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Quality Assurance Commission
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Prophylaxis of early-onset neonatal sepsis caused by group B streptococci

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Summary

Infections of newborns and small infants caused by serogroup B streptococci (GBS, "group B streptococci"), which occurred in Western industrialized nations with an incidence of ≥ 1/1000 live births before the introduction of preventive measures, can be divided into an early (90% of the cases) and a late form (10%) based on the time of their occurrence. The early form of GBS disease ("early-onset neonatal GBS [EOGBS] disease"), is acquired intrapartum and appears within 7 days after birth. It has a poor prognosis with a foudroyant course, high morbidity (sepsis, pneumonia, meningitis) and a mortality rate of 10-30% in premature newborns and 2-3% in term ones. The "late-onset neonatal GBS (LOGBS) disease" is acquired postpartum (after 7 days of age) and mostly manifests as meningitis. To prevent EOGBS disease, the most effective approach currently available is the administration of an intrapartum antibiotic prophylaxis based on a routine prenatal screening strategy. Intrapartum antibiotic prophylaxis reduces the incidence of EOGBS disease by 80-90%, but has no effect on the incidence of LOGBS disease.

Anal-vaginal colonization with GBS is detected in 10-30% of all pregnant women; Swiss data show a prevalence of 20%. Various international gynaecologic-obstetrical societies recommend general screening for anal-vaginal GBS colonization and prophylactic antibiotic administration intrapartum for all pregnant women who are tested positive and to those with unknown carrier status and risk factors for EOGBS disease. A few societies only propose antibiotic prophylaxis in the presence of risk factors (without universal screening).
Studies have shown that, in practice, antibiotics are administered more reliably on a screening basis than on a risk factor basis when indicated. In any case, a clear strategy is necessary in the care of women during pregnancy and childbirth in order to prevent GBS-related neonatal sepsis without increasing the risk of infections caused by other pathogens or promoting the development of resistance against antibiotics. The aim of this expert letter is to present and recommend a concept for screening and treatment and possible alternatives.

General screening of all pregnant women for GBS colonization at 35-37 weeks of gestation is recommended — Ia

The negative predictive value of an examination ≤ 5 weeks before delivery is 95-98%, but decreases with longer intervals. Screening must be performed with a vaginal and perianal smear (using the same swab), analysed in the lab by enrichment in a selective GBS broth culture medium to achieve a high sensitivity and specificity. Screening can be dispensed in patients with GBS bacteriuria in the current pregnancy, as well as in patients who gave birth to a child who suffered from GBS sepsis. In such cases, prophylactic administration of antibiotics intrapartum without prior screening is indicated. In hospitals with the possibility to perform a rapid PCR test in cases of rupture of membranes prior elective C-section, screening at 35-37 weeks can be omitted. Intrapartum antibiotic prophylaxis should be administrated in all pregnant women tested positive for GBS. Treatment of GBS colonisation before onset of labor or premature rupture of membranes (PROM) is not indicated, because vaginal colonisation mostly recurs after antibiotic treatment due to persistence of GBS in the rectum. Exceptions are at-risk pregnancies (e.g. active preterm labor or preterm PROM), where treatment against GBS should be initiated.

Practical implementation of the screening — Ia

Screening is performed by culture from a vaginal and perianal (or transanal) swab. No speculum examination is required, as GBS are mostly present in the outer third of the vagina, and a single swab can

