

# Mortality from early onset group B streptococcal infection in the United Kingdom

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## Abstract

**Aims**—To assess the assumption that group B streptococcal infection is less common in the United Kingdom than it is in the United States.

**Methods**—All stillbirth and neonatal death records in the former Northern Health Region were scrutinised to determine how many babies had died of infection in 1981–96, and what had been the cause.

**Results**—Fifty one of 630 206 live born babies had died of confirmed group B streptococcal infection after becoming symptomatic within 48 hours of birth (0.8 neonatal deaths per 10 000 live births). There were a further 27 deaths from infection without a confirmed microbiological diagnosis, and 17 stillbirths from confirmed group B streptococcal infection.

**Conclusions**—The incidence of death from early onset infection was marginally higher than the officially estimated rate for the United States before widespread prophylaxis was attempted. Strategies for perinatal prevention deserve greater attention in the United Kingdom.

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Keywords: group B streptococcal infection; congenital infection; perinatal death

Group B streptococcal infection has been the most common cause of severe, early onset neonatal infection in much of the developed world over the past three decades. It does not, however, seem to be responsible for more than 2% of diagnosed neonatal sepsis in Africa, India, the Middle East or South East Asia.<sup>1</sup> More recently in the United States it has been seen as a major, potentially preventable, cause of perinatal death.<sup>2</sup> Guidelines on prevention have been published by various professional bodies<sup>3–5</sup> and widely adopted in the United States and parts of Australia.<sup>6</sup>

Whether group B streptococcus is a major cause of sepsis or death in this country (and the rest of Europe) is less clear. The only previous large scale population based study in this country was carried out 20 years ago by the Public Health Laboratory Service, but was unfortunately only published in symposium format.<sup>7</sup> We present the incidence of death due to early onset group B streptococcal infection from a large, geographically defined United Kingdom population and compare it with other large studies from Europe, the United States and Australasia.

## Methods

The former northern health region covers a population of 3.1 million people, and has tightly defined geographical borders with few cross border referrals. Cases were identified using data for the years 1981–96 held by the Northern Region's Perinatal Mortality Survey.<sup>8</sup> The records in this large well validated database contain carefully cross audited information on cause of death, but the obstetric, paediatric, and pathology case notes of the 301 non-malformed infants classified as dying from infection within 28 days of birth were all reviewed afresh during the course of this study. Cases were defined as early onset where there was clear documented evidence of symptoms compatible with group B streptococcal infection in the first 48 hours of life.

During the 16 years there was no policy for the routine screening of maternal group B streptococcal carriage, and no widespread policy of prevention using intrapartum antibiotic prophylaxis.

## Results

There were 630 206 live births during the study and 51 deaths in babies with confirmed early onset group B streptococcal infection. The clinical course in all the babies was compatible with a diagnosis of severe sepsis. In 37 cases the diagnosis was made on the basis of a positive deep culture: blood (n=26), blood and cerebrospinal fluid (n=3), blood and tracheal aspirate (n=7), or tracheal aspirate (n=1). In 11 cases group B streptococci were isolated at necropsy and there was histopathological evidence of infection, but no cultures had been taken (n=7) or organisms isolated (n=4) during life. In two cases where no deep cultures were performed group B streptococci were isolated on superficial swabs (one of whom had pneumonia confirmed at necropsy but with no microbiological evidence), and in one case blood cultures were negative, no necropsy was performed, but group B streptococci were isolated from superficial swabs.

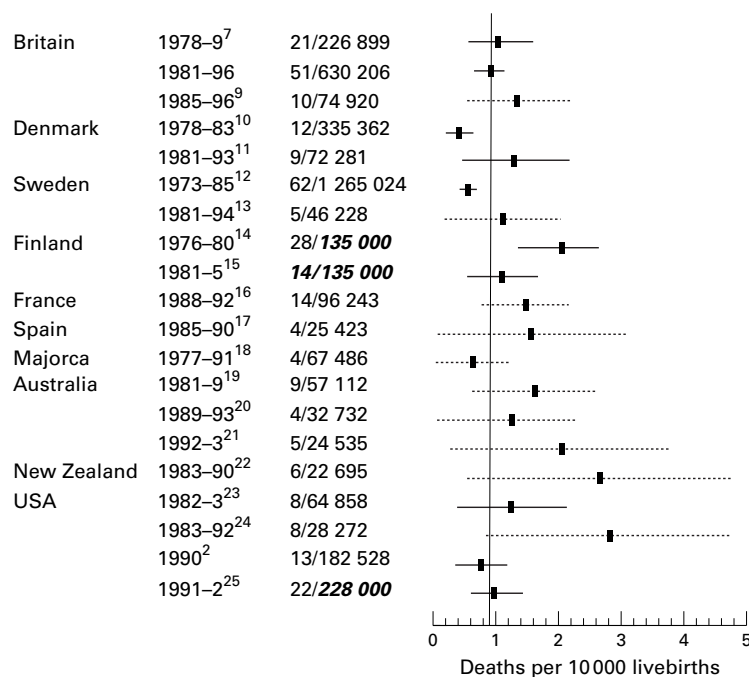
Another 27 babies had strong clinical evidence of infection in the first 48 hours, but no satisfactory microbiological diagnosis. Features of infection were present in all 21 who came to necropsy. Many of these babies had probably also died from group B streptococcal infection. Eight were born to mothers colonised with the organism, and in a further four, antibiotics had been given before delivery. No cultures were ever obtained from the mother or baby in a further seven cases.

