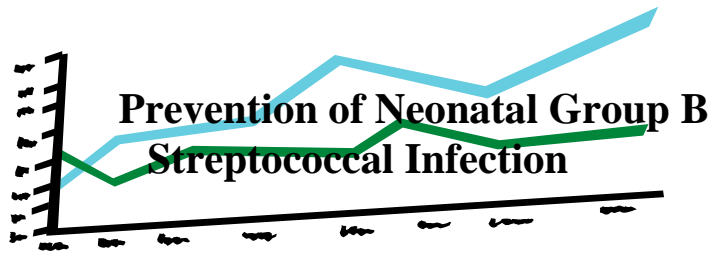


Polls and Surveys



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Since the 1970's, GBS has become the most prevalent life threatening neonatal infection of the industrialized world, affecting 0.3 – 0.5 / 1000 lives in the USA with substantial morbidity¹.

The organism

GBS or *Streptococcus agalactiae* is a facultative gram positive, of which there are 8 distinct serotypes of which types Ia, III and V account for 70-80% of cases of invasive neonatal diseases in the USA^{2,3} and the UK⁴.

Clinical spectrum

Normal commensal of female genital tract recoverable from 10-25% of pregnant women in most populations⁵⁻⁷.

Carriage is intermittent and repeat sampling increased detection rate to 30%^{8,9}.

Transperineal spread from the GIT is the source: low vaginal and rectal swabs give a higher yield than high vaginal and cervical swabs.

Neonatal colonization

Between 3-12% of neonates are colonized with GBS in the 1st week, 35-70% in infants of colonized mothers^{9,10} usually same serotype as mother¹¹.

Vertical transmission is commoner if there is GBS bacteriuria¹², cervical carriage¹³, heavily ed. mother¹⁰. Although transmission of the organism following intrapartum chemoprophylaxis occurs, it usually follows inadequate dose regimens¹⁴.

Neonatal invasive disease

Early onset GBS (EOGBS) disease accounts for 80% and occurs in the 1st week due to vertical transmission. It presents within 24 hours in 95% usually as pneumonia or septicemia¹⁵.

Late onset disease occurs after the 1st week presenting as septicemia or meningitis, due to either vertical transmission (50%), or nosocomial spread. The serotypes of late onset is not the same maternal types.

Prior to the introduction of intervention for EOGBS the incidence in the US was 1-2.3/1000 livebirths in 91-92^{16,17}. The same investigation showed rates to have fallen within few years cumulating to the introduction of IP penicillin or ampicillin.

In high risk females. To date, studies have been published with rates of 0.24-1.15/1000 livebirths.

Table 1. Risk factors for the development of early-onset group B streptococcus (EOGBS) disease

Stage	Risk factor
<i>Pregnancy</i>	Age less than 20 years ⁵ African-American descent ²³ Australian Aboriginal descent ⁶ Previous baby affected by EOGBS ³³
<i>Antepartum</i>	Multiple pregnancy ³⁴ GBS bacteriuria in pregnancy ¹⁹ Heavy GBS colonization ¹⁶ Low levels of anti-GBS capsular antibodies ³⁵ Prelabour rupture of the membranes ³⁶
<i>Intrapartum</i>	Preterm delivery ³¹ Fever over 38°C ³⁷ Ruptured membranes for more than 18 hours ³⁷

Neonatal morbidity and mortality

In the 70's mortality exceeded 50% in invasive disease¹⁸. In the US the case fatality rate fell to 5% mainly in premature neonates.^{19,20} 15-50% of survivors may suffer neurological sequels as cognitive dysfunction, deafness or visual impairment.^{20,21}

Prevention of neonatal disease

IP chemoprophylaxis

Brocanch et al²⁸ have demonstrated an 88% reduction in EOGBS incidence by applying CDC guidelines in 94% of all vaginal deliveries.

The recommended agent of choice is Penicillin G because its narrow spectrum reduces the emergence of resistance in other organisms unlike ampicillin.¹

The regimen is penicillin. G 3 gm loading (IV) then 0.5 gm / 4 hours till delivery²⁹, starting as soon as possible after the onset of labor to avoid delivery prior to antibiotic treatment. Antibiotics should be given at least 4 hours prior to delivery,^{30,31} more recent evidence saying that only 2 hours is enough.

Penicillin-allergic women should receive Clindamicin 900mg/8 hours³⁰, although resistance is seen in 15%³².

There are two possible strategies for selecting women for IV chemoprophylaxis and both of them are endorsed by the American academy of Pediatrics²⁹ and the ACOG³³. In addition, the two strategies can be combined²⁹.

Risk based strategy

Give chemoprophylaxis for any woman with any of the following

1. Previous infant with invasive GBS disease.
2. Labor (<37 weeks).
3. ROM (37 weeks).
4. Fever in labor > 38°C.
5. ROM > 18 hours prior to delivery.

This prevents nearly 70% of cases of EOGBS by give chemoprophylaxis to 20% in laboring women.^{27,34} Reports suggest that as few as 50% of mothers of infants with EOGBS have identifiable risk factors.^{35,36}

Screening based strategy

All pregnant women are offered bacteriological screening at 35-37 weeks of gestation. Women presenting in labor before culture results are available should be offered chemoprophylaxis.

Cultures obtained in the last 5 weeks of pregnancy have been shown to be more predictive

of carrier status than cultures obtained early in pregnancy.

Yancey et al³⁷ showed a positive predictive value of 89% and a negative predictive value of 97% for cultures taken at 35 weeks. The rate of detection can be increased by sampling the rectum as well (27%) as opposed to the lower vagina alone (22%).³⁸

If all culture positive women are treated, 25-27% of women in labor would receive antibiotics^{27,34}, resulting in the prevention of 86-90% of infant cases.^{29,34}

This method is therefore more effective, but more expensive than the risk based one, as it requires treating more women³⁹.

