

London Neonatal Operational Delivery Network (ODN) infection prevention & control (IPC) guidance for colonisation or infection with multi-drug resistant bacteria

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1. Introduction

Across London it is recognised that babies face delays in transfer between neonatal units, both for escalation of care when requiring either high dependency or intensive care, or repatriation for lower dependency care. Reasons for this include:

- Limitations on neonatal unit cot capacity
- Limitations on neonatal nurse staffing
- Concerns about colonisation with multi-drug resistant (MDR) organisms and the need for enhanced IPC precautions
- Lack of side room availability

Work done by the London Neonatal ODN has demonstrated a lack of uniformity in Trusts' IPC practices. This document is intended to advise and support Trusts on standards and expectations for management of IPC concerns, particularly with regard to MDR organisms, in order to improve the efficiency of transfer of babies between neonatal units and to guide on safe, evidence-based IPC practice.

This guidance has been developed by a working party supported by the Neonatal ODN, Public Health England (London) and the Directors of Infection Prevention & Control (DIPC) Forum, with broad clinician representation as follows:

- All 3 neonatal ODN sectors (north west London, north east and north central London, south London)
- All levels of neonatal unit (Neonatal Intensive Care Unit (NICU), Local Neonatal Unit (LNU), Special Care Unit (SCU))
- Neonatal medical and nursing staff
- IPC nurses
- Microbiology & Infectious Diseases

This document provides:

- Overarching principles for IPC in the context of ensuring smooth functioning of the ODN and excellent clinical care (see box)
- Information on organisms of concern that have an impact for IPC and clinical care (refer to section 2.1)
- Information on classification of IPC precautions and advice on practice (refer to 2.2)
- Guidance on screening for MDR organisms (refer to section 3)
- Advice on IPC in the context of transfer of babies between neonatal units in the ODN (refer to section 4)

2. Overarching principles

- IPC guidance supports risk management for patient care but should not be a barrier to patients receiving the right care, in the right place, at the right time
- Standard infection prevention and control precautions are expected as a minimum for all episodes of patient care
- With limited capacity and side room availability, Trusts are expected to risk assess their patient population and care for those requiring enhanced precautions within an appropriate ward environment. This is current practice across all NHS provider services.
- Education and training of staff and visitors, including the importance of hand washing, or using hand sanitiser, before and after contact with the patient or the patient's environment, remain the mainstay of infection control (1)
- Infants transferred between neonatal units should not be isolated in side rooms routinely following admission from other neonatal units
- Referrals and repatriation should not be refused on the basis of colonisation or infection
- This guideline is limited to guidance on MDR organisms and does not cover advice for viruses and other organisms that are transmitted via droplet or airborne route
- This document is not designed to provide detailed guidance for the management of outbreaks of infection and/or colonisation in individual units. Units should work with their local IPC teams in these circumstances.

3. General information

This section provides some basic information on the microbiology of organisms of concern that may colonise or cause infection in babies on neonatal units. The resistance to antibiotics inherent in the organisms highlighted below can all be spread through plasmid-mediated (mobile genetic element) enzymes. The organisms have great potential for spread through contact.

3.1 Bacteria & resistance patterns

ESBL: Enterobacteriales that produce an extended-spectrum β -lactamase (ESBL)

ESBL in this document refers to any organism that has a class A β -lactamase enzyme, that hydrolyses and (usually) confers resistance to:

- '2nd and 3rd generation' cephalosporins, e.g. cefuroxime, cefotaxime, ceftazidime and ceftriaxone
- 4th generation cephalosporins e.g. cefepime, cefpirome, but not cephamycins (eg cefoxitin)

ESBLs occur in *Enterobacteriales*. This is a large family of Gram negative bacteria which includes *E. coli*, *Klebsiella* species, *Enterobacter* species, *Serratia* and *Citrobacter*.

ESBLs are clinically important because they can break down cephalosporins that are used in the treatment of many severely ill patients. Delayed recognition and inappropriate treatment of severe infections caused by ESBL-producers with cephalosporins has been associated with increased mortality.

