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Review

The current and future roles of neonatal infection surveillance programmes in combating antimicrobial resistance

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ABSTRACT

Neonatal sepsis is an important cause of morbidity and mortality, particularly in premature or low birth weight babies. Hospital-acquired blood stream infections represent a significant and largely preventable cause of disease in this population. Neonatal units have been identified as a common site for the development and transmission of antimicrobial-resistant pathogens, a significant issue in modern medicine.

Neonatal surveillance programmes collect prospective data on infection rates and may be used to optimise therapy, benchmark practice and develop quality improvement programmes. Despite this, the number of networks is relatively few and these are largely concentrated in resource-rich nations. Furthermore, surveillance definitions may vary between programmes impairing our ability to draw comparisons between them. Better harmonisation is required between networks to ensure that they achieve their potential as a valuable tool for benchmarking of hospital-acquired infection rates between units.

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1. Introduction

Infants are at a substantial risk of infection during the neonatal period, especially those who are born prematurely or with a very low birth weight (VLBW) [1]. Infection remains a significant cause of morbidity and mortality [2]. In addition, neonatal intensive care units (NICUs) are common sites for the acquisition of antimicrobial-resistant pathogens which may not be susceptible to first-line treatment regimens [1]. Failure to treat early with appropriate antimicrobials may therefore lead to poor outcomes. It is necessary to have a thorough understanding of the current epidemiology of neonatal infections in order to be able to select the best antimicrobial combinations for empiric treatment. This epidemiology is currently poorly defined both in terms of the common causative pathogens of neonatal infection and their antimicrobial resistance rates [3]. Neonatal infection surveillance programmes are an important means of collecting these data in order to optimise antimicrobial treatment protocols and prevent the development of resistance.

2. Neonatal sepsis

2.1. Classifications of neonatal sepsis

Neonatal sepsis has classically been divided into two distinct clinical groups which aim to categorise the infection episode by the likely source of the responsible pathogen. This classification system guides first-line empiric antibiotic therapy as clinical presentations are typically non-specific and it is necessary to initiate treatment before a positive culture result is available [1]. Early-onset sepsis (EOS) is variably defined as occurring before 48 or 72 h of life and is the result of vertical transmission of pathogens from the mother during labour or delivery [2]. It typically presents as a fulminant, systemic illness and in resource-rich countries is predominately caused by Group B Streptococci (GBS) and *Escherichia coli* [2]. Late-onset sepsis (LOS) (>48 or 72 h) is generally acquired via horizontal transmission of pathogens from the environment. LOS in preterm infants on resource-rich NICUs is usually due to hospital-acquired infection, particularly in units which do not admit infants from home [1]. It typically has a more gradual onset and lower mortality rate than EOS with the most common pathogens being Coagulase-negative Staphylococci (CoNS) and Enterobacteriaceae [1]. Common causative organisms for neonatal sepsis are shown in Table 1.

Infants admitted to NICUs are at a high risk for developing healthcare-associated infections (HAIs) [6]. These are considered hospital-acquired if occurring more than 48 h after admission to hospital, with hospital-acquired bloodstream infections (HABSIs) representing one of the most important HAIs in NICUs [6]. HABSIs are often related to certain clinical practices, such as the insertion of invasive devices including central venous catheters (CVCs) in the context of the reduced immunological function and birthweight of premature infants [6]. In particular, central-line bloodstream infections (CLABSIs) occurring secondary to CVCs are an important and largely preventable cause of HABSI in the NICU [6].

2.2. Variations in definitions

Debate exists over the most appropriate cut-off point for EOS with 24 h, 72 h, 4 days and 7 days having all been used as alternatives to 48 h. Whilst the GBS literature has universally accepted the 7 day cut-off for EOS, other papers from the USA have almost invariably used 72 h and a few isolated studies have separated EOS from very early-onset sepsis to specifically analyse the first 24 h of life. Lengthening the EOS period minimises the chances of missing any relevant cases and may be useful to describe the epidemiology of pathogens such as GBS which are known to be vertically transmitted. However, it risks misclassifying cases of horizontally acquired sepsis as vertically transmitted. By contrast, whilst the majority of cases of EOS occur on the first day of life, a definition of 24 h risks missing a significant proportion of vertically acquired infections. There is still no widely accepted definition in the literature but in general it is accepted that a definition of 48 or 72 h is most likely to represent the transition between these two routes of infection [3].

Difficulties also arise when trying to differentiate true positive CoNS cultures from those representing sample contaminations. Several previous studies have defined CoNS infection as clinical sepsis in the presence of two or more positive cultures from separate sites [7]. In practice however, this definition is often impractical with problems

Table 1
Common causative pathogens of neonatal sepsis in resource-rich countries [3–5].

	Early-onset sepsis (%)	Late-onset sepsis (%)
Gram-positive bacteria	70–85	70–90
Group B Streptococci (GBS)	30–60	<5
Coagulase-negative Staphylococci (CoNS)	<1	45–85
S. aureus	<5	5–15
Enterococci	<5	10–15
Gram-negative bacteria	15–30	15–25
E. coli	10–20	5–10
Other Enterobacteriaceae	<1	10–15
Fungi	<1	5
Candida albicans	<1	3–4

Table 2
Risk factors for neonatal sepsis [1].

	Risk factors
Early-onset sepsis	Known maternal GBS colonization
	Premature rupture of membranes
	Prolonged rupture of membranes >18 h
	Maternal fever or chorioamnionitis
	Preterm delivery
	Multiple pregnancies
	Traumatic delivery
Late-onset sepsis	Disruption of intrinsic neonatal barriers (e.g. skin)
	Prolonged use of an indwelling intravascular catheter
	Invasive procedures (e.g. endotracheal intubation)
	Lack of enteral feeding with breast milk
	Prolonged use of antibiotics (particularly broad spectrum)
	Necrotising enterocolitis
	Premature or VLBW infants

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