

CDC *Vital Signs* Town Hall Teleconference

Stopping Carbapenem-resistant Enterobacteriaceae Infections:
Making Health Care Safer

March 12, 2013
3:30–4:30 pm EDT

Coordinator: Welcome and thank you for standing by. At this time, participants will be on a listen only mode until the question and answer portion. And at that time, if you'd like to ask a question, press star 1. Today's conference is also being recorded. If you have any objections, please disconnect at this time.

And now, I'd like to turn the call to your host today to Dr. Judith Monroe.
Ma'am, you may begin.

Judith Monroe: Thank you, operator. Good afternoon, everyone. I'm Dr. Judith Monroe. I direct the Office of State, Tribal, Local and Territorial Support here at CDC, and I'm really excited to have all you join the call today and it's exciting to see so many hospitals and health departments joining us to discuss this really important topic.

Before we get started, I do have a few housekeeping details. First remember to go online and download today's PowerPoint presentation so you can follow along with the presenters. So if you're in front of your computer, the web address is www.cdc.gov/stltpublichealth, all one word. There's a link directly to the town hall website under highlighted products and resources on the right side of the page. On this page, you can also view the bios for each of the presenters today. This is where we will be adding the audio recording and the transcript for today's teleconference, and those will be available in about a week.

So today, we're here to discuss the latest *Vital Signs* report on stopping carbapenem-resistant Enterobacteriaceae, or CRE infections. This is an important public health topic because untreatable and hard to treat infections from CRE are on the rise among patients in medical facilities.

CRE infections in the blood stream are fatal for up to half of patients who contract them. CRE was relatively uncommon in the US before the year 2000, and yet over the last ten years, one type of CRE infection has been reported in healthcare settings across 42 states.

On today's call, we are going to hear from three esteemed colleagues. They will share the latest insights regarding CRE, what can be done to help prevent the spread, and more information beyond that.

First, we will hear from Dr. Alexander Kallen, Medical Epidemiologist in the Division of Healthcare Quality Promotion at CDC's National Center for Emerging and Zoonotic Infectious Diseases. He will provide a summary of this month's *Vital Signs* report.

Dr. Kallen will then hand the call over to Dr. Wendy Bamberg, Medical Epidemiologist and Healthcare-Associated Infections Program Manager at the Colorado Department of Public Health and Environment.

Dr. Bamberg will share information about how Colorado increased awareness of CRE and the process of making CRE a reportable condition in healthcare settings.

Dr. Bamberg will then turn the call over to Mr. Zintars Beldavs, Manager of Healthcare-Associated Infections at the Oregon Health Authority. Mr. Beldavs will discuss the development of the Drug-Resistant Organism Prevention and

Coordinated Regional Epidemiology Network. That's the DROP-CRE network for short, and talk about how they've been successful in Oregon.

Please note, there will time for questions after the presentations today but you can get into the queue to ask a question at any time during the teleconference, and you do that by pressing star 1, and record your name when prompted.

So now, let me turn the call over to Dr. Kallen.

Alexander Kallen: Great. Thanks. This is Alex Kallen and I am going to take the next few minutes just to kind of highlight some of the important parts that were in the most recent CDC *Vital Signs* on carbapenem-resistant Enterobacteriaceae (CRE) and I'll - but first, I want to put this in a little bit of context using the first two slides.

So moving to the slide that's entitled Enterobacteriaceae, so the last part of CRE, or Enterobacteriaceae, really is a huge family of bacteria that are very common cause of both healthcare and community infections. In fact, this includes bacteria like E. Coli which is now the second most common cause of healthcare-associated infections reported to our National Healthcare Safety Network (NHSN) and also very common cause of community acquired urinary tract infections.

And if you go back through time, these bacteria - these Enterobacteriaceae - which are common inhabitants of our human GI tract, these have had issues with resistance over the years beginning with just basic antibiotics like penicillins and cephalosporins and then in the last 10 years or 20 years, the emergence of very, even more resistant bacteria that we're able to not be affected by very high generation cephalosporins and penicillins.

But until relatively recently, we've always had this class of antimicrobials called the carbapenems to fall back on. And if you actually look back through NHS Center and before that NNIS (National Nosocomial Infections Surveillance) our surveillance system that preceded an NHSN, carbapenem resistance was very rare in this country before about 2000.