Carbapenem resistant organisms (CRO):

Organisms can be resistant to carbapenems (CRO) irrespective of the organism species or mechanism. Some *Enterobacteriales* are also able to produce ‘carbapenemases’ which is a term used to mean any β -lactamase enzyme that hydrolyses carbapenems (doripenem, ertapenem, imipenem and meropenem). They are hence sometimes referred to as Carbapenemase Producing *Enterobacteriales* (CPE). Carbapenems are antimicrobial drugs of last resort and are crucial for preventing and treating life-threatening nosocomial infections.

Many carbapenemases confer resistance or reduced susceptibility to all or nearly all members of the β -lactam class, not just to carbapenems. They are also often resistant to quinolones e.g. ciprofloxacin and aminoglycosides e.g. amikacin and gentamicin.

Bacteria with acquired carbapenemases are of IPC concern. However some can also be intrinsic (found naturally) in a few clinically significant bacteria, such as *Stenotrophomonas maltophilia*, *Aeromonas* species, ‘chryseobacteria’ including *Elizabethkingia meningoseptica* and *Acinetobacter baumannii*.

Classification of Carbapenemases:

Adapted from PHE guidance (10).

Enzyme type	Antibiotic activity spectrum	Organisms affected
KPC	All β -lactams	<i>Enterobacteriales</i> <i>Pseudomonas aeruginosa</i> <i>A. baumannii</i>
NDM IMP VIM	All β -lactams except aztreonam	<i>Enterobacteriales</i> <i>Pseudomonas</i> species <i>Acinetobacter</i> species
OXA	Carbapenems	<i>Enterobacteriales</i> <i>A. baumannii</i> and rarely <i>Pseudomonas aeruginosa</i>

GES	Some are ESBLs and others are carbapenemases	<i>Enterobacteriales</i> <i>Pseudomonas aeruginosa</i>
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KPC: *Klebsiella pneumoniae* carbapenemase (KPC); NDM: New Delhi metallo-beta-lactamase (NDM-1); IMP (active on imipenem) metallo-beta-lactamase; VIM: Verona integron-encoded metallo-beta-lactamase; OXA: OXA beta-lactamases; GES: GES-type extended-spectrum β -lactamases (ESBLs).

Aminoglycoside resistant organisms

Resistance to aminoglycosides such as gentamicin and amikacin can occur in a variety of organisms including *Pseudomonas aeruginosa* and *Enterobacteriales*.

There are a variety of mechanisms by which this can occur, including bacterial production of inactivating enzymes. Inactivating enzymes can be encoded by plasmids or associated with transposable elements. Plasmid exchange and dissemination of transposons facilitate the acquisition of drug resistance.

AmpC beta-lactamase resistance

Several of the *Enterobacteriales* species, such as *Enterobacter*, *Citrobacter*, and *Serratia* encode an inducible, chromosomal AmpC beta-lactamase.

Due to their ability to express this enzyme, treatment failure can be observed with the use of third generation cephalosporins and piperacillin/tazobactam. Some AmpC producing isolates may be resistant to all beta-lactams except carbapenems.

Meticillin resistant Staphylococcus aureus (MRSA)

Meticillin was the first penicillinase resistant penicillin and has been widely used in testing susceptibility of *S. aureus* to penicillinase resistant β -lactam agents. MRSA refers to any *S.aureus* that is oxacillin and cefoxitin resistant. This is reflected clinically as flucloxacillin resistance. They are also often resistant to other classes of antibiotics including aminoglycosides e.g. amikacin and gentamicin.

Vancomycin resistant Enterococci (VRE)

Vancomycin-resistant enterococci (VRE) are differentiated from other strains of *Enterococcus* by an increased minimum inhibitory concentration and hence resistance to vancomycin with the presence of vancomycin-resistance gene clusters. VRE can be seen in *E. faecalis* and *E. faecium* strains but are more common in *E. faecium*. Resistance to both teicoplanin and vancomycin is observed and this presents limited treatment options.

