Department of State Health Services
Health Service Region 1
Epidemiology Response Team

EPI Tōme
Newsletter

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"Please be kind…report on time!"

Multi-Drug Resistant Organism Reporting

Additions to the Texas 2014 Notifiable Condition List include two categories of multi-drug resistant organisms: Carbapenem Resistant *Enterobacteriaceae* (CRE) and Multi-drug Resistant *Acinetobacter* (MDR-A). These two notifiable conditions became officially reportable on April 20, 2014.

CRE

Enterobacteriaceae are a family of bacteria that include *Klebsiella* species and *Escherichia coli*, both of which can be found in the normal human gut flora. Occasionally these bacteria spread beyond the intestines and cause infections such as pneumonia, urinary tract infections, wound infections, bacteremia, and meningitis.

Carbapenems are a class of beta-lactam antibiotics that have a broad spectrum of antibacterial activity; and because of their high resistance to most beta lactamases, they are often considered the last resort in treating serious gram negative bacterial infections. There are currently four carbapenem drugs licensed in the United States, which include doripenem, imipenem, meropenem, and ertapenem.

Carbapenem beta lactamases (carbapenemases) hydrolyze most beta-lactam antibiotics, including carbapenems, allowing bacteria possessing these enzymes to become resistant to all beta-lactam class antibacterial agents. In the recent years, two especially troubling carbapenases have emerged: *Klebsiella pneumoniae* carbapenemase (KPC) and New Delhi metallo-beta lactamase (NDM-), a carbapenemase. KPC, the most common carbapenemase in the United States, was first detected in 2001 (originating in the U.S.). NDM was first recognized in 2009 from a patient that received medical care in India. First detected in the U.S. in 2010, 69 cases of NDM producing CRE have reported in the states as of January 2014.

Genes that express KPC and NDM are located on transmissible plasmids, and though first associated with *Klebsiella pneumoniae* (CRE-*Klebsiella*), KPC can be expressed by *Escherichia coli* (CRE– *E. coli*), other *Enterobacteriaceae*, *Pseudomonas* species, and *Acinetobacter baumannii*. NDM expression has been detected in *K. pneumoniae, E. coli,* and *Acinetobacter*. CRE can have additional antibiotic resistance mechanisms that enable them to be non-susceptible to many other classes of antibiotics.

CDC's Antibiotic Resistance Threats - Hazard Levels

Urgent	High-consequence antibiotic threats because of significant risks are identified across the seven antibiotic resistance factors (see below). These threats may not currently be widespread, but have to potential to do so and require urgent public health attention to identify infections and limit transmission.
Specific threats	*Clostridium difficile*, Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)
Serious	Significant antibiotic resistance threats. For varying reasons, such as low or declining domestic incidence or reasonable availability of therapeutic agents, they are not considered urgent, but these threats will worsen or become urgent without ongoing public health monitoring and prevention activities
Specific threats	Multidrug-resistant (MDR) *Acinetobacter*, drug resistant *Campylobacter,* fluconazole-resistant *Candida* (a fungus), extended spectrum beta-lactamase producing Enterobacteriaceae (ESBLs), vancomycin-resistant *Enterococcus* (VRE), MDR *Pseudomonas aeruginosa*, drug-resistant non-typhoidal *Salmonella*, drug resistant *Salmonella typhi*, drug resistant *Shigella*, methicillin resistant *Staphylococcus aureus* (MRSA), drug resistant *Streptococcus pneumoniae*, drug resistant tuberculosis (MDR and XDR)
Concerning	Bacteria for which the threat of antibiotic resistance is low, and/or there are multiple therapeutic options for resistant infections. These bacterial pathogens cause serious illness. Threats in this category require monitoring and in some cases rapid incident or outbreak response.
Specific threats	Vancomycin-resistant *Staphylococcus aureus* (VRSA), erythromycin-resistant *Streptococcus* Group A, clindamycin-resistant *Streptococcus* Group B

Antibiotic Resistance Factors:
(1) clinical impact, (2) economic impact, (3) incidence, (4) 10 year projected incidence, (5) transmissibility, (6) availability of effective antibiotics, and (7) barriers to prevention.

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CRE can cause infections in almost any part of the body including bloodstream infections, ventilator- associated pneumonia, and intra-abdominal abscesses. Based on information from a CDC pilot surveillance system most CRE infections involve the urinary tract, often in people who have a urinary catheter or have urinary retention. The CDC, in their "Antibiotics Resistance Threats in the United States, 2013" report, categorizes CRE as a high-consequence antibiotic threat because of significant risks identified across several criteria (see table on page 1).

