Aneurin Bevan University Health Board

Infection Prevention and Control Policy

Control of Multi-Drug-Resistant Gram-Negative Bacilli

N.B.  Staff should be discouraged from printing this document. This is to avoid the risk of out of date printed versions of the document. The Intranet should be referred to for the current version of the document.
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1 EXECUTIVE SUMMARY

The Gram-Negative Bacilli (GNB) are a large group of bacteria that includes coliforms (such as *E. coli* and *Klebsiella*), *Pseudomonas* and *Acinetobacter*. While some GNB regularly cause infections such as UTI in uncomplicated patients, they are especially important in patients undergoing intensive care, chemotherapy or complex medical and surgical procedures, when they may cause opportunistic infections such as wound infections, sepsicaemia and hospital-acquired pneumonia.

The ability of these organisms to acquire resistance to virtually all antimicrobial agents presents both a therapeutic problem and a hazard from cross-infection in the healthcare setting, as well as in the community at large. Such resistance is increasing worldwide and is a global concern. It is imperative that strains that have acquired multiple drug resistance (MDR) are controlled to prevent dissemination of potentially untreatable infections.

As well as being part of the normal bacteria of the body, Gram-negative bacilli may be found in moist environments and provide a source of organisms that can take advantage of failure of standard cross-infection procedures. During an outbreak, colonization without symptoms is more common than infection, but colonized patients may quickly become seriously ill. Staff may be transiently colonized during an outbreak but are rarely clinically infected themselves.

1.1 Scope of Policy

The policy applies to all healthcare workers working within Aneurin Bevan Health Board.

2 AIMS

This policy’s aim is that any suspected or known case of infection caused by Multi-Drug-Resistant Gram-Negative Bacilli (MDR-GNB) is managed appropriately.

This policy will support the implementation of the Welsh Standards for Health Services, particularly standard number 13a: ‘Organisations and services comply with legislation and guidance on Infection Prevention and Control and decontamination in order to eliminate or minimise the risk of healthcare-associated and community-acquired infections.’
3 POLICY STATEMENT

The Organisation’s aim is to provide optimum treatment for patients with known or suspected MDR-GNB infection and ensure staff are aware of the required infection control procedures. The Organisation’s policy for control of MDR-GNB will be continually monitored and updated in line with current professional guidelines.

4 RESPONSIBILITIES

All staff must have access to the policy via the Organisation intranet or locally held paper copy in the Infection Control Manual.

Every employee has a duty to adhere to the policy at all times.

All Managers are responsible for ensuring the policy is implemented and adhered to within their sphere of influence.

5 TRAINING

Training will be carried out as part of Level One training where awareness of the Infection Control Manual and its Infection Control Policies will be promoted. Specific training (Level Two) on the management of patients with suspected or known MDR-GNB disease will be provided to staff on request and targeted for members of staff on wards where such patients will be cared for and for those Organisation staff who may encounter these patients in community-based practice.

6 MONITORING & EFFECTIVENESS

The Infection Prevention and Control Team will monitor compliance through surveillance and audit.

7 FURTHER INFORMATION

7.1 Coliforms

Coliforms (such as E. coli, Klebsiella, Enterobacter) are part of the normal colon bacteria and patients may become infected with organisms derived from their own bowel flora (or that of their mother for newborn babies who become colonized during delivery). Some patients, especially those receiving antibiotics and those who are severely ill, may acquire extensive colonization of their skin, particularly with Klebsiella, and their skin then acts as a source of organisms for the contamination of staff hands and transmission to
other patients. Colonization of the stomach and upper airway can follow administration of Proton Pump Inhibitor or H₂ histamine antagonist drugs, and the susceptible patient may then develop pneumonia.

Resistance to gentamicin is often a marker for resistance to many other antibiotics and potential for epidemic spread. Coliforms that show gentamicin or broad-spectrum cephalosporin or carbapenem antibiotic resistance need to be prevented from becoming disseminated amongst patients. Once on staff hands, coliforms survive well and thus it is important that staff hand disinfection is carried out between patient contacts. Epidemic coliform infection may be due to bacterial contamination of an item of equipment or fluid, which acts as a common source of infection for several patients. Examples include contaminated enteral feeds or inadequately disinfected bedpans or other equipment that is reused by different patients. Aerosols from infected body fluids may cause cross-infection.