VRE can be selected out by selection pressure with vancomycin therapy and can colonise the gastrointestinal tract but can also be found on the skin due to faecal shedding. Colonisation with VRE generally precedes infection, but not all patients with colonisation will become infected.

Panton-Valentine Leukocidin (PVL) producing Staphylococcus aureus (PVL-SA)

Although not necessarily a MDR organism, PVL-SA is considered in this guidance as an organism of concern due to potential for serious illness and transmission.

Panton-Valentine Leukocidin (PVL) is a toxin that destroys white blood cells and is a virulence factor in some strains of *Staphylococcus aureus*. Strains of PVL-SA producing disease have emerged in the UK and worldwide. PVL-SA may be meticillin-sensitive (MSSA) or meticillin-resistant (MRSA).

Like other *S. aureus* strains, PVL-SA predominantly cause skin and soft tissue infections (SSTI), but can also cause invasive infections.

3.2 IPC practice and precautions

3.2.1 Standard IPC precautions

All Trusts with Neonatal Units are expected to have comprehensive IPC policies and guidance, with specific reference to IPC within the neonatal environment. It is advised that the following should be considered in this guidance:

- Hand hygiene (1), including handwashing, use of hand sanitiser and skin care for hands damaged by frequent decontamination
- Contact and other transmission-based precautions
- Decontamination of equipment, including mobile technology
- Use of personal protective equipment (PPE)
- Waste disposal
- Management of invasive devices
- Cleaning of the environment
- Antimicrobial stewardship
- Visitor policies
- Parent information

Parents and visitors should be taught good hand hygiene technique and there should be clear visual information displayed demonstrating these principles in clinical and non-clinical areas on a unit.

Hand hygiene on a unit should be audited regularly and the results of audit and learning outcomes fed back to the clinical staff.

3.2.2 Contact precautions

Transmission-Based Precautions are the second tier of basic IPC and are used in addition to standard IPC precautions for patients who may be infected or colonised with certain infectious agents (7,8). There are 3 types of transmission-based precautions: contact, droplet and airborne.

Contact precautions are most important in preventing transmission of bacterial, particularly MDR, organisms (refer to section 3.2.3). The principles of contact precautions include:

- Ensure appropriate patient placement
 - Baby can be nursed in an open ward in most circumstances

- This should be based on a risk assessment depending on the pathogen and the site from which the pathogen is isolated
- Contact precautions signage should be displayed and be clearly visible at all times.
- Ensure excellent hand hygiene practice at all times
- Appropriate use of PPE, including gloves and aprons/gowns (6)
 - Gloves, aprons/gowns and hand sanitiser dedicated to the patient should be available at the cot side
 - Gloves predominantly provide protection to the wearer against blood and bodily fluids and should be worn for all such patient contact. The need to use gloves for other patient care may be decided after risk assessment. Advice may vary in different units on the use of gloves in babies under contact precautions.
 - There is a risk with MDR colonisation that contamination of staff uniforms can lead to spread of bacteria. The following practice regarding use of aprons and gowns is recommended:

Handling of infant	PPE required
Not held close to the body by staff	Apron
Held close to the body by staff	Gown

- PPE should be donned before delivering direct patient care and discarded appropriately before leaving the patient zone in order to reduce spread of pathogens
- Hand hygiene must be performed immediately before donning and after removing PPE
- Limiting transport and movement of patients to medically-necessary purposes only.
 - Contact precautions should be observed during any transfer but patient care should not be compromised due to use of PPE
- Use of single use and/or dedicated patient-care equipment where possible
 - If use of shared equipment for multiple patients is unavoidable, clean and disinfect such equipment before use on another patient according to local IPC guidance
- Prioritise cleaning and disinfection of the patient zone (1) focusing on frequently-touched surfaces and equipment in the immediate vicinity of the patient
 - Once the baby is discharged or transferred, a deep (terminal/ enhanced) cleaning process (according to the local IPC policies) should take place
- Ensure infected waste and linen streams are used as per Trust policy

Where a baby from a multiple birth is under contact precautions, units should consider placing siblings under contact precautions too, regardless of colonisation status.

