Epidemiological Alert:

First finding of carbapenemases of type New Delhi Metallo-β-lactamase (NDM) in Latin America

22 November 2011

Due to the recent finding of carbapenemases of New Delhi metallo-β-lactamase (NDM) type in isolations of *Klebsiella pneumoniae* in Guatemala, the Pan American Health Organization/World Health Organization (PAHO/WHO) emphasizes the importance of the surveillance and detection in the Region of this resistance mechanism that increases morbidity and mortality of healthcare associated infections.

In August 2010, reports indicated the emergence of a mechanism of resistance in enterobacteria that caused outbreaks and was related to an increase in morbidity and hospital mortality in India, Pakistan and England. Subsequently, it was also reported in Europe, Japan, Australia, Canada and the United States of America. Due to its geographical origin, the mechanism was named "New Delhi metallo-β-lactamase " (NDM).

In Latin America, the circulation of metallo-β-lactamase of type VIM had been reported mainly in nonfermenting Gram-negative bacilli, as *Pseudomonas aeruginosa*, *Acinetobacter baumanni*, and to a smaller degree in enterobacteria; however, NDM had not been detected. NDM type metallo-β-lactamase have spread to different countries via the related Enterobacteriaceae as *Klebsiella pneumoniae*, an agent commonly related to hospital infections.

Since 2008, when the first case was detected in a patient in Sweden that had traveled to India, there have been reports of dissemination of this mechanism and its circulation in other countries. In 2010, Canada and the United States of America detected cases in travelers coming from India. In Latin America, there had not been reports of the circulation of this mechanism, until Guatemala recently reported two isolations of *Klebsiella pneumoniae*.

What are carbapenemases?

They are enzymes present in negative gram bacteria that inactivate the carbapenems and, generally, all betalactam antibiotics.

The consequences for the treatment of the infections caused by these bacteria are important since there is practically no therapeutic arsenal for the infections caused by the pathogens producing carbapenemases.

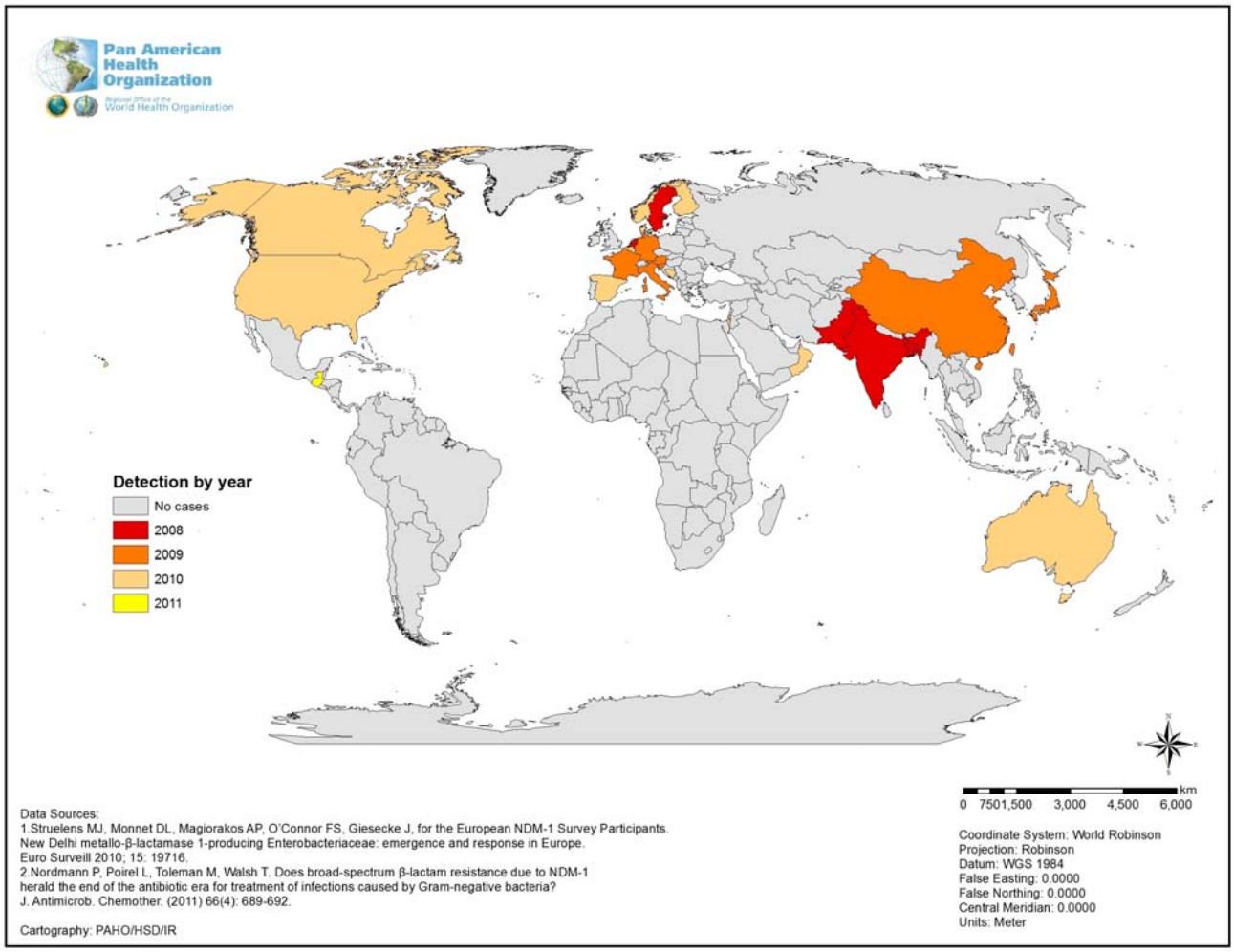
Two carbapenemases families exist: the type serin beta-lactamases (KPC and SME) and metallobetalactamases (VIM, IMP, and NDM); although there are molecular differences between the two families both inactivate the carbapenems and in general betalactam antibiotics, with the exception of aztreonam in the metallobetalactames.

