a] if colonizing isolate is resistant to clindamycin ***or*** susceptibility is unknown

UPDATED NEONATAL GUIDANCE

- Background :

- Over ٢٠ years have passed since the first clinical and pathologic descriptions of neonatal early-onset bacterial infection focused on the identification of factors that signal risk of this potentially fatal complication of birth.

- Such risk factors derive from an understanding of the pathogenesis of EOS as primarily resulting from ascending colonization of the uterine compartment and fetus with maternal genitourinary and gastrointestinal flora, with colonization and pathologic infection of the fetus and newborn.

- factors that can be used to identify newborns at high enough risk of GBS specific (and all-bacterial cause) early infection to warrant laboratory investigation and empiric antibiotic treatment :
- Maternal age
- maternal race
- obstetric interventions during labor
- indications of intrauterine infection (including the obstetric diagnosis of chorioamnionitis, “foul-smelling” amniotic fluid, intrapartum maternal fever, and maternal and fetal tachycardia),
- duration of ROM
- presence of meconium- stained fluid
- GBS colonization
- gestational age at birth
- twin gestation
- neonatal instability at birth
- have all been associated with increased risk, though many of these factors are not independent predictors of neonatal infection.

- Recommendations for newborn evaluation contained in the CDC ١٩٩٦, ٢٠٠٢, and ٢٠١٠ GBS prevention documents focused on the categorical use of single specific risk factors and did not distinguish between term and preterm newborns.

Although motivated by the aim of preventing sepsis-associated morbidity and mortality, these approaches have been associated with high rates of laboratory testing and empiric antibiotic administration to term infants compared with the current incidence of confirmed disease and antibiotic administration to the majority of preterm newborns.

Chorioamnionitis as a Risk Factor for GBS EOD

- Infants born to women diagnosed with chorioamnionitis are at elevated risk for EOS.
- However, the subjective nature of this diagnosis has presented difficulties for obstetric and neonatal clinicians, particularly among women laboring at term gestation.

- ACOG recently opted to transition away from use of the term chorioamnionitis to “intra-amniotic infection.”

- ACOG highlights the uncertainty in this diagnosis and now provides classifications for definitive and suspected intra-amniotic infection:

✓ A definitive diagnosis of intra-amniotic infection is made with amniotic fluid analysis and/or culture, or with placental histopathologic examination.

✓ Intra-amniotic infection is suspected on the basis of a single maternal intrapartum temperature greater than ۱۰۲٫۲°F (۳۹٫۰°C), or in cases of maternal temperature of ۱۰۰٫۴°F to ۱۰۲٫۰°F (۳۸٫۰°C–۳۸٫۹°C) occurring in combination with maternal leukocytosis, purulent cervical discharge, or fetal tachycardia.

- Isolated maternal fever is defined as maternal temperature of ١٠٠٫٤°F to ١٠٢٫٠°F (٣٨٫٠°C–٣٨٫٩°C) without associated signs and can also signal evolving intra-amniotic infection.

- ACOG recommends the administration of intrapartum antibiotics when there is concern for suspected or confirmed intra-amniotic infection or isolated maternal fever.

- AAP ٢٠١٩ uses the highest maternal intrapartum temperature in recommended risk assessment algorithms among infants born at ٣٥ ٠/٧ weeks' or greater gestation, rather than the more subjective obstetric clinical diagnosis.

- Among those born at less than or equal to ٣٤ ٦/٧ weeks' gestation, AAP ٢٠١٩ uses the term "any concern for intra-amniotic infection" because the signs and symptoms may be subtle and complex among women at risk for preterm delivery.

Strategies for GBS EOD Risk Assessment Among Infant Born at ≥٣٥ Weeks' Gestation

- CDC ٢٠١٠ provided a single strategy for GBS EOD risk assessment, based on the categorical presence or absence of specific single risk factors as well as the adequacy of indicated GBS IAP.

- Studies addressing the clinical use of CDC ٢٠١٠ guidance demonstrate that approximately ٥% to ١٠% of infants born at ٣٥ to ٣٦ weeks' gestation received empiric antibiotics using this approach.

- AAP ٢٠١٩ follows the AAP ٢٠١٨ revised guidance on the care of infants at risk for all-bacterial cause EOS and offers ٣ possible approaches.

each approach has its advantages and disadvantages,

- **Categorical Risk Assessment :**
- Modeled on the CDC ٢٠١٠ guidelines, the revised algorithm removes reliance on the obstetric diagnosis of "chorioamnionitis" and uses a cutoff value for maternal intrapartum temperature aligned with the ACOG ٢٠١٧ recommendations on intra-amniotic infection.