When mother is known to be colonised with MDR organisms, consider instituting contact precautions for the baby pending admission swabs. Risk assessment should be undertaken prior to stepping down precautions.

For babies under contact precautions, parents should be given additional information and support to enable them to fully participate in the care of their baby whilst minimising the spread of resistant organisms around the unit.

Additional measures

Closed incubator

A closed incubator should not be considered to be an extra barrier against transmission of MDR organisms. It is recommended that babies are nursed in an appropriate incubator or cot as dictated by the age, size and clinical and developmental requirements of the baby.

Side room

Although nursing a baby in a side room may provide additional reassurance and units with side room availability may use them as part of their IPC processes, it is not necessary to prevent transmission of MDR organisms. Therefore, the absence of side room capacity must not prevent transfer of babies between neonatal units.

It is recognised that CRO are considered to pose such a high risk that units may choose to nurse colonised babies in a side room, if one is available, in addition to undertaking contact precautions (refer to section 5). Such decisions are not mandated by this guideline and should not prevent network transfers and repatriations.

3.2.3 Recommended IPC precautions in MDR colonised babies

The need for enhanced precautions and the level of precautions advised will depend on the organism and the resistance pattern. Trust neonatal unit and IPC staff should work together to risk assess the situation and decide on the right level of IPC precautions, according to the organism, staffing, availability of room(s) for isolation and the presence of other IPC concerns in the unit.

Nursing with contact precautions, including appropriate use of gloves and aprons/gowns, is considered adequate for infants with the following:

- MRSA
- Gram-negative organisms resistant to aminoglycosides or cephalosporins
- Extended spectrum beta-lactamase producing organisms (ESBLs)
- AmpC-producing organisms
- VRE
- PVL-producing *S. aureus*

There may be circumstances where following local risk assessment, IPC staff advise contact precautions for babies colonised or infected with other organisms.

CROs are considered particularly worrying, due to both the high risk of transmission between patients and the severely limited antibiotic options for treatment of invasive infection. Isolation in a side-room (if available) should be considered for CROs, if facilities exist and safe staffing allows along with the use of gowns and gloves.

3.2.4 Other levels of transmission-based precautions

Droplet

Used for infections caused by organisms that are spread in small droplets. Some infectious agents transmitted by the droplet route also may be transmitted by the direct and indirect contact routes. In contrast to contact transmission, respiratory droplets carrying infectious pathogens transmit infection when they travel directly from the respiratory tract of the infectious individual to mucosal surfaces of the recipient, generally over short distances. Respiratory droplets are generated when an infected person coughs or sneezes. Procedures such as suctioning and endotracheal intubation can produce aerosols that may similarly lead to organism transmission.

Examples include *Bordetella pertussis*, influenza virus, adenovirus, rhinovirus, respiratory syncytial virus (RSV) and *Neisseria meningitidis*.

Airborne

Used for infections caused by organisms that are spread through the air from one person to another (examples: Tuberculosis, Measles, Varicella zoster). Airborne transmission occurs by dissemination of either airborne droplet nuclei or small particles in the respirable size range containing infectious agents that remain infective over time and distance. Microorganisms carried in this manner may be dispersed over long distances by air currents and may be inhaled by susceptible individuals who have not had face-to-face contact with (or been in the same room with) the infectious individual.

These precautions pertain to organisms that are currently excluded from this guideline. Local IPC specialist advice should be sought for any baby who requires droplet or airborne precautions. If such a baby needs to be transferred between hospitals, detailed discussions between consultants and the infection prevention and control teams in both units are required.

4. Screening

It is advised that all neonatal units should, as a minimum, perform screening swabs for key organisms on all babies admitted after ex utero transfer.

