

Infection Prevention and Control Gram Negative Resistant Bacteria Policy

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1. Introduction

Multi-Drug resistant (MDR); Extremely-Multi Drug (XDR) and Pan drug resistant (PDR) and Carbapenem Resistant Gram negative Bacteria (CPE)

The issue of antimicrobial resistance in commonly occurring pathogens (bacteria) is a worldwide concern.

The lack of new antibiotics in development mean the treatment options available for serious or resistant infection (e.g. Carbapenem antibiotics) should only be used when there is a clear indication and in consultation with an infection specialist (Microbiologist, Infectious Diseases specialist).

Gram negative resistance can be categorised to guide staff on appropriate infection prevention and control measures:

- Multidrug resistant (MDR)
- Extremely drug resistant (XDR)
- Pan drug resistant (PDR)
- Carbapenem resistant organisms (CPE)

MDR, XDR, PDR

The terms MDR, XDR and PDR can be applied to Enterobacteriaceae, Pseudomonas species and Acinetobacter species.

The exact criteria for meeting these categories is different depending on which bacteria is being considered and is not uniform across all Gram negative bacteria.

The definitions are summarised below.

Carbapenem Resistant Organisms (CPE)

Carbapenem resistance can arise through a variety of mechanisms in Gram negative bacteria. These include

- loss of bacterial outer membrane proteins (porin loss)
- Increased production of some resistance enzymes (e.g. extended beta lactamase (ESBL) production with increased AmpC production).

The most concerning bacteria are those that can produce a carbapenemase enzyme. When the bacterial class involved is Enterobacteriaceae (i.e. coliforms) then such organisms are referred to as Carbapenemase Producing Enterobacteriaceae (CPE). Carbapenemase enzymes can be harboured by bacteria and are not categorised as CPE e.g. carbapenemase producing Pseudomonas species and Acinetobacter species resistant to carbapenems.

It is not uncommon for Carbapenem Resistant Organisms (CRO) to have the ability to be resistant to multiple other antimicrobial classes, not just carbapenems, which can restrict treatment options substantially.

Pan Drug Resistance (PDR)

Until recently, CPE bacteria were in most cases still susceptible to colistin which could be relied upon as a treatment option. However, it is now recognised that colistin resistance can

be found in transmitted between bacteria Gram negative bacteria with the MCR-1 gene. This has been recognised as an emerging global threat by the World Health Organisation.

All of these MDR, XDR, PDR, and CPE Gram negative bacteria may manifest as infections with the same clinical features as other infections. The only way to establish if the infection is caused by a drug resistant strain is through laboratory testing.

Infection prevention and control measures are an essential integral part of any strategy to control Gram negative resistant bacteria. This is achieved through robust risk assessment, early diagnosis, early containment and early appropriate antimicrobial treatment.

2. Aim of the policy

To ensure that all health care workers (HCWs) understand and apply appropriate infection prevention and control precautions when providing care and treatment for patients with suspected or confirmed MDR, XDR, CPE or PDR

3. Key objectives

To ensure consistency across NHS Lothian

- Minimise the risk of cross infection
- To describe best practice
- To optimise patient and staff safety
- To minimise adverse events

4. Policy scope

This policy is designed to safeguard patients, staff and the wider public from the risk of infection from Gram negative resistant bacteria.

This policy applies to all staff employed by NHS Lothian and locum staff on fixed term contracts and volunteer staff.

5. Identification, care and management of a patient with MDR, XDR or PDR colonisation or infection.

5.1 Overview

The ways that the bacteria are spread are the same (e.g. faecal oral spread, respiratory spread, touched surfaces or fomite spread) regardless of whether the bacteria is drug resistant or not. Transmission based precautions prevent further spread.

The clinical significance of an MDR or XDR organism will vary depending on whether the patient has colonisation or active infection. The significance of the result is also influenced by:

- the specimen type from which the bacteria grew
- anatomical site of any infection
- whether the remaining antimicrobial choices are suitable for the patient

The infection prevention and control advice may vary from patient to patient depending on the situation encountered.