### 7.2 ESBL and AmpC – Producing Bacteria

“ESBL” stands for Extended Spectrum Beta-Lactamases, which are enzymes produced by certain bacteria that destroy, and so confer resistance to, a wide range of antibiotics. ESBL enzymes are most commonly produced by two types of bacteria – *E coli* and *Klebsiella* – making the infections they cause much more difficult to treat.

“AmpC” is another enzyme that causes similar concerns, particularly in *Enterobacter, Citrobacter, Serratia* and some *Proteus* species.

ESBL or AmpC-producing bacteria are mainly resistant to penicillins and cephalosporins, two of the most important and widely used classes of antibiotics. They may also be resistant to other antibiotics such as gentamicin and ciprofloxacin. Serious infections often require the use of potent carbapenem antibiotics such as imipenem.

There is evidence that ESBL and AmpC-producing bacteria are carried in faeces, which may imply spread via the food chain, thereby producing a reservoir of multi-resistant bacteria in the gut. It is also possible for these bacteria to be passed from person to person on contaminated hands or by poor practice in urinary catheter care. It is urinary infections that happen most commonly with ESBL bacteria (both in hospital and in the community), though wound and chest infections and septicaemia also occur.
The infection control principles for ESBL and AmpC are the same as for other multiresistant bacteria transmissible by touch – i.e. ‘contact’ precautions in addition to routine ‘standard’ precautions and scrupulous hand hygiene.

### 7.3 Carbapenemase Producers

Carbapenem antibiotics (imipenem, meropenem, ertapenem and doripenem) are invaluable for the treatment of infections due to MDR-GNB, including those with ESBL or AmpC. Carbapenem-resistant coliform bacteria remain rare but are emerging worldwide, including in Wales. Of particular concern are coliform bacteria that have acquired a carbapenemase enzyme that renders this type of antibiotic ineffective. Several types occur, some with particular geographic associations, e.g. type NDM-1 with the Indian Subcontinent. These enzymes are easily spread amongst bacterial strains already resistant to multiple antibiotics. The transmission characteristics and pathogenesis of these multi-resistant strains are the same as those of more sensitive organisms, but the infections are much more difficult or even impossible to treat. For this reason, it is vital that healthcare organisations prevent their spread. See the Appendix.

### 7.4 Multi-resistant Acinetobacter baumannii (MRAB)

Acinetobacters are environmental organisms that are widespread both in and outside healthcare premises. The main species associated with human infection is *Acinetobacter baumannii*. It is widely prevalent in static water and is frequently found in the hospital environment and easily cultured from fomites and other equipment, particularly in an outbreak.

Acinetobacters are generally organisms of low virulence. Most commonly, they are found colonising the skin, respiratory tract and urine of patients. Those who are most susceptible are: immunosuppressed; in intensive care and similar high-density environments; and/or on broad spectrum antibiotics, particularly those with little activity against *A. baumannii*.

Acinetobacters are occasionally invasive, causing wound infections, nosocomial pneumonia and urinary infection. Multi-antibiotic resistant forms of *A. baumannii* (MRAB) occur and can be difficult to treat. It is important to distinguish colonisation from infection to avoid the unnecessary use of antibiotics, which may make the clinical situation worse, as well as reinforcing the selective pressure.
that allows multi-resistant organisms to propagate in the environment.

*A. baumannii* is intrinsically resistant to most commonly available antibiotics. Hence it is able to survive in the hospital environment, and also to colonise susceptible patients being treated with broad-spectrum antibiotics. Strains that cause infection are liable to be even more resistant than colonising strains. Injudicious use of antibiotics, particularly fluoroquinolones (e.g. ciprofloxacin) or carbapenems (e.g. imipenem) leads to the emergence of more resistant forms of colonising strains.

Occasional strains are resistant to ALL antibiotics currently available. Recommended management is – when possible and prudent – to withhold antibiotics and hopefully allow the patient to recover their normal colonising flora. Close liaison between the clinical team and the Microbiologists is essential if this course of action is to be followed.