Key organisms are currently considered to be meticillin-resistant staph aureus (MRSA) and carbapenem-resistant organisms (CRO).

Recommended screening swabs are:

- Nose and groin swabs for MRSA
- Rectal or perianal swabs, or stool sample for CRO

There is no evidence that screening regularly and more widely for other organisms, such as bacteria that do not have significant antibiotic resistance, is useful in reducing invasive infections.

Additional screening swabs may be undertaken according to local Trust policy. These may include:

- Additional admissions screens for other MDR Gram negative organisms
- Admission swabs for inborn babies
- Weekly swabs for all inpatients
- Weekly swabs at times of colonisation or outbreak (2,3)

Although there is some evidence that there is a correlation between colonisation and subsequent infection, it is not clear that the timing of detection of colonisation is sufficiently early to influence management, that routine swabbing adequately predicts the distribution of pathogens (and antimicrobial resistance) associated with invasive infection, that it impacts on clinical outcomes, or that it is cost effective (9). However, it may provide useful information about transfer of key organisms within a neonatal unit and to direct unit antibiotic policy.

5. Transfer & repatriation

5.1 Prior to transfer

There should be information provided to the receiving hospital regarding a baby's infection/colonisation status, where available, at the time of referral. Effective communication between staff in healthcare settings will help facilitate efficient patient transfers and are crucial in reducing transmission of infection.

A discharge summary documenting the baby's infection status should be completed so that the transport team and receiving unit have a detailed record of the baby's infection/colonisation history.

The most recent microbiology results from the referring unit should be accepted by the receiving unit and should not delay transfer of care. Documentary evidence of results, where available, should be provided by the referring unit. There should be no requirement for 'discharge screening'.

Referrals and repatriation should not be refused on the basis of colonisation or infection. Appropriate IPC precautions and prioritisation should be in place to ensure referrals can be accepted.

5.2 Following transfer

The practice of routinely isolating infants in side-rooms when transferred from other units is unnecessary. The vast majority of colonisations are with organisms that will be seen on all units and are spread via contact.

There is evidence (4,5) that nosocomial spread occurs due to direct contact with the patient or patient environment, thus contact precautions used in a nursery (see section 3.2) should negate the need for a side room.

From arrival, incoming babies should be nursed with contact precautions until local unit admission screening swab results are available.

If screening swabs are negative for key organisms (see 3.1), babies should be nursed as for other inpatients on the receiving unit using standard IPC precautions (refer to 3.2.1). There

is no evidence, in the presence of appropriate hand hygiene, that gloves and aprons should be used during routine patient contact with babies who are *not* colonised with MDR organisms (6).

The need for enhanced precautions and the level of precautions advised will depend on the organism and the resistance patterns. Refer to section 3.2.3 for advice on precautions for babies colonised with MDR organisms.

6. Knowledge gaps and research opportunities

This guidance is based on best available evidence and consensus. It is recognised by the working group that there are significant gaps in the evidence base for IPC in neonatal units. The following are specific areas where further research could usefully inform future practice:

- Use of plastic aprons versus gowns as part of standard IPC and transmission-based (especially contact) precaution practice
- Usefulness of a closed incubator as an additional measure to reduce transmission of MDR organisms
- Efficacy and safety of decolonisation in reducing infection or transmission in the neonatal population
- Impact on colonisation and infection outcomes of routine weekly screening versus no screening
- Clinical and cost-effectiveness of routine weekly screening to prevent infections
- Impact of maternal colonisation on colonisation and infections of babies and on spread of infections in neonatal units

7. Glossary

CPE	Carbapenemase-producing <i>Enterobacteriales</i>
CRO	Carbapenem-resistant organisms
DIPC	Director of Infection Prevention & Control
ESBL	Extended-spectrum β -lactamase
IPC	Infection prevention & control
LNU	Local Neonatal Unit (level 2 Neonatal Unit)
MDR	Multi-drug resistant
MRSA	Meticillin-resistant <i>Staphylococcus aureus</i>
NICU	Neonatal Intensive Care Unit (level 3 Neonatal Unit)
ODN	Operational Delivery Network
PHE	Public Health England
PPE	Personal protective equipment
RSV	Respiratory syncytial virus
SCU	Special Care Unit (level 1 Neonatal Unit)
VRE	Vancomycin-resistant <i>Enterococcus</i>