- MDR bacteria are defined as having non-susceptibility to at least one agent in three or more antimicrobial categories.
- XDR bacteria are defined as having non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e. the bacteria remains susceptible to only one or two categories)
- PDR bacteria are resistant to all antimicrobial categories and so there are no approved antimicrobial agents that have activity against these strains.

Appendix 1 summarises the relevant antimicrobial classes (and their component antibiotics) which require to be considered for Gram negative bacteria depending on whether they are Enterobacteriaceae, Pseudomonas species or Acinetobacter species.

·	The Gram negative bacteria for which this policy applies are:		
Causative Organism	 Enterobacteriacaea Pseudomonas aeruginosa Acinetobacter species 		
Clinical Manifestation	Can cause infection at any body site/system. Some patients may be colonised (not have acute infection)		
Period of Infectivity	Although acute infections may be successfully treated, for infection prevention and control purposes, patients are considered to be indefinitely colonised with these organisms as there is no effective means of demonstrating los of carriage from the bowel flora. Therefore all precautions will apply for every acute hospital admission.		
Mode of Transmission	 Dependent upon the organism and site of infection Contact Droplet Airborne. 		
Reservoirs	Patients, contaminated equipment, water, staff, environment		
Population at Risk	 Patients with previous exposure to multiple antimicrobial agents (particularly carbapenems) 		

Table 1: Summary Overview

	 Patients in high risk specialities particularly: ITU, HDU, renal, Transplant. Oncology/haematology Neonatal units Neurosurgery
Vaccine Preventable	No
Notifiable Disease	No

5.2 Case Definitions

Table 2: Case definitions

Multidrug resistant organism (MDR)	Any organism with non susceptibility to at least one antimicrobial agent in ≥3 antimicrobial categories
Extremely drug resistant organism (XDR)	Any organism with non susceptibility to at least one antimicrobial agent in all but 2 or fewer antimicrobial categories.
Pan drug resistant organism (PDR)	Any organism with non susceptibility to all antimicrobial agents in all antimicrobial categories.
Carbapenem Resistant Organism (CRO)	Gram negative bacteria of any genus (e.g. Enterobacteriaceae, Pseudomonas species or Acinetobacter species) which is resistant to the carbapenem class of antibiotic by any resistance mechanism or combination of mechanisms (e.g. porin loss, ESBL with AmpC production or carbapenemase production).
Carbapenemase Producing Enterobacteriaceae (CPE)	Gram negative bacteria of the Enterobacteriaceae genus (coliforms) which are resistant to carbapenems by means of producing a carbapenemase enzyme.

Confirmed case (MDR/XDR/PDR/CRO/CPE)	Laboratory confirmation of Gram negative bacteria which meets the definitions above.	
Possible case (MDR/XDR/PDR)	Any patient who is colonised or has a confirmed infection with a resistant organism which meets the above definitions. Where initial antimicrobial susceptibility testing identifies multiple resistances but further testing is in progress.	
Possible case CPE	Laboratory identification of an Enterobacteriaceae (coliform) which demonstrates resistance to one or more carbapenem antibiotics but for which the resistance mechanism has not yet been determined.	

If initial laboratory testing suggests the organism may be a CPE, reference laboratory confirmation may be required if
initial screening for common carbapenemase enzymes in
Edinburgh by PCR is negative of inconclusive.

5.3 Risk Assessment

The infection prevention and control clinical risk assessment (CRA) is now on TRAK and must be completed on every hospital admission. The actions generated from this should be followed for all patients.

All previously known MDR, XDR, PDR and CPE patients will have a TRAK alert on their record.

5.3.1 CPE Risk Assessment

Clinical risk assessment (CRA) assists in the early identification of patients who are colonised or are at high risk of being colonised with CPE.

If a patient is deemed to be at increased risk of CPE on CRA, they must screen in line with the CPE <u>Screening Protocol</u>

If the patient has ever been previously positive for CPE, the admission CRA should be bypassed and the patient immediately managed as a **confirmed case** of CPE (see section 6).

Actions required if a screening swab (any of the 3 taken) or clinical sample grows: see section 6

5.4 Laboratory diagnosis/sampling

Microbiological sampling should be performed

- when there is a diagnostic need
- according to laboratory guidance

Samples should be obtained using Standard Infection Control Precautions.

