

## **Group B streptococcus in pregnancy and delivery**

Knut Hordnes  
Babill Stray-Pedersen  
Pål Øian  
Anne Karin Brigtsen

### **Definitions**

Group B streptococci (*Streptococcus agalacticae*; GBS) can cause serious infections in newborns in the form of sepsis and/or meningitis. GBS can also cause maternal infections as endometritis or wound infection after cesarean section.

**Early onset disease** starts within the first seven days of life. This condition is strongly related to maternal colonization, and is the most important clinical problem.

**Late onset disease** debuts from 7-89 days of life and does not have the same clear relationship with GBS colonization of the birth canal (see below), but is believed to have a nosocomial background.

Early GBS disease can be prevented by antibiotics to the mother, in contrast to late disease. This chapter is aimed at the reduction of early disease.

### **Etiology**

GBS colonization occurs in the vagina and rectum, with a slightly lower incidence of cervix. The intestine is considered to be a reservoir for the bacteria. Carrier status may be chronic, intermittent or transient.

In early disease, the fetus becomes infected with GBS by ascending infection after rupture of membranes or through fetal passage through the birth canal.

### **Epidemiology**

Among pregnant women is 10-35% carriers, and 50-70% of their children will be colonized by GBS at birth. Of these children will 1-2% develop so-called early GBS disease. Such serious infections occurs in different countries in 0.5-3 per 1000 live births, in Norway 0.5 per 1000 live births (1, 2). The mortality in newborns at term is now dropped to about 5% but is significantly higher in affected premature infants (3). For survivors of meningitis 30-50% have neurological defects. In Norway 0-4 children dies annually of early and late GBS disease (2).

### **Risk Factors**

Clinical risk factors are previous child with GBS disease, recurrent GBS urinary tract infection (UTI) or asymptomatic bacteriuria (ABU), preterm birth or preterm rupture of membranes, prolonged rupture of membranes, fever and /or other signs of intrauterine infection. Mothers with high GBS density in the birth canal and low amounts of antibody are at high risk of having an affected child (4).

## **Diagnostics**

GBS may be detected by culture in blood agar or by PCR methodology (5, 6). The sample is taken from the inner part vagina and rectum. It may be taken with the same swab, and by the woman herself. Indications and procedure depends on local conditions and the choice of method, see below.

## **Methods**

Two alternative methods are presented, the first method based on common culture diagnostics that are presently commonly available. The other method based on rapid diagnosis by PCR is considered to be better but is currently not available in most hospitals.

Important preconditions for the choice of method is

- Antibiotic treatment of pregnant carriers is ineffective: After 1-2 weeks of oral antibiotic treatment of pregnant carriers is 20-30% still carriers, and at birth is almost 70% of women were still colonized (7).
- Intravenous antibiotic prophylaxis in connection with childbirth is effective against early-onset GBS disease (1, 8). The problem is to identify women who are in need of such treatment, diagnosis by culture takes two to three days and access to good rapid detection of GBS (PCR) is limited. Strategy for prophylaxis must therefore either be based on **screening** of all pregnant women, or by identification of women at risk based on the **clinical risk factors** (8).

We have selected two alternative methods, both based on risk factors. Justification for the choice of methods is presented at the end of the chapter.

## **1. Method based on culture diagnostics**

### **Sampling**

#### **Indications**

- It should be advised not to take routine tests for detection of group B streptococci in healthy, symptom-free pregnant women (IV).
- Sample should be taken for all women
  - with amniotic rupture without contractions before 37 weeks. Sampling should be repeated every week until birth.
  - presenting with contractions before 34 weeks

#### **Procedure**

The sample should be taken from the outer part of the vagina and rectum and may be taken with the same sample brush. The sample is placed in the transport medium and sent to the laboratory clearly stating the indication.

