expected. It is clear that mammalian development requires the functional and complementary presence of at least parts of both maternal and paternal genome. Affects on embryonic and fetal growth and behaviour have been observed. The challenge now is to determine how many childhood and adult disorders also are associated with genomic imprinting.

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Neonatal infections with coagulase negative staphylococci

Staphylococci are members of the family of bacteria Micrococccaceae. They are Gram positive, catalase positive cocci that form grape like clusters (from the Greek staphyle: bunch of grapes, coccus: grain or berry). The classification of staphylococci is extremely complex and has been revised repeatedly over the last 30 years. More and more new species have been recognised, so that there are now 19 distinct species recognised by Bergey's Manual of Systematic Bacteriology (1986). The coagulase test is one of several tests used by clinical laboratories to distinguish Staphylococcus aureus from other staphylococci. 'Coagulase negative staphylococci' is a term used to describe species that do not coagulate plasma under the defined conditions of the coagulate test.

Coagulate negative staphylococci are frequent blood culture isolates from neonates in many intensive care units. 1 2 Neonatal infections with coagulate negative staphylococci are hospital acquired and are usually diagnosed after the first week of postnatal life. 3 Quantitative blood culture techniques have shown that the numbers of coagulate negative staphylococci in the blood of premature neonates with bacteraemia may exceed 1000 colony forming units/ml. Defective opsonisation and phagocytosis may allow these large numbers of coagulate negative staphylococci to be cleared. Staphylococcus hominis is the species most frequently associated with neonatal infection, although other species such as Staphylococcus hominis, Staphylococcus warneri, and Staphylococcus haemolyticus have also been implicated. The strains involved in neonatal infection are usually resistant to a wide range of antibiotics. 4 Antibiotic resistant strains are spread from neonate to neonate on the hands of medical and nursing staff leading to colonisation of the skin of premature neonates in intensive care units within the first week of life. 5 Apart from the skin, another major reservoir of antibiotic resistant coagulate negative staphylococci is the bowel of neonates, where numbers may exceed 10 10 colony forming units/g dry weight.

Many strains of coagulate negative staphylococci secrete a complex mucopolysaccharide, 6 which has been termed 'extracellular slime substance'. Electron microscopy studies suggest that it stabilizes the attachment of coagulate negative staphylococci to the surfaces of foreign bodies such as intravascular catheters. 9 The influence of extracellular slime substance on the adherence of coagulate negative staphylococci to the immature skin of premature neonates is not known. Extracellular slime substance has been reported to have a number of immunomodulating effects such as inhibiting antibody binding to the staphylococcal cell wall, reducing the chemotactic response of neutrophils, and interfering with T and B cell function. 10 Although extracellular slime substance is probably important in stabilising the attachment of bacteria on surfaces, its importance in determining pathogenicity is controversial. 11 It is not produced by all clinically significant isolates of coagulate negative staphylococci and other bacterial surface characteristics such as bacterial cell surface hydrophobicity may be more important determinants of pathogenicity. 11

It is not possible to sterilise the skin and therefore a proportion of percutaneously collected samples will be contaminated with cutaneous flora. Use of quantitative blood culture techniques may help to differentiate blood culture contamination from bacteraemia. 12 The proportion of blood cultures collected from neonates and children that are contaminated with coagulate negative staphylococci has been estimated to 7–10%. 13 This proportion is similar to that reported for blood cultures collected from neonates with necrotising enterocolitis. 14

There is no evidence that coagulate negative staphylococci can cross intact skin. Intravascular catheters frequently become colonised with antibiotic resistant strains, 17 and neonatal bacteraemia with coagulate negative staphylococci is frequently associated with the use of intravascular catheters. 5 15 18 It is likely that infected catheters are the most common source of neonatal infection with coagulate negative staphylococci. The mechanisms by which bacteria
colonise intravascular catheters are poorly understood. Bacteria may be washed into the catheter after contamination of infused fluids or migrate from the cutaneous surface along the outside of the catheter. The relative importance of these two routes of catheter colonisation in neonates is not known. In addition to catheter associated infections, coagulase negative staphylococci may cause wound infections and urinary tract infections after urological surgery. Meningitis with coagulase negative staphylococci in neonates is usually associated with ventricular drainage devices.

The clinical signs of bacterial infection in neonates are non-specific. Rapid tests such as buffy coat examination and tests for neutrophil activation or acute phase protein response may improve the accuracy of diagnosis at the onset of episodes of suspected infection.

In contrast to Gram negative infections, neonatal mortality associated with infections caused by coagulase negative staphylococci is unusual. The clinical signs of infections with coagulase negative staphylococci are often minor with insidious onset of signs such as lethargy, increased frequency of apnoea, hypotonia, and poor peripheral perfusion. Delayed treatment may lead to disseminated disease, however, and so treatment with an appropriate antibiotic should be initiated as soon as infection with coagulase negative staphylococci is suspected and the appropriate diagnostic samples have been taken. Isolates of coagulase negative staphylococci from neonates are often resistant to penicillin and aminoglycosides, but are also commonly resistant to a range of other antibiotics such as chloramphenicol, cloxacillin, and erythromycin. Unless specific tests are performed, resistance to β-lactam antibiotics may not be detected by the laboratory. Resistance of neonatal coagulase negative staphylococcal isolates to the glycopeptide antibiotics, vancomycin and teicoplanin, has not been reported and these are the antibiotics of choice for treating suspected neonatal infections with coagulase negative staphylococci. Strains of vancomycin resistant S. haemolyticus were isolated from the peritoneal dialysis fluid of an adult. Rifampicin inhibits a wide range of micro-organisms, including staphylococci at very low concentrations, but must be used with another antibiotic to avoid the rapid emergence of rifampicin resistance. Ventriculitis or meningitis associated with use of intraventricular drainage devices can be controlled with intravenous vancomycin combined with oral or intravenous rifampicin, but eradication of the infection usually requires removal of the colonised device. In neonates with suspected catheter associated infections, peripheral intravenous catheters associated with local signs of inflammation should be removed. Whether or not central lines colonised with coagulase negative staphylococci should be removed from neonates is controversial. There are no published comparative studies of treatment regimes for neonates with infected central lines.

The frequency of neonatal infection with coagulase negative staphylococci may be reduced by restricting the duration of use of intravascular catheters, avoidance of contamination of infusion system connections, better care of the catheter insertion site, and delegation of responsibility for the management of central lines to a specialist team. Better understanding of the mechanisms leading to bacterial colonisation of catheters and of the interaction between intravascular catheters and developing skin may lead to new strategies for preventing infections with coagulase negative staphylococci in premature neonates.

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