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NH-HAN

NH DIVISION OF Public Health Services
Improving health, preventing disease, reducing costs *for all*
Department of Health and Human Services

Call to Action to Prevent Emergence and Spread of Antibiotic Resistant Infections

Key Points and Recommendations:

- NH DPHS is releasing the first annual New Hampshire Statewide antibiogram to track antibiotic resistance patterns, and to provide a tool clinicians can use to guide antibiotic prescribing. The 2016 State Antibiogram is attached, and can be accessed through the following link: https://www.dhhs.nh.gov/dphs/cdcs/hai/publications.htm. We include key clinical messages about treating common infectious syndromes below.

- Antibiotic prescribing drives the development of resistance; and antibiotic resistant infections are more difficult to treat, require more toxic and costly medications, and patients have worse clinical outcomes as a result.

- Antibiotic misuse is a problem that requires a multidisciplinary approach to implement antibiotic stewardship initiatives and improve antibiotic prescribing around New Hampshire.

- To facilitate learning and discussion around these issues, the NH DPHS is hosting a State Antibiotic Resistance Symposium scheduled for May 23, 2018 at the Grappone Conference Center in Concord, NH. Registration information will be forthcoming.

- For questions or concerns, or for more information about how to be involved in statewide antibiotic stewardship work, please call (603)- 271-4496 and ask to speak with the Healthcare-Associated Infections (HAI) Program.

The Problem of Antimicrobial Resistance:

At least 30% of all outpatient antibiotic prescriptions are estimated to be unnecessary (*JAMA 2016;315(17):1864-1873*). More than 50% of hospitalized patients receive some antibiotics during their admission, and 30% receive at least one dose of a broad-spectrum antibiotics (*MMWR Mar 7 2014;63(9):194-200, JAMA Intern Med 2016;176(11):1639-1648*). Inappropriate antibiotic prescribing has contributed to the emergence and spread of highly antibiotic resistant infections throughout the United States.

Carbapenem-Resistant Enterobacteriaceae (CRE): Carbapenemase producing CRE (CP-CRE) were first introduced into the U.S. around the year 2000 and have spread to every state in the U.S.: https://www.cdc.gov/hai/organisms/cre/trackingcre.html. CRE was made a mandatory reportable disease in NH in November 2016, and since then we have received 50 confirmed reports of CRE. Three had a plasmid-mediated mechanism of carbapenemase production, which is a concerning type of resistance because it can easily spread to other bacteria.

Mcr-1: The mcr-1 gene makes bacteria resistant to the antibiotic colistin, which is used as a last-resort antibiotic to treat patients with infections caused by multidrug-resistant bacteria, including carbapenem-resistant Enterobacteriaceae (CRE). The mcr-1 gene is carried on a plasmid making it easily transferred between bacteria. In June 2016, the CDC issued a national health alert about the first human infection in the U.S. identified with a bacterium carrying the mcr-1 gene (https://emergency.cdc.gov/han/han00390.asp). Since then, multiple other states have identified bacteria carrying the mcr-1 plasmid: https://www.cdc.gov/drugresistance/tracking-mcr1.html

Candida auris: *Candida auris* is an emerging multidrug-resistant yeast that can cause invasive infections with high mortality, has been found to contaminate patient environments, and can be spread person-to-person in healthcare settings. In June 2016, the Centers for Disease Control and Prevention (CDC) issued a clinical alert about the global emergence of the multidrug-resistant yeast *Candida auris* (https://www.cdc.gov/fungal/diseases/candidiasis/candida-auris-alert.html). Since that time, states in the Northeast have experienced difficult to control outbreaks of *Candida auris* in the healthcare setting: https://www.cdc.gov/fungal/diseases/candidiasis/tracking-c-auris.html.

