


Treatment of Lancefield group B streptococcal infections

Lancefield group B streptococci (Streptococcus agalactiae) are a cause of serious perinatal sepsis, producing both high morbidity and mortality rates (Eickhoff, Klein, Daly, Ingall & Finland, 1964; Franciosi, Knostman & Zimmerman, 1973; Baker, Barrett, Gordon & Yow, 1973). Although uniformly sensitive to penicillin and ampicillin (Finch, French & Phillips, 1976) they require higher concentrations to inhibit growth, than do strains of Streptococcus pyogenes (Matsen & Coughlan, 1972).

Streptococcus agalactiae is isolated from a wide range of clinical specimens and reports suggest that the increase in isolation rates (Finn & Holden, 1970) is real rather than apparent, following the increased awareness of this particular organism. However, this experience has not been universal (Stokes & Mehtar, 1977). There appears to have been no change in the susceptibility to penicillin of strains isolated in the past ten years (Baker, Bette & Barrett, 1976) although occasional reports have shown strains producing clinical disease with high MICs of 0.12 mg/l to penicillin (Dormand & Adams, 1976). In addition there has been a series of case reports of recurrent group B streptococcal infection in infants who have received an adequate course of chemotherapy. (Dormand & Adams, 1976; Broughton, Mitchell, Grossman, Hadley & Cohen, 1976; Truog, Davis & Ray, 1976; Walker, Santos & Quintero, 1976).

These reports together with mean mortality rates of 23% and 55% for neonatal group B streptococcal meningitis and septicemia respectively (Anthony & Okado, 1977), has provided the impetus to investigate possible alternative treatment regimens.

The relevance of in vitro methods to determine antimicrobial susceptibility with a fixed inoculum size of about 10⁴ organisms/ml, has been questioned (Baker, 1977). There is evidence to suggest that some infants with group B streptococcal meningitis have between 10⁸-10¹⁰ viable bacteria/ml of cerebrospinal fluid. By increasing the inoculum size to 10⁴ organism/ml the MIC of penicillin is increased to >2-4 mg/l (Baker, 1977); this is close to penicillin levels that can be achieved in the cerebrospinal fluid, with a daily dose of 250,000 units/kg (Baker, 1977).

Antibiotic combinations of a penicillin and an aminoglycoside against a variety of streptococci frequently demonstrate in vitro synergism. Streptococcus agalactiae is no exception although experience is limited and some of the information conflicting. For example Schauf, Deveikis, Riff & Serota (1977), were only able to demonstrate synergism with clinically achievable levels of ampicillin and gentamicin in two strains. On the other hand these authors also reported some interesting observations from kinetic studies, plotting time-killing curves for ampicillin (1-2 mg/l) in combination with gentamicin (10 mg/l) and have shown a 1-4 log₁₀ reduction in colony counts after 4 h incubation, compared with results for ampicillin alone. Furthermore the killing rates for ampicillin alone are much slower for group B streptococci than for Streptococcus pyogenes, but are usually complete by 18 h incubation.

The clinical relevance of these observations remains to be determined. In an experimental mouse model improved survival and accelerated clearing of bacteremia has been reported, using combined therapy with ampicillin and
Leading articles

Aminoglycoside ototoxicity

The ototoxicity of gentamicin has been recognized since first human trials in the early 1960s, but is usually not clinically apparent. Although vestibular disturbances may present as vertigo or ataxia, and cochlear impairment may lead to perceptive deafness, otological damage must usually be sought by vestibular function tests or audiometry. Even so, the commonest audiometric changes are detectable only at high frequencies (in excess of 4000 Hz), and are usually reversible once the drug is discontinued (Jackson & Arcieri, 1971). Damage to neuroepithelial cells is permanent, and hair cells have no regenerative capacity, but in fact, some improvement in function almost always occurs. The mechanism of ototoxicity is not fully understood, but aminoglycosides may disturb endolymphatic ionic homeostasis by interfering with cell membrane potassium/sodium transport mechanism. Hair cells may be destroyed by osmotic gradient changes, or possibly by a direct toxic effect. Initial alterations in osmotic gradient are reversible, but there seems to be a point beyond which reversibility is no longer possible (Neu & Bendush, 1976).

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