Carbapenem-Resistant *Enterobacteriaceae (CRE)* & Multi-drug Resistant *Acinetobacter (MDR-A)*

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Objectives

- What is CRE/ MDR-A
- Transmission
- Who is at risk
- Control measures/ infection prevention
- The Environment
- Additional recommendations
- Supplemental measures

What is Enterobacteriaceae?

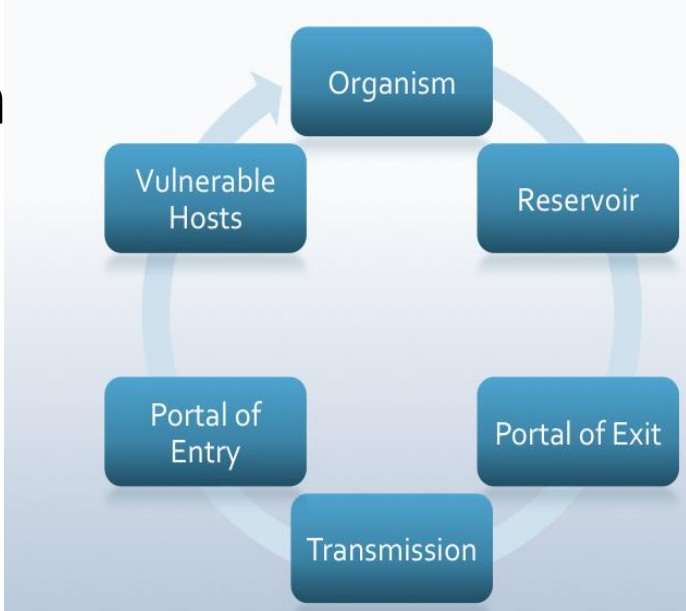
- Large family of gram-negative bacilli
  - *E. coli, Klebsiella, Enterobacter*
- Normal part of the GI tract
- Common cause of infections
  - Community
  - Health care-associated

What is *Acinetobacter*?

- Common in soil & water
- *A. baumannii* – 80% of reported infections
- Can cause variety of illnesses
  - Little risk to the healthy

Transmission

- Person-to-person
  - Contact with positive patients
  - Contact with wounds or stool
- Medical devices or equipmen
- Inanimate objects



Who is at Risk?

- CRE & MDR-A infections are more common in patients who have:
  - Frequent or prolonged hospital stays
  - Prolonged antibiotic use
  - Indwelling medical devices
    - Foley's
    - Central lines
  - Chronic medical conditions
    - COPD, asthma
    - History of surgery
    - Decubitus

Why are these Important?

- Complex resistance
- Rapid transmission in health-care settings
- Limited treatment options available
- High mortality rates

By Poon Chian Hui

A NEWLY found superbug from India that has been making news around the world infected two patients here early this year – before anyone knew what they were dealing with – but was successfully dealt with and contained.

The Ministry of Health (MOH) told The Straits Times that the patients had infections from bacteria with the New Delhi metallo-beta-lactamase-1 (NDM-1) gene identified last month.

The gene has the ability to shield bacteria from all antibiotics, turning them into drug-resistant superbugs.

It was found in the samples from the two patients last month, after hospitals went back and tested past samples.

"Following reports of NDM-1 in other countries and the availability of newer and more s… found two … this year tha… said an MOH…

One was … sought medi… the other ha… Bangladesh f…

They had … times to the … The patient…

New superbug found in two patients here

resistant bacteria when they showed signs of illness besides the one they had gone in for – an indication they might also be infected with a superbug.

Both were quickly isolated from other patients after bacteria in their urine samples were found to be resistant to drugs.

Both cases successfully contained as experts urge health officials to track deadly bacteria

NDM-1 made the headlines after a study published on Aug 11 in The Lancet medical journal said the gene was detected in British patients in 2007, and appeared to have originated from India. So far, it has occurred mainly in two gut bacteria – *Escherichia coli* (E. coli) and *Kleb…*

…triggered a global reaction as …le to resist even the most …s of antibiotics known as car…

…now been reported in place… United States, France, Ger… …alia, Hong Kong and Japan. …a Belgian man became the …atality.