Evidence-levels

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be used. Although some organisations recommend transanal rectal swab collection, new data show such a small difference that justifies avoiding the unpleasant transanal exam. Self-sampling can also be performed. The swabs shall be inserted in a tube containing transport medium and can be stored at room temperature of 4-22 C° for up to four days. For the microbiology laboratory, the sample should be clearly labelled with the order for GBS cultivation to enable further processing on selective special culture media, which can significantly improve the detection rate of GBS. In pregnant women with a history of allergy to penicillin, antibiotic sensitivity analysis should be requested from the laboratory, particularly with regard to clindamycin and erythromycin. To avoid overdiagnosis of penicillin allergy, PEN-FAST Score could be used in unclear cases. Data from Switzerland show a resistance rate of GBS to clindamycin of 14-28% and to erythromycin of up to 30%. Laboratories are required to detect erythromycin-induced resistance to clindamycin using the so-called D-test. This microbiological peculiarity is the reason for resistance testing against erythromycin, although this antibiotic is no longer recommended for GBS prophylaxis. Clindamycin may only be used in cases of severe penicillin allergy (see below) if sensitivity has been demonstrated. Sensitivity testing in women without penicillin allergy is not necessary, as all GBS are sensitive to penicillin. PCR-based tests (standard and rapid) are now available (caution: do not confuse with non-PCR-based rapid tests such as antibody-based ELISA tests) to detect GBS colonization with relatively high sensitivity and specificity at the onset of labor. PCR does not allow for resistance detection. For these reasons, culture in selective media is still the gold standard for screening of GBS colonization. However, rapid PCR tests are useful in cases of labor with unknown GBS status.	
Prophylactic antibiotics should be administered intravenously intra-partum in the following cases: • positive GBS result performed ≤ 5 weeks before delivery; • previous child suffering from GBS neonatal infection; • GBS bacteriuria in the current pregnancy; • unknown carrier status at the time of birth and one of the following risk factors: Premature birth < 37 weeks' gestation, rupture of membranes ≥ 18 h, intra-partum fever ≥ 38.0° C (if inflammation infection intrapartum syndrome is suspected, broad-spectrum antibiotics should be administered instead of GBS prophylaxis) • women with a GBS result more than 5 weeks ago (positive or negative) should be considered as unknown carrier status and therefore receive antibiotic prophylaxis only if above risk factors are present	Ia
Prophylactic administration of antibiotics for prevention of EOGBS sepsis is not recommended for: - positive GBS culture results and elective caesarean section (no contractions, no rupture of the membranes). Perioperative AB prophylaxis is indicated for maternal indication before the start of surgery or after delivery of the newborn (cord clamping). - asymptomatic pregnant woman (without signs of labor / rupture of membranes) with GBS colonization (high rate of recurrent GBS colonization and of resistances).	Ia
Choice and dosage of antibiotics (1st dose at the start of labor or premature rupture of membranes): • **1st choice: penicillin G**, 5 million E i.v., then 2.5-3 million E i.v. every 4 h, or **amoxicillin**, 2 g i.v., then 1 g i.v. every 4 hours. • **For mild penicillin allergy (erythema): cefazolin** 1 g i.v., then every 6 h 1 g i.v**.** • **In case of severe penicillin allergy (anaphylaxis, angioedema, respiratory distress, urticaria), proceed according to the resistance test: clindamycin** 0.9 g i.v., every 8 h. Erythromycin is no longer recommended. • **In case of resistance to clindamycin: vancomycin** 1g i.v. every 12 h until birth.	Ia
Start and duration of antibiotic administration intra-partum Prophylaxis is best effective if started at least 4 hours prior to birth. The first dose of antibiotics should therefore be administered as early as possible at the onset of labor or at rupture of membranes, and continued in the above mentioned fixed dosage interval until birth / cord clamping. Meanwhile, no obstetric intervention should be undertaken solely to achieve the 4-hour interval between first dose of antibiotics	Ia