Guidance regarding laboratory tests and sampling can be found at: <u>http://www.edinburghlabmed.co.uk/Pages/default.aspx</u>

Clearance samples are not required for any MDR, XDR, PDR, or CPE. A single negative stool or rectal swab sample does not indicate absence of carriage of these organisms. Patients may remain colonised in parts of the digestive tract that cannot be sampled, become re-colonised or become re-infected.

Exposure to antimicrobial treatment, repeated hospital admission, prolonged hospital stay and hospital care/dialysis/treatment outside of Scotland also appears to increase this risk of further recolonisation or reselection of antimicrobial resistance.

5.4.1 CPE sampling

Patients who are identified as having an increased risk of CPE carriage from the admission risk assessment should be screened as per protocol – 3 faecal samples (either rectal swab or stools samples) taken 48 hours apart. Preferably one sample should be a stool sample.

Action required if there are 3 consecutive CPE negative screening results: step down any enhanced precautions, isolation not required. Apply SICPs.

If a patient is known to have CPE- please state this on any specimen request for microbiology (if known, please provide the name of the organism and enzyme).

5.4.2 Treatment

Clinical teams must liaise with an infection specialist (Microbiology or Infectious Diseases) to identify alternative suitable antimicrobial therapies.

6. Infection Prevention and Control Precautions

The Health Protection Scotland Toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae in Scottish acute settings should be used.

The <u>daily checklist</u> should be completed on each shift and discussed at each safety brief.

For all patients, with any confirmed MDR, XDR, PDR, CRO or possible or confirmed CPE strict application of standard and transmission based precautions must be applied.

6.1 Isolation

Where there is a conflicting demand on isolation room accommodation, staff must consult the NHS Lothian <u>Prioritisation of Isolation Rooms</u> document and prioritise isolation rooms for patients with possible or confirmed CPE. CPE are considered as requiring mandatory isolation in NHS Lothian. The IPCT or duty Microbiologist may be contacted for further advice but ideally this should only be required during normal working hours and not as an emergency.

- Isolate in single room with en-suite facilities. If no en-suite available, a dedicated commode must be provided.
- The door to the isolation room must be kept closed at all times
- The appropriate TBP poster should be clearly displayed outside the patient room
- If unable to isolate, the Infection Prevention and Control Team should be informed and a risk assessment completed.
- Once patient is isolated, a terminal clean of the bay should be undertaken.

Note though that for PDR, CRO and CPE isolation is mandatory.

6.2 Visitors

- Visitors should discuss entering the isolation room with the nurse in charge prior to entering the room.
- Visitors should be encouraged to decontaminate their hands before and after visiting.
- Visitors should not use patient toilets.

6.3 Hand hygiene

• Use soap and water or alcohol based hand rub before and after patient or environmental contact in line with the WHO five key moments

6.4 Equipment

- Dedicated or single use equipment must be used
- Minimal equipment should be taken into the room
- Equipment must be cleaned daily using Chlorclean
- Electric fans must be removed from the room these can increase dispersal of bacteria through the ward environment
- Prior to removal from the isolation room, all reusable equipment must be decontaminated using Chlorclean
- On patient discharge all equipment must be cleaned prior to removal from the room with Chlorclean

6.5 Environment

- Minimal items should be kept in the room to allow for effective cleaning
- Increase frequency of domestic cleaning <u>twice</u> daily
- Ensure frequent touch surfaces are cleaned carefully
- All nursing and domestic cleaning in the isolation room must be undertaken using Chlorclean
- On transfer or discharge, the patient room should be terminally cleaned, including curtain change, in line with the <u>Terminal Cleaning Protocol</u>.
- Under certain circumstances (all PDR and some CPE/CRO), the IPCT may advise that a terminal clean should be followed by decontamination with hydrogen peroxide vapour before the room can be occupied by a new patient

6.6 Personal Protective Equipment

- Disposable gloves
- Yellow disposable aprons
- long-sleeved gowns for all contact for CPE

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• Surgical mask and eye protection and long sleeved gowns may be worn where there is a risk of blood/body fluid contamination as per SICPs

6.7 Waste

• All waste should be classed as clinical waste (orange bag) and disposed of inside the isolation room.

