NDM-1 : The new superbug

Both the Health Protection Agency in the UK (in July 2009) and the CDC (in June 2010) warned of a new emerging carbapenemase, Metallo Beta-Lactamase \( \text{bla}_{\text{NDM-1}} \) (NDM-1). In August 2010, an article in *The Lancet Infectious Diseases* triggered a media storm and brought the public’s attention to the world’s newest superbug when 37 strains of NDM-1 were found in the UK and 99 strains were found in India. NDM-1 is reported to be highly resistant to all antibiotics, including carbapenems – considered to be the last line of defense in antibiotic treatments.

Q&A : NDM-1

What is NDM-1?
- NDM-1 is a Metallo Beta-Lactamase essentially found in *Enterobacteriaceae* (principally *E. coli* and *K. pneumoniae*).
- NDM-1 stands for New Delhi Metallo-beta-lactamase-1, since it was first identified in a Swedish patient of Indian origin, who had been admitted to a hospital in New Delhi, India in 2008.
- The NDM-1 gene produces an enzyme which makes bacteria resistant to almost all \( \beta \)-lactams, including carbapenems (imipenem, meropenem, ertapenem, doripenem). Carbapenems are powerful, broad-spectrum antibiotics, which are often considered to be the last line of defense against multi-resistant strains of bacteria, such as *E. coli* and *K. pneumonia*.

How does it spread?
The gene for NDM-1 is found on plasmids (DNA strands), which can easily spread from one strain of bacteria to another, particularly in patients receiving antibiotic treatment.

Where has it spread so far?
- So far, the large majority of cases have been reported in India, Pakistan and Bangladesh.
- However, cases have also been reported in the United Kingdom (37), the U.S. (3), France (2), Sweden (1), as well as Australia, Hong Kong, Canada, Belgium, Germany, the Netherlands, Kenya, and Oman. Cases found outside of the Indian sub-continent have been linked to patients recently receiving medical care or cosmetic surgery in that region.

Why is it a major healthcare risk?

Lack of effective antibiotics
- NDM-1 bacteria are resistant to most antibiotics (fluoroquinolones, aminoglycosides and \( \beta \)-lactams), except tigecycline and colistin.
- Currently, there are few new antibiotics against Gram-negative bacteria in development and none that are effective against NDM-1.

High risk of rapid NDM-1 transmission
- The NDM-1 type of plasmidic resistance means it can transfer easily to other bacteria and has been identified in several different and unrelated bacterial strains. Transmission can be accelerated by "medical tourism", and by the high level of population exchanges between India and Pakistan and other countries around the globe. NDM-1 is found in *E. coli* - the most frequent cause of urinary tract infections, which is commonly found in the community. The fact that *E. coli* is a typical community-acquired bacteria may also accelerate the spread of NDM-1 resistant strains, since the resistance is not limited to the healthcare setting.
- The spread of this new resistance gene is strongly facilitated by the following conditions:
  - low level of hygiene
  - overpopulation
  - hot, humid climate
  - widespread over-the-counter use of antibiotics
How is NDM-1 different from other types of carbapenemases?

There is no major difference from other carbapenemases (same shortage of antibiotics), except that NDM-1 occurs in *E. coli*, therefore presenting a greater risk factor since it could potentially migrate in the community.

What can be done to prevent it?

Standard infection control/hygiene measures applied in the case of nosocomial or community-acquired infections can be applied to reduce the transmission of NDM-1.

**Healthcare Setting**

Key measures for prevention are:
- increased screening (particularly all patients transferred from overseas hospitals)
- isolation of carriers and reinforced hygiene measures
- prudent use of antibiotics
- monitoring and surveillance of antibiotic resistance

**Individual Precautions**

Actions which can help to reduce the transmission of *E. coli* and therefore NDM-1 include:
- frequent, thorough handwashing
- cleanliness when preparing and consuming food
- reinforcing precautions when in contact with persons with a urinary tract infection/diarrhea
- reinforcing contact precautions if you yourself have a urinary tract infection/diarrhea

Can it be treated?

It is difficult to treat patients infected by bacteria which harbor this new resistance mechanism, since NDM-1 is highly resistant to almost all antibiotics, including carbapenems. Currently, it appears that two antibiotics (tigecycline and colistin) are still effective, but resistance can occur. The severity of infections involving NDM-1 can vary from mild to fatal.

Where can I learn more?