In 2001, there was a report of a new type of resistance that was emerging in these bacteria that was identified in a *Klebsiella* isolate that was found from a surveillance program in North Carolina in 1996. And this really was the emergence of what we call carbapenemases as a resistance mechanism for this family of bacteria. Carbapenemases are enzymes that break down these carbapenem antibiotics as well as all the penicillins and cephalosporins, for the most part, and what happens since the emergence of these in 2000 is kind of a rapid spread of this one particular type of carbapenemase called KPC, or *Klebsiella pneumoniae* carbapenemases across the US.

In addition, there are other carbapenemases that we're starting to see more frequently, including one called the New Delhi metallo-beta-lactamase (NDM). These are enzymes that are found more commonly in other parts of the world that are now spreading mainly through people who have received healthcare outside the US into the United States.

And if you move to the second, or the third slide which shows a map of the United States, this really shows the emergence and spread of carbapenemase producing CRE in the United States beginning, again as I said, in about 2001. And this - all the colored states are states that have had reported to us or where we at CDC have confirmed at least one carbapenemase producing CRE. And as you can see, most of the states - all of the states - that are colored there had one of these KPCs that I mentioned and as matter in other states have had other enzymes that again are more common outside the United States.

So why are these epidemiologically important? We've tried to highlight this in the MMWR portion of the *Vital Signs*, and I think it blows down to about 5 points. The first is I mentioned is these bacteria - this Enterobacteriaceae - are very common causes of infection. And although we see this resistance that we're going to talk about today primarily in healthcare, it certainly does, second of all, have the ability to spread outside of healthcare into community settings. These organisms are highly drug resistant and even in the best case scenarios the treatment options are extremely limited.

These organisms are also capable of transferring their resistance. Not only can we spread these bacteria from one person to another on healthcare worker hands but they're capable of spreading the resistance genetic elements from one bacteria to the other. And lastly as you heard in the introduction, these bacteria are associated with very high mortality rates when causing invasive infections.

The key points to the *Vital Signs* on the next slide boil down to really three. First, the CRE are increasing when you look at NHSN, the percent of Enterobacteriaceae that are resistant to carbapenemase increased from about 1% in 2001 to 4% to 2011. However, if you look specifically to Klebsiella in 2011, 10% of Klebsiella reported to NHSN were resistant to carbapenems.

But the good news is that most hospitals don't see CRE regularly. In fact, if you look at NHSN in 2012 for the first six months, only about 4% of hospitals reported at least one CRE. Unfortunately, when you look at long-term acute care hospitals, this was higher, about 18% of LTACHs (long term acute care hospitals) reported one CRE in the first half of 2012.

And as I mentioned, when you look in our surveillance systems that we maintained to the Emerging Infection Program, most CRE are still healthcare associated. However, this is certainly something we don't want to see happen where this bacteria move from healthcare into community settings.

On the next slide, the good news about CRE is that there are interventions that are available to help prevent CRE transmission and slow the dissemination of this organism. This basically boils down to what we're calling detect and protect which kind of is - it would basically as identifying colonized or infected patients and then using appropriate transmission-based precautions to prevent transmission by things like contact precautions, et cetera.

When looking in the United States, facilities have used this CDC recommendations to control outbreaks of CRE and actually places outside the United States have used this in a regional way, in other words, applying these interventions not just an individual facilities but across regions to prevent the transmission of these organisms across whole regions and there's a great example in MMWR what Israel has done, with kind of our regional nationwide regional approach to preventing CRE transmission.

On the next slide, I just wanted to highlight our CDC CRE Toolkit. This expands and updates our regional guidance on CRE which came out in 2009 in MMWR, and provides recommendations for prevention for both facilities and in the second half regions that want to - health departments and regions who want to tackle this problem.

Lastly, what we wanted to highlight some of the things that states can and have done to try and prevent - slow the prevention of the - spread of these organisms and you'll hear more about this from Mr. Beldavs and Dr. Bamberg

in a minute, but what I think it boils down to is highlighted on the slide that says detect and protect.

First, I think it's important that states and regions have a sense of the CRE prevalence and trends in your region. Health departments, I think, are well positioned to help coordinate regional CRE tracking and control efforts. States can also work with facilities to make sure that accepting facilities are alerted when patients are transferred from one facility to the other. States can also work to develop lab capacity to assist with CRE identification and transmission especially being able to identify the mechanisms that underlie the resistance.

States can also provide education about CRE to healthcare facilities, infection prevention, et cetera. And also I do want to highlight as you'll hear in the story from Oregon that really it's important to be proactive especially in states that rarely, or have not yet been affected by CRE.