6.8 Linen

• All linen should be classed as infectious and disposed of using alginate bags into red laundry bags.

6.9 Blood/body fluid spillages

• As per <u>SICPs</u>

6.10 Communication

- Ensure the patient is provided with a <u>Patient Information Leaflet</u> and provided with opportunity to discuss any concerns or questions with staff that are familiar with the organism, its risks and its management.
- The IPCT will apply a permanent TRAK alert to advise clinical teams of results to inform future care and management during subsequent admissions
- Ward staff must ensure that all HCWs involved in patient care are advised of the result and appropriate management at ward handover. This Policy and Quick Reference Guide should be made available at this time
- A <u>daily checklist</u> should be kept throughout the patient's stay.

6.11 Moving between wards, departments and hospitals (including operating theatres, radiology and endoscopy units)

- Patients may require to be transferred to other departments or hospitals for investigation or treatment based on clinical need.
- Where possible, the patients should be seen/treated at the end of scheduled activity to allow staff adequate time to complete terminal cleaning
- The clinical need of critically ill patients should always take priority and their appropriate investigation or management should not be delayed due to their carriage of antimicrobial resistant Gram negative bacteria
- Adequate communication is essential to ensure that, appropriate infection prevention and control management is implemented during transfer
- The transportation service (e.g. Scottish Ambulance Service, hospital transport service) must also be informed to allow for post-transfer decontamination of equipment in line with local procedures.
- If the patient is transferred out of hospital or out of NHS Lothian, a summary of the patient alert and current management must be included in this discharge communication and the infection prevention and control team and microbiologists at

the receiving hospital should be advised of the transfer in advance of the patient's arrival.

6.12 Management in Outpatient Settings

Some patients may have an anticipatory care plan documented in TRAK. The IPCT can be called for assistance in managing patients in this setting.

7. Infection Prevention & Control out of hospital (e.g. GP, Care Home)

A summary of the patient alert and current management must be included in the patient's discharge communication.

Community staff (including GPs, district nurses, social care staff and other community healthcare workers) must apply SICPs at all times when providing care.

In a shared care environment, an individual who is colonised (a carrier) and who is not at high risk of infecting others does not need to be isolated and should be allowed to use communal facilities. If possible, the individual should be given a single room with en-suite facilities, including toilet. If not possible, they should not share a room with an immunocompromised individual. SICPs should always be used by carers and affected individuals should be enabled to practice effective hand hygiene, especially when using the toilet.

Where an individual is in their own home and shares a bed or bedroom with a partner or family member, consult your usual IPC advisor to assist in making a risk assessment.

Domiciliary carers should be reminded of their responsibility to maintain effective IP&C measures to prevent spread within the individual's home or to other clients on their case list.

8. Care of the Deceased

For information on specific requirements and restrictions see <u>Appendix 12: National Infection</u> <u>Prevention and Control Manual</u>.

An Infection and Contamination Control Notification Form must be completed for every deceased patient.

Where repatriation of the deceased to another country is required, please contact the Health Protection Team for advice and any required documentation.

9. Management of contacts, contact tracing or screening

Screening of patients in the same location as the affected patient is not normally required. The Infection Prevention and Control Team may recommend screening if investigating an increased incidence or cluster of the same bacteria within an area. This would be as a recommendation of a Problem Assessment Group (PAG) or Incident Management Team (IMT).

- Screening of contacts will be advised by IPCTor ICD
- Screening of patients in the same location as the affected patient is NOT normally required if the case was identified on admission and isolated immediately.
- Household contacts of CPE cases should be identified by the CPE Clinical Risk Assessment on TRAK on admission to a healthcare facility and managed accordingly
- Management of any positive contacts will be decided through an IMT
- Staff screening is not normally required and would only be considered as a recommendation of a PAG or IMT and would be done in conjunction with Occupational Health Services and Partnership in line with the <u>HAI Staff Screening Policy</u>

10. Treatment guidance

Refer to the NHS Lothian <u>Microguide</u> for further information regarding appropriate antimicrobial prescribing.

Specific queries can be discussed with an infection specialist; see Contacting Microbiology.