Another 23 babies of 20 or more weeks gestation were born dead between 1987–96 with overt maternal group B streptococcal sepsis or

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**Figure 1** Prevalence of neonatal death from early onset group B streptococcal infection (studies involving at least 20 000 births only). The black bars show the 95% confidence intervals for population based studies, and the hatched bars the confidence intervals for other (potentially less representative) hospital based studies. Denominator figures in bold italics are estimates; the enumerator figure in bold italics is calculated from the stated rate. The vertical line is the average for population based studies.

necropsy evidence of group B streptococcal infection; 17 of these were 24 or more weeks gestation at delivery (median gestation 32 weeks) and would, therefore, now be classified as stillborn. Seven of these died during labour.

Of the 51 confirmed neonatal deaths, 33 (66%) were symptomatic at birth and 49 (96%) symptomatic by 18 hours. Median birthweight was 1770 g (range 520–4740 g), median gestation 31 weeks (range 24–41 weeks), and median age of death 18 hours (range 1 hour to 9 days). Ten mothers were delivered at term (37–41 weeks gestation): only four had ruptured membranes for more than 24 hours before delivery, and none had a recorded intrapartum temperature of more than 37.5°C. In only 5/51 cases had antibiotics been given before delivery. There were six multiple pregnancies associated with seven deaths. We were not able to detect any change in prevalence over the 16 year period.

### Discussion

Our data give a minimum incidence of 0.8 deaths per 10 000 live births due to early onset group B streptococcal infection, a rate very similar to that predicted for the United States<sup>3</sup> and comparable with that in other parts of Europe and Australia. Figure 1 shows mean death rates from early onset group B streptococcal infection in other large studies carried out over the past 20 years in Britain,<sup>7–9</sup> other parts of Europe,<sup>10–18</sup> Australasia<sup>19–22</sup> and the United States.<sup>2–25</sup> Several studies defined early onset cases as those presenting in the first week.<sup>2–7 10–12 14 15 18 23</sup> If this criterion had been used in this study the incidence would have

been almost unchanged as there were only two additional deaths presenting between 2 and 6 days of age.

The incidence in this study is similar to the rate found during the 1978–9 Public Health Laboratory Service study<sup>7</sup> even though this was the study that caused *The Lancet* to imply that early neonatal infection was less common than in the United States,<sup>26 27</sup> a misperception now reflected in many United Kingdom textbooks. Earlier commentators may have made erroneous comparisons between the Public Health Laboratory Service data which were population based, and United States studies of the same era<sup>28</sup> which were largely hospital based. Studies reporting data from tertiary referral centres are subject to several biases, and frequently live birth denominator data are not accurate. We have, where possible, contacted and confirmed with the original authors both the enumerator and denominator data for other large studies in our figure. Figure 1 illustrates the difference between population and hospital based studies.

Although this study is retrospective, death from infection, as opposed to infection per se, is relatively easily defined and permits good comparison with other studies. Many units in the United Kingdom are currently participating in a large Medical Research Council funded ORACLE trial (preterm antibiotic uncertainty study) and do not therefore have written policies for intrapartum antibiotics similar to that proposed by the Centers for Disease Control and Prevention<sup>3</sup> in the United States; and in this region only two of 14 obstetric units have a written policy for certain group B streptococcal risk groups. Our study strongly suggests that a decision not to adopt a policy of intrapartum antibiotic prophylaxis for certain risk groups in the United Kingdom (similar to the strategies now widely adopted in the United States and parts of Australia) cannot be based on an assumption that the incidence of lethal early onset infection is different.

In the recent annotation on this subject<sup>29</sup> it was suggested that "...when the incidence of early onset group B streptococcal infection is low ... expensive preventative measures may not be justified." This may well be correct, but should be seen in context. Our study, the Public Health Laboratory Study,<sup>7</sup> and the Oxford study<sup>9</sup> (albeit with wide confidence intervals) all estimate the incidence of death to be about 0.1 per 1000 live births, a figure not dissimilar to the rate of fatal intracerebral bleeding potentially prevented by vitamin K prophylaxis. Controlled studies of the incidence of infection and relative risk factors for this country are urgently required to determine the optimum strategy for reducing the incidence of perinatal group B streptococcal disease.

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