Categorical Risk Assessment
• Thresholds for risk factors are used to identify infants at increased risk
• Risk factors include
o Signs of newborn clinical illness (no guidance provided; determine details locally)
o Maternal intrapartum temperature ≥100.4°F (≥38.0°C)
o Inadequate IAP in a GBS-colonized mother
• Blood culture and empiric antibiotics recommended for infants with signs of clinical illness or maternal intrapartum temperature ≥100.4°F
• Clinical observation for 36–48 hours after birth recommended for infants born in the setting of inadequate IAP in the absence of other risk factors

- Blood culture and empiric antibiotic therapy are recommended for infants who are clinically ill and for infants born to mothers with an elevated intrapartum temperature.

- Clinical observation for ٣٦ to ٤٨ hours after birth is recommended for infants born with inadequate maternal IAP; this timing was shortened from a full ٤٨ hours to allow for local discretion in discharge timing.

- An advantage of this approach is that it is familiar to most neonatal clinicians and has been studied extensively.
- It is limited by poor discrimination and wider use of empiric antibiotics compared with other approaches.

Multivariate Risk Assessment (Neonatal Early-Onset Sepsis Calculator)

- **Multivariate Risk Assessment :**
- The neonatal early-onset sepsis calculator is available as a web-based online tool (https://neonatalsepsiscalculator.kaiserpermanente.org).

- The “calculator” is a combination of ٢ multivariate prediction models developed for estimating risk of all bacterial causes of EOS, not only GBS EOD, with clinical recommendations for observation, blood culture, and empiric antibiotics provided at specific levels of estimated risk.

- The calculator provides individualized estimates for the baseline probability of infection using variables known at birth.
- The newborn’s clinical status for the first ٦ to ١٢ hours after birth can be used to obtain updated risk estimates; clinical criteria for illness are provided on the calculator website.

- Advantages of this approach are that it provides more individualized management and overall lower use of empiric antibiotics.

- A limitation is that it requires that centers develop workflows for risk calculation and newborn observation.

Multivariate Risk Assessment (Neonatal Early-Onset Sepsis Calculator)
• Available at https://neonatalsepsiscalculator.kaiserpermanente.org
• Calculator combines factors known at birth with newborn clinical condition to provide estimated risk of early-onset infection
• Factors considered:
o Gestational age at birth
o Highest maternal intrapartum temperature
o Duration of ROM
o Maternal GBS status
o Type and duration of IAP (clindamycin and vancomycin given for any duration should not be considered adequate IAP)
o Newborn clinical condition (detailed guidance is provided)
• Website provides recommended clinical actions (enhanced observation, blood cultures, empiric antibiotics) at different levels of estimated risk
o Evolving clinical condition can be used to update the risk estimates over the first 6-12 hours after birth
o Centers may use these recommendations or locally determine actions at specific levels of risk

- **Risk Assessment Based on Enhanced Observation :**
- With this risk assessment approach, infants are categorized as at risk or not at-risk for GBS EOD (Table ٣), but are evaluated and administered empiric antibiotics only if they are ill appearing at birth or develop signs of illness after birth.

Risk Assessment Based on Enhanced Observation
• Risk factors include
o Signs of newborn clinical illness (no guidance provided; determine details locally)
o Maternal intrapartum temperature ≥100.4°F (≥38.0°C)
o Inadequate IAP in a GBS-colonized mother
• If infant has signs of clinical illness, empiric antibiotics are administered
• In all other cases, regardless of the risk factors and circumstance of birth and IAP, infants are followed by close, serial clinical assessment and administered empiric antibiotics if signs of illness develop

- This approach requires serial, structured clinical assessments from birth through ٣٦ to ٤٨ hours of age. Small cohort studies demonstrate that this approach will expose fewer infants to empiric antibiotic treatment compared with a categorical or multivariate risk assessment approach.

- An advantage of this risk assessment is the potentially low rate of empiric antibiotic administration.

- Disadvantages of this approach include the need for centers to define what constitutes “ill-appearing” and to develop care and documentation structures for close serial reassessments.