Carbapenem resistance and NDM-1 - Q&A from the UK Health Protection Agency
http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/CarbapenemResistance/GeneralInformation/

CDC MMWR (Morbidity and Mortality Weekly Report) June 25, 2010 / Vol. 59 / No. 24 / Page 250
http://www.cdc.gov/mmwr/PDF/wk/mm5924.pdf

Diagnostic Solutions for NDM-1

bioMérieux is actively committed to the fight against bacterial resistance and offers a complete range of products for the detection and screening of the most frequently found resistance mechanisms. For carbapenemase-producing *Enterobacteriaceae*, and namely NDM-1, the current bioMérieux ID/AST solutions are:

**VITEK® 2 / Advanced Expert System™ (AES) / Etest®**

NDM-1 is a Metallo Beta-Lactamase essentially found in *Enterobacteriaceae* (principally *E. coli* and *K. pneumoniae*).

VITEK® 2 AST cards and Etest® accurately provide MIC results to specific carbapenem drugs that are commonly used to treat infections caused by resistant *Enterobacteriaceae* strains. Using these MIC results, Advanced Expert System™ (AES) analyzes the antimicrobial susceptibility pattern of each organism and can actually determine the carbapenemase resistant phenotype. The ability of AES to detect resistant phenotypes is crucial for helping clinicians guide therapy and predict clinical outcomes. Also, bioART™ offers an additional tool that can be customized to alert users to carbapenem resistance patterns.

Contact your local bioMérieux representative or visit www.biomerieux-usa.com/connection to receive information on additional Etest® laboratory tools that we can provide to assist in the assessment of highly resistant strains.
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Automation: Vision and Making the Case
Linda C. Bruno, M.A., MT (ASCP)
Associate Administrative Director
Director of Laboratory Operations, Manager of the Microbiology,
Molecular Pathology, and Tissue Typing HLA Laboratories
University of Illinois, Chicago

What’s New
Douglas Matthews
Marketing Manager
bioMérieux

A New Paradigm for Antibiotic Susceptibility Testing
Paul Bourbeau, Ph.D
Laboratory Director
Geisinger Medical Center

Sepsis, Know From Day 1: Procalcitonin
Karen Watters
Clinical Implementation Specialist
bioMérieux

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### Healthcare Associated Infections (HAIs)

BioMérieux's suite of HAI solutions help to identify and control the spread of Multi-Drug Resistant Organisms (MDROs) with same-day testing and effective MRSA screening capabilities. They also help to reduce HAI-related costs.

### Reducing HAIs

- **HAIs are one of the top 10 causes of death in the U.S.**
  - Identify and control the spread of MDROs with same-day testing capabilities.
- **Reduced reimbursement**
  - Reduce HAIs through proactive surveillance of potential sources of infection.
- **MRSA adds 8.5 days to length of stay, on average**
  - Minimize HAI-related costs (average direct cost of $8832) with effective MRSA screening.

### Your Suite of Solutions

**chromID™**
- ChromID VRE and chromID MRSA: Two highly sensitive and specific chromogenic media used to screen for two of the most common causes of HAIs:
  - Methicillin-resistant *Staphylococcus aureus*
  - *Enterococcus faecium* and *E. faecalis* showing acquired vancomycin resistance
- Pre-prepared and ready to use

**NucliSENS® EasyQ® MRSA**
- A real-time amplification and detection assay for the rapid screening of MRSA
*U.S. availability pending clinical trial completion and FDA clearance; currently available in Europe

**DiversiLab®**
- Augment current infection prevention surveillance activities with rapid strain typing to identify the source of MDROs and help stop the spread of HAIs

**VIDAS® C. difficile Toxin A & B**
- Allows for the identification and treatment of infected patients quickly and avoids unnecessary patient isolation, particularly for elderly individuals

### Esoteric Testing

Early detection and diagnosis is critical for the selection of appropriate patient treatment regimens. BioMérieux's esoteric suite of solutions provide rapid, specific, high value tests to support emergency and critical care medicine decisions for better patient management.

### Getting better information, faster

- **Physicians are inundated with information**
  - Early detection and diagnosis for appropriate treatment regimens.
- **Patient risk assessed with limited precise information**
  - Specific biomarkers deliver critical information and add clarity for better patient management.
- **Physicians need reliable, actionable information as quickly as possible**
  - Rapid, high medical value tests support emergency and critical care medicine decisions.