### 7.5 Pseudomonads

*Pseudomonas* species and related organisms such as *Stenotrophomonas maltophilia*, unlike the coliforms, are only occasionally found in the normal gut, although hospital patients may become colonized. Moist equipment such as ventilators, suction catheters and contaminated fluids constitute a reservoir of pseudomonads which can provide a source of organism for the direct colonization and infection of patients. Pseudomonads are intrinsically resistant to many antibiotics and multi-resistant strains can be extremely difficult to treat. Invasive disease is associated with a high mortality.

### 8 SPECIAL UNITS

Areas of particular concern in relation to risk of transmission of coliforms, acinetobacters and pseudomonads are neonatal, paediatric and adult critical care units; ophthalmology clinics and surgery; units caring for burns and neutropenic patients; endoscopy units; and hydrotherapy pools.

### 9 PREVENTIVE AND CONTROL MEASURES

As there are a number of different types of MDR-GNB that are of greater or lesser concern, the appropriate response is flexibly applied as judged by the Consultant Microbiologists / Infection Prevention and Control Team.
9.1 **Health Board engagement**

It is critical that the Board and its Executive make it a high priority to minimise spread of MDR-GNB and are supportive of all prevention and eradication measures. A containment plan is outlined below.

9.2 **Laboratory methods**

The microbiology laboratory will continuously review and optimise its methods for the detection of the various types of MDR-GNB and refer suspected bacterial strains for confirmation and for epidemiological purposes to appropriate reference laboratories of Public Health Wales or the Health Protection Agency. Screening specimens for MDR-GNB will be examined from associated patients and the environment when cases occur, as deemed appropriate by the Medical Microbiologist / Infection Control Doctor.

9.2.1 Definitions of problem resistance

Organisms with the following resistance problems are of particular concern:
- Coliforms resistant to carbapenems.
- Coliforms resistant to drugs from two or more the classes of fluoroquinolones, aminoglycosides, or third-generation cephalosporins.
- Pseudomonads resistant to three or more classes of antibiotics
- Acinetobacters resistant to carbapenems.

9.3 **Antibiotic stewardship policies**

Excessive use of broad-spectrum antimicrobials will encourage the emergence of multi-resistant organisms. A Health Board Antimicrobial Working Group will ensure that stewardship measures are in place to promote optimal and safe usage to minimise the acquisition and spread of resistance. Antimicrobial prophylaxis for surgery should be as narrow spectrum as clinically possible, preferably restricted to a single dose, in all but the most exceptional circumstance.

9.4 **Disinfection of equipment**

An effective decontamination strategy is required. Moist respiratory equipment, (such as ventilator tubing, nebulizers and humidifiers that come into direct contact with the patient) is easily contaminated. It is important that the correct procedures for decontamination are followed and that the equipment is properly
dried before use for subsequent patients. Follow the manufacturer’s instructions or consult the Cleaning and Disinfection section of the Infection Control Manual. Disinfectors such as bedpan washers must be maintained and checked regularly to ensure that adequate temperatures are being reached (normally 80°C for at least one minute), and records of maintenance must be kept.

9.5 Reusable drugs

All creams, ointments and gels and liquids used with medical equipment (e.g. nebulizers) must be stored in such a way as to prevent contamination and patient-to-patient spread of Gram-negative organisms. Single-use disposables are preferred if they are available.

9.6 Hand hygiene

All staff who have contact with patients must employ good hand disinfection practices and use disposable gloves and aprons when hand contamination is likely. The routine use of alcohol-based hand rubs will generally be replaced by use of soap and water for hand hygiene for critical resistance events.

9.7 Healthcare environment

Spread can be minimised by effective enhanced and terminal cleaning with chlorine-based disinfectants. All shared services and high-contact areas such as lavatories, bathrooms, etc., should be cleaned at least daily and kept dry. Sink traps inevitably harbour organisms which cannot be completely removed by disinfectants. It is therefore important not to splash water from the sink to adjacent areas.