- If using this approach, centers must dispense with the concept of “missing cases” of GBS EOD and accept that the identification of illness in a previously well-appearing infant is an anticipated outcome.

Risk Assessment for Infants born at <٣٥ Weeks' Gestation

- The CDC ٢٠١٠ guidelines recommended evaluation and empiric antibiotic administration for all newborns with "signs of neonatal sepsis."
- Because of the overlap between the physiologic instability characteristic of preterm infants and signs of neonatal sepsis, large proportions of preterm infants (particularly those born with extremely low birthweight) are administered empiric antibiotics at birth for risk of GBS EOD and all causes of bacterial EOS.
- AAP ٢٠١٩ recommends categorizing risk among preterm infants using delivery characteristics.

- Infants delivered in the setting of :
- preterm labor
- prolonged ROM
- intra-amniotic infection
- cervical insufficiency

or otherwise unexplained in utero fetal distress should be considered at higher risk for GBS EOD and should be given empiric antibiotics

Infants are considered at high risk of GBS disease and other causes of early-onset infection, if delivered in the setting of:
• Preterm labor
• Prelabor, preterm ROM
• Concern for intra-amniotic infection
• Cervical insufficiency

- Infants delivered preterm solely because of maternal indications, such as preeclampsia or intrauterine growth restriction, and delivered via cesarean section before the onset of labor, with ROM at the time of delivery, can be considered to be at low risk for GBS EOD regardless of IAP administration.

- The rationale for this recommendation is that these infants are neither delivered because of concern for intra-amniotic infection nor subject to the risk from ascending colonization and infection provided by labor and vaginal delivery.

- AAP ٢٠١٩ recommends that such infants can be treated without initiating empiric antibiotics.

❑ Infants delivered preterm vaginally or via cesarean section for maternal or fetal indications, but after induction of labor and/or ROM before delivery, present a challenge for GBS EOD risk assessment.

- Infants delivered preterm vaginally or via cesarean section for maternal or fetal indications, but after induction of labor and/or ROM before delivery, present a challenge for GBS EOD risk assessment.

- Although not delivered because of maternal infection, they are subject to the risks of labor and vaginal delivery.

- ✓ AAP ٢٠١٩ recommends that such preterm **infants be considered at high risk for GBS** EOD if GBS IAP is inadequate (when indicated), or if obstetric concern for intra-amniotic infection arises during the course of induced labor and delivery, or if the infant has significant respiratory or cardiovascular instability after birth.

Infants are considered at low risk of GBS disease and other causes of early-onset infection, if delivered with all of the following:

Infants are considered at low risk of GBS disease and other causes of early-onset infection, if delivered with all of the following:
• For maternal/fetal non–infection-related indications *and*
• By cesarean section *and*
• No labor or attempts to induce labor *and*
• ROM at the time of delivery

Infants are considered at high risk of GBS disease and other causes of early-onset infection if:

Infants are considered at high risk of GBS disease and other causes of early-onset infection if:

- Delivered vaginally or by cesarean delivery, with induction of labor or ROM before delivery for maternal/fetal non–infection-related indications *and*
- Indicated, adequate GBS IAP was not given *or*
- Infant has respiratory or cardiovascular instability after birth

In preterm infants at high risk, blood cultures should be performed and empiric antibiotics administered. Preterm infants at lower risk may be cared for without blood cultures or empiric antibiotics, at the discretion of the care team

Empiric and Definitive Antibiotic Therapy

- Unchanged from CDC ٢٠١٠, AAP ٢٠١٩ endorses the use of ampicillin and an aminoglycoside as empiric antibiotic treatment for suspected GBS EOD, because GBS almost universally remains susceptible to b-lactam antibiotics.

- that broader spectrum empiric therapy should be considered when there is strong clinical concern for ampicillin-resistant infection, especially among very preterm and/or critically ill newborns.

- The evaluation and empiric treatment for GBS LOD falls into the general guidance for evaluation of the
- febrile young infant among otherwise healthy infants in the community.

- Although the approach to such infants may have local variations, AAP ٢٠١٩ guidance endorses the use of ampicillin and ceftazidime among infants of age ٨ to ٢٨ days, and ceftriaxone for those ٢٩ to ٩٠ days of age.
- In both instances, empiric vancomycin should be added if there is concern for meningitis.
- Among those continuously hospitalized in the NICU, empiric antibiotic choice for infants beyond ٧٢ hours of age is informed by local microbiology and individual infant technicalities of care but should include agents active against GBS.