…ay, scientists at the Inter…

science Conference on Antimicrobial Agents and Chemotherapy urged the health authorities to track bacteria with the gene.

The conference in the United States, which ended yesterday, is the world's largest gathering of infectious disease specialists, attracting about 12,000 people.

Drug-resistant superbugs are not new and include methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*.

MRSA is a serious infection found mostly in hospital settings, while the latter usually infects the lungs.

The NDM-1 gene is a part of a bigger problem of drug resistance brought about by the abuse of antibiotics worldwide.

To fight the spread of these bugs, local hospitals have comprehensive infection control measures.

Hospital staff practise strict hand hygiene and are audited regularly.

Inpatients are also screened for existing superbugs such as MRSA.

There are also antibiotic stewardship programmes to help doctors prescribe the right type and dosage of antibiotics to minimise the rise of drug resistance.

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More in tomorrow's edition of Mind Your Body

The rise of the superbug

SGH's Director of Infection Control clues us in on the importance of simple hygiene habits to combat the superbug

Combating the deadly superbug is a responsibility everyone must share by practising good hygiene to prevent the transmission of the bacteria, said Dr Ling Mui Lin (below), Director of Infection Control.

Although antibiotics might work in overcoming an MRSA infection, anyone infected with the bug will largely have to count on his own immune system to get better. It is not surprising that for elderly people with weaker constitutions, an MRSA infection can be fatal.

MRSA can infect people in different ways. The most common is via a skin infection that may look like a pimple or a boil. Occasionally, it can spread to other organs in the body and become life-threatening.

A new antibiotic that is able to fight MRSA and other types of superbugs is …be available for many years to …le that is worrying, the good …at good hygiene practices can …spread of the bacteria signifi… Dr Ling.

…mmise that actively screens …atients for MRSA and promotes …alcohol hand rubs and cleanli… …wards has led to "a drop over …the number of hospital patients …ith MRSA", said Dr Ling.

…fection rate is now about 0.3 …atient days, but we are aiming …be added.

…spread through contact – shak… …or touching something that an …ted person has touched. "These …riers shed bacteria in places …have been," said Dr Ling.

…t is more likely for someone to …d with MRSA in hospital, it is …ut anyone who is warded will …e, she said. It is still possible to …ISA in the community.

…id off," said Dr Ling. "Those …ve become resistant. Over …resistant strains develop …l. This scenario sets up the …of the superbug."

…its continually undertake …s develop new drugs to …th the growth of such new …acteria, but it takes years …ug to be available for use. …s creativity, knowledge …t 10 years to create a new …But by the time it comes …already be ineffective in …tain types of bacteria. …ng out of time and ideas."

Help stop the superbug

A new gene which turns bacteria into powerful drug-resistant strains has landed in Singapore. Here is how you can protect yourself. POON CHIAN HUI reports

A new superbug gene, as yet unnamed, landed in Singapore at the beginning of this year, long before it hit headlines around the world.

But its visit was discovered only last month, when the Ministry of Health (MOH) tested past bacteria samples of patients after it got a name – New Delhi metallo-beta-lactamase-1 (NDM-1).

As reported in The Straits Times yesterday, the NDM-1 gene sneaked into Singapore with two people flying in from India and Bangladesh.

This new strain, like the existing methicillin-resistant Staphylococcus aureus (MRSA), has the ability to turn bacteria into superbugs that are resistant to powerful antibiotics.

While this episode underlined the airtight hospital infection control measures here, the public should not let their guard down.

Superbugs may not always be confined to sick people in hospitals, said Associate Professor Raymond Lin, the head of National University Hospital's (NUH) microbiology department.

"Antibiotic-resistant

ST PHOTO: ABDAN RAUF

Staff nurse Lee Si Ying screening a patient at the National University Hospital for superbug MRSA by taking a swab from his nose.