Drug-resistant gonorrhea: In January 2017, New Hampshire announced a statewide gonorrhea outbreak after seeing a 260% increase in gonorrhea cases compared to prior years (https://www.dhhs.nh.gov/dphs/cdcs/alerts/documents/gonorrhea.pdf). The CDC has listed gonorrhea as one of the top three national urgent antibiotic resistant threats due to the propensity of *Neisseria gonorrhoeae* bacteria to develop resistance to antibiotics. With inappropriate treatment, the prospect of highly drug-resistant gonorrhea is growing. Reports of ceftriaxone-resistant gonorrhea are beginning to emerge, including a recent report from Quebec Canada: https://wwwnc.cdc.gov/eid/article/24/2/17-1756_article.

Highly-resistant bacteria: Other antibiotic-resistant infections are also becoming increasingly common in the healthcare setting. Gram-negative bacteria that produce extended-spectrum beta-lactamases (ESBLs), and multi-drug resistant Pseudomonas and Acinetobacter infections, as examples, are making infections more difficult to treat (https://www.cdc.gov/drugresistance/biggest_threats.html).

Public Health Action:

NH DPHS is taking an aggressive approach to identify, investigate, and prevent spread of high-priority infections, such as CRE and *Candida auris*, because they are still uncommon in New Hampshire.

To evaluate and address the problem of antibiotic overuse and antibiotic resistance in New Hampshire, we have formed a statewide collaborative Antibiotic Resistance Advisory Workgroup (ARAW) composed of individuals from many different healthcare specialties, including: healthcare providers (clinicians from local hospitals, urgent care facilities, long-term care facilities, dentists), infection preventionists, microbiologists, pharmacists, and veterinarians, to discuss and address the issues; and to work with us on promoting appropriate use of antibiotics (i.e. “antibiotic stewardship” initiatives).

As a first step, we will monitor antibiotic resistance through collection and assessment of hospital antibiogram data (hospital antibiograms are reportable in NH by statute). The data reported for calendar year 2016 has been combined into a statewide antibiogram. The antibiogram provides a summary of antibiotic susceptibility patterns for selected bacterial pathogens and antibiotics, separated by urine and non-urine sources. The purpose of the state antibiograms is to:

1. Annually evaluate antibiotic resistance trends in order to guide public health actions and promote/develop antibiotic stewardship initiatives.

2. Create a tool for clinicians to assist rationale choice of antibiotics for common infectious syndromes in order to empirically treat more appropriately and avoid overuse of broad spectrum antibiotics. The antibiograms can be found attached to this HAN or at the following link with additional information: https://www.dhhs.nh.gov/dphs/cdcs/hai/publications.htm. We have also attempted to summarize some key points about appropriate antibiotic prescribing below based on the antibiograms data (see "Clinical Implications" below).

Clinical Implications:

The recommendations below serve as guidance to clinicians treating patients empirically for some of the most common infections encountered in patient care. Each patient should be treated based on a clinician's assessment of the type of infection and acuity, and a patient's antibiotic regimen should always be tailored to culture results once they return.

Uncomplicated Urinary Tract Infections (UTIs)

- Asymptomatic bacteriuria should not be treated with antibiotics in most cases. Treatment may be indicated during pregnancy, before certain urologic procedures, and in first three months after renal transplant.
- The most common Gram-negative bacteria isolated from urine were *Escherichia coli* (70% of isolates) followed by *Klebsiella* spp. (15%) and *Proteus mirabilis* (5%). *Pseudomonas aeruginosa* was only cultured from 3.5% of urine specimens.
- Nitrofurantoin remains the most likely active agent against *Escherichia coli* (98% susceptible), followed by cephalexin (predicted by cefazolin, 91% susceptible). Trimethoprim-sulfamethoxazole and ciprofloxacin are less likely to be active, and we recommend avoiding ciprofloxacin as first-line therapy because of the potential for toxicity and *Clostridium difficile* infection.
- Fosfomycin may also be considered for *E. coli* (and enterococcal) UTIs. While most hospital laboratories do not routinely test susceptibilities for this antibiotic, testing can be requested. National data show >90% of *E. coli* are susceptible to fosfomycin.