Definitive Treatment for Invasive Neonatal GBS Disease
• Penicillin G is the preferred antibiotic for definitive treatment of early-onset and late-onset neonatal GBS disease; ampicillin is an acceptable alternative
• Duration of therapy is based on site of GBS isolation (bacteremia vs meningitis vs organ-specific infection)
• Dosing is based on gestational age at birth and postnatal age at treatment; see Table 1 in the AAP 2019 document for details

TABLE 2. **Comparison of CDC 2010 and ACOG 2020/AAP 2019 GBS Prevention Guidance**

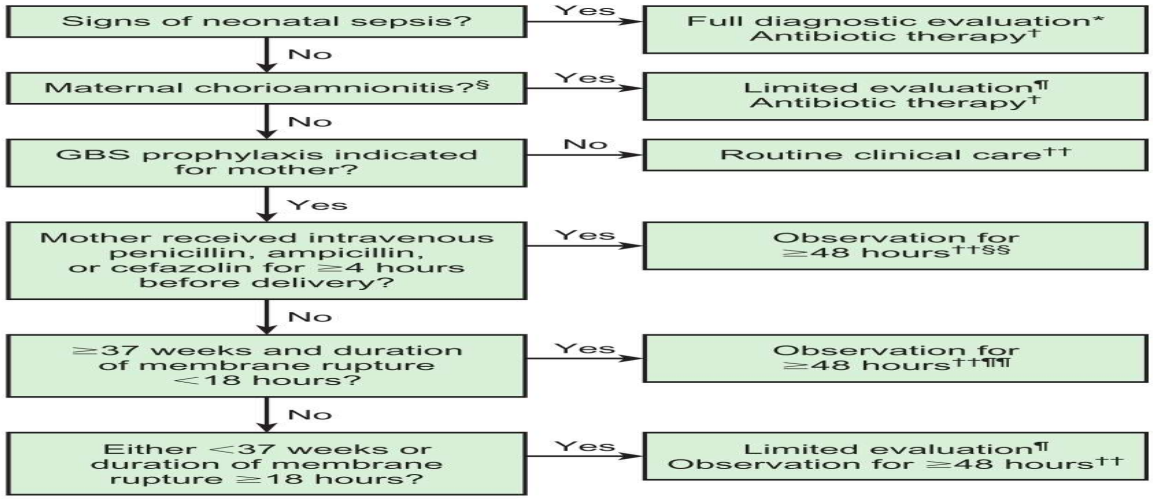
CDC 2010	ACOG 2020
Differences	
Recommended timing for antenatal GBS screening culture at 35 0/7–37 6/7 weeks' gestation	Recommended timing for antenatal GBS screening culture changed to 36 0/7–37 6/7 weeks' gestation
No recommendation regarding confirmation of reported penicillin allergy	Pregnant women with any history of allergy to penicillin may undergo skin testing to confirm or refute penicillin allergy
For pregnant women with history of penicillin allergy: Request antibiotic susceptibility testing on laboratory requisitions for antenatal GBS screening cultures	For pregnant women with history of penicillin allergy: Clearly state the penicillin allergy on laboratory requisitions for antenatal GBS screening cultures to ensure antibiotic susceptibility testing
If a pregnant woman presents in labor at ≥37 0/7 weeks' gestation with unknown GBS status, IAP should be administered if intrapartum risk factors are present	If a pregnant woman presents in labor at ≥37 0/7 weeks' gestation with unknown GBS status, IAP should be administered if intrapartum risk factors are present; IAP may also be considered if the woman was GBS positive in a prior pregnancy
When indicated, 1 g of vancomycin should be administered intravenously every 12 hours	When indicated, vancomycin should be administered over 1–2 hours, based on weight and baseline renal function (20 mg/kg intravenously every 8 hours; maximum of 2 g per single dose)
CDC 2010	ACOG 2019