The CDC estimates there are 140,000 health-care associated *Enterobacteriaceae* infections each year, with approximately 9,300 caused by CRE. Approximately 600 deaths result each year from infections with CRE-*Klebsiella* spp. and CRE-*Escherichia coli.* As of February 2014, CDC has confirmed at least one type of carbapenemase-producing CRE in healthcare facilities in 47 states.

CRE-*Klebsiella* spp. and CRE-*Escherichia coli* are the two reportable carbapenem-resistant Enterobacteriaceae (CRE) in Texas.

MDR-A

Acinetobacter species are pleomorphic, aerobic, gram-negative bacilli that are commonly found in water and soil. Within the genus *Acinetobacter*, more than 25 species have been described. However, the most important species affecting humans is *A. baumannii*, a member of the phenotypically similar group *A. calcoaceticus-A.baumannii* complex.

A. baumannii is often cultured from hospitalized patients, sputum or other respiratory fluids, wounds, and urine. Isolates of *A. baumannii* usually represent colonization, rather than true infection. However, in critically ill patients, *A. baumannii* can cause life-threatening infections. Pneumonia and blood stream infections are the most common, but *Acinetobacter* can infect any organ or tissue. These infections are typically associated with central lines, arterial lines, and mechanical ventilation. In addition to hospital-related infections, *A. baumannii* can cause community acquired pneumonia.

A. baumannii expresses several resistance mechanisms (inherent and acquired) to antimicrobials including beta-lactamases, aminoglycoside-modifying enzymes, alteration to antibiotic targets, porin mutations, and enhanced efflux pumps.

Historically, *Acinetobacter* had been treated with combinations of beta-lactam drugs and aminoglycosides. In recent years however, *Acinetobacter* has become increasingly resistant to multiple antibiotic classes and some strains are resistant to the 8 drug classes available for treatment, including carbapenem, one of the last resort drugs for treatment. *Acinetobacter* species that are resistant to at least 3 classes of antimicrobials are considered "multidrug resistant" (MDR-A). See Case Classification on Page 5.

In hospital settings, the primary mechanism of transmission for *Acinetobacter* is contact transmission, either by directly, person-to-person, or indirectly, through an intermediate contaminated object or person. *Acinetobacter* is resistant to drying, can form biofilms, and subsequently, can survive for days in the hospital environment. *Acinetobacter's* attributes of resiliency, multidrug resistance, ability to colonize, and contact transmission present challenges in preventing and controlling this organism in healthcare settings.

According to the CDC, an estimated 12,000 healthcare-associated *Acinetobacter* infections occur each year and approximately 63% (7,300) are considered multidrug resistant. *Acinetobacter* accounts for about 2% of healthcare associated infections, though the proportion is about 7% for critically ill patients on mechanical ventilators. Approximately 500 deaths occur annually.

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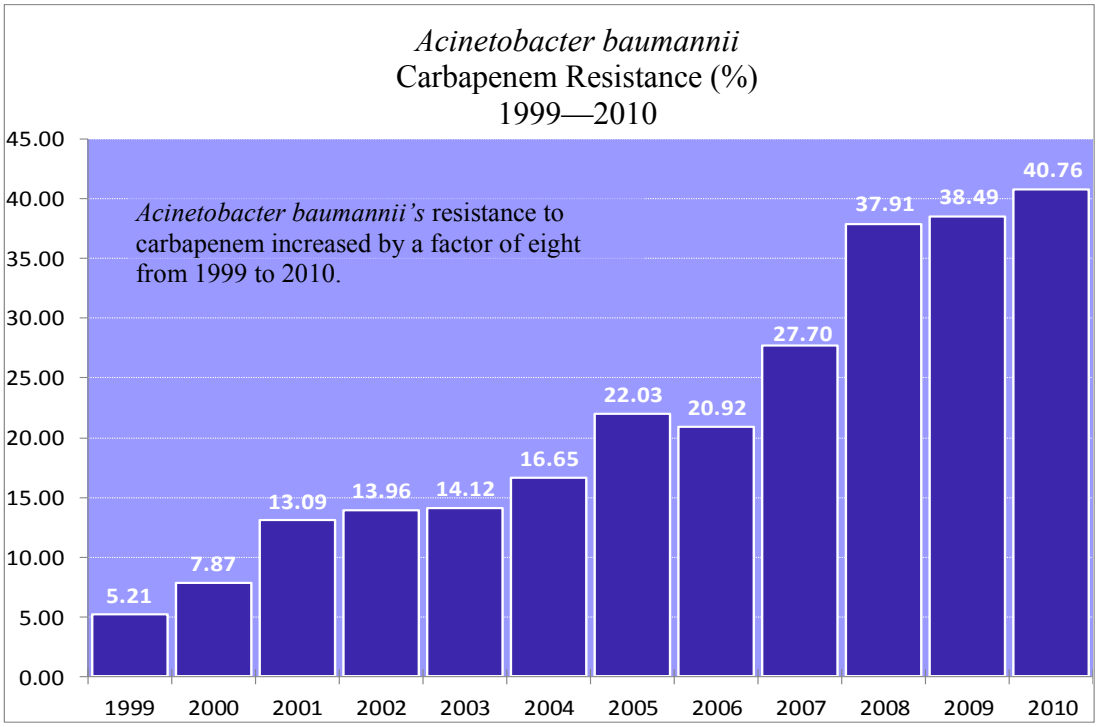