Community Acquired Pneumonia (CAP)

- 32% of *Streptococcus pneumoniae* (pneumococcus) isolates are resistant to azithromycin (predicted by erythromycin susceptibility). As a result, azithromycin should not be prescribed when there is concern for pneumococcal pneumonia (e.g., when the syndrome is acute and/or focal consolidation is evident on the chest X-ray).
- National data shows that 44% of outpatient prescriptions are written for acute respiratory conditions, at least half of which are viral and will not respond to antibiotics (JAMA 2016; 315:1864-73). As the number one antibiotic prescribed in the outpatient setting is azithromycin, it is critical to reduce unnecessary use to prevent further resistance from developing in the community (Clinical Infectious Disease 2015; 60:1308-16).
- Preferred agents to treat an acute outpatient bacterial pneumonia suspected due to *Streptococcus pneumoniae* include amoxicillin, amoxicillin-clavulanate, and cefuroxime.
- The respiratory fluoroquinolones (i.e., levofloxacin and moxifloxacin) remain highly active against *Streptococcus pneumoniae;* however, quinolones should typically be avoided when

treating outpatient CAP because of the toxicities of the class, their ability to induce *Clostridium difficile* infection even months after these antibiotics have been used, and the availability of alternatives. The U.S. Food and Drug Administration (FDA) Drug Safety Communication now advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections (https://www.fda.gov/Drugs/DrugSafety/ucm500143.htm).

- For patients with community acquired pneumonia that require hospitalization, we recommend treatment with ceftriaxone and either doxycycline or azithromycin (for atypical bacterial pathogens).

Skin and soft tissue infections (SSTIs)/Cellulitis

- Most SSTIs are due to either *Staphylococcus aureus* or streptococcal infection.
- 68% of all non-urine *Staphylococcus aureus* isolates were methicillin-sensitive (MSSA). Because the majority of SSTIs will be due to either MSSA or streptococcal infection, a first generation cephalosporin (e.g., cephalexin or cefazolin) is the recommended empiric treatment. Oxacillin susceptibility predicts cephalosporin and beta-lactam/beta-lactam inhibitor susceptibility.
- In the case of a skin abscess, however, empiric outpatient therapy with either trimethoprim-sulfamethoxazole or doxycycline (98% and 88% susceptible, respectively) is the preferred antibiotic treatment because of the possibility for MRSA. This is typically prescribed following incision & drainage of the abscess.
- Clindamycin should not be prescribed empirically for MRSA, because 32% of isolates are resistant.

Intra-abdominal infections

- *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Proteus* spp., streptococci, and *Bacteroides fragilis* are the most common bacterial pathogens in intra-abdominal infections. Enterococci are often present in polymicrobial infections, but typically can be ignored, particularly when selecting an empiric regimen. *Pseudomonas aeruginosa* is not a common pathogen in intra-abdominal infections.
- Ampicillin-sulbactam shows poor activity against *E. coli*, so this drug should not be used empirically for mixed aerobic-anaerobic intra-abdominal infections, particularly for infections requiring hospitalization.
- Ceftriaxone (a third-generation cephalosporin) maintains good activity against *E. coli* and *Klebsiella* isolates, which together make up about 50% of the Gram-negative bacteria cultured from non-urine sources. Thus, ceftriaxone plus metronidazole is a reasonable empiric inpatient regimen for intra-abdominal infections.
- For serious, life-threatening intra-abdominal infections, piperacillin/tazobactam or cefepime plus metronidazole maintain high activity against the primary pathogens listed above.

Healthcare-associated Gram negative aerobic infections

- Meropenem remains remarkably active against Enterobacteriaceae. The rates of carbapenem-resistant Enterobacteriaceae (CRE) in the state are very low. We recommend that antimicrobial stewardship programs continue to restrict the use of carbapenem

antibiotics, because healthcare settings with more liberal use of carbapenems have seen a more rapid rise in carbapenem-resistance.

