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INFECTION PREVENTION: SSI PREVENTION AND DECOLONIZATION/PROPHYLAXIS FOR *S. AUREUS* (MR&SSA)

Hi, I'm Patchen Dellinger, surgeon from the University of Washington, and I'm going to talk with you today about decolonization and prophylaxis for Staph aureus, and I mean both methicillin-resistant and sensitive Staph aureus, and see how this relates to infection prevention in surgical patients.

Now if we look at the population at large we can learn that about 20% of the human population always has at least one strain of Staph aureus in their nose, whereas about 20% of the population almost never has Staph, and then other remaining 60% sometimes are colonized and sometimes are not.And when we look at the prevalence, if you just went and cultured 100 people in a row, among the general population you'd get about somewhere between 30% and 40% with Staph.Among healthcare workers it's actually not increased, if anything perhaps a little less.Patients admitted to the hospital tend to be similar to the general population, but there's increase in patients with diabetes who are hemodialysis patients and IV drug users.

When you look at colonization and the risk of infections, this very old paper from 1963 shows an 8% infection rate in patients with no colonization, a 21% infection rate in patients with colonization of more than 1,000 colonies of Staph in their nose, and not an elevated infection rate in patients with low numbers of Staph.In a similar study, Kalmeijer and colleagues, in the year 2000, looked at the infection rate in patients with negative cultures for Staph; 1.5% compared to patients with positive cultures 8%.Of those with positive Staph cultures, two-thirds were heavily colonized and one-third lightly colonized.And when a multi-variant analysis was done it was primarily heavy colonization that was associated with Staphylococcal surgical site infections.

Trish Perl and colleagues published a paper in the New England Journal in 2002, looking at the utility of using mupirocin for eliminating Staph aureus nasal colonization.They found that patients who received three to five doses of mupirocin, given twice daily, had an 83% elimination of Staph in the nose.Six doses of mupirocin caused a 93% elimination.And patients with placebo had no loss of Staph in the nose.When they looked at the risk of a Staph aureus surgical infection there was a significant reduction in patients who had been treated preoperatively with mupirocin compared to those who had received a placebo.

Van Rijen and colleagues looked at the use of mupirocin to prevent Staph aureus surgical site infections, and they looked at four prospective randomized trials and showed a significant – a very suggestive reduction in surgical site infections, a 37% reduction which, however, just missed statistical significance with the confidence limit crossing one.When they looked at any type of postoperative Staph aureus nosocomial infection they found that there was a significant reduction in a subsequent meta-analysis looking at any type of infection and a greater number of articles.

More recently, Bode and colleagues, in the Netherlands, looked at a prospective study of the effectiveness of eradicating Staph aureus from patients who tested positive at hospital admission.Five hospitals participated, and almost 7,000 patients were screened.More than 1,200 of them were positive by PCR for Staph aureus.Of this group, 917 agreed to be randomized, either to have an eradication

regimen for Staph aureus or not.Their regiment was to use mupirocin twice daily in the nose for five days, along with a chlorhexidine body wash once daily for five days.

What they found was that there was a significant reduction, from 4.4% to .9%, deep surgical site infections, and a significant reduction of any surgical site infections, from almost 8% down to 2.5%.What the study did not address in its publication was how long before surgery you needed to start the decolonization.And in this study from the Netherlands, unlike most practice in the United States, the patients typically were admitted to the hospital before operation, whereas in our practice the patient usually shows up in the hospital about two hours before the operation, and thus, the logistics of testing a patient before an operation, finding out who's positive, and getting them some kind of treatment is much more complicated.

I was able to correspond with Jan Kluytmans, and he told me that 90% of the surgical patients were admitted the day before the operation and received only one or two decolonization treatments prior to operation.Even so, there was a significant reduction in surgical site infections in the patients who were decolonized.They did continue the decolonization treatments postoperatively for those patients who'd had only a couple of treatments beforehand, and whether that part makes a difference at this point is not known.They did calculations and showed that the number of patients you should screen in their population to prevent one Staph aureus infection was 250, and the number of Staph aureus carriers who should be treated to prevent the Staph aureus infection was 23.

So should we just treat every surgical patient with mupirocin?That would be simpler and you wouldn't have to do cultures and figure out ahead of time who needs to be treated.But, wait, mupirocin is actually a type of antibiotic, and we know that overusing antibiotics can lead to resistance.In fact, at the University of Geneva, they have been using mupirocin for quite some time in their effort to reduce MRSA, and they looked at mupirocin sensitivity, either sensitive, low-level resistance, or high-level resistance, and they found over the last ten years that they have had a two- to four-fold increase in minimum inhibitory concentrations, meaning that they have had an increase in resistance in their hospital.

They had a decolonization program going on now, at the time this article was written, for 12 years, and had mupirocin resistance increase from 9% to 81%, mostly with low-level resistance.But when they looked at their treatments they found that 75 patients who failed to have their MRSA colonization successful with mupirocin had decolonization factors, and they had increased resistance.So there was an increase in mupirocin and chlorhexidine resistance that was three times higher in patients that had a failure of decolonization.There was also an increase for patients with prior hospitalizations, open wounds who were receiving inactive antibiotics or who had central venous catheters.