The Development of Resistance

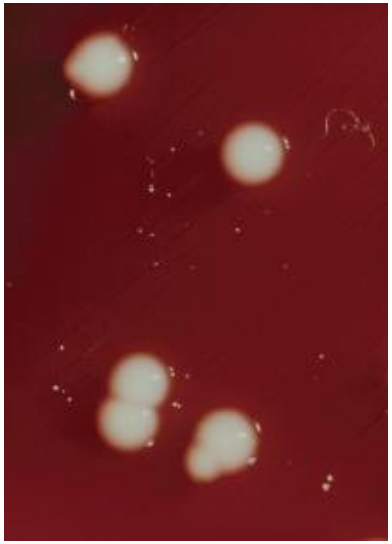
- Production of β-lactamases
  - Resistance to penicillin's
- Production of Extended Spectrum β-lactamases
  - Resistance to β-lactams, monobactams & 3rd gen ceph.
- Production of Carbapenemase
  - Resistance to Carbapenems: Imipenem, meropenem, doripenem, ertapenem
- Identified pan-resistant strains

Resistance Mechanisms

- Mechanisms for Enterobacteriaceae to be CRE
  - Active efflux of antibiotic
  - Structural mutations + overproduction of β-lactamases
  - Production of carbapenemases

Carbapenemases in the U.S.

- *Klebsiella pneumoniae* carbapenemase (KPC)
- Metallo-beta-lactamases (MBL)
  - New Delhi (NDM)
  - Verona integron-encoded (VIM)
  - Imipenemase (IMP)



Klebsiella pneumoniae

**All of these are enzymes that make a bacteria be labeled as “CRE”

What does the Texas Administrative Code (TAC) say?

- Reporting of CRE-*E. coli* or CRE-*Klebsiella* as defined in the Centers for Disease Control and Prevention, National Healthcare Safety Network (NHSN) Manual, Patient Safety Component, Protocol for Multidrug-Resistant Organism and Clostridium difficile Infection (MDRO/CDI) Module, or its successor.

- Multi-drug resistant (MDR) *Acinetobacter*--MDR-*Acinetobacter* as defined by …

Reporting Requirements

Texas Notifiable Conditions

24/7 Number for Immediately Reportable – 1-800-705-8868

Report confirmed and suspected cases.

Unless noted by *, report to your local or regional health department using number above or find contact information at http://www.dshs.state.tx.us/idcu/investigation/conditions/contacts/