## 1. Antibiotic therapy and prophylaxis in pregnancy

**The finding of GBS** in the vagina and/or the rectum is in itself not an indication for giving antibiotics in pregnancy (Ia). The finding should be noted at the "Helsekort for gravide" (Health card for pregnant women) for treatment during labor if risk factors should appear (see point C).

**UTI and ABU** (> 100,000 bacteria per ml) should be treated, whether GBS or any other microbe. If GBS is the identified agents, the information should be applied to the "health card ". Antibiotics should then be given during labor, see below. It should not be a general screening for ABU, but women who have had recurrent UTI should be investigated, see "Retningslinjer for svangerskapsomsorgen" (Guidelines for antenatal care) (9).

Indications for antibiotics are:

- **Amniotic rupture without contractions from week 23+0 to week 33+6:**  
Antibiotics should be administered initially intravenously for 3 days, then orally for a week. Then repeat the culture test weekly until birth. When re-detection of GBS in one of the weekly control samples: Oral antibiotic for 1 week. Discontinuation. Continue with weekly samples until birth. If detection of GBS in one of the weekly control samples: Oral antibiotic until birth.
- **Amniotic rupture without contractions from week 34+0 to week 36+6** (without any clinical signs of infection) antibiotics should be given intravenously after culture sample is taken. By rupture of membranes after 34 weeks the aim is delivery within 1-3 days, if necessary by induction (see Chapter "Preterm vannavgang" (Preterm rupture of membranes (PPROM) and primary rupture of membranes at/near term (PROM)) (10).

## 2. Antibiotic prophylaxis during vaginal birth

Antibiotics should be given intravenously to women who have one of the following conditions:

1. Previous birth of one or more children with severe GBS disease (IV)
2. GBS UTI or ABU in the present pregnancy (II)
3. Detection of GBS in the birth canal / rectum (for any reason) and have one of the following risk factors:
  - 3.1. preterm birth (before 37 weeks)
  - 3.2. amniotic rupture of about 18 hours before the baby is born (the limit is indicative: it is not due to start antibiotics when the woman is sleeping, or the birth is imminent)

### **3. Antibiotic treatment**

Suspected intrauterine infection is an indication for treatment with antibiotics intravenously (see antibiotic choice). Suspicion may be based on an overall clinical assessment of signs and symptoms in the mother: fever, vaginal discharge, uterine tenderness, and fetal tachycardia. The assessment is clinical and emphasis should be given to the strength of signs and symptoms. Delivery should be considered. The timing and mode of delivery should be considered in relation to the clinical situation and the progress of labor.

### **2. Method based on rapid diagnosis by PCR**

#### **Sampling procedure**

The sample should be taken from the outer part of the vagina and rectum with the same swab. Same sample brush can be used for both PCR and culture diagnostics if analysis will be performed in the same laboratory. If commercial PCR diagnostic test is taken use the appropriate own brush for this, and a separate sample swab is sent simultaneously for culturing.

#### **Indications for sampling and antibiotic prophylaxis**

The indications for sampling are identical with the indications for giving antibiotics if GBS is detected. These are:

- Previous child with GBS disease.
- Preterm birth or preterm rupture of membranes (before 37 weeks)
- Rupture of membranes more than 18 hours after 37 weeks

#### **Antibiotic treatment**

As in Method 1.

#### **Choice of antibiotics**

##### Prophylaxis

1. First choice is benzylpenicillin (Penicillin®) 1.2 g (2 mill. IU) intravenously every 4 hours (II)
2. By penicillin allergy or other high risk for anaphylaxis give clindamycin (Clindamycin®) 900 mg intravenously every 8 hours or erythromycin (Abbotcin®) 500 mg intravenously every 6 hours
3. In the presence of known GBS resistance to clindamycin or erythromycin give vancomycin (Vancomycin®) 1 g intravenously every 12 hours

4. On completion of intravenous antibiotics continue with oral erythromycin (eg. Abbotycin®) 250 mg tablets x 4 for a week. Control scheme and possibly restart as above

#### Treatment

In cases of suspected intrauterine infection regardless of gestational age give combination benzylpenicillin (Penicillin®) 1.2 g (2 mill. IU) intravenously every 4 hours and gentamicin (Garamycin®, Gensumycin®) 5 mg / kg Once daily. Treatment beyond 1-2 days for this indication is rarely necessary, but if so risk of nefro- and ototoxicity should be considered. By duration over 2-3 days blood concentration of gentamycin should be measured.