Quick Reference Guide: MDR, XDR & CPE

Organism:	Multi-drug resistant Gram-negative bacteria	
Signs & symptoms:	Variable depending on the site of infection	
Transmission (spread):	Contact, droplet, airborne – dependent on site of colonisation/infection.	
	Discuss with IPCT.	
Person to person spread possible?	Yes	
Incubation period:	n/a	
People most at risk:	All patients. NNU, ITU, Neurosurgery, Oncology and Haematology are at particular risk.	
Treatment:	As per the reported antimicrobial susceptibilities or as appropriate for the clinical manifestation or drug intolerances.	
Key management &	For MDR,XDR, PDR and CPE:	
(MUST DO'S):	 Isolate all suspected or confirmed cases when possible or use the NHS Lothian Isolation Prioritisation Policy. 	
	 Discuss with Infection Prevention and Control if isolation not possible. 	
	• Transmission based precautions to be put in place as per route of transmission.	
	Appropriate isolation poster to be used.	
	Correct PPE selected.	
	Dedicated patient care equipment.	
	All linen to be treated as infected.	
	 Enhanced/increased frequency of cleaning of equipment and environment with Chlorclean, particularly in toilet areas. 	
	 Document all risk assessments and communications in patient notes. 	
	 For CPE, the CPE daily checklist should be implemented 	

Appendix 1: Antimicrobial categories to consider when categorising Gram negative bacteria as MDR or XDR (taken from Magiorakos *et al*, 2011)

Enterobacteriaceae

Antimicrobial category	Antimicrobial agent	Species with intrinsic resistance to antimicrobial agents or categories (51) ^a
	Gentamicin	Providencia rettgeri (P. rettgeri), Provindencia stuartii (P. stuartii)
Aminoglycosides	Tobramycin	P. rettgeri, P. stuartii
	Amikacin	
	Netilmicin	P. rettgeri, P. stuartii
	Ceftaroline (approved only for	
Anti MRSA conhalosporins	Escherichia coli, Klebsiella	
Anti-MIKSA cephalosponiis	pneumonia, Klebsiella	
	oxytoca)	
Antipseudomonaol penicillins +	Ticarcillin-clavulanic acid	Escherichia hermannii (E. Hermanii)
β-lactamase inhibitors	Pipercillin-taxobactam	E. hermanii
	Ertapenem	
Carbapenems	Imipenem	
Carbaponomo	Meropenem	
	Doripenem	
		Citrobactor freundii (C. Freundii),
		Enterobacter aerogene (E.areogenes),
		Enterobacter cloacae (E. Cloacae), Hafnia
None-extended spectrum	Cefazolin	alvei (H. Alvei) Morganella morganii (M.
cephalosporins; 1 st and 2 st		Morganii), Proteus penneri (P. Penneri),
generation cephalosporins		Proteus vulgaris (P. vulgaris), P. Rettgeri, P
		M. Marganii, D. Dannari, D. Vulgaria, S.
	Cefuroxime	Marcescens
Extended-spectrum	Cefuroxime or ceftriaxone	
Cephalosporins; 3 rd and 4 th	Ceftazidime	
generation cephalosporins	Cefepime	
Conhomusing	Cefoxitin	C. Freundii, E.areogenes, E. Cloacae, H. Alvei
Cephanycins	Cefotetan	C. Freundii, E.areogenes, E. Cloacae, H. Alvei
Fluoroquinolones	Ciprofloxacin	
Folate pathway inhibitors	Trimethopri-	
	sulhamethoxazole	
Glycylcyclines	Tigecycline	M. Morganii, Proteus mirabilis (P. Mirabilis), P. Penneri, P. Vulgaris, P. Rettgeri, P. stuartii
Monobactams	Aztreonam	
Penicillin's	Ampicillin	Citrobacter koseri (C. Koseri), C. Freundii, E.areogenes, E. Cloacae, E. Hermanii, H. Alvei, Klebsiellae spp., M. Morganii, P. Penneri, P. Vulgaris, P. Rettgeri, P. Stuartii, S. Marcescens
Penicillins + + β-lactamase	Amoxicillin-clavulanic acid	C. Freundii, E.areogenes, E. Cloacae, H. Alvei, M. Morganii, P. Rettgeri, P. Stuartii, S. Marcescens
	Ampicillin-sulbactam	C. Freundii, C. Koseri, E. Cloacae, H. Alvei, P. Rettgeri, S. Marcescens
Phenicols	Chloramphenicol	
Phesphonic acids	Fosfomycin	