In another study, Murphy and colleagues examined patients who were going to have orthopedic operations, and they screened the patients in the nose, throat and groin for MRSA.Any patient who tested positive got a five-day decolonization program using mupirocin and polymyxin, and chlorhexidine body wash.And they agreed that the patient could not go to surgery until they had a negative MRSA screen, and the patient had to be admitted for operation within three months of the negative screen.However, you can see a potential problem here.In other words, a patient could go as long as two, two-and-a-half months after a negative screen before having an operation.

All patients at operation received cefuroxime as their prophylactic antibiotics.And basically what they found was that patients who had previously had a MRSA screen positive, even though they had been

decolonized, had a 7-fold higher hip infection rate and an 18-fold higher knee infection rate if they had previously been colonized with MRSA.So I think if you are going to decolonize the patient, it's pretty important that you do so close to the time of operation in order to be sure that you're decolonization has been effective.And for reasons I'll show you in a minute, anybody with a history of MRSA should probably receive vancomycin at the time of their operation, even if you have decolonized them.

Now what about using vancomycin for everyone?Well there are some problems with that as well.In this very nice cardiac surgical study done in Israel, Finkelstein and colleagues randomized patients to get either cefazolin or vancomycin in a hospital where they said they had a high rate of MRSA.What they found was that their overall infection rate was not different, but there was twice the number of methicillin-sensitive infections in the patients who received vancomycin compared to those with cefazolin.And there was a higher rate of MRSA infections in patients getting cefazolin compared to vancomycin.So this suggests that vancomycin is an inferior drug for methicillin-sensitive Staph.

More recent information became available only about one to two months ago in this very interesting study from Australia, looking at over 22,000 patients having either cardiac surgery or arthroplasty.And this was an observational study, not a randomized prospective study.But they looked at the odds ratio for any surgical site infection.As you would expect, the odds ratio was positive with a higher infection rate for any patient with a longer operation, for patients with a higher risk index.But, look, there was a 40% higher infection rate in patients who received vancomycin compared to patients who received a cephalosporin for their prophylaxis; that's any surgical site infection.And if you look at methicillin-sensitive surgical site infections, there were almost three times as many of these in patients who received vancomycin compared to patients who received cefazolin.

So what I conclude from this and the Finkelstein study is that vancomycin, which is essential to give for patients with MRSA or high risk of MRSA, is less effective for patients with methicillin-sensitive Staph.And it's very clear that patients with methicillin-sensitive Staph in their nose are at higher risk for infection.In fact, in the Bode study, which showed very clearly that decolonization reduced infection rate, Bode had no MRSA colonies at all.All of the patients in that study had methicillin-sensitive Staph.And something to remember is that once a patient gets an infection the results are just as disastrous with methicillin-sensitive as with methicillin-resistant Staph.The treatment you use is a different antibiotic, but the consequences to the patients are equally severe whether the Staph was resistant or sensitive.

Chambers did a meta-analysis in the Journal of Surgical Infections in 2010 and looked at 12 to 14 studies, looking at the use of glycopeptides, and concluded that there is no evidence glycopeptides are more effective than beta-lactams for prophylaxis of surgical site infections.And here we see the fourth plot with all of the different studies looking at this, and you can see that basically there was no benefit across the board with many different types of studies for using vancomycin in preference to cefazolin.Here, another way of looking at the same information.

Now the joint commission and the University of Iowa, working together with an advisory panel, recently put together this proposed strategy for dealing with patients having operations where Staph aureus is a potential serious pathogen.And the classic cases would be orthopedic cases, craniotomy cases, and cardiac surgical cases.And perhaps it would make sense to add hernia operations with replacements of large pieces of mesh.So what they suggest is that when the patient is scheduled for surgery, if possible, you screen the patient for Staph aureus, either MRSA or MSSA.And if you have the screening results and you know that the patient is positive for Staph aureus, you ask whether the colonies are MRSA or

sensitive Staph.If MRSA, decolonize with mupirocin and do chlorhexidine bathing, and use cefazolin plus vancomycin.You need the vancomycin because of the MRSA, but you should use cefazolin also because of the risk of sensitive, and also the small but measurable risk of gram-negative infections which are not covered by vancomycin.

On the other hand, if the patient had methicillin-sensitive Staph in the nose, also this patient would benefit from decolonization and chlorhexidine bathing, but does not need vancomycin and can receive cefazolin as well.If, on the other hand, the colonization is negative, the patient's nose is not colonized, then simply chlorhexidine bathing and cefazolin is in order for most patients.However, if the patient is known to be at high risk for MRSA, and this would be patients coming from a place with a high endemic rate of MRSA or patients recently hospitalized, treated with antibiotics, coming from a nursