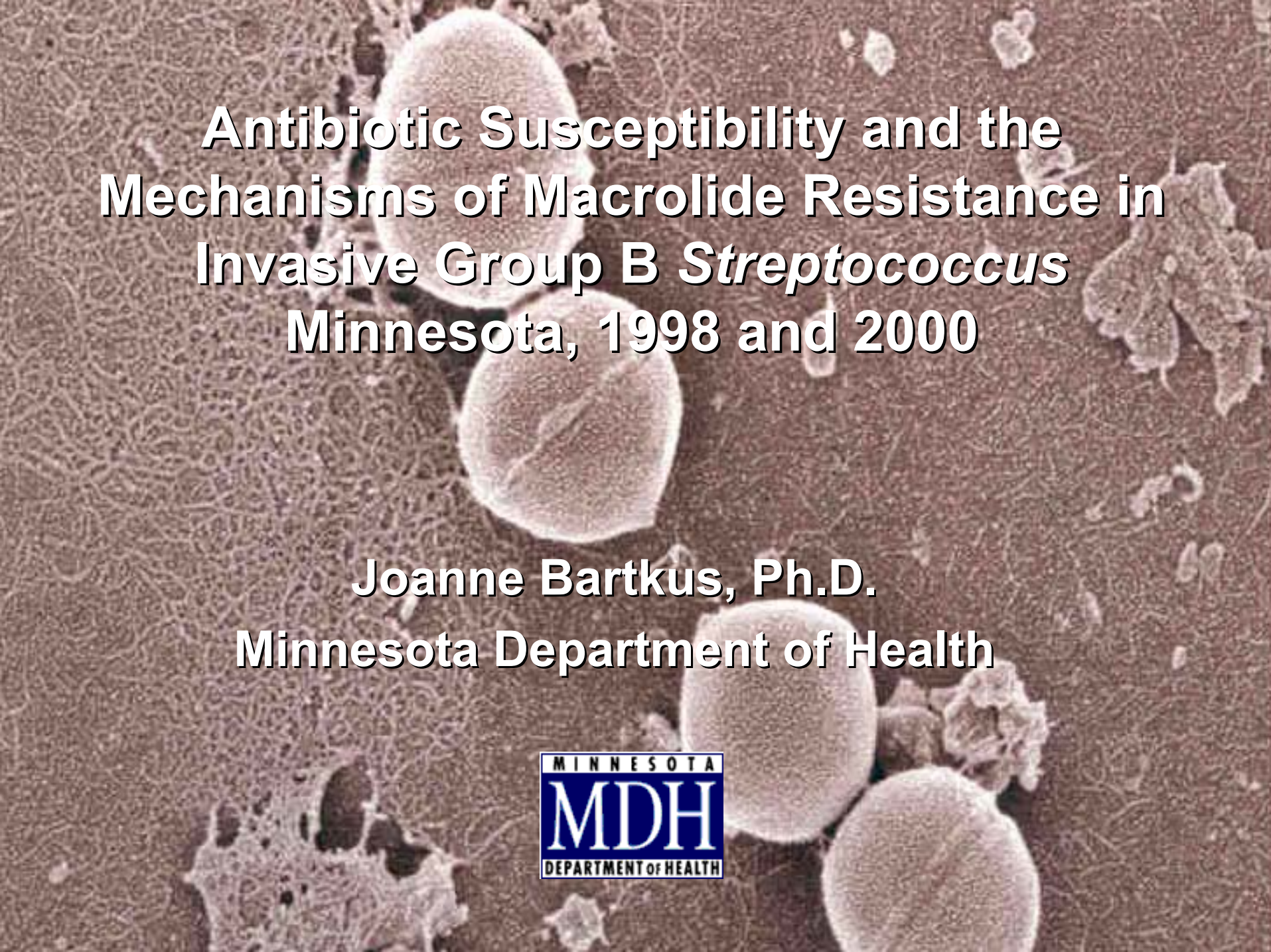

Antibiotic Susceptibility and the Mechanisms of Macrolide Resistance in Invasive Group B *Streptococcus* Minnesota, 1998 and 2000

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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

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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

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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

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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