Here at CDC, we continue to work to monitor the presence and risk factors for CRE infections throughout both the NHSN and the Emerging Infection Program. We are providing ongoing support for CRE outbreaks as well as laboratory expertise especially for confirming resistance mechanisms.

We are continuing to work with the partners to better enhance our detection methods and prevention programs and, of course, working to help improve antibiotic prescribing practices.

Next, I'm going to turn it over to Wendy Bamberg who's a medical epidemiologist with the Colorado Department of Public Health and Environment, to talk about what they've done in Colorado. Wendy.

Wendy Bamberg: Thank you, Dr. Kallen. As Dr. Kallen greatly pointed out, CRE is a public health problem and as he mentioned, these are difficult to treat organisms with high mortality rate up to half of all invasive infections can lead to death.

It has been identified in at least 42 states currently, including Colorado, but thankfully transmission is preventable through appropriate infection control measures. Understanding the scope of the CRE problem in Colorado will help us prevent CRE infections. Although we know that CRE is present in Colorado, the specific problems and incidence of CRE has been unknown.

So I wanted to show you a piece of the CDC 2012 CRE Toolkit pictured here. And in order for us to really gather more information on CRE in Colorado, we at the state health department needed to develop a plan. So the CDC CRE Toolkit which is available online has important information for both healthcare facilities and health departments for the prevention of CRE.

The toolkit states health departments should understand the prevalence or incidence of CRE in their jurisdiction by performing some form of regional surveillance for these organisms. Two proposed methods for understanding the prevalence and incidence of CRE are highlighted in the red box - making CRE a reportable condition or performing a surveillance infection prevention at laboratories.

So the survey in Colorado that took place are first efforts to try to understand the CRE problem in our state. We went about this by asking 63 clinical laboratories statewide to complete a web-based survey in order to understand current testing method used to detect CRE, and also to try to gather actual numbers if the laboratories knew this and if they did an estimates of CRE that were detected by each laboratory.

So, 25 laboratories or 40% statewide completed the survey. The numbers and estimates of CRE provided by the laboratories was used to try to estimate the numbers of CRE isolates seen in Colorado over a one-year period of time.

Then the data from this survey showed that by these estimates that approximately 418 to 620 isolates per year might be seen in Colorado. However, I emphasized that these are very rough estimates and one thing we discovered during the survey was that there was vast confusion among laboratorians over the definition of CRE.

And CRE was often confused with other multi-drug resistant organisms such as extended-spectrum beta-lactamases, or ESBL that were more common. Thus, it was very likely that these estimates were way too high.

The next - our next step was to engage healthcare partners. We wanted to know from our partners if gathering data on CRE in Colorado, which would be extra work for clinical laboratories and healthcare providers, would actually be useful for them as well. So we created a working group to determine the utility of gathering data on CRE and the best method to accomplish this.

The working group consists of physicians and infection control experts, infectious disease pharmacists, laboratorians, public health officials, and the hospital association in Colorado. The group recommended systematically tracking CRE and was very interested in seeing specific and accurate data on CRE in Colorado as a state as well as specific regions of the state.

And the cleanest and most accurate way to accomplish our goal of systematically tracking CRE was to make CRE a reportable condition in Colorado.

Since the burden of reporting would fall to laboratories, the state health department engaged laboratories, healthcare facilities and providers in the process of making CRE reportable in order to make this successful.

The process itself resulted in an increased awareness of CRE and its public health importance and the health department again hearing various reports to CRE and receiving questions even before reporting began.

So in August of 2012, several months before reporting of CRE began, Colorado hospital reported two cases of CRE specifically carbapenem-resistant *Klebsiella Pneumoniae* to the health department. The infection prevention and infectious disease physician from hospital A were part of the CRE working group and so they were aware of our ongoing efforts to track CRE in Colorado.

It was interestingly found that these two cases plus an additional six cases detected through the investigations by the hospital, the health department, and CDC were positive for the New Delhi metallo-beta-lactamase, or NDM, enzymes. NDM is very rare in the United States. Prior to this outbreak, there were only 16 cases of NDM reported to CDC in the US.

This was the first NDM-producing CRE detected in Colorado and the largest NDM outbreak in the United States to date. This outbreak really illustrated the importance of public health collaboration with healthcare partners in order to understand CRE in their region. And we really feel that if it hadn't been through these efforts to try to make CRE reportable during those efforts, we might not have heard about these two cases and might not have found these NDM cases.

