

PENICILLIN (Comment)

Protecting babies from maternally acquired, early onset, bacterial infection

Group B streptococcal infection: A range of bacteria commonly colonise the vagina, and colonise the baby at birth, but it rare for any to infect the baby during delivery. Indeed viral infections, such as hepatitis B and HIV, are much more often acquired by the baby during delivery. While group B streptococcus (GBS) infection is but one of many potential bacterial pathogens, it is the single commonest pathogen, and the pathogen on which most attention had been focused in the last twenty years. Indeed prenatal screening for this condition is now established practice in North America, Australasia and many parts of Europe.⁶ The UK and Finland stand out as the only two countries to have consciously resisted this trend,^{11,12} and this is, at least in part, because the incidence of early onset neonatal infection in the UK is less than a third of what it was in America before clinicians in that country started to offer regular screening and intrapartum prophylaxis.

Policy in the USA since 2002, has been to recommend universal rectal and vaginal culture-based screening at 35–37 weeks, and to give IV antibiotics (usually penicillin or ampicillin) every four hours during labour to all who prove culture positive.² Antibiotics are also often given to those who present in labour before screening has been done and, as a result, between a third and a half of all women now get prophylactic intravenous antibiotics during labour or delivery.³ However, risk factors for early onset neonatal infection are not the same in the UK as they are America. Recent studies have shown that 37% of neonates with early onset infection in the UK are born preterm, but only 14% in America; 45% have had prolonged rupture of the membranes in the UK, but only 14% in America.⁷ The implication is that what may be a cost effective strategy in America is not necessarily a cost effective strategy in the UK, and a study recently completed as part of the UK's Health Technology Assessment (HTA) Programme has now shown that this is indeed the case.^{13,14} If this is true for the UK it may also be true for other countries where GBS infection is less common than it is in America.

Cost effectiveness is, however, only one consideration. Such a policy certainly further medicalises pregnancy, and only works if women can be prevailed upon to come into hospital at the first sign of labour. The added value of such a policy is also diminished in a climate where, as a result of the ORACLE trial findings, oral antibiotics are increasingly being used to delay labour when pregnancy is complicated by preterm pre-labour rupture of membranes.⁵ Infection of intrapartum origin is a relatively uncommon cause of disability, and seldom causes death in the term baby, but it is often lethal in the preterm baby, and screening does not pick these up. Widespread antibiotic use could also have adverse consequences, and there is already concern that it may be starting to cause other, more resistant, pathogens to become more common.

The HTA report also concluded that the strategy currently recommended in the UK (an *intravenous* antibiotic for every mother who had had a previous baby with GBS infection, or an earlier vaginal swab or urine culture that was GBS positive and every mother who became pyrexial during labour, and an *oral* antibiotic for every mother experiencing preterm pre-labour rupture of membranes) is not cost effective either.⁴ It concluded that it **would** be cost effective to give penicillin or ampicillin to *all* mothers being delivered before 37 weeks gestation, but the suggestion that this should even apply to babies born by elective Caesarean section is known to have been reached by a misreading of the available data. While there are good grounds for giving cefoxitin to every mother having a Caesarean delivery immediately after the baby is delivered, this is done to minimise the risk of post-operative *maternal* complications (as the *Formulary's* monograph on that antibiotic makes clear). There is no evidence that such a policy is of any benefit to the baby.

It is certainly true that infection of intrapartum origin is commoner after preterm delivery, and that any infection is much more likely to cause disability or death when it occurs to a preterm baby. Infection is, however, excessively rare after elective caesarean delivery, and relatively uncommon after premature labour unless the membranes ruptured before labour started. It is certainly commoner when the mother is pyrexial in labour, but fever is very uncommon in early labour and the commonest cause of fever in late labour is epidural analgesia (where temperature typically rises by 1°C within seven hours). The prime indication for giving an antibiotic during preterm labour is when the membranes are known to have ruptured before labour began. Controlled trial evidence suggests that, in this situation, oral erythromycin (q.v.) may well delay delivery for long enough to be of some real benefit,⁵ but it is doubtful whether any oral antibiotic is the most secure way of preventing some maternal pathogen from infecting the baby during delivery. If such treatment is merited it should almost certainly be given parenterally.

What about other pathogens? GBS is but one of a range of pathogens capable of infecting the baby during delivery, as several surveys have shown. Only about a third of all the potentially lethal pathogens are sensitive to penicillin, and only about two thirds are sensitive to ampicillin¹ (a fraction that seems to have declined significantly during the last ten years⁸⁻¹⁰). It seems illogical, therefore, to use an antibiotic that is only effective against half to two thirds of the organisms that may be threatening the baby's very survival at this time. The more logical approach would be a combination of IV penicillin (or ampicillin) and IV gentamicin. The findings of two recent UK studies (see table) strongly support such an approach.^{1,15}

Organisms responsible for sepsis of intrapartum origin in the UK

Provisional data in early sepsis collected by the NeonIN Collaborative Group's in 2006-7,¹⁵
and from a study of all perinatal death in the north of England 1981-2005¹

Organism	Culture proven early sepsis ¹⁵		Intrapartum or neonatal death from sepsis ¹	
Group B <i>Streptococci</i>	39	49%	82	38%
Other <i>Streptococci</i>	6	7%	16	7%
<i>Listeria monocytogenes</i>	3	4%	11	5%
<i>Haemophilus influenzae</i>	1	1%	6	3%
<i>Staphylococcus aureus</i>	12*	14%	3	1%
<i>Escherichia Coli</i>	13	16%	32	15%
<i>Bacteroides</i>	0	-	5	2%
Other gram negative organisms	4	5%	13	6%
Viral, protozoal or fungal infection	2	3%	12	5%
Unequivocal sepsis, organism undetermined	-	-	37	17%
Total	80	100%	217	100%

* 10 of these were coagulase negative Staphylococci

Conclusion: To minimise these risks this *Formulary* has, for the last seven years, recommended that “all women going into unexplained spontaneous labour before 35 weeks gestation should be given both IV penicillin and IV gentamicin” and that, “in pregnancies more mature than this there are good grounds for giving IV penicillin throughout labour to reduce the risk of GBS infection if the membranes are known to have ruptured more than 6 hours before labour starts.” IV penicillin “should also be offered to all known carriers, and to mothers becoming pyrexial ($\geq 38^{\circ}\text{C}$) during labour.” Even this policy results in antibiotics being given to between 40 and 60 women during labour to provide optimal treatment for just one baby with bacterial sepsis of intrapartum origin. However most other policies result in antibiotics being given to many more women than this. Indeed it is said that a third of all women in America are currently being treated with either penicillin or ampicillin during labour,³ and this could be one reason why an increasing proportion of all coliform infections are becoming resistant to ampicillin. What is also clear is that the baby also needs treatment for 7 days if symptomatic even if no pathogen is grown.¹⁶

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