Graph Data Source: The Center for Disease Dynamics, Economics & Policy Resistance Map, Carbapenem-Resistant *Acinetobacter baumannii*
http://www.cddep.org/resistancemap/bug-drug/AB-CP#.U39mWstOW70, Accessed 05/23/2014

Table 1: Select reportable conditions, including confirmed, probable, and suspect cases (as applicable) in DSHS HSR 1, including all public health jurisdictions. Six month comparison (October through March for the time period October 1, 2011 through March 31, 2014.) Data source: Texas NEDSS Database. Data extracted: 05/05/2014. Time period based on Event Date. These counts are generated by DSHS HSR1. 2014 data is preliminary and subject to change.

	October 2011 through March 2012							October 2012 through March 2013							October 2013 through March 2014										
Condition	Oct	Nov	Dec	Jan	Feb	Mar	6 mo. Total	Oct	Nov	Dec	Jan	Feb	Mar	6 mo. Total	Oct	Nov	Dec	Jan	Feb	Mar	6 mo. Total	2014 thru Mar	2013 Total	2012 Total	2011 Total
Amebiasis						1	1						1	1				2			2	2	1	1	
Botulism, foodborne																3	1				4		4		
Campylobacteriosis	16	6	8	12	7	6	55	14	16	7	10	3	11	61	28	13	10	5	4	7	67	16	188	178	136
Creutzfeldt-Jakob Disease																							1		2
Cryptosporidiosis	2						2		2	1	2	1		6	3	3	3		2	3	14	5	29	8	31
Cyclosporiasis																							1		
Encephalitis, West Nile								1						1	4						4		28	2	
Haemophilus influenzae, invasive																							1		
Hantavirus pulmonary syndrome																				1	1	1			
Hemolytic uremic synd., postdiarrheal						1	1								1						1		1	1	6
Hepatitis A, acute			1	1			2								1	1				1	3	1	5	2	4
Hepatitis B Viral Infection, Perinatal																								1	
Hepatitis B, acute		1	1				2				1	1	1	3									4	2	6
Hepatitis C, acute																								1	3
Influenza-associated pediatric mortality						1	1																	1	
Legionellosis								1						1									2	1	5
Listeriosis																		1			1	1	1		4
Lyme disease																							1	1	
Malaria		1					1						1	1				1			1	1	4	1	1
Mumps	1	1					2																1		2
Neisseria meningitidis, invasive													1	1		1					1		2	1	1
Pertussis	1	2		4			7		4		3		2	9	18	24	23	17	15	4	101	36	162	21	16
Salmonellosis	28	19	13	9	11	8	88	13	18	10	5	6	13	65	20	18	11	5	6	4	64	15	151	172	220
Shiga toxin-producing Escherichia coli	1		1	2		2	6	4		1			1	6	2	1		3	2	2	10	7	9	16	21
Shigellosis	24	18	21	14	10	15	102	17	32	3	1	5	3	61	3	2		1			6	1	31	178	210
Spotted Fever Rickettsiosis		1					1			1				1										1	1
Streptococcus pneumoniae, inv. disease	4	15	14	14	9	18	74	5	6	9	15	7	7	49	9	4	6	10	12	13	54	35	74	90	127
Streptococcus, invasive Group A	2	1	2			2	7		3	5	4	3	8	23		1	6	3	3	5	18	11	29	19	19
Streptococcus, invasive Group B	6	6	6	3	1	3	25	3	3	5	4	5	4	24	6	4	3	3	3	5	24	11	45	51	46
Typhoid fever (Salmonella typhi)																									1
Vancomycin-intermediate Staph aureus			1				1																		1
Varicella (Chickenpox)	2	6	13	8	7	6	42	5	8	4	4	2	6	29	8	3	4	2	2	2	21	6	47	61	62
Vibrio vulnificus infection																								1	
Vibriosis, other or unspecified																								2	
West Nile Fever																							32	1	
Yersiniosis													1	1									1		

