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CRE - update issued on laboratory detection and infection control measures

As the epidemiology of carbapenem resistant enterobacteriaceae (CRE) in Ireland has significantly changed since the previous interim alert document (circulated by the SARI subcommittee for the Development of Guidance against Multidrug Resistant Organisms in January 2011and published in the February issue of Epi-insight, available here), a further update on the recommended laboratory detection and infection control measures to be taken in all acute hospitals in Ireland is given here.

In July 2010, the European Centre for Disease Control (ECDC) graded Ireland as having only sporadic occurrence of CRE.[1] Recently, there has been an outbreak of CRE affecting an acute hospital in the mid-west of Ireland. Two additional cases have also been reported from a Dublin hospital where one of the cases had a recent history of admission to the mid-west hospital. The epidemiology in Ireland has therefore shifted to regional/inter-regional spread of CRE. The Irish epidemiology is worryingly similar to other European countries, where sporadic occurrence was followed by single hospital outbreaks with subsequent spread to regional and national centres.

In order to prevent CRE from becoming endemic in Ireland, prompt laboratory detection of CRE in any clinical isolate, and identification and targeted screening of patients deemed to be at-risk of CRE rectal carriage is crucially important.

CRE became a notifiable infectious disease in Ireland in March 2011. Under the category of an 'Unusual cluster or changing pattern of illness that may be of public health concern', medical practitioners and clinical directors of diagnostic laboratories are requested to notify all cases of colonisation or infection with carbapenem-resistant enterobacteriaceae (CRE) to the relevant Medical Officer of Health. CRE should be notified once carbapenem resistance and the underlying resistance mechanism have been confirmed by a reference laboratory. In the event that suspected CRE (awaiting reference laboratory confirmation) is implicated in an outbreak, it is advised that this be notified as soon as possible and that all appropriate outbreak control measures are established immediately.

The SARI subcommittee for the Development of Guidance against Multidrug Resistant Organisms recommends that prompt identification and screening of at-risk patients is prioritised in every healthcare facility in Ireland. The committee plans to circulate draft guidance for consultation in summer 2011. The following reflects the interim guidance of the committee:

1. Laboratory guidance for screening of enterobacteriaceae for carbapenemase production

Early laboratory detection is of paramount importance to prevent spread of CRE. Currently both EUCAST and CLSI clinical breakpoints will not detect all carbapenemase harbouring enterobacteriaceae. Although the clinical significance of carbapenemase producing isolates with carbapenem MICs below the clinical breakpoints has not been determined, detection of these isolates is important from an infection prevention

Health Protection Surveillance Centre
25-27 Middle Gardiner St
Dublin 1

Tel: +353 (0) 1 8765300
Fax: +353 (0) 1 8561299
info@hpsc.ie
www.hpsc.ie

and control and public health perspective.

Currently the majority of carbapenem resistance in enterobacteriaceae in Ireland is caused by non carbapenemase mediated resistance mechanisms, most frequently a combination of a permeability defect (porin loss) with either ESBL or AmpC beta-lactamase production. As ertapenem is the carbapenem mostly affected by this mechanism, screening for carbapenemase production with ertapenem alone (Ertapenem ≥ 0.5 mg/l) will yield a substantial number of isolates with non-carbapenemase mediated resistance. In contrast a meropenem screening breakpoint of ≥0.5 mg/l (zone diameter screening breakpoint for meropenem (10µg disk) ≤23 mm[2,3]) should reliably detect carbapenemase producers without increasing laboratory workload significantly due to low specificity.

Automated susceptibility testing equipment alert rules should be set to the relevant screening breakpoints. Screening zone diameters should be utilised in templates used for disk diffusion testing. It is important to use the correct inoculum as a small decrease in the inoculum might lead to inaccurate susceptibility results.

Isolates found to have MICs equal to or higher than screening breakpoints, using automated susceptibility testing or disk diffusion testing should have the susceptibility test result confirmed by an appropriate quantitative method such as gradient strip on Mueller-Hinton agar or broth dilution. Confirmed CRE should undergo further phenotypic and molecular testing.

Currently, there is no designated reference laboratory for confirmation of suspected carbapenem resistance in Ireland. As the epidemiology of CRE in Ireland could evolve quickly and microbiology laboratories throughout the country might potentially have to give preliminary identifications rapidly, all laboratories should aim to gain competency in identification and phenotypic preliminary confirmation of CRE isolates.

The modified Hodge test although sensitive has low specificity for carbapenemase detection. Class A carbapenemases (e.g. KPC) can be detected by double-disk synergy test and combined disk test using ABPA (aminophenylboronic acid) as an inhibitor. For class B metallo-enzymes DPA (dipicolinic acid) can be used as an inhibitor in double-disk synergy or combined disk testing. Combination disks can be prepared locally or can be purchased.[4] If a laboratory does not have the capacity to perform confirmatory phenotypic and/or molecular tests internally, the isolates should be referred promptly to a laboratory with the capacity to perform the tests to an acceptable standard. Both EUCAST and CLSI recommend reporting susceptibility results at face value.

2. Patient screening recommendations for CRE in Ireland

During March 2011, the Health Service Executive (HSE) issued further guidance applicable to all acute healthcare facilities in Ireland to screen the following patients for CRE carriage:

- Patients who have been inpatients for more than 48 hours in healthcare facilities outside Ireland in the previous year
- Patients who have been inpatients in HSE-Mid West healthcare facilities in the past year
- Patients transferred from HSE-Mid West healthcare facilities to another healthcare facility
    - Patients who have attended HSE-Mid West or foreign healthcare facilities as day patients e.g. for dialysis, should have a risk assessment performed in consultation with the local infection prevention and control team.

It is recommended that healthcare facilities put in place robust measures to ensure prompt identification and screening of the above patients.

Several screening methodologies have been published. [5-10] For CRE surveillance in rectal swab or faecal cultures, the use of MacConkey or CLED agar with the placement of an ertapenem or a meropenem (10 µg)

disc, with or without prior culture in enrichment broth, is an acceptable method. An inhibitory zone diameter of ≤ 27mm may be used as a criterion for identifying colonies for further analysis. Acceptable alternative laboratory methods in CRE surveillance include the use of certain commercially manufactured selective screening media (such as ChromID ESBL or CHROMagar KPC medium), or the inoculation of swabs in carbapenem-containing enrichment broth followed by subculture onto MacConkey or CLED medium.

3. Infection control measures to be taken for potential/confirmed cases of patients with CREs[5,11,12,13]

- Every patient with a history of CRE detected in any clinical or screening specimen regardless of whether the isolate is considered to reflect colonisation or infection should be isolated with strict application of contact precautions. Such patients should be considered to be colonised with CRE indefinitely. There are no known criteria for deeming a patient as being no longer colonised with CRE
- Any patient from whom a suspected CRE is detected (awaiting reference laboratory confirmation of carbapenem resistance) in any clinical or screening specimen should be isolated with strict application of contact precautions. The requirement for ongoing isolation will be determined by the findings of the reference laboratory
- Any patient who is considered to be in an at-risk category for CRE carriage (see point 2 above) should ideally be isolated with application of strict contact precautions pending the results of rectal screen. In the event that isolation facilities are limited, priority for isolation should be given to any patient with diarrhoea, productive of respiratory secretions, faecal or urinary incontinence or actively draining wounds.
- Where a case of CRE colonisation or infection is identified, contact identification and screening should be is conducted.
- Because CRE are carried in the bowel flora, they are highly transmissible, particularly when affected patients have diarrhoea or high dependency on healthcare professionals for personal and medical care. Where direct physical contact with the patient is anticipated, the usual personal protective equipment (PPE) recommendations are advised, including the donning of a long sleeved disposable gown to protect the clothing of the healthcare professional.
- It is recommended that where a patient is identified as being colonised or infected with CRE, that direct patient care is carried out by a staff member assigned to caring for that patient only. If this proves difficult to implement, given the resources of an individual ward, it is recommended that a risk assessment be performed by the infection prevention and control team. Priority should be given to providing dedicated staffing for any patient who has a high level of dependency, diarrhoea, productive respiratory secretions, faecal or urinary incontinence or actively draining wounds.

Dr Karen Burns & Dr Kirsten Schaffer (Committee Chairperson) on behalf of the SARI subcommittee for the development of guidance for prevention of multi-drug resistant organisms, apart from MRSA.

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