CDC 2010	ACOG 2019
Differences	
Full newborn diagnostic evaluation includes (a) blood culture; (b) CBC with WBC differential and platelets at birth, and/or at 6–12 hours of age; (c) lumbar puncture; and (d) chest radiograph (if indicated) *Limited* newborn diagnostic evaluation includes (a) blood culture and (b) CBC with WBC differential and platelets at birth, and/or at 6–12 hours of age	CBC with WBC differential and platelets are no longer routinely recommended as part of the newborn diagnostic evaluation for GBS EOD, because of poor sensitivity and modest likelihood ratios for predicting early-onset infection
Full or limited newborn diagnostic evaluation for GBS disease should be performed and newborn empiric antibiotics administered if: (a) newborn has signs of sepsis (full) (b) maternal chorioamnionitis is present (limited) (c) inadequate GBS IAP was given and infant is born <37 0/7 weeks' gestation (limited) *or* ROM ≥18 hours (limited)	Separate risk stratification strategies should be used for infants based on gestational age: • *Infants born ≥35 weeks' gestation*: 1 of 3 possible approaches are recommended—categorical risk assessment, multivariate risk assessment, or risk assessment based on enhanced observation • *Infants born <35 weeks' gestation*: Management should be based on circumstances of preterm delivery
Maternal chorioamnionitis diagnosis is made based on obstetric clinical judgment	Among infants born ≥35 weeks' gestation, the obstetric clinical diagnosis of maternal chorioamnionitis is replaced by consideration of highest maternal intrapartum temperature
No detailed discussion of GBS late-onset disease epidemiology, risk assessment, or empiric therapy	Includes discussion of GBS late-onset disease epidemiology and risk assessment

CDC 2010	AAP 2019
No recommendations for definitive therapy for GBS disease	Provides a table with dosing guidelines for treatment of GBS bacteremia and meningitis with ampicillin and penicillin G, based on gestational age at birth and postnatal age during treatment.

Recommendations Common to CDC ٢٠١٠, AAP ٢٠١٩, and ACOG ٢٠٢٠

Recommendations Common to CDC 2010, AAP 2019, and ACOG 2020
• Optimal management is based on antenatal GBS vaginal-rectal culture results
• Antenatal GBS vaginal-rectal culture is not necessary for women diagnosed with GBS bacteriuria during pregnancy or for women with a prior infant with GBS disease; these women should be administered GBS IAP
• Women undergoing planned cesarean delivery before the onset of membrane rupture or labor do not require GBS IAP regardless of GBS status
• Centers able to perform rapid, point-of-care nucleic acid amplification tests for GBS may use this technology for the care of pregnant women who present in labor with unknown GBS status and no additional risk factors
• Risk factors used to administer GBS IAP to pregnant women with unknown GBS status include preterm gestation (<37 0/7 weeks) with prelabor ROM and/or preterm labor; intrapartum maternal temperature ≥100.4°F (≥38°C); or ROM ≥18 hours
• Penicillin, ampicillin, or cefazolin given >4 hours before delivery is considered adequate IAP; clindamycin and vancomycin given for any duration should not be considered as adequate IAP for the purpose of newborn risk assessment
• Penicillin G is the recommended antibiotic for definitive treatment of confirmed GBS disease; ampicillin is acceptable alternative



* Full diagnostic evaluation includes a blood culture, a complete blood count (CBC) including white blood cell differential and platelet counts, chest radiograph (if respiratory abnormalities are present), and lumbar puncture (if patient is stable enough to tolerate procedure and sepsis is suspected).

† Antibiotic therapy should be directed toward the most common causes of neonatal sepsis, including intravenous ampicillin for GBS and coverage for other organisms (including *Escherichia coli* and other gram-negative pathogens) and should take into account local antibiotic resistance patterns.

§ Consultation with obstetric providers is important to determine the level of clinical suspicion for chorioamnionitis. Chorioamnionitis is diagnosed clinically and some of the signs are nonspecific.

¶ Limited evaluation includes blood culture (at birth) and CBC with differential and platelets (at birth and/or at 6–12 hours of life).

†† If signs of sepsis develop, a full diagnostic evaluation should be conducted and antibiotic therapy initiated.

§§ If ≥37 weeks' gestation, observation may occur at home after 24 hours if other discharge criteria have been met, access to medical care is readily available, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

¶¶ Some experts recommend a CBC with differential and platelets at age 6–12 hours.

Fig. 211.4 Algorithm for secondary prevention of early-onset group B streptococcal disease among newborns. (*From Verani JR, McGee L, Schrag SJ, Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention: Prevention of perinatal group B streptococcal disease—revised guidelines from CDC 2010,* MMWR Recomm Rep *59[RR-10]:22, 2010.*)

functionally active type-specific antibody that was efficiently transported to the fetus. Vaccines containing GBS surface proteins have been considered as a means to provide protection against strains of multiple