Antimicrobial category	Antimicrobial agent	Species with intrinsic resistance to antimicrobial agents or categories (51) ^a
Polymyxins	Colistin	M. Morganii, P. Mirabilis, P. Penneri, P. Vulgaris, P. Rettgeri, P. Stuartii, S. Marcescens
Tetracyclines	Tetracyline	M. Morganii, P. Mirabilis, P. Penneri, P. Vulgaris, P. Rettgeri, P. Stuartii
	Doxycycline	M. Morganii, P. Penneri, P. Vulgaris, P. Rettgeri, P. Stuartii
	Minocycline	M. Morganii, P. Penneri, P. Vulgaris, P. Rettgeri, P. Stuartii

Criteria for defining MDR, XDR and PDT in Enterobacteriaceae

MDS: non-susceptible to \geq 1 agent in \geq 3 antimicrobial categoris.

XDR: non susceptible to \geq agent in all but \leq 2 categories.

PDR: non-susceptible to all antimicrobial agents listed.

^aWhen a species has intrinsic resistance to an antimicrobial agent or to the whole category, that agent or categoty must be removed from the list in this table prio to appling the criter for the definitions and should not be counted when calculating the number of agents or categories to which the bacterial isolate is non-susceptible. <u>http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/ARHAI/Pages/public_consultation_clinical_microbi</u> <u>ology_infection_article.aspx</u>

Pseudomonas aeruginosa

Antimicrobial category	Antimicrobial agent
Aminoglycosides	Gentamicin
	Tobramycin
	Amikacin
	Netilmicin
Antipseudomonal carbpenems	Imipenem
	Meropenem
	Doripenem
Antipseudomonal cephalosporins	Ceftazidime
	Cefepime
Antipseudomonal fluoroquinolones	Ciprofloxacin
	Levofloxacin
Antipseudomonaol penicillins + β-lactamase inhibitors	Ticarcillin-clavulanic acid
	Piperacillin-tazobactam
Monobactams	Aztreonam
Phosphonic acids	Fosfomycin
Polymyxins	Colistin
	Polymyxin B
Criteria for defining MDR, XDR and PDT in Pseudomona	as aeruginosa
MDS: non-suscentible to >1 agent in >3 antimicrobial categories	

MDS: non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial categories.

XDR: non susceptible to \geq agent in all but \leq 2 categories.

PDR: non-susceptible to all antimicrobial agents listed.

http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/ARHAI/Pages/public_consultation_clinical_microbi_ ology_infection_article.aspx

Acinetobacter species

Antimicrobial category	Antimicrobial agent
Aminoglycosides	Gentamicin
	Tobramycin
	Amikacin
	Netilmicin
Antipseudomonal carbpenems	Imipenem
	Meropenem
	Doripenem
Antipseudomonal fluoroquinolones	Ciprofloxacin
	Levofloxacin
Antipseudomonaol penicillins + β-lactamase inhibitors	Piperacillin-tazobactam
	Ticarcillin-clavulanic acid
Extended-spectrum cephalosporins	Cefuroxime
	ceftriaxone
	Ceftazidime
	Cefepime
Folate pathway inhibitors	Trimethopri-sulhamethoxazole
penicillins + β-lactamase inhibitors	Ampicillin-sulbactam
Polymyxins	Colistin
	Polymyxin B
Tetracyclines	Tetracyline
	Doxycycline
	Minocycline
Criteria for defining MDR, XDR and PDT in Acinetobacter spp.	
MDS: non-susceptible to ≥1 agent in ≥3 antimicrobial categories.	
XDR: non susceptible to \geq agent in all but \leq 2 categories.	
PDR: non-susceptible to all antimicrobial agents listed.	
http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/ARHAI/Pages/public consultation clinical microbi	
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