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Appendix 1

London Infection Control and Prevention Task & Finish Group membership

Chairs

Tim Watts. Consultant Neonatologist, Guy's & St Thomas' NHS Foundation Trust

Nabeela Mughal, Consultant Microbiologist, Chelsea & Westminster Hospital NHS Foundation Trust

Representatives from Neonatology (consultants and nurses)

Christina Kortsalioudaki	Consultant Neonatologist	University College Hospitals NHS Foundation Trust
Rashmi Gandhi	Consultant Neonatologist	Kings College Hospital NHS Foundation Trust (King's)
Sijo Francis	Consultant Neonatologist	St George's University Hospitals NHS Trust
Narendra Aladangady	Consultant Neonatologist	Homerton University Hospital NHS Foundation Trust
Mark Thomas	Consultant Neonatologist	Chelsea & Westminster Hospital NHS Foundation Trust
Sunit Godambe	Consultant Neonatologist	Imperial College Healthcare NHS Trust
Mojgan Ezzati	Consultant Neonatologist	Lewisham & Greenwich NHS Trust
Jenni Jagodzinski	Lead Nurse	London Neonatal ODN
Elaine McNally	Neonatal Matron	Barking, Havering & Redbridge University Hospitals NHS Trust
Kim Padfield	Neonatal Senior Sister	Kings College Hospital NHS Foundation Trust (Princess Royal)
Basani Mabyalane	Neonatal Lead Nurse	Homerton University Hospital NHS Foundation Trust

Representatives from Microbiology/Infectious Diseases

Alleyna Claxton	Consultant Microbiologist	Homerton University Hospital NHS Foundation Trust
James Hatcher	Consultant Microbiologist	Great Ormond Street Hospital for Children NHS Foundation Trust
Aarti Shah	Consultant Microbiologist	Barking, Havering & Redbridge University Hospitals NHS Trust
Stephanie Paget	Consultant Microbiologist	Royal Free London NHS Foundation Trust

Tacim Karadag	Consultant Microbiologist	Lewisham & Greenwich NHS Trust
Albert Mifsud	Consultant Microbiologist	Public Health England, Barts Health NHS Trust
Ellie Alexander	Consultant Microbiologist & Paediatric Infectious Diseases	Public Health England
Paul Heath	Consultant in Paediatric Infectious Diseases	St Georges, University of London & St Georges University Hospitals NHS Trust

Representatives from Infection Prevention & Control

Bronwen Shuttleworth	Lead Nurse IPC for Neonatal Unit	University College Hospitals NHS Foundation Trust
Shona Perkins	Paediatric IPC Lead Nurse	Guy's & St Thomas NHS Foundation Trust
Shona Ross	IPC Clinical Nurse Specialist	Kingston Hospital NHS Foundation Trust
Helen Dunn	IPC Lead Nurse	Great Ormond Street Hospital for Children NHS Foundation Trust
Sheila Howard	Nurse Consultant & Deputy DIPC	Lewisham & Greenwich NHS Trust

Appendix 2

Risk Assessment in IPC

Hazard	Something that can cause adverse effects eg multi-drug resistant (MDR) organism colonisation (hazard) leading to an outbreak (adverse effect)
Risk	An uncertain event or set of events that, should it occur, will have an effect upon the achievement of objectives. A risk is the likelihood that a hazard will actually cause its adverse effects, together with a measure of the impact should these adverse events occur.
Risk assessment	Identifying measures to control risk – think about what might cause harm and decide whether you are taking reasonable steps to prevent that harm eg infection control measures to prevent spread of MDR organisms