
Joanne Bartkus, Ph.D.
Minnesota Department of Health
Group B Streptococcal (GBS) Disease

- GBS most common cause of invasive bacterial disease in neonates
- GBS also an important pathogen in maternal and non-pregnant adults
- Early-onset neonatal disease has decreased from 1.7 cases per 1,000 live births in 1993 to 0.4 per 1,000 live births in 1999
- Decreased incidence of early-onset GBS disease attributed to recent prevention efforts
Prevention of GBS Disease

- Administration of intrapartum antibiotic prophylaxis to prevent early-onset disease
- Penicillin or ampicillin is the first-line agent in non-allergic women
- Erythromycin or clindamycin treatment recommended for women with allergies to penicillin
Antimicrobial Susceptibility of GBS

- GBS remain susceptible to first-line antimicrobial agents, penicillin and ampicillin.
- Resistance to macrolides (erythromycin) and lincosamides (clindamycin) have emerged in GBS.
- Studies in U.S. have found 9% to 19% erythromycin resistance and 2% to 15% clindamycin resistance.
- Few studies have evaluated erythromycin resistance mechanisms.
Erythromycin Resistance Mechanisms in GBS

- Two common resistance mechanisms in GBS
  - Methylation of 23S rRNA, encoded by *erm* gene
  - Macrolide efflux, encoded by *mef* gene
Macrolide Resistance Mechanisms

Macrolides (e.g. Erythromycin)
Lincosamides (e.g. Clindamycin)
Streptogramin B
Regulation of $erm$ Methylase

Constitutive

$erm_C$

Methylase

Inducible

$erm_I$

Methylase

Macrolides
Inducible MLS Phenotype

Zone of Inhibition

Blunted Zone
Study Objectives

• Determine the prevalence of erythromycin and clindamycin resistance in invasive GBS isolated in Minnesota in 1998 and 2000

• Characterize erythromycin resistance mechanisms among invasive GBS isolates
Surveillance Methods

• Active statewide laboratory-based surveillance for invasive GBS disease
• Conducted since 1995 as part of Emerging Infections Program Active Bacterial Core Surveillance Network
• Surveillance includes isolate collection and medical record review from early and late onset, maternal and adult cases
Laboratory Methods

- Antimicrobial testing by broth microdilution
- PCR for detection of $erm$ (A, B, C, TR) and $mef$
- Double disk diffusion for inducible MLS phenotype
- PFGE analysis
## Invasive GBS Disease
### Minnesota, 1998 and 2000

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases Reported</th>
<th>Isolates Collected</th>
<th>Susceptibility Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>230</td>
<td>200</td>
<td>101 (51%)</td>
</tr>
<tr>
<td>2000</td>
<td>294</td>
<td>237</td>
<td>220* (93%)</td>
</tr>
</tbody>
</table>

*Includes all adult isolates*
Percentage of GBS Isolates Resistant to Erythromycin and Clindamycin
Minnesota, 1998 and 2000

- Erythromycin (Macrolide = M)
  - 1998: 21%
  - 2000: 23%
  - n = 71

- Clindamycin (Lincosomide = L)
  - 1998: 8%
  - 2000: 12%
  - n = 35
Erythromycin MIC Values Among Erythromycin-Resistant Isolates
Minnesota, 1998 and 2000
Distribution of Resistance Mechanisms by Genotype

Percent

mef  ermTR  ermB  ermB/mef  none

1998

2000
Distribution of Phenotypes Among Erythromycin Resistant GBS Isolates
Minnesota, 1998 and 2000

The bar chart shows the distribution of phenotypes among erythromycin resistant GBS isolates in Minnesota, 1998 and 2000. The phenotypes are categorized as M, MLS Inducible, and MLS Constitutive.

- M: 1998 - 100%, 2000 - 10%
- MLS Inducible: 1998 - 0%, 2000 - 60%
- MLS Constitutive: 1998 - 0%, 2000 - 40%
Distribution of Erythromycin MIC Values by Resistance Determinant

Minnesota, 1998 and 2000

Number of Isolates

MIC (ug/ml)

0 5 10 15 20 25

erm
ermB constitutive
ermB inducible
ermTR
mef

2 4 8 >8
PFGE Analysis of Resistant GBS
Data Summary

• No increase in erythromycin resistance from 1998 and 2000
• Trend toward in resistance to clindamycin during that time period
• Resistance determinants predominantly $mef$ in 1998 GBS isolates and predominantly $ermB$ in 2000 isolates
• Many $ermB$ were inducible MLS phenotype, appeared clindamycin-susceptible by broth microdilution
Clinical Implications

• Potential for clindamycin resistance in GBS probably underestimated because most laboratories do not test for inducible MLS resistance

• Clindamycin should not be used for therapy or prophylaxis of erythromycin-resistant GBS strains
Acknowledgements

Acute Disease Investigation and Control

Craig Morin, M.P.H.
Ruth Lynfield, M.D.

Public Health Laboratory

Jennifer Adams
Sara Vetter
Elizabeth Thompson
Anita Glennen