- Mild-to-moderate infections caused by extended spectrum beta-lactamase (ESBL) producing bacteria (e.g., uncomplicated urinary tract infections caused by ESBL *E. coli*) do not always require treatment with a carbapenem. Alternatives include: trimethoprim-sulfamethoxazole (Bactrim), nitrofurantoin, fosfomycin, and ciprofloxacin. These alternatives should be considered, when susceptible, to limit the overuse of carbapenem antibiotics and to reduce the potential adverse outcomes from unnecessary intravenous antibiotics.
- *Pseudomonas aeruginosa* is most commonly a healthcare-associated infection, including in catheter-associated urinary tract infections and ventilator-associated pneumonia. The most active antibiotics based on the state antibiogram data are piperacillin-tazobactam, ceftazidime, cefepime, and meropenem. Providers should be aware that 14-17% of isolates are non-susceptible to ciprofloxacin/levofloxacin, and 20% of isolates are non-susceptible to aztreonam (for non-urine isolates). If selecting one of these antibiotics, a combination regimen may be warranted. Among the aminoglycosides, tobramycin remains the most active.

For any questions regarding the contents of this message, please contact NH DHHS, DPHS, Bureau of Infectious Disease Control at 603-271-4496 (after hours 1-800-852-3345 ext.5300).

To change your contact information in the NH Health Alert Network, call 603-271-5194 or neil.twitchell@dhhs.nh.gov.

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From:	Benjamin P. Chan, MD, MPH – State Epidemiologist
Originating Agency:	NH Department of Health and Human Services, Division of Public Health Services

Attachments: 2016 State Antibiogram

NH DIVISION OF Public Health Services
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Department of Health and Human Services

New Hampshire Statewide Antibiogram 2016

All Sources Other Than Urine

Percent Susceptible

Bureau of Infectious Disease Control
Infectious Disease Surveillance Section

Gram Negative Organisms	Total Number of Isolates	Percent Susceptible																								
		Ampicillin	Ampicillin/Sulbactam	Piperacillin/Tazobactam	Cefazolin	Cefuroxime	Cefoxitin	Cefotetan	Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Ertapenem	Meropenem	Imipenem	Doripenem	Ciprofloxacin	Levofloxacin	Moxifloxacin	Amikacin	Gentamicin	Tobramycin	Tigecycline	Tetracycline	Trimethoprim/Sulfamethoxazo
Escherichia coli	2162	60	63	97	87	90	85	100*	94	93	95	93	100	99	100	100*	83	77	---	92	93	93	100	71	82
Enterobacter aerogenes	117			93					86	84	100	91	100	100	92	100*	99	100	---	100	100	99	95	88	98
Enterobacter cloacae	541			90					82	86	92	87	97	99	96	99*	96	96	---	99	97	97	99	88	91
Klebsiella pneumoniae	875		86	96	93	91	94	100*	97	97	98	97	100	100	99	100*	96	96	---	99	95	94	88	88	90
Klebsiella oxytoca	355		74	97	56	93	97	---	96	97	97	93	100	100	100	100*	99	100	---	99	99	99	100	94	98
Proteus mirabilis	568	73	89	100	87	96	96	---	97	98	97	96	99	100		98*	79	83	---	98	91	93			75
Serratia marcescens	327			85					92	86	100	88	100	100	95	99*	95	95	---	99	98	89	95	7	97
Citrobacter freundii	149			97					85	86	99	87	100	100	98	100*	93	95	---	99	93	94	100	82	87
Morganella morganii	124		7	97			74	---	93	92	98	88	99	99		---	92	95	---	100	95	97	25	20	86
Pseudomonas aeruginosa	1208			96						93	91	80		93	89	94*	86	83		95	85	97			
Acinetobacter baumannii	115		84	77					54	85	81			98	---	---	82	88		95	88	91	---	89	83
Stenotrophomonas maltophilia	315									42								79							94
Haemophilus influenzae	385	68	89*			95			99					---			95*	---	100*					85	68