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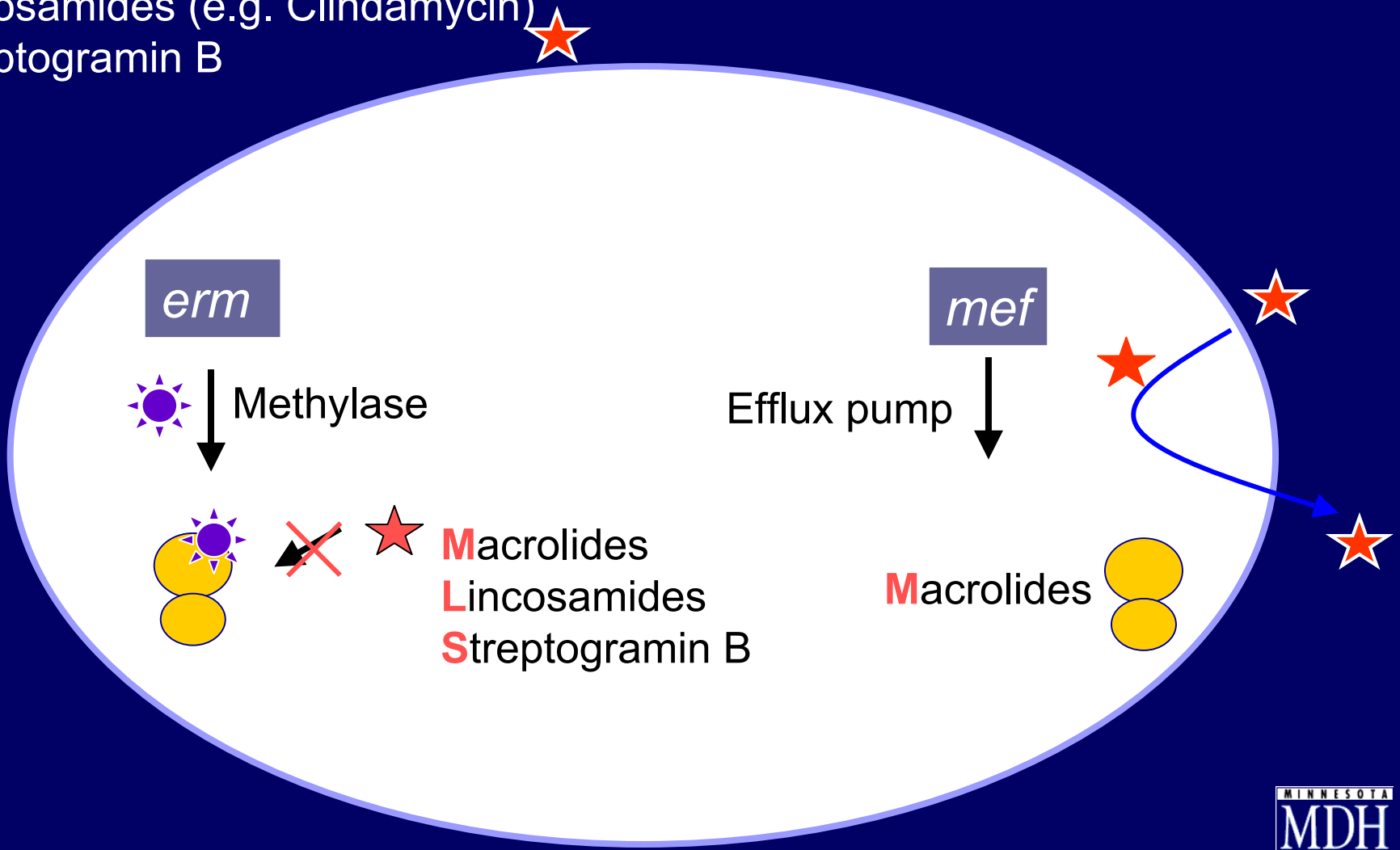
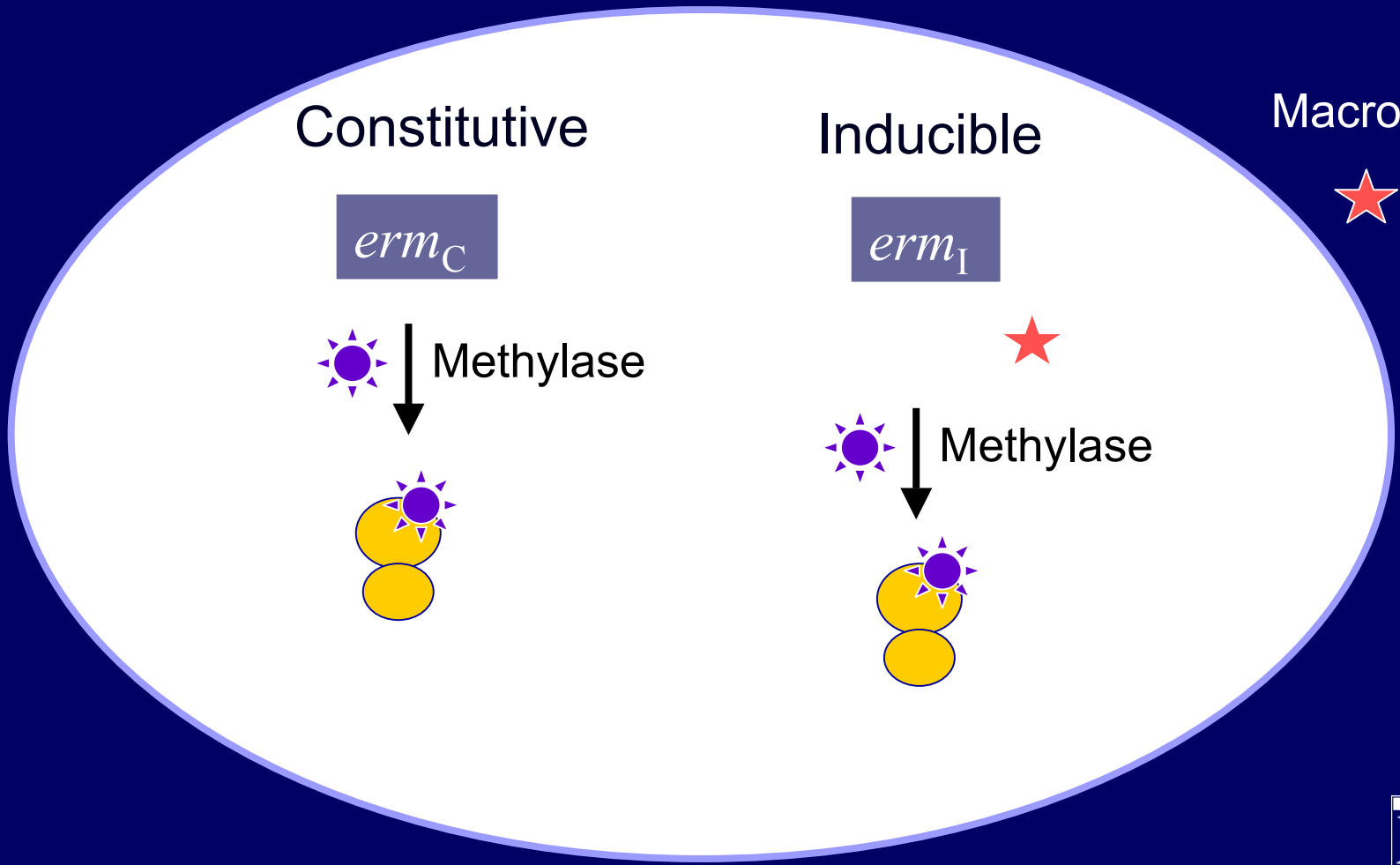
Macrolide Resistance Mechanisms

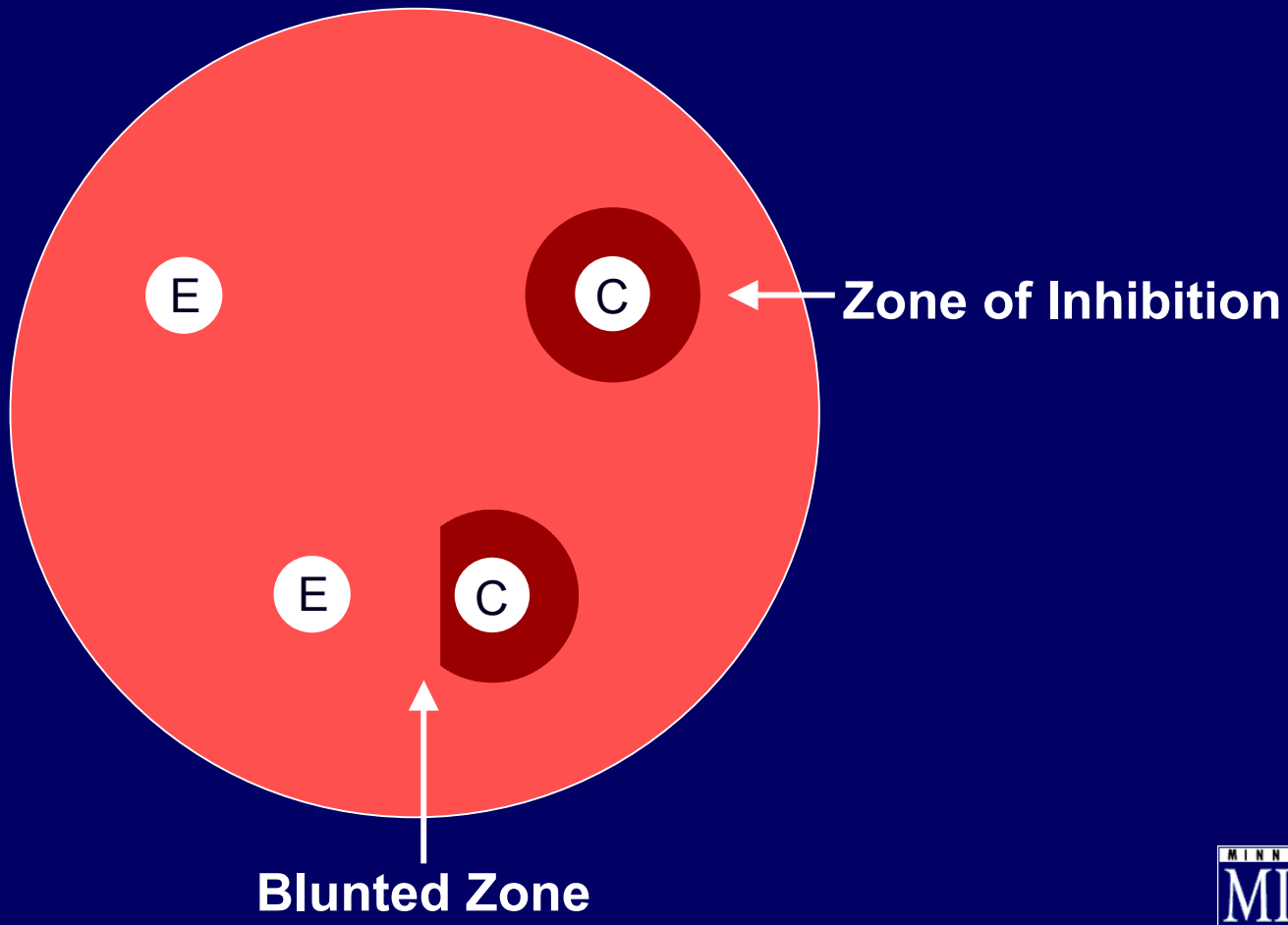
Macrolides (e.g. Erythromycin)
Lincosamides (e.g. Clindamycin)
Streptogramin B



Regulation of *erm* Methylase



Inducible MLS Phenotype



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

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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

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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

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Invasive GBS Disease
Minnesota, 1998 and 2000

Year	Cases Reported	Isolates Collected	Susceptibility Testing
1998	230	200	101 (51%)
2000	294	237	220* (93%)

*Includes all adult isolates

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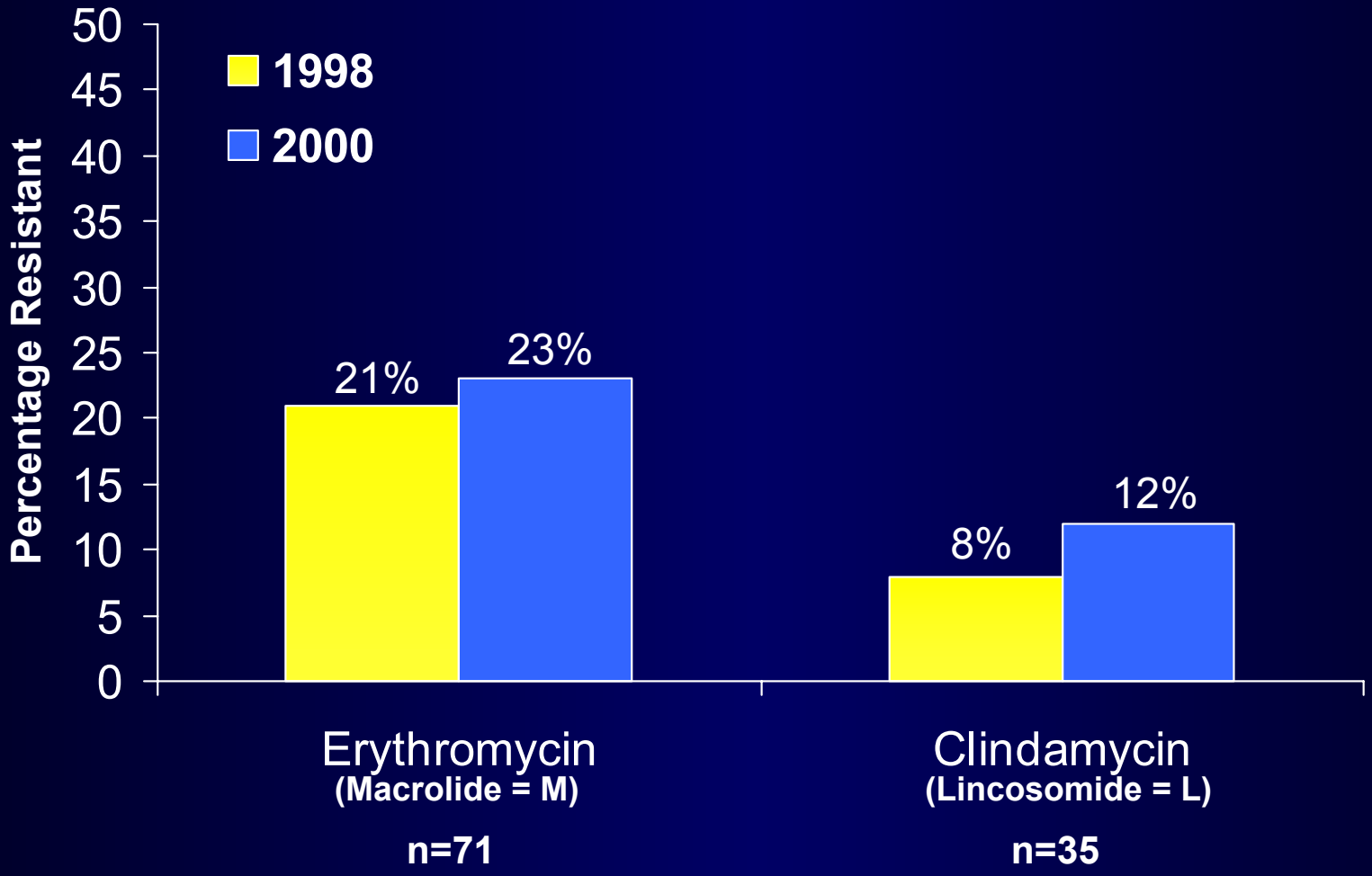
Percentage of GBS Isolates Resistant to Erythromycin and Clindamycin

Minnesota, 1998 and 2000



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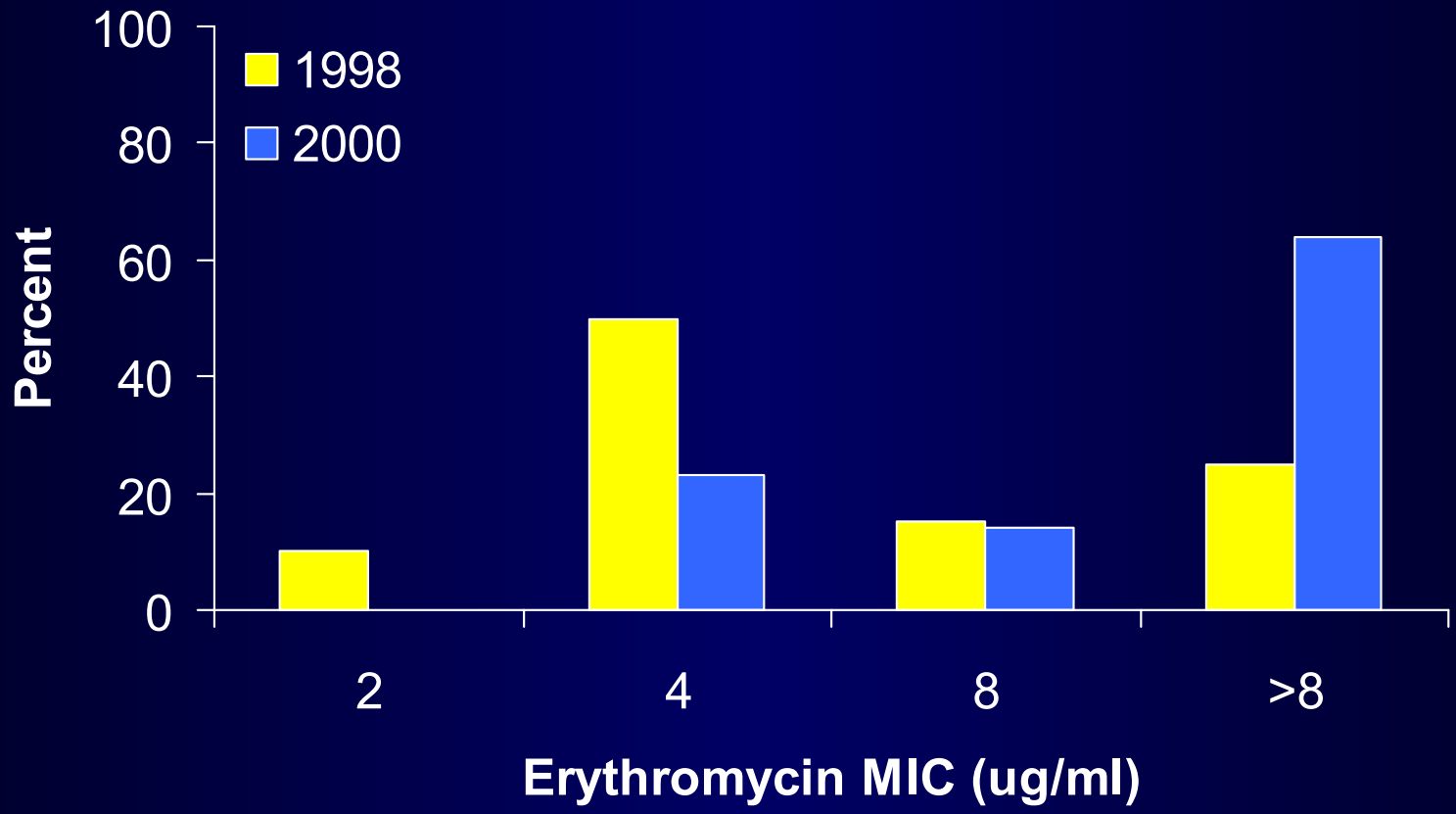
Erythromycin MIC Values Among Erythromycin-Resistant Isolates

Minnesota, 1998 and 2000



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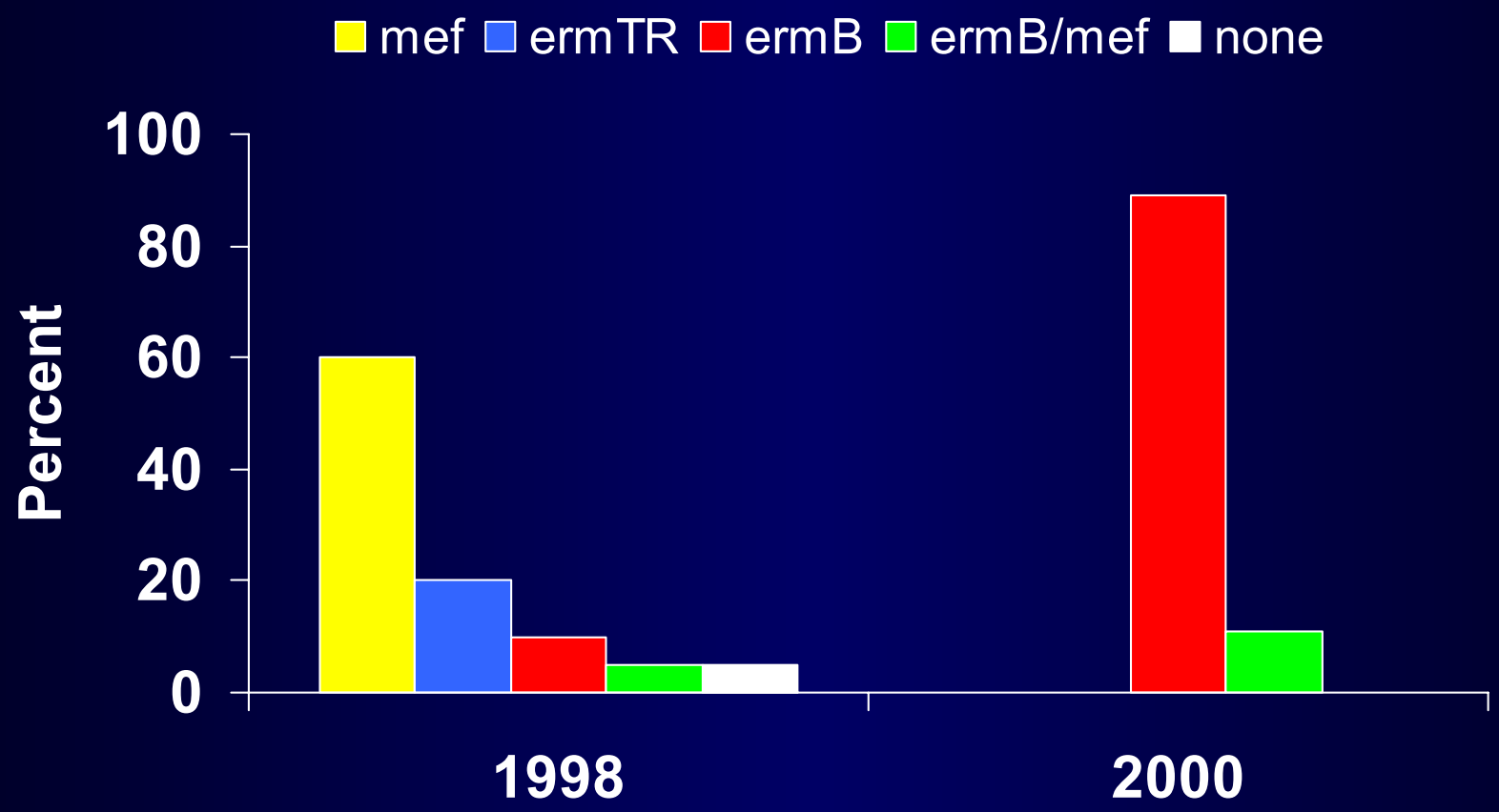
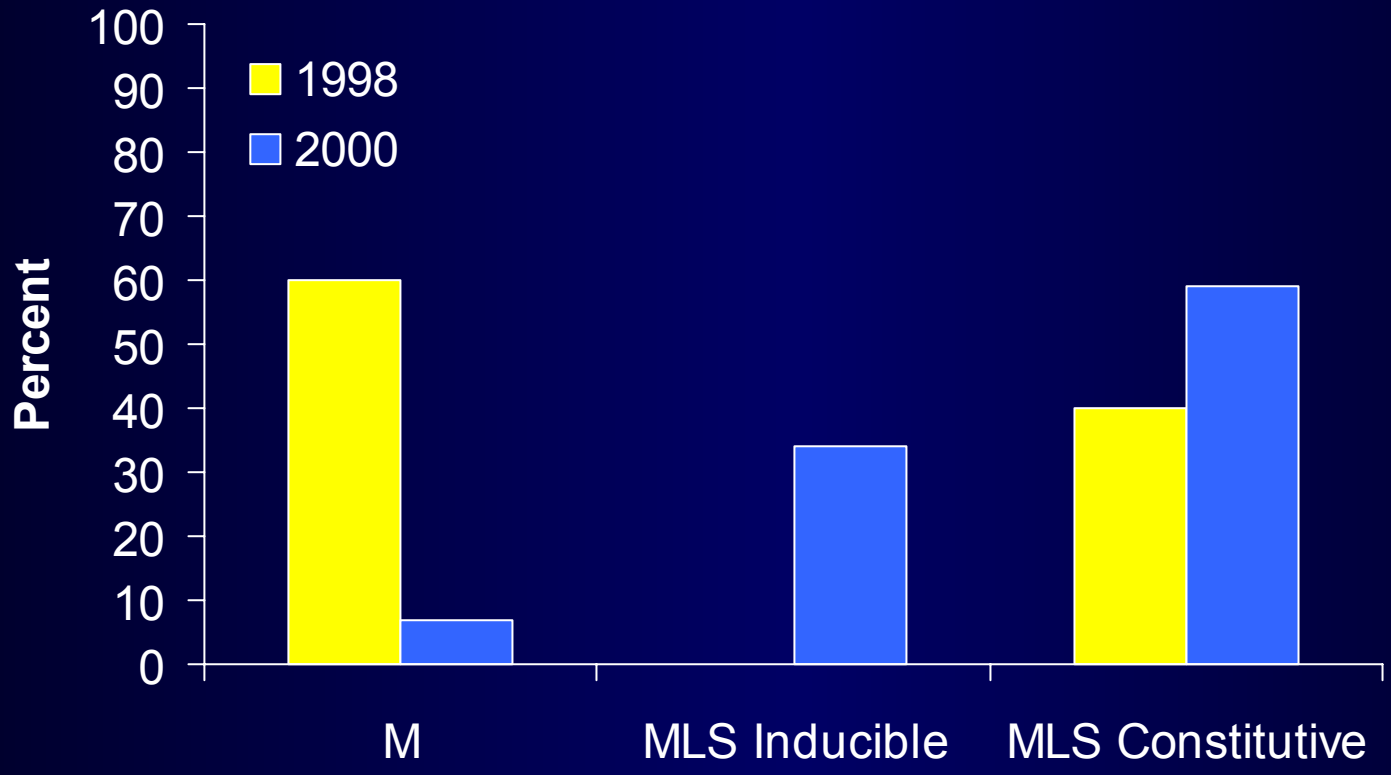
Distribution of Resistance Mechanisms by Genotype



Distribution of Phenotypes Among Erythromycin Resistant GBS Isolates

Minnesota, 1998 and 2000



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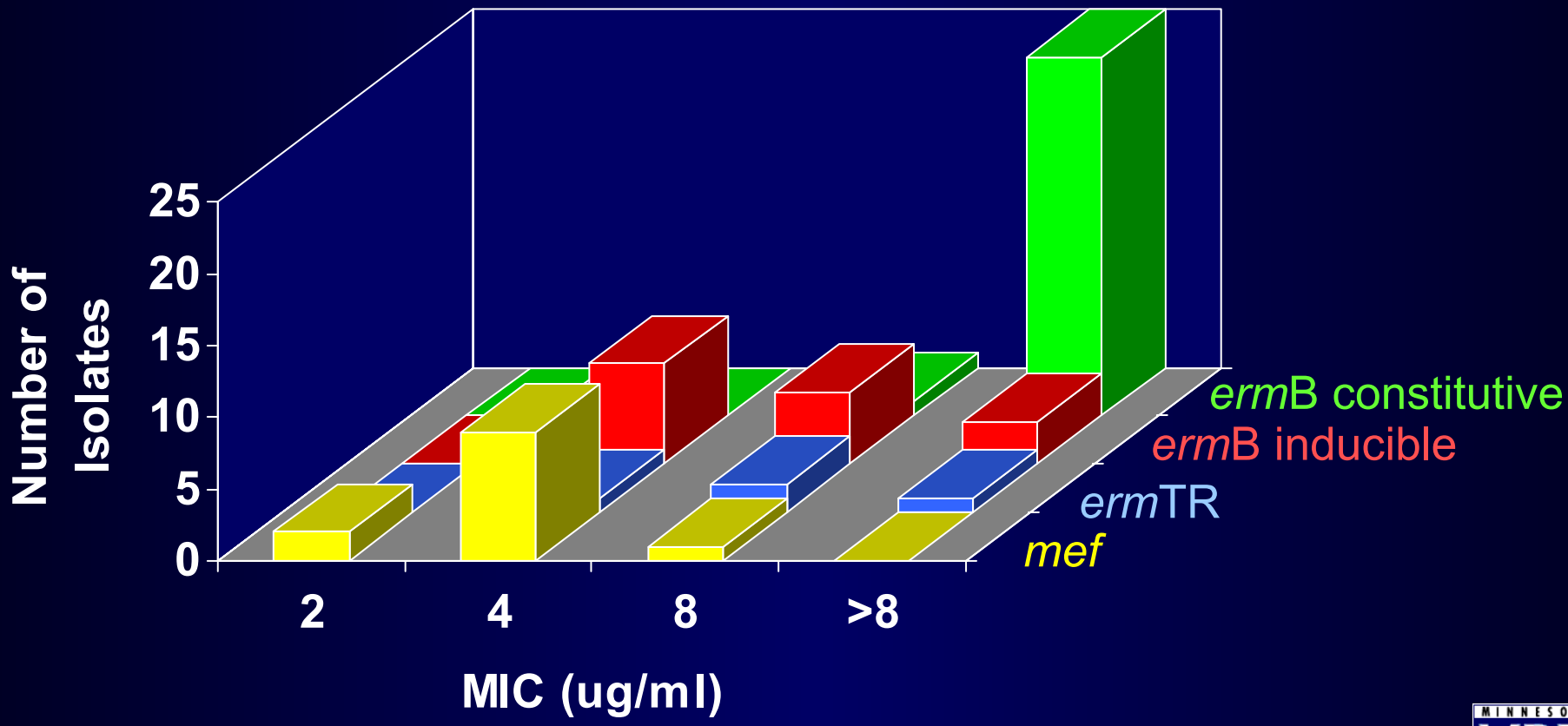
Distribution of Erythromycin MIC Values by Resistance Determinant