So I'm in slide number 19. On November 30, 2012, Colorado made CRE a reportable condition. The specific definition that we used for CRE reportability is on this slide, it includes E. Coli, Klebsiella and Enterobacter species that are intermediate or resistant to at least one carbapenem antibiotics, and resistant to all third-generation cephalosporins tested or E. Coli, Klebsiella and Enterobacter that test positive for carbapenemase production through Modified Hodge Tester (MHT), disk diffusion, PCR, or any other method.

Slide number 20. So there are several objectives the state health department in Colorado has for performing this CRE surveillance. It's important to note that Colorado is fairly early in the emergence of CRE. We likely will have low numbers of cases.

Therefore, we feel that performing this surveillance is an opportunity for prevention. When cases of CRE are reported to the state health department, we use this as an opportunity to provide education and guidance to the facility during the period of time that the facility is actually - has a patient with CRE in their facility.

The ultimate goal of our surveillance is to prevent the transmission of CRE. Providing education to the healthcare providers in real time reinforces the importance of infection control measures and communication between facilities when transferring patients with CRE.

We are also able to review with the facility the CDC recommendation to screen other patients that might be at risk of acquiring CRE due to the epidemiologic links with the reported case patient.

We expect this to be a much more effective way of providing education than only providing general education to facilities that might not see a case of CRE until several months or even years later.

We are also able to use this surveillance to provide education to laboratories that might detect cases of CRE rarely. We plan to provide statewide and regional aggregate data back to facilities and to the public that state that might include specific organisms, body sites of isolation, and facility type, such as hospital, long-term acute care hospitals, and nursing homes.

As another surveillance system, we can track rates overtime and will also be able to detect outbreaks. We will also be able to check community onset cases, should they occur.

Slide number 21. The data showed in this slide are preliminary and are likely to change as surveillance continues, but the first two months of surveillance data in December and January showed that Colorado has low numbers of cases of CRE currently, which is what we expected - 10 cases reported so far for December and 12 cases for January, for a total of 22 cases.

Enterobacter species showed on the first two lines of the table are the most common bacteria reported so far, and most cases, 16 cases, reported so far are from urine cultures.

Due to the low numbers, our plan to contact each facility with the patients with CRE in order to provide education and support and answer facility questions has been successful during the early stages of surveillance.

This concludes my presentation and I would like to introduce Zintars Beldavs, HAI Program Manager at the Oregon Health Authority.

Zintars Beldavs: Thank you, Wendy. So I'm here to talk about what we're doing in Oregon. Soon after initiating surveillance for CRE as part of the Emerging Infections Program, we realized we were really in a lucky position of having very little CRE.

When seeing what was happening in the rest of the country, and the potential scary consequences of CRE becoming endemic, we realized that we had a prime opportunity to see if it's possible to prevent the spread of CRE from even really starting.

I'm just going to give a brief overview of how CRE looks in Oregon and the multifaceted plan that we're enacting which is focused on rapid detection and appropriate response statewide across the continuum of care.

So, we initially became interested in CRE by participating in the Emerging Infection Program Multi-State Gram-negative Surveillance Initiative. So this is also called MuGSI. It's - actually we're back on slide one still.

So during the initial set of stage of our work with this initiative and before it even start formal surveillance, we were notified of a Klebsiella Pneumoniae carbapenemase, KPC. This was obviously concerning to us so we decided to both formally pursue the MuGSI project which provided a surveillance structure and needed carbapenemase testing along with making CRE reportable statewide.

Our initial concern was somewhat alleviated. After we started full statewide surveillance of CRE, we found that we had very few cases. We had identified 37 CRE to this point - only three of which are KPCs. One of these was the one that helped initiate surveillance. One was identified retrospective surveillance,

and one was recently identified. All three of these cases had recent travel and medical care and states where KPCs are considered endemic.

In September of 2012, we initiated the Drug-Resistant Organism Prevention and Coordinated Regional Epidemiology Network, and that's a little bit of a mouthful so we just call it DROP-CRE. The primary goal of this network is to establish and maintain ability to detect, control, and prevent the spread of MDROs (multi-drug resistant organisms) with an initial focus on CRE.

And as you might imagine to make a network like this workable requires considerable collaboration. We started by including three, key local experts from the major teaching hospital, a local university and (RBA) in the core group. This includes Dr. Chris Pfeiffer from the Portland VA who serves as our medical director.

We also have an advisory committee consisting of key stakeholders throughout the state. This advisory committee includes ID physicians and IPs from hospitals, a QIO representative, long-term care and long-term acute care representatives, an APIC (Association for Professionals in Infection Control and Epidemiology) representative, Dr. Alex Kallen who heard of previously from CDC , and physicians - ID physicians throughout the states. So the advisory committee is helping to assist in development of a response plan to CRE.