Reporting Contacts

A – I	When to Report	I – Y	When to Report
*Acquired immune deficiency syndrome (AIDS)[1, 2]	Within 1 week	Influenza, Novel[3]	Call Immediately
Amebiasis[3]	Within 1 week	*Lead, child blood, any level & adult blood, any level[6]	Call/Fax Immediately
Amebic meningitis and encephalitis[3]	Within 1 week	Legionellosis[3]	Within 1 week
Anaplasmosis[3]	Within 1 week	Leishmaniasis[3]	Within 1 week
Anthrax[4, 5]	Call Immediately	Listeriosis[4, 5]	Within 1 week
Arbovirus infection[4, 5]	Within 1 week	Lyme disease[3]	Within 1 week
*Asbestosis[7]	Within 1 week	Malaria[3]	Within 1 week
Babesiosis[3]	Within 1 week	Measles (rubeola)[3]	Call Immediately
*Botulism (adult and infant)[4, 5, 8]	Call Immediately	Meningococcal infections, invasive[4, 5]	Call Immediately
Brucellosis[4, 5]	Within 1 work day	Multi-drug-resistant *Acinetobacter* (MDR-A)[9, 10]	Call Immediately
Campylobacteriosis[3]	Within 1 week	Mumps[3]	Within 1 week
*Cancer[11]	See rules[11]	Pertussis[3]	Within 1 work day
Carbapenem resistant *Enterobacteriaceae* (CRE)[9, 12]	Call Immediately	*Pesticide poisoning, acute occupational[13]	Within 1 week
Chagas' disease[3]	Within 1 week	Plague (*Yersinia pestis*)[4, 5]	Call Immediately
*Chancroid[3]	Within 1 week		
Chickenpox (varicella)[14]	Within 1 week		
*Chlamydia trachomatis infection[3]	Within 1 week		
*Contaminated sharps injury[15]	Within 1 week		
*Controlled substance overdose[16]	Call Immediately		
Creutzfeldt-Jakob disease (CJD)[3]	Within 1 week	Rubella (including congenital)[3]	Within 1 work day
Coronavirus, novel causing severe acute respiratory disease[3,17]	Call Immediately		
Cryptosporidiosis[3]	Within 1 week		
Cyclosporiasis[3]	Within 1 week		
Cysticercosis[3]	Within 1 week		
*Cytogenetic results (fetus and infant only)[18]	See rules[18]	*Spinal cord injury[20]	Within 10 work days
Dengue[3]	Within 1 week	Spotted fever group rickettsioses[3]	Within 1 week
Diphtheria[3]	Call Immediately	*Staph. aureus*, vancomycin-resistant (VISA and VRSA)[3, 5]	Call Immediately
*Drowning/near drowning[20]	Within 10 work days	Streptococcal disease (group A, B, *S. pneumo*), invasive[3]	Within 1 week
Ehrlichiosis[3]	Within 1 week	*Syphilis – primary and secondary stages[3, 21]	Within 1 work day
Escherichia coli infection, Shiga toxin-producing[4, 5]	Within 1 week		
*Gonorrhea[3]	Within 1 week		
Haemophilus influenzae type b infections, invasive[3]	Within 1 week		
Hansen's disease (leprosy)[3]	Within 1 week	*Traumatic brain injury[20]	Within 10 work days
Hantavirus infection[3]	Within 1 week	Trichinosis[3]	Within 1 week
Hemolytic Uremic Syndrome (HUS)[3]	Within 1 week	Tuberculosis (includes all *M. tuberculosis* complex)[3, 22]	Within 1 work day
Hepatitis A (acute)[3]	Within 1 work day	Tularemia[4, 5]	Call Immediately
Hepatitis B, C, and E (acute)[3]	Within 1 week	Typhus[3]	Within 1 week
Hepatitis B identified prenatally or at delivery (acute & chronic)[3]	Within 1 week	*Vibrio* infection, including cholera[4, 5]	Within 1 work day
Hepatitis B, perinatal (HBsAg+ < 24 months old)[3]	Within 1 work day	Viral hemorrhagic fever, including Ebola[3]	Call Immediately
*Human immunodeficiency virus (HIV) infection[1, 2]	Within 1 week	Yellow fever[3]	Call Immediately
Influenza-associated pediatric mortality[3]	Within 1 work day	Yersiniosis[3]	Within 1 week

In addition to specified reportable conditions, any outbreak, exotic disease, or unusual group expression of disease that may be of public health concern should be reported by the most expeditious means available.

Carbapenem resistant *Enterobacteriaceae* (CRE)[9, 12] — Call Immediately

Multi-drug-resistant *Acinetobacter* (MDR-A)[9, 10] — Call Immediately

Staph. aureus, vancomycin-resistant (VISA and VRSA)[3, 5] — Call Immediately

Defining CRE

CDC – CRE Toolkit

An Enterobacteriaceae that is

- Nonsusceptible to imipenem, meropenem or doripenem

  AND

- Resistant to all the following third-generation cephalosporins that were tested: ceftriaxone, cefotaxime and ceftazidime

CDC – NHSN MDRO Protocol

E.coli or any Klebsiella spp. testing non-susceptible to imipenem, meropenem or doripenem by standard susceptibility testing methods or by a positive result for any method FDA-approved for carbapenemase detection from specific specimen sources.

If you have an E.coli or Klebsiella that meets this criteria – report it.