and birth. The administration of antibiotics can be stopped after delivery unless there is a maternal indication to continue with antibiotics. In women with GBS colonisation, there is no contraindication for mechanical labor induction (with balloon catheter or dilapan) or bathtub use during birth.	
Management of newborns at risk Newborns who appear ill at birth or during clinical observation should be evaluated immediately by a neonatologist or pediatrician and treated empirically with antibiotics. Although evidence is limited, asymptomatic newborns are at risk for early-onset infection (e.g., intrapartum fever (>38°C) or incomplete maternal AB prophylaxis) from GBS colonized mothers with or without intrapartum AB prophylaxis, from mothers with unknown GBS status or from GBS-negative mothers with risk factors and should be closely monitored for 48 hours. Close clinical monitoring requires a documented description of the newborn's condition at least every 4 hours (general condition (vigilance, muscle tone), breathing (frequency, moaning, oxygen requirements), drinking feeding behaviour, skin coloration (mottled, icteric, cyanotic), (if applicable), capillary refill time (normal: < 2 - 3 seconds) and, temperature (conspicuous: <36.5° or <37.5°C, measure rectally if necessary) by an experienced nurse or midwife. This should preferably be done in the hospital.	IIb
Alternative concept: No general screening, prophylaxis based solely on risk factors No pregnancy screening and intrapartum antibiotics only administered if one of the following risk factors is present: Preterm birth < 37 0/7 weeks' gestation, rupture of membranes ≥ 18 h, fever ≥ 38.0° C (or other signs of infection at the time of birth), GBS neonatal disease in a prior child or GBS bacteriuria during current pregnancy. Comparing studies have however shown that this strategy is less effective for preventing EOGBS disease. Women who choose this strategy must be informed about this fact. We do not recommended this policy as shown less effective than the general screening strategy	IV
Procedure in premature rupture of membranes at term (≥ 37 0/7 weeks' gestation) Intrapartum antibiotics should be started immediately in cases of known GBS colonization, a history of a prior child affected by neonatal GBS sepsis or GBS bacteriuria during pregnancy. In addition, direct induction of labor should be initiated without delay within 6-12 hours. Studies have shown that this management reduces the prevalence of early-onset GBS neonatal sepsis from 15% to 2%.	Ib
Procedure in threatened premature labor (< 37 0/7 weeks' gestation) - IN CASES OF PPROM < 34 WEEKS: Give antibiotics effective against GBS for 7-10 days (according to local antibiotic recommendation, e.g. Azithromycin combined with Amoxicillin)	Ia
- In CASES OF PPROM after 34 0/7 weeks: Either expectant management or immediate delivery in patients with PROM between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation is a reasonable option. If expectant management is chosen, it should include careful monitoring of symptoms and signs of maternal infection, chorioamnionitis, and antepartum hemorrhage. Care should be individualized through shared decision making, and expectant management should not extend beyond 37 0/7 weeks of gestation. Latency antibiotics are not appropriate in this setting. This monitoring may be done best in a hospital setting.	Ib
Recommendations summary: **Early-onset GBS sepsis of the newborn is a potentially lethal condition, which can be prevented by intrapartum antibiotic prophylaxis** **GBS colonisation has a prevalence of 20-25% in pregnant women in Switzerland** **General screening of all pregnant women for GBS colonization at 35 0/7 - 37 0/7 weeks' gestation is recommended** **Screening is performed by culture from a vaginal and perianal swab**	

Intrapartum intravenous antibiotic prophylaxis is recommended in positive GBS result performed ≤ 5 weeks before delivery, previous child suffering from neonatal GBS disease, or GBS bacteriuria in the current pregnancy **For unknown carrier status at the time of labor (including result >5 weeks prior birth), prophylaxis is only recommended if one of the following risk factors exists: Premature birth < 37 0/7 weeks' gestation, rupture of membranes ≥ 18 h or intra-partum fever ≥ 38.0° C**	

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Classification of evidence levels

Ia	Evidence obtained from meta-analysis of randomised controlled trials.
Ib	Evidence obtained from at least one randomised controlled trial.
IIa	Evidence obtained from at least one well-designed controlled study without randomisation.
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study.
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grades of recommendations

A	Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)
B	Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)
C	Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

Good practice point

✓	Recommended best practice based on the clinical experience of the guideline development group.

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References with the authors

Conflict of interest declaration:
Authors: no conflict of interest

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