9.8 Pharmaceutical preparations

Drugs and other products should be reconstituted or prepared according to the guidance of the Medicines and Healthcare Products Regulatory Agency (MHRA) or other professional institutions. Suspected contamination of commercially purchased products must be reported to the MHRA for investigation. Further guidance on reporting pharmaceutical contains full guidance on reporting pharmaceutical product defects: http://howiis.wales.nhs.uk/sitesplus/documents/866/ABHB0010%20Medicines%20Management%20Policy%20-%20Issue%203.pdf
9.9 Infection surveillance

The Infection Prevention and Control Team undertake surveillance of all laboratory reports in order to identify patients who are colonized or infected with resistant coliforms, acinetobacters or pseudomonads. Resistance to gentamicin, broad-spectrum cephalosporins (e.g. cefotaxime, ceftazidime) or carbapenems are the usual markers for multi-resistance, which will require measures to prevent colonization or infection of other patients. Incident tracking, epidemiological graphs and tables will be prepared if transmission is detected.

9.10 Patient isolation

The Infection Prevention and Control Team in conjunction with appropriate clinical managers will identify places for effective isolation, e.g. en-suite rooms and cohort areas with dedicated commodes, and consider criteria for any ward closure and re-opening to new admissions. In some circumstances it will be necessary implement the containment action immediately, with meticulous adherence to ‘Standard’ and ‘Contact’ Precautions that will be advised.

In many sporadic cases, there will be no evidence of cross-infection, as resistant strains can arise through selective antibiotic pressure. Restriction of admissions to the unit may be necessary, depending on the number of patients affected and the number of infections compared with colonization.

9.11 Screening

Identification of further asymptomatic colonized and infected cases may need screening of patients in the affected unit – both index patients and secondary case contacts – with the intention of immediate isolation of cases found, determining the extent of spread and to enable flagging, when appropriate, both of case records and electronically on PAS systems. If flagged patients are re-admitted they must be placed in isolation pending discussion with the Infection Prevention and Control Team and possible re-screening.

Weekly screening of continuing patients and patient screening on discharge from affected units until the MDR-GNB organism is eliminated may be advised. Occasionally it may be necessary to screen staff and close household contacts of cases. Typically, rectal
swabs and urine, together with oropharyngeal or respiratory secretions from intensive care patients, and skin swabs from burns patients will be required.

Patients at high risk for being positive for carbapenemase-producing MDR-GNB should be screened on admission, e.g. known positives, those with prior hospitalization or dialysis in countries where such strains are prevalent – currently: India, Pakistan, Greece, USA, Israel, Turkey, Middle East and North Africa.

9.12 Patient transfer

Adequate communication to other healthcare providers is essential to ensure that, if required, appropriate isolation is maintained if patients are transferred between units, with prior notification to the receiving care team. The transportation service must also be informed to allow for post-transfer decontamination by the procedures in their internal policy.

10 REFERENCES


Guidance for Control of Infections with carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in Acute Care Facilities. Centers for Disease Control and Prevention, MMWR, 2009; v58, pp256-260. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5810a4.htm
11 APPENDIX

As part of the routine admission procedure, assess all patients on admission for carbapenemase-producing Enterobacteriaceae status. If no known risk, screening is not required. Send routine clinical microbiological samples as clinically indicated.

Carbapenemase-producing Enterobacteriaceae identified in a routine clinical sample?

- Yes, therefore:
  - Recent laboratory confirmation is during this admission episode or confirmed at the transferring healthcare facility. Treat as positive case (see below).
  - Laboratory: Save isolate and send to AMR-I&I reference laboratory.

- No
  - NO further action
  - Inform IPC team and clinicians immediately
  - Isolate/maintain isolation (with en-suite facilities)
  - Reinforce strict standard precautions
  - Inform patient of infection carrier status
  - Flag patient notes with result
  - Instigate Carbapenemase-producing Enterobacteriaceae IP&C Plan
  - Consider convening incident/outbreak control team
  - Identify and screen contacts as indicated
  - Review clinical management including use of antimicrobials and devices (whether latter required)
  - Maintain robust communications
  - Communicate patient’s positive status to GP and other community care providers on discharge/transfer

Result: Presumptive positive

Patient is suspected case of colonization or infection

- Take rectal swab & isolate patient (with en-suite). Apply strict standard precautions

- Result Negative
  - Patient should remain in isolation until a further two consecutive samples test negative – samples being taken 48 hours apart (i.e. Day 0 [initial sample], day 2 and day 4)

- Result Positive
  - Confirm positive?