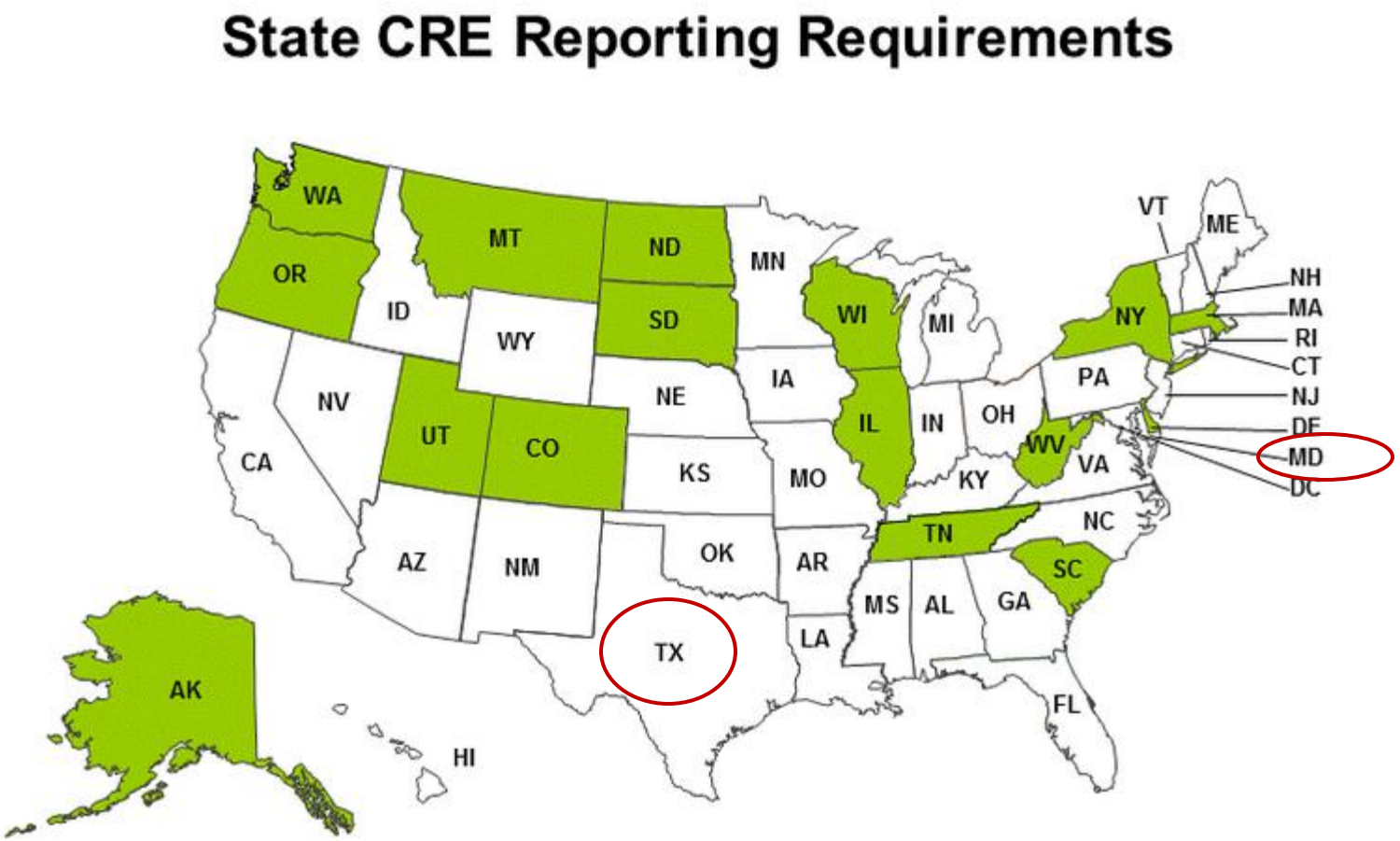
Defining MDR-Acinetobacter

Nonsusceptible to at least 1 antibiotic in at least 3 antimicrobial classes of the following 6 antimicrobial classes:

Beta-Lactam	Aminoglycosides	Carbapenems	Fluoroquinolones	Cephalosporins	Sulbactam
Piperacillin Piperacillin/ tazobactam	Amikacin Gentamicin Tobramycin	Imipenem Meropenem Doripenem	Ciprofloxacin Levofloxacin	Cefepime Ceftazidime	Ampicillin/ sulbactam

If you have an Acinetobacter that meets this criteria – report it.

APIC Updated 1/6/14



Lab Detection for CRE

- Clinical and Laboratory Standards Institute (CLSI) breakpoints for determining carbapenem susceptibility
  - Breakpoints were lowered to improve detection
- Modified Hodge Test
  - Tests for carbapenemase
- Other methods

Case Examples

Reportable or not?
Case 1

>100,000 CFU/ML KLEBSIELLA PNEUMONIAE
THIS ISOLATE DOES NOT PRODUCE A CARBAPENAMASE

SUSCEPTIBILITY RESULTS:

KLEPNE	MIC	INTERP
AMIKACIN	<=2	S
AMOX/CLAV ACID	>=32	R
AMPICILL/SULBAC	>=32	R
AMPICILLIN	>=32	R
CEFAZOLIN	>=64	R
CEFOTAXIME	>=64	R
CEFUROXIME	>=64	R
ERTAPENEM	>=8	R
GENTAMICIN	>=16	R
IMIPENEM		R
LEVOFLOXACIN	>=8	R
NITROFURANTOIN	128	R
PIPER-TAZOBACT	>=128	R
TMP/SMX	>=320	R
TOBRAMYCIN	8	I

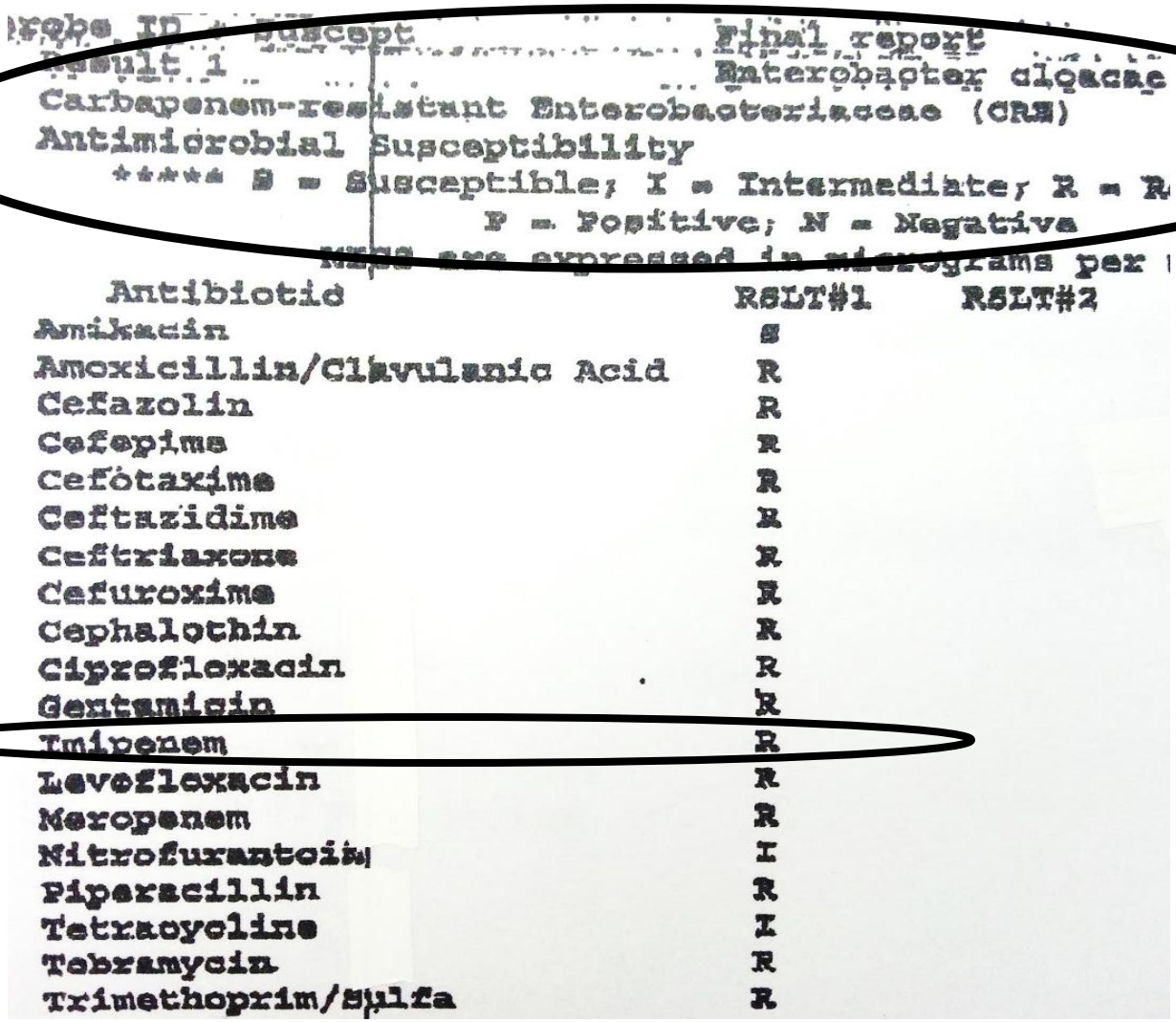
Reportable or not?
Case 2

Isolate (Final)
Klebsiella pneumoniae
ESBL-POSITIVE .
HODGE TEST POSITIVE
TESTING PERFORMED AT LABCORP .
Carbapenem-intermediate or resistant organism

Isolate (Final)
Pseudomonas aeruginosa

	Isolate ***Carbapenem-intermediate or resistant organism***		Isolate Pseudomonas aeruginosa	
MIC (mcg/ml)				
Amikacin (AK)	+>=64	R	>=64	R
Ampicillin (AM)	+>=32	R		
Ampicillin/Sulbactam (A/S)	+>=32	R		
Cefazolin (CFZ)	+>=64	R		
Cefepime (CPM)	+>=64	R	16	I
Ceftazidime (CAZ)	+>=64	R	4	S
Ceftriaxone (CRO)	+>=64	R	>=64	R
Ciprofloxacin (CP)	+>=4	R	>=4	R
Gentamicin (GM)	+>=16	R	>=16	R
Imipenem (IMP)	+<=0.25	S	>=16	R
Levofloxacin (LVX)	+>=8	R	>=8	R
Piperacillin/Tazo (TZP)	+>=128	R	>=128	R
Tobramycin (TO)	+>=16	R	>=16	R
Trimethoprim/Sulfa (SXT)	+>=320	R	>=320	R

Reportable or Not?
Case 3



Probe ID ... Suscept ... Final report
Result 1 ... Enterobacter cloacae
Carbapenem-resistant Enterobacteriaceae (CRE)
Antimicrobial Susceptibility
***** S = Susceptible; I = Intermediate; R = R
P = Positive; N = Negative
MICs are expressed in micrograms per

Antibiotic	RSLT#1	RSLT#2
Amikacin	S	
Amoxicillin/Clavulanic Acid	R	
Cefazolin	R	
Cefepime	R	
Cefotaxime	R	
Ceftazidime	R	
Ceftriaxone	R	
Cefuroxime	R	
Cephalothin	R	
Ciprofloxacin	R	
Gentamicin	R	
Imipenem	R	
Levofloxacin	R	
Meropenem	R	
Nitrofurantoin	I	
Piperacillin	R	
Tetracycline	I	
Tobramycin	R	
Trimethoprim/Sulfa	R	

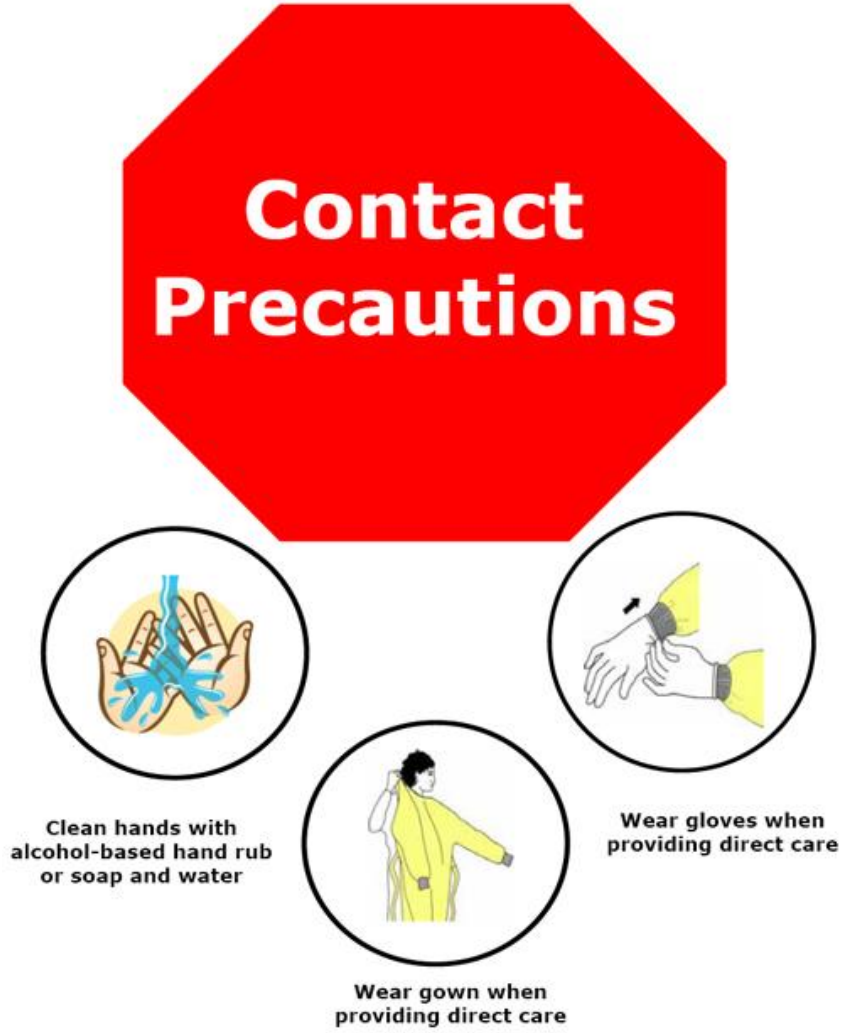
Facility Level Recommendations

- Lab detection and notification of CRE
  - Facility antibiogram
- Retrospective surveillance
  - Perform surveillance (6-12mos) to find unreported CRE
- Intra and inter-facility communication of patients
- Hand hygiene survey
  - Accessibility of product
- EVS and healthcare worker training
  - High touch areas and practice adherence

Facility Level Recommendations continued…

Core prevention measures:

1. Hand hygiene
2. Contact precautions
3. Patient and staff cohorting
4. Limit use of devices
5. Antimicrobial stewardship
6. CRE screening



Facility Level Recommendations continued…

Supplemental measures

1. Active surveillance testing
   - Reactive vs. Proactive
2. Chlorhexidine bathing

LTAC Specific Recommendations

- Resident placement
  - Low vs. high risk
- Modified contact precautions
- Occupational and physical therapy
  - Controlled vs. uncontrolled secretions/excretions
- Social activities
  - Infection risk vs. psychological risk
- Admission of CRE+ patients is ok

Contacts

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<u>All Other Regions</u>

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