Gram Positive Organisms	Total Number of Isolates	Penicillin	Ampicillin	Oxacillin	Ampicillin/Sulbactam	Cefazolin	Cefuroxime	Ceftriaxone	Ceftaroline	Levofloxacin	Moxifloxacin	Tetracycline	Trimethoprim/Sulfamethoxazol	Clindamycin	Erythromycin	Vancomycin	Linezolid	Daptomycin	Rifampin
Methicillin-**Sensitive** Staphylococcus aureus (MSSA)	6524	15		100	99	100	---	100	100*	93	96	96	99	83		100	99	100	99
Methicillin-**Resistant** Staphylococcus aureua (MRSA)	3048								100*	55	66	88	98	67		100	99	100	99
Enterococcus faecalis	877	99	99		---											98	99	100	
Enterococcus faecium	149	16	27		---											43	96	93	
Enterococcus spp. *(all hospital data)*	1390	87	89		---											91	99	99	
Coagulase negative staphylococcus	1638	12		56	48	51		51		74	84	85	69	69		100	99	100	99
Streptococcus pneumoniae	439	89	---	---	---		84	93		98	99*	84	86	91	68	100	100*		

	Indicates data have been censored because of intrinsic resistance and/or inappropriate clinical use.
---	Indicates data have been censored because of insufficient sample. CLSI guidelines suggest total isolate counts of less than 30 are excluded.
*	Indicates data for which 3 or less hospitals reported and result may not be geographically representative.

Please find the full version of the Antibiogram and Executive Summary report on our website at: https://www.dhhs.nh.gov/dphs/cdcs/hai/publications.htm

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New Hampshire Statewide Antibiogram 2016

Urine Only Sources

Percent Susceptible

Bureau of Infectious Disease Control
Infectious Disease Surveillance Section

Gram Negative Organisms	Total Number of Isolates	Ampicillin	Piperacillin/Tazobactam	Cefazolin	Cefuroxime	Cefoxitin	Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Ertapenem	Meropenem	Imipenem	Doripenem	Ciprofloxacin	Levofloxacin	Amikacin	Gentamicin	Tobramycin	Tigecycline	Tetracycline	Trimethoprim/Sulfamethoxazole	Nitrofurantoin
	Percent Susceptible																						
Escherichia coli	24330	66	96	91	95	96	96	96	97	96	97	100	100	100*	87	86	96	94	95	100	81	83	98
Enterobacter aerogenes	374		91				86	89	99	92	99	100	94	100*	99	99	100	100	100	99	94	99	19
Enterobacter cloacae	681		85				79	82	94	84	94	99	97	100*	94	95	100	98	97	95	86	84	30
Klebsiella pneumoniae	4600		98	96	94	95	97	97	98	97	100	100	100	100*	97	98	100	98	98	98	86	93	46
Klebsiella oxytoca	687		94	50	88	98	95	97	97	95	100	100	100	100*	97	98	99	99	97	99	94	95	85
Proteus mirabilis	1620	76	100	90	98	98	98	99	98	97	100	100		99*	78	80	99	90	92			78	
Serratia marcescens	262		88				90	86	98	88	100	100	99	100*	94	97	99	99	90	96	3	98	
Citrobacter freundii	624		96				82	83	100	86	100	100	85	100*	95	96	99	96	96	99	85	89	95
Morganella morganii	218		99			81	92	87	97	90	100	99		95*	87	87	97	90	94	11	14	84	
Pseudomonas aeruginosa	1220		97					95	92	82		93	86	98*	79	77	97	86	94				
Acinetobacter baumannii	84		---				56	91	93			77	---	---	95	90	95	99	98	---	85	85	

Gram Positive Organisms	Total Number of Isolates	Penicillin	Ampicillin	Oxacillin	Cefazolin	Ceftriaxone	Ceftaroline	Levofloxacin	Tetracycline	Trimethoprim/Sulfamethoxazole	Clindamycin	Vancomycin	Linezolid	Daptomycin	Rifampin	Nitrofurantoin
Methicillin-**Sensitive** Staphylococcus aureus (MSSA)	591	24		97	100	100	100*	78	97	99	82	100	100	100	100	100
Methicillin-**Resistant** Staphylococcus aureua (MRSA)	401						100*	19	97	98	52	100	100	99	98	99
Enterococcus faecalis	2612	97	97									99	98	100		98
Enterococcus faecium	200	24	25									40	97	93		44
Enterococcus spp. *(all hospital data)*	4015	92	93									97	99	92		95

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