Another key component to establish an effective and workable plan was to understand the needs and capabilities of those that are working in a field. So we performed three surveys - these are statewide surveys - to understand where there might be gaps in knowledge to address in Oregon.

The groups that we targeted were hospital infection control, long-term care, and laboratories. And a few things that we found that were - one was there really wasn't strong capability in Oregon to identify carbapenemase producers such as KPCs. Only 19% of microbiology laboratories perform a Modified Hodge Test and none use PCR to detect carbapenemase.

The needs assessment also showed that education is a key need. The long-term care needs assessment showed that only 50% of long-term care facilities were aware of CRE. Infection control in hospitals were more aware but they clearly also could benefit from assistance as a definition of CRE varied widely.

We also - and there were definite challenges with communicating whether patients have MDROs (multi-drug resistant organisms) and transfer. Fifty-five percent are aware of MDRO status on admission and 58% agree that receiving facilities are provided this information.

The needs assessment also showed that we could help provide important education across the continuum of care. We want to make sure that everyone that needs to know about CRE is aware of what it is, how to identify it, and how to respond when it is found.

As a result, we're bringing speakers both from within our group and national experts from CDC and elsewhere who were on-site to talk at meetings and conferences throughout the state centered on long-term care, microbiology, infectious diseases, critical access hospitals, infection prevention, and our antimicrobial stewardship and MDRO collaboratives.

Along with speakers, we are creating education materials including patient information sheets, a CRE-focused communicable disease summary and

newsletters. So this is a newsletter that comes out every month and we have a specific issue that will soon be coming out focused on CRE; and updating our website with pertinent information for CRE surveillance and response.

We also learned that enhancing and standardizing laboratory capacity both locally at our state public health lab and at microbiology laboratories throughout Oregon is important for us to be able to rapidly and accurately identify CRE and carbapenemase producers.

Our lab now has capacity to do a modified Hodge Test and is developing capacity to do PCR to determine whether or not isolate is a carbapenemase producer and identify the specific carbapenemase produced.

We're also working, assist laboratories with ensuring that they are providing isolates according to the standard definition and attempting to implement workable electronic laboratory reporting to streamline the process of use to report CRE.

So what happens when we actually identify a CRE? Well, in Oregon, we have developed a CRE toolkit and this borrows heavily from CDC's toolkit but we've modified it for our own definition and specific needs.

The toolkit provides overviews for responding to identified CRE for laboratories, hospital infection control, and for long-term care settings. And you can see these are just some algorithms that we've developed that are part of the toolkit to make it kind of a step-by-step process where facilities can relatively easily walk through what they should actually do.

But we're also working on a case-by-case basis with CRE in particularly carbapenemase produces in Oregon. Any case that has detected receives a

complete medical record review and we offer assistance with infection control response.

In Oregon, we consider a single KPC to be an outbreak and respond by discussing with infection control staff our recommendations which may include appropriate precautions, surveillance cultures, and potentially prevalence study if there's an indication of spread.

And the consultation can either occur during a phone call or potentially we will actually go on-site and help with designing these prevalence studies and other needed infection control measures.

The same day that our initial draft protocol is completed, we actually have a bit of a trial by fire situation. So we were notified of our third KPC and also a highly resistant *Acinetobacter baumannii* outbreak. We had assisted and responsibility situations and I can say at this point, we have no reason to feel that KPC has actually been transmitted within Oregon. Next slide, please.

Along with identifying and responding to CRE, another key component of preventing spread know when patients with CRE transferred - are transferred between facilities.

First, we have very detailed information on each case entered into our state, MDRO database and it results from a complete medical record review. And I just want to mention that we are using the information from MuGSI the case report form to create this database and so this is created - we have also created a simplified CRE tracking form that were providing facilities and we're working to identify other methods to tract the transfer of CRE.

Another thing is that we realize that CRE does not understand state borders, so we have initiated discussions with surrounding states to try to develop methods to identify when CRE might be transferred to, or from Oregon.

We're also working on collaborating with other states on more detailed testing of CRE that might provide important information to understand the specifics of epidemiology and the molecular biology of CRE.

And I think that about covers a fast overview. I'd also like to thank all of the people involved both in the internal group and the network as a whole. As you can see, we have considerable membership and we also have other people that have assisted that aren't part of the formal group. Thank you very much.

Judith Monroe: This is Judy Monroe again. So let me thank all of the presenters. These were excellent presentations.