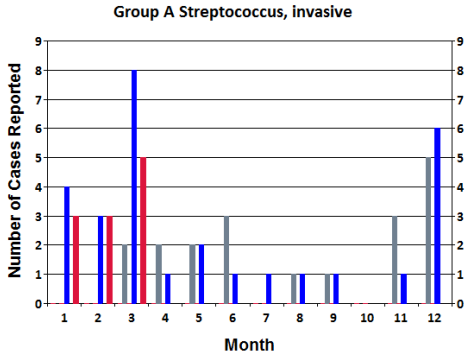
Note: West Nile Encephalitis and West Nile fever were not officially reported in the NEDSS database during 2011 and 2012.

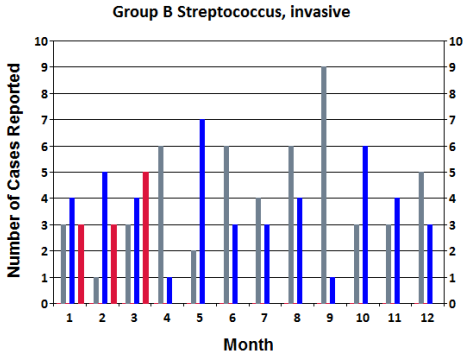
Chart 1: Select reportable conditions, including confirmed, probable, and suspect cases (as applicable) in DSHS HSR 1, including all public health jurisdictions, for the period January 01, 2012 through March 31, 2014 by Month/Year. Time period is based on Event Date.
Data source: Texas NEDSS Database. Data extracted: 05/05/2014. These counts are generated by DSHS HSR1. 2014 data is preliminary and subject to change.

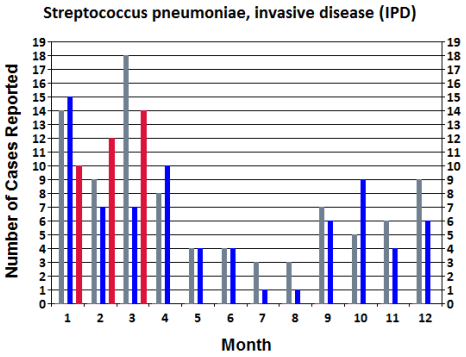
LEGEND

2012 2013 2014

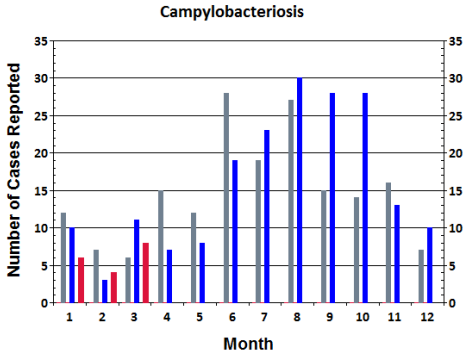
Invasive Streptococcal Disease

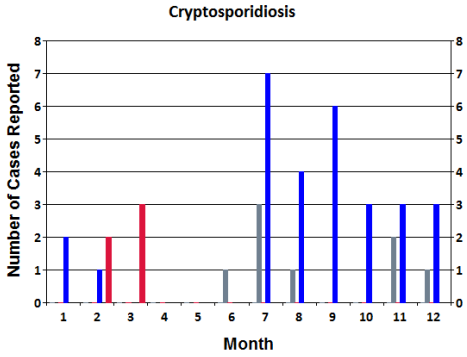


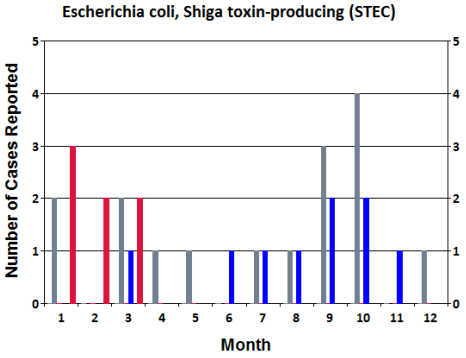


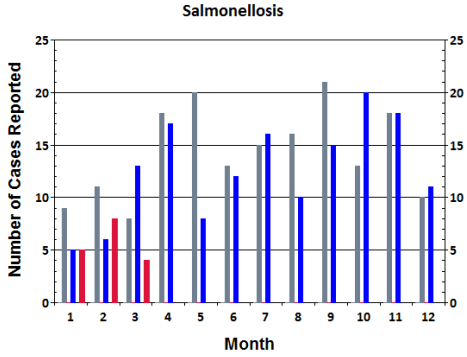


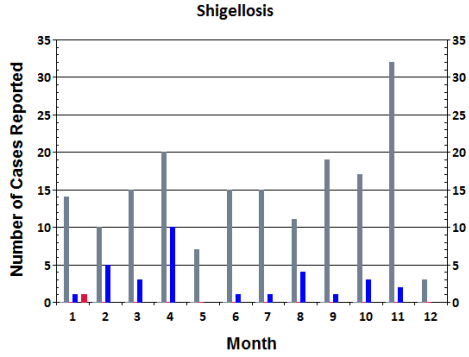
Foodborne/Waterborne Disease

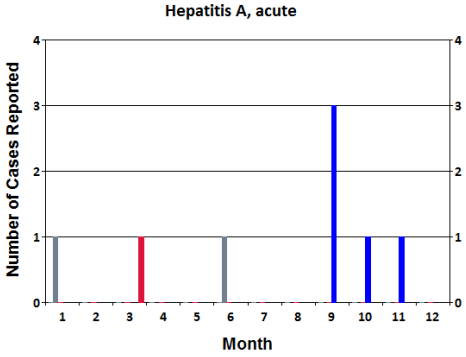




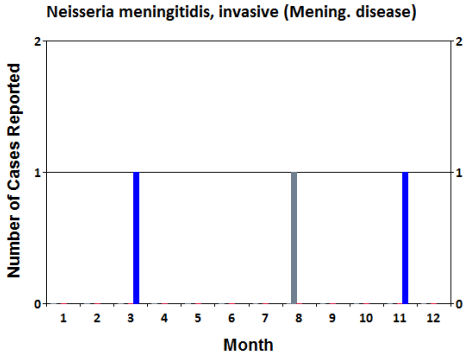


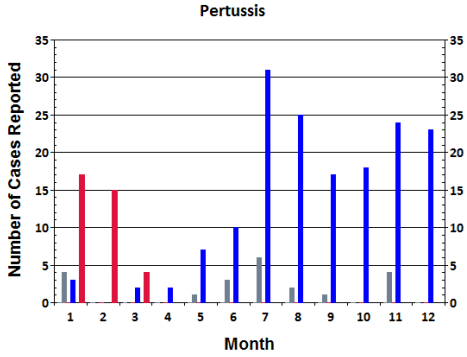


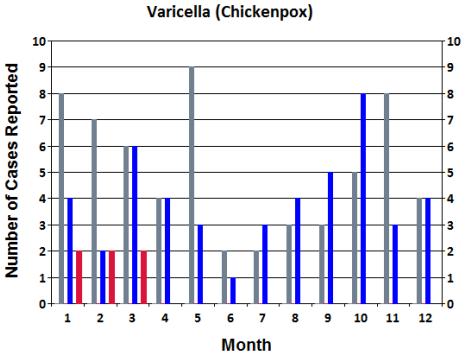




Other Vaccine Preventable Disease







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Reporting

CRE and MDR-A are immediately reportable conditions. Isolates from any body site should be reported, including colonization and surveillance cultures. Reporting forms can be found on the Texas Department of State Health Services (DSHS) Infectious Disease Control Unit's (IDCU) website: http://www.dshs.state.tx.us/idcu/investigation/forms/ or the DSHS Health Service Region 1 (HSR1) website: http://www.dshs.state.tx.us/region1/surveillance.shtm#Report1.

When reporting, please include supporting laboratory reports with isolate identification and susceptibility results.

Report immediately by calling (806) 744-3577.
Fax reporting forms and supporting documentation to DSHS HSR 1 Epidemiology, (806) 783-6466.

Case classification

CRE Case Classifications

Confirmed: *Klebsiella* species or *Escherichia coli* from any body site/source that possess/contain a gene sequence specific for carbapenemase (a positive PCR result).

Probable: *Klebsiella* species or *Escherichia coli* from any body site/source that is:

- Positive for carbapenemase production by a phenotypic test (e.g., Modified Hodge Test), OR
- Non-susceptible (i.e., intermediate or resistant) to at least one of the following carbapenems: doripenem, meropenem, or imipenem

	MIC (µg/mL)		
	Susceptible	Intermediate	Resistant
Doripenem	≤1	2	≥4
Imipenem	≤1	2	≥4
Meropenem	≤1	2	≥4

MDR-A Case Classification

Confirmed: *Acinetobacter* species from any body site/source that meets the confirmed laboratory criteria for MDR-A

- Laboratory criteria: Non-susceptible (i.e., resistant or intermediate) to at least one antibiotic in at least 3 antimicrobial classes of the following 6 antimicrobial classes:

Class	Examples		
Beta-Lactams	Piperacillin	Piperacillin/ tazobactam	
Aminoglycosides	Amikacin	Gentamicin	Tobramycin
Carbapenems	Imipenem	Meropenem	Doripenem
Fluoroquinolones	Ciprofloxacin	Levofloxacin	
Cephalosporins	Cefepime	Ceftazidime	
Sulbactams	Ampicillin/ Sulbactam		

Control measures for healthcare facilities to prevent spread of MDROs.

- Practice antibiotic stewardship.
- Know if patients with CRE or MDR-A are hospitalized at your facility and stay aware of MDRO infection risks. Inquire if patients have received medical care elsewhere or have traveled.
- Request immediate alerts when the lab identifies a MDRO infection in a patient at your facility.
- Ensure the patients with MDRO are placed on contact precautions.
- Limit use of invasive devices on all patients to the extent possible.
- Remove temporary devices as soon as possible.
- If the patient was received from another healthcare facility and the patient is subsequently identified as having a MDRO, notify the transferring facility of the patient's MDRO status.
- Upon discharge of a patient with MDRO, if the patient is being transferred to another healthcare facility, notify the receiving facility of the patient's MDRO status.
- If feasible, cohort patients with the same MDROs.
- If feasible, cohort healthcare and support staff attending to patients with like MDROs.
- If the patient has CRE and is in a non-private room, consider screening the cohabitant for CRE via rectal swab. See CDC Laboratory Protocol http://www.cdc.gov/hai/pdfs/labsettings/klebsiella_or_ecoli.pdf
- If the patient has MDR-A and is in a non-private room, consider screening the cohabitant for MDR-A. Candidate body sites include nose, throat, axilla and/or groin, rectum, open wounds, and endotracheal aspirates.

Control Measures for patients with MDRO

- Instruct the patient to complete all antibiotic regimens and not to save or share medications.
- Encourage the patient to inform medical staff of their MDRO status, including future medical visits to other facilities.
- Remind the patient while visiting a health care facility or physician's office to wash or sanitize hands frequently.
- While in a healthcare setting, urge the patient to stay involved in their care by inquiring about infection control measures such as hand washing and room/equipment disinfection. Have the patient insist that healthcare providers wash or sanitize their hands upon entering and leaving the room.
- If the patient is no longer in a healthcare setting, encourage routine disinfection of frequently touched surfaces at home.

Sources:

Texas Department of State Health Services, Infectious Disease Control Unit, "Multi-drug Resistance Organism Guidance for Carbapenem-resistant Enterobacteriaceae (CRE) and Multi-drug Resistant Acinetobacter (MDR-A)."

Centers for Disease Control and Prevention, "Antibiotic Resistance Threats in the United States, 2013", http://www.cdc.gov/drugresistance/threat-report-2013/

Association for Professionals in Infection Control (APIC), "Guide to the Elimination of Multidrug-resistant Acinetobacter baumannii Transmission in Healthcare Settings", 2010. http://www.apic.org/resource_/eliminationguideform/b8b0b11f-1808-4615-890b-f652d116ba56/file/apic-ab-guide.pdf