- Yes
  - Can be removed from isolation (unless another reason for continuing isolation). No further action

- No
  - All samples negative but previously known positive?

    - Yes
      - Note: Previously positive individuals with subsequent negative screen can revert to a positive state, especially after a course of antibiotics – careful risk assessment is required if removing from isolation

    - No
      - Reinforce strict standard precautions

- Review by date: 24/November/2017
### Control of Multi-Drug-Resistant Gram-Negative Bacilli

**Title:** Control of Multi-Drug-Resistant Gram-Negative Bacilli

**Owner:** Infection Prevention & Control Team

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### Key

- **High risk**
  - Isolate immediately in a side room with en suite facilities (or dedicated commode) and retain in isolation as follows:
    - Suspected case: isolate until 3 consecutive NEGATIVE screens (if still in hospital). Should any sample screen positive treat as confirmed case.
    - Known case or case confirmed via clinical / screening sample (further screening not required) – isolate throughout hospital stay.
  - Either: cohort patient in line with toolkit and in discussion with your IPAC team.
  - OR, if not possible to cohort, nurse with strict emphasis on maintaining compliance with standard precautions and optimal environmental cleaning (without fail).
  - AND submit further 2 samples to achieve 3 consecutive NEGATIVE screens if still in hospital. Should any sample test positive treat as confirmed case.

- **Medium risk**
  - Isolate in side room with en suite facilities (or dedicated commode) if possible (see increased transmission risks) until first screening result demonstrates NEGATIVE. If not possible to continue isolation (in line with toolkit) then:
    - EITH/ER: cohort patient in line with toolkit and in discussion with your IPAC team.
    - OR, if not possible to cohort, nurse with strict emphasis on maintaining compliance with standard precautions and optimal environmental cleaning (without fail).
  - AND submit further 2 samples to achieve 3 consecutive NEGATIVE screens if still in hospital. Should any sample test positive treat as confirmed case.

- **Low risk**
  - Increased transmission risks: the following factors which increase transmission risk should be taken into account when prioritising side rooms, they are patients with:
    - Diarrhoea
    - Incontinence (urine or faeces)
    - Discharging wounds
    - A high risk of wandering and unable to comply with good hygienic practices
    - Medical devices in situ
    - Ventilatory support requirements
  - Additionally:
    - Risks posed from inadequate decontamination of equipment where there is high contact with body fluids e.g. endoscopes.

**NOTE:** This matrix is intended to inform preparation of a roll-out plan. The gold standard for any patient admitted who is a suspected case of carbapenemase-producing Enterobacteriaceae (infected and/or colonised) is to isolate immediately and manage in line with the Acute trust toolkit. However, where risk prioritisation is required (due to competing priorities) the above matrix is intended as a guide to planning for this.

It is advised that roll-out should commence in high risk care environment(s) (some trusts are already taking a more aggressive approach by screening all admissions to these areas). If transmission events occur or prevalence increases in your trust, it is strongly advised to expedite full implementation of the toolkit.

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### Table: Risk Prioritisation of Infection Prevention and Control (IPAC) Measures

<table>
<thead>
<tr>
<th>The Patient History</th>
<th>Direct medical transfer from or specified / augmented care unit in country or UK care setting with known high prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known or recently confirmed case of carbapenemase-producing Enterobacteriaceae</td>
<td>Medical transfer from country with known high prevalence</td>
</tr>
<tr>
<td>History of hospitalisation in last 12 months in country or UK care setting with known high prevalence</td>
<td>Identified as contact of positive case (colonisation or infection)</td>
</tr>
<tr>
<td>Medical transfer from history of hospitalisation in last 12 months in country with no reported problems</td>
<td>No risk factors identified on admission</td>
</tr>
</tbody>
</table>

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1. Refer to Acute Trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae found at:

2. Screening not required for known or recently confirmed cases.


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