Minnesota, 1998 and 2000



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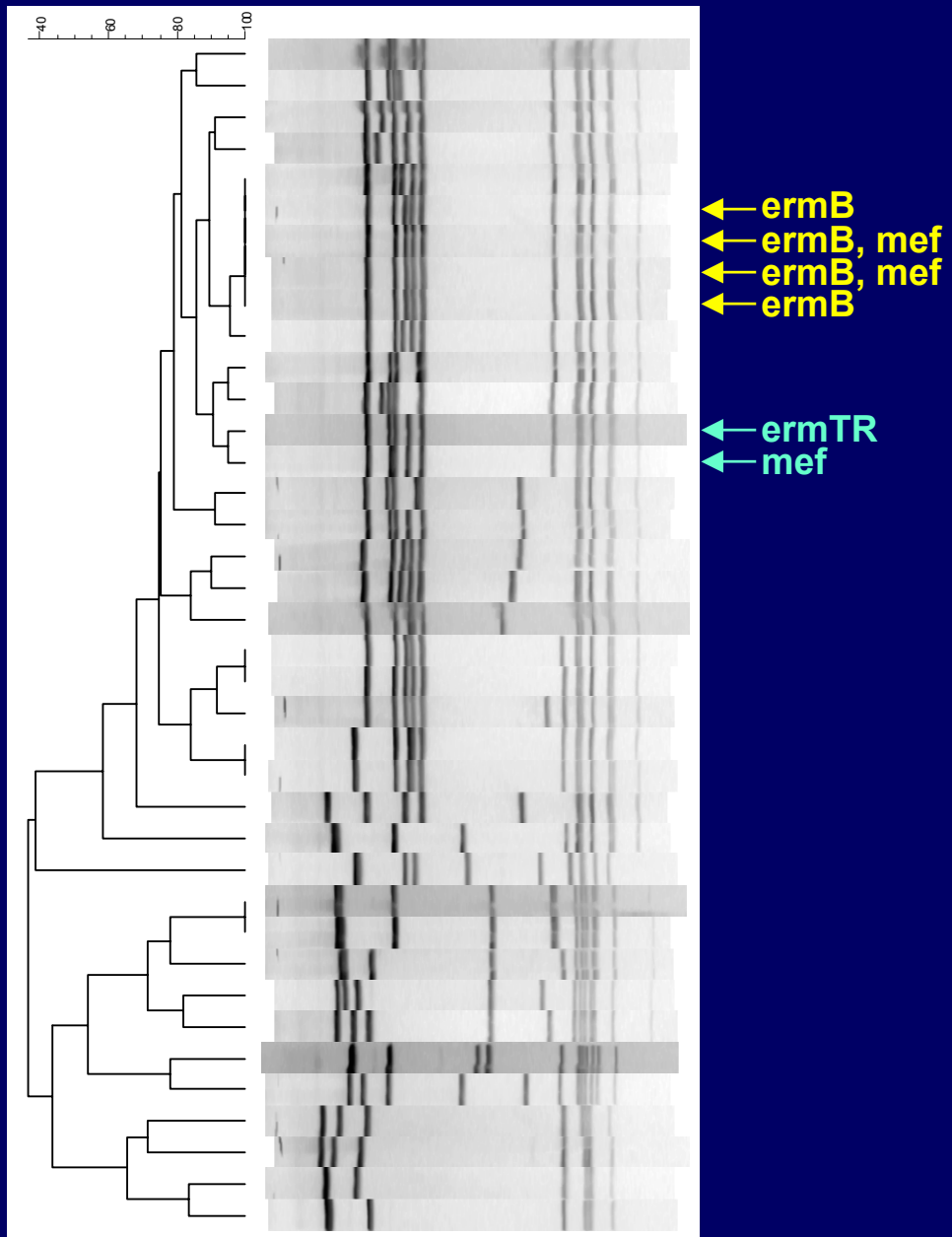
PFGE Analysis of Resistant GBS



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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 *erm*B in 2000 isolates
- Many *erm*B were inducible MLS phenotype, appeared clindamycin-susceptible by broth microdilution

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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

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