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PLAIN LANGUAGE SUMMARY

Antibiotic treatment for neonatal sepsis: changing trends and future directions

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Neonatal sepsis, which is a serious infection in newborns, is a major global health crisis, causing over 550,000 newborn deaths annually. It is most common and deadly in low-income and middle-income countries. Premature infants are at the highest risk, with mortality in babies with extremely low birth weight being of over 20%.

Understanding the infection

Neonatal sepsis is categorized into two main types, based on when the infection occurs:

- **Early-onset sepsis:** Occurs within the first 72 hours after birth.
  - **Cause:** Typically acquired from the mother before or during delivery.
  - **Main bacteria (in high-income countries):** Group B *Streptococcus* (GBS) and *E. coli*.
  - **Prevention:** Universal screening and antibiotic treatment for pregnant women who are positive for GBS have significantly reduced early-onset GBS cases.
  - **Management:** Guidelines recommend risk assessment tools, like the Sepsis Calculator, to determine which babies truly need antibiotics, thus reducing unnecessary exposure.

- **Late-onset sepsis:** Occurs after 72 hours of life, often due to hospital-acquired (nosocomial) infections.
  - **Cause:** Associated with prolonged hospital stays, medical devices (like central lines and ventilators), and immature immune systems, especially in premature babies.
  - **Main bacteria (in high-income countries):** Coagulase-negative *Staphylococci* are most common, followed by Gram-negative organisms like *E. coli* and *Klebsiella*.
  - **Other infections:** Late-onset sepsis can manifest as ventilator-associated pneumonia, catheter-related bloodstream infections and urinary tract infections.

The problem of resistance and fungal threats

A critical issue is the rising incidence of antibiotic resistance, especially to common drugs like aminoglycosides and cephalosporins, driven by the frequent, broad-spectrum use of antibiotics in the neonatal intensive care unit (NICU).

In addition to bacterial infections, fungal infections (mainly *Candida*) are a major cause of late-onset sepsis, particularly in babies with extremely low birth weight, with high mortality. In NICUs with high rates of fungal infection, preventative antifungal medication (like fluconazole prophylaxis) is recommended.

Antibiotic stewardship

To combat resistance and minimize side effects (such as neurodevelopmental delay) from unnecessary antibiotic exposure, antimicrobial stewardship programmes are essential.

- **Goal:** Ensure timely, effective treatment while dramatically reducing unnecessary antibiotic use.
- **Key strategies:**
  - Implementing evidence-based guidelines and standardized treatment protocols.
  - Using risk assessment tools to accurately identify infants with an infection.
  - Rapidly de-escalating therapy (switching to narrower-spectrum drugs or stopping them entirely)

once culture results confirm no infection or identify a sensitive organism.
- Implementing 'care bundles' (e.g. strict hand hygiene and central line maintenance) to prevent hospital-acquired infections.

Effective stewardship, driven by multidisciplinary teams, has been shown to significantly reduce antibiotic use and decrease the prevalence of multidrug-resistant bacteria in NICUs, ultimately leading to better outcomes for vulnerable newborns.