Carbapenemases is produced and disseminated by means of plasmids, signifying that the risk of dissemination between species is very high.

On 17 November 2011, the International Health Regulations National Focal Point (IHR NFP) published an epidemiological alert of the isolation of strains of multiresistant *Klebsiella pneumoniae* by carbapenemase type New Delhi metallo-β-lactamase (NDM) in Guatemala. According to the published alert, the National Health Laboratory confirmed the presence of NDM in two strains of *Klebsiella*

pneumoniae that were provided by two national reference hospitals located in Guatemala City.[1] The Guatemala IHR NFP is conducting epidemiological research to know the origin and the implications of the finding. The National Institute of Infectious Diseases Dr. Carlos G. Malbrán in Argentina carried out the molecular analysis of the strains. Additional molecular analyses are underway to determine the type of NDM and the pulsed field gel electrophoresis, which in turn will help to find the genetic relation of these strains with those circulating elsewhere in the world.

Map. Global distribution of Enterobacteriaceae with NDM enzime, 2008-2011



Surveillance in Latin America

After the PAHO/WHO epidemiological alert on KPC type carbapenemases was issued in June 2010, PAHO/WHO with support of the antimicrobial service of the National Institute of Infectious Diseases "Dr. Carlos G. Malbrán"[2] held training sessions

[1] Information available at: http://epidemiologia.mspas.gob.gt/vigepi/2011/Oficio%20Circular%2018-2011%20171111.pdf

[2] Responsible for the external program of quality assurance of the Latin American Surveillance Network of the Resistances to the Antimicrobial, coordinated by PAHO.

and established the regional protocol for the detection of carbapenemases, including NDM, which strengthened surveillance and detection and diagnosis capacity of the Latin American Surveillance Network Antimicrobial Drug Resistance (ReLAVRA).

Laboratory Detection

The first line of defense to contain these multiresistant pathogens includes the laboratories, along with adequate detection of the mechanism and prevalence research. Authorities, including committees of healthcare associated infection control and national level health authorities must be provided with information to alert other hospital centers.

Through the ReLAVRA network, the laboratories in the Region have the tools for the phenotypical detection of NDM carbapenemases. The strain is molecularly standardized in the same national reference laboratory, or it may be sent for its molecular confirmation to the Regional Reference Laboratory, the Institute of Infectious Diseases Dr. Carlos G. Malbrán.

Recommendations

a) Methods of surveillance and epidemiological research:

1. Increase the participation of laboratories in the surveillance systems for the early detection of outbreaks, for the purpose of early guidance of control measures.

2. Apply the regional protocol for the detection of carbapenemases and strain reference in suspected cases at the national reference laboratories level.[3]

3. Send the suspected strain to the national or regional reference laboratory for confirmation and molecular typing of carbapenemases.

4. Disseminate the information and recommendations to alert health workers and decision-makers at all levels.

b) Antimicrobial treatment:

Limited clinical experience indicates that antibiotic combinations produce better results than monotherapy. However, it is not possible to issue a general recommendation of antimicrobial treatment due to the lack of solid evidence on its

[3] NOTE: It is recommended that the sentinel laboratories, faced with gram-negative hospital pathogens, follow the regional protocol (http://bit.ly/ProtocoloDeteccionCarbapenemases) for the detection of these mechanisms of resistance and hand over the first strain detected to a health institution for confirmation by the national reference laboratory.

effectiveness. Because of the complexity of the treatment, infectious disease specialists must prescribe it.

c) Infection prevention and control measures:

The prevention and control measures against infections in hospitals are intended for patients who are colonized and with infection by the NDM pathogen.

In addition to standard precautions, **contact precautions** should be applied.

Recommendations:	• Hand washing using water and soap or glycerinated alcohol. • Use of gloves and gowns for close contact with patients and for contact with secretions. • Isolation in individual room or cohort. • Separation between beds of at least 1 meter. • Cleaning the surroundings with chlorine (bleach) dilution (1:10).

References

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