Combined approach

Boyer and Gottof⁴⁰ advocated an alternate strategy where treatment is offered only to culture positive patients with risk factors. It has reduced the women treated to 5% and prevented up to 75% of EOGBS disease.

This strategy is attractive because it greatly decreases the risk of treatment but is still more expensive than the risk based option³⁹, and will not prevent all cases that could have been prevented, had the based method been used.

Current recommendations

The group B streptococcus working group has been set up by the public health lab service (PHLS) which has produced interim "good practice" recommendation.

Pending the availability of further UK epidemiological data, such as the UK-wide British pediatric surveillance unit study involving all maternity units.

The "good practice" recommendations

1. Do not perform routine bacteriological screening as there is currently little evidence to support this.
2. Give intrapartum antibiotics specifically for GBS to the following women:
 - GBS infection of a previous baby.
 - GBS found incidentally in the vagina or urine at any stage in pregnancy.
3. Use broad spectrum antibiotics with GBS cover in:
 - Diagnosed or suspected chorioamnionitis.
 - Prolonged PROM (> 18 hours).
4. Consider IV antibiotic prophylaxis in the following cases:
 - Preterm labor.
 - Prolonged PROM or fever in labor.

Controversial clinical scenarios***Elective CS with intact membranes***

CDC recommends that IP CP be given to known GBS carriers before CS with intact membranes³⁰. A recent publication, has contradicted this by stating that the risk of GBS disease in such case is very low concluding that chemoprophylaxis is therefore unnecessary.⁴²

PROM without labor

CDC guidelines³⁰ recommend that a low vaginal and rectal swab for GBS be obtained, antibiotics should either be given empirically till cultures are negative or once cultures are positive.

The guidelines do not mention the length of treatment, Hager et al.⁴² recommend antibiotics for 48 hours together with a repeat culture. If negative stop, if positive IV Antibiotics for 5-7 days, authors have evidence to support any patient with positive culture in pregnancy should receive chemoprophylaxis in labor.

If positive, the culture should be repeated in 5 weeks as the possibility of a negative culture becomes positive is 5%.³⁷

Elective PTL

Although previously assumed to be low risk, a recent case report argued that swabs should be taken before delivery or chemoprophylaxis given.⁴³

Disadvantages of intrapartum prophylaxis***Potential severe allergic side effects of penicillin***^{27,41}***Antibiotic resistance***⁵⁴**Erythromycin and Clindamycin**

Ampicillin usage has been associated with increased incidence of ampicillin-resister Gram. negative neonatal sepsis positive increase mortality.^{45,46}

Cost

A risk based approach could be financially justified when the cost of treating cases is lower than microbiological screening.

Medicalisation of labor

The introduction of 4 hourly IV antibiotics can medicalise an otherwise normal labor, making the woman less likely to deliver at home or in a midwife-run unit^{47, 48}.

Increased demands for prenatal counseling and increased maternal anxiety

Women attending booking clinics are given a lot of counseling problems. Of which they retain very little.^{49,50} Added to this is the negative psychological effect that this may have⁵¹.

Medicalisation of the neonatal period

If a mother has received inadequate or no chemoprophylaxis, many neonatologists feel uneasy about an early discharge from the hospital. However, there is no current evidence to support the use of extra interventions for these infants.^{52,53}

A screening based approach has less intervention than a risk-based approach.⁵⁴⁻⁵⁶ But both are associated with more intervention in the healthy neonate than would be the case without these guidelines.^{57,58}

Failure to prevent disease

Intrapartum chemoprophylaxis does not prevent 100% of cases of EOGBS disease⁵⁹. More than 80% of failed cases are associated with Chorioamnionitis or maternal fever, and are due to an established fetal infection.¹⁵

Postnatal antibiotics prophylaxis

This strategy reduces the incidence of EOGBS disease in term infants but has no effect on low birth weight infants or on late-onset disease.¹

Universal postpartum prophylaxis has been shown to increase overall mortality rates attributable to Penicillin-resistant pathogens.⁶⁰

Vaccines

Studies in the 1970's established a relationship between GBS capsular polysaccharides and invasive GBS infection²⁵. Vaccines have since seen developed against various GBS serotypes.

Summary

To sum up, it appears that the following can be concluded:

A risk-based approach would raise treatment costs with a lower efficacy, more patients needing treatment of course entailing side-effects and drug resistance.

A bacteriological screening approach would maximize efficacy, but also raise costs. Side effects would decrease due to lower numbers of patients needing treatment.

A risk-based selection of bacteriologically positive patients would have lower numbers of patients needing treatment and fewer costs, but

Polls and Surveys

slightly less efficacy than sure bacteriological screening.

While a combined approach of treating all patients at risk, irrespective of their culture results and all patients with positive or unknown cultures, irrespective of their risk status would maximize the efficacy of a prevention program but with maximum costs and maximum incidence of side effects.

The choice between different approaches depends on the load of disease in a given population, the cost-benefit ratio between expenses of treating the disease and expenses of preventing it, as well as doctors' and patients' preferences and equipment availability.

Conclusions

1. The incidence of neonatal GBS disease can be reduced by intrapartum chemoprophylaxis.
2. A reduction in neonatal mortality has not been demonstrated.
3. There is insufficient evidence to show whether a clinical or screening based approach is more effective.
4. The "good practice" recommendations of PHLS group B working group:
 - a) Previously affected infant²³.
 - b) PPROM²⁶.
 - c) GBS bacteriuria¹².
 - d) Vaginal colonization⁶¹.
5. The introduction of universal microbiological screening would have huge financial implications and would be hard to justify with current evidence.

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Prevention of Neonatal GBS Infection

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