#### **Background for the choice of strategy**

The aim is to reduce the incidence of severe GBS disease in newborns. At the same time measures must be proportionate to the scale of the problem, and it is particularly important to avoid massive use of antibiotics with possible serious consequences in the short and long term.

USA has selected screening of all pregnant in weeks 35-37, and treatment of all GBS-positive women (4). This strategic choice is mainly based on Schrage et al (8) who find that the many mothers with sick children have no clinical risk factor, and that the screening-based approach prevents most sick children. However, a major weakness of the screening based strategy is that premature infants born before week 35-37 have the highest mortality, but are not identified and will thus not receive treatment. On the other hand, many pregnant women who give birth at term receive unnecessary treatment because they will not be colonized at birth even if GBS is detected in weeks 35-37. The positive predictive value of carrier state at term by culture in weeks 35-37 are 54% (6). The proportion of pregnant women who will receive treatment will equal the carrier rate, thus up to 35% (5). Kunnskapsenteret (The Norwegian Centre of Knowledge) summarizes that around 0.1-0.2% of those given antibiotics will benefit from it, and concludes that there is no basis for recommending screening rather than risk-based strategy (12).

In Sweden, a national GBS prevalence study found that 30% of mothers are carriers. The presence of at least one of the classical risk factors (<37 weeks, membrane rupture > 18 hours, fever > 38 ° C) was 17%. Around 40% of pregnant women with sick children had no risk factor, but in the cases where the baby died, at least one risk factor was present and in these cases none of these women had received antibiotics (13). The study provides good evidence that the risk-based strategy effectively prevents fetal death, and this strategy involves significantly less antibiotic use than screening based strategy.

The authors also point out that in the risk-based strategy, antibiotics are given to women who due to the risk factors (premature birth, prolonged rupture of membranes) are monitored in hospital anyway and intravenous antibiotics may be given relatively

safe. If antibiotics should be given at birth on the basis of positive GBS screening a 3-6 weeks before birth, the woman should need to be hospitalized solely because of GBS and the risk of serious allergic reaction associated with intravenous penicillin. A normal birth can otherwise take place at midwifery unit (or home).

It is therefore chosen a risk-based strategy, not unlike former Norwegian guidelines (9, 14). The strategy is conservative since only pregnant women at highest risk are included (rupture of membranes before 37 weeks), and it is estimated that 6-8% of the mothers will receive antibiotic (14).

The optimal strategy is considered to be PCR rapid diagnosis in a defined risk situation. The range of clinical risk factor may then be extended somewhat (preterm birth, prolonged rupture) without unreasonably high use of antibiotics. This could provide effective, targeted antibiotic use, limited to around 5% of the mothers (namely 30% carriers among 17% of clinical risk factors) (13).

This guideline represents a compromise in that it is primarily based on risk factors, but also takes into account that a positive GBS result may be present, obtained by any indication or wild screening. This is consistent with RCOGs Guidelines (11). The guideline also takes into consideration that rapid diagnosis by PCR is possible and we encourage the increased availability of this method. This guideline also addresses the fact that infections in the smallest premature infants are not GBS but are dominated by *E. coli*, often ampicillin resistant strains (3).

This guideline is consistent and overlaps with the guideline for Preterm rupture of membranes and preterm birth (10).

### **Evidence level**

These are indicated in the text with respective mortality, and assessment of level corresponded with RCOG Guidelines (11).

### **Literature**

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