### Your Suite of Solutions

**VIDAS® and miniVIDAS®**
- Multiparametric, automated immunoassay systems with a broad test menu encompassing sepsis, infectious diseases, cardiac and tumor markers, thyroid, reproductive hormones, and serology assays

**High Medical Value Biomarkers include:**

1. **VIDAS® B-R-A-H-M-S PCT™**: Rapid procalcitonin assay used with critically ill patients to assess risk for progression to severe sepsis and septic shock
2. **VIDAS® D-Dimer Exclusion™**: First FDA cleared assay for exclusion of Pulmonary Embolism (PE) and Deep Vein Thrombosis (DVT) for outpatients with signs and symptoms of venous thromboembolism (VTE)
3. **VIDAS® C. difficile Toxin A & B**: Allows for the identification and treatment of infected patients quickly and avoids unnecessary patient isolation, particularly for elderly individuals
Microbial Identification and Susceptibility Testing
Rapid and precise identification and susceptibility testing results are critical to guide antimicrobial therapy and manage infectious diseases. bioMérieux’s Microbial Identification and Susceptibility Testing suite includes a complete solution of advanced automation, informatics and lean practices for streamlined testing and results within hours.

Combat growing microbial resistance to antibiotics
- **Antimicrobial resistance is on the rise**
  Microbial identification and susceptibility testing results within hours for targeted therapy.
- **Increased testing volume**
  Advanced automation with lean practices to streamline testing.
- **Complex identification and susceptibility algorithms**
  Consolidated testing platforms.

Your Suite of Solutions

**VITEK® 2**
- Rapid, accurate and automated microbial identification and susceptibility testing system provides results within hours
- **OBSERVA™**: A single workstation manages patient data integration from the BacT/ALERT® 3D

**BacT/ALERT®**
- Automated, modular system for continuous microbial detection and sepsis management

**Etest®**
- Internationally recognized and supported by more than 3,000 scientific references for its antimicrobial resistance testing range

**Specifications:**
Fifteen dilution MIC reagents are available for the following areas:
- Antimicrobial susceptibility testing
- Antifungal susceptibility testing
- Antimycobacterial susceptibility testing*
*For research use only

**VITEK 2 MS™**
- Identification of microbial pathogens within minutes*
*Availability pending clinical trial completion and FDA clearance

**PREVI™ Isola**
- Automated pre-poured media streaking instrument that provides improved workflow efficiency through a patented award winning robotic system. The PREVI Isola manages 90% of the steps required to process liquid microbiology specimens.

Your Suite of Solutions (cont.)
- **Advanced Expert System™ (AES)**: Provides intelligence for resistance detection by analyzing MIC patterns and detecting phenotypes for most organisms tested on VITEK® 2
- **Smart Carrier Station™**: A unique concept in test preparation that saves time, offers full traceability and enhances productivity

**PREVI™ Color Gram**
- Automated, standardized Gram staining system that saves lab technician time while economically reducing reagent usage and biohazard waste

**NucliSENS® easyMag®**
- IVD-labeled automated nucleic acid extraction instrument and reagents offering unparalleled versatility and reduced plastics waste
- Nucleic acid binding to NucliSENS® magnetic silica particles
- Same reagents for all protocols
- Workflow Flexibility

**Myla™**
- An intelligent middleware solution that is designed by microbiologists for microbiologists. This browser-based application can be assessed throughout your institutional network and helps put you in charge of organizing and optimizing your microbiology laboratory workflow

**LEAN Lab Design Services**
- A new service for microbiology laboratories to dramatically reduce turnaround time and increase productivity by utilizing the principles of Lean Six Sigma

LEAN Lab
Microbiology laboratories are facing an increasing pressure to reduce turn around time and increase productivity. bioMérieux’s LEAN Lab suite of solutions provides high throughput automated instruments, advanced informatics and a set of services to assist microbiology laboratories to optimize their workflow processes and increase efficiency.

Creating a more efficient lab
- **Projected shortage of 100,000 skilled technologists by 2012**
  Optimize microbiologists’ time to perform skilled tasks.
- **Increasing workloads, decreasing budgets**
  Automate and standardize workflow.
- **Faster turnaround time for quality patient care**
  Implement process change to provide rapid results.

Your Suite of Solutions

**PREVI™ Isola**
- Automated pre-poured media streaking instrument that provides improved workflow efficiency through a patented award winning robotic system. The PREVI Isola manages 90% of the steps required to process liquid microbiology specimens.

YOUR SUITE SUCCESS

Turn to page eight to learn more about your Suite Success
Recent advances in technology and process management have had a dramatic effect on the workload of hospital microbiologists. Hospital microbiologists are under pressure to decrease response times while addressing the need for new testing capabilities to detect multi-drug resistant organisms. New tests, such as MRSA screening of patients at time of admission, are adding additional pressure to a profession that already is overburdened by a severe labor shortage and a decline of new microbiologists entering the field. The average age of these professionals in the U.S. is 51 years, with only two new clinical laboratory scientists entering the profession for every seven that leave. This situation is putting tremendous workload and economic pressures on microbiology laboratories.

Numerous innovative products have been developed in recent years to automate some of the routine tests performed in the microbiology laboratory. Innovation alone, however, is not enough to alleviate the burden placed on microbiologists for faster, more reliable tests. That’s why many laboratory managers and directors are adopting Lean in the laboratory. Lean is a tool for eliminating waste while maximizing productivity, reducing errors and cost, and improving turnaround times. "Nonvalue-added tasks" typically refer to manual tasks that hinder the flow of information. This includes administrative processes, plate streaking, waiting on batch test runs, traveling between instruments, or shuttling specimens around the laboratory. While important to the workings of the laboratory, these processes are not value-added time. The goal of Lean is to minimize the time spent on routine processes so that microbiologists can focus their time on value-added tasks. These tasks provide clinicians with the information they need to make important clinical decisions so they can begin treatment more quickly. Lean principles also allow clinicians to optimize or revise treatments based on the patient’s current medical condition.

In 2009, bioMérieux, a world leader in the field of in vitro diagnostics, partnered with Guidon Performance Solutions, a leading provider of Lean and Six Sigma performance management consulting, to provide objective Lean lab assessments to our customers. Using Lean, our customers can make decisions that optimize their value-added services. The assessments include a microbiology laboratory “roadmap” that provides recommendations for adjusting processes, reorientating existing equipment, maximizing staff time, and automating various portions of the microbiology lab continuum.

"Imagine peeling back the roof of a microbiology lab and this is what you would see over time," said Ron Wince, President and CEO of Guidon Performance Solutions. "A map of laboratory movement would look just like spaghetti."

The goal of a Lean lab assessment is to identify redundant motion and repetitive processes so that the laboratory can run more efficiently and productively. The assessment begins with a meeting between Guidon and laboratory management. At this time, the Lean team reviews the types of samples that are processed, current staffing, current quality control standards, and laboratory operations, i.e., time and motion. The assessment typically takes between four and six days to complete. The LEAN team physically follows patient samples from receipt to delivery to quantify the arrival pattern of the samples, duration of each step, cycle times, and staff interaction with specimens. It is not unusual to find slow times and rush times, particularly because sample processing is coordinated with the laboratory’s staffing matrix.

At the kick-off meeting, Guidon provides training on ways to reduce or eliminate waste, improve laboratory workflow and increase turn around times. When the analysis is complete, the LEAN team meets with the entire laboratory staff to review and discuss the best measures for reducing waste and cycle times while increasing laboratory efficiency. In most cases, the Lean team identifies several areas where improvement can increase their productivity by as much as 20 percent. In some cases, additional discussions with laboratory managers, in combination with benchmark studies, may improve efficiency by as much as 50 percent.

**LEAN Lab Assessment Improves Quality, Efficiency, and Turnaround Time**

By: Christian Borjesson
Senior Director, Microbiology
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Guidon’s Lean team also may recommend reconfiguring parts of the laboratory to reduce travel time and excessive motion. One way to accomplish this is to rearrange equipment and work areas so that vital equipment is clustered together in functional groups, thereby avoiding any bottlenecks. One effective method is to adopt a cellular flow process, where the sample passes from one end to other end, which reduces time and motion among laboratory personnel. This relatively simple change can result in as much as a 50 percent improvement in sample processing times.

LEAN, while not new to the healthcare industry, is a new endeavor for microbiology laboratories. Microbiology laboratories tend to take a more conservative approach than other hospital laboratory early adopters do, such as clinical chemistry laboratories. Recent advances in technology and Lean’s proven record of accomplishment with other hospital laboratories have made microbiology managers and directors more receptive to Lean Laboratory Design. The shortage of laboratory personnel is forcing microbiology laboratories to rethink how they process specimens. Lean gives laboratory management the tools they need to identify their weaknesses and fortify their strengths.

Contact us at www.biomerieux-usa.com/connection to schedule a LEAN team visit to your laboratory.
Want to learn more about your Suite Spot? Complete this form and fax it to 919-620-2615, or visit www.biomerieux-usa.com/connection

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*U.S. availability pending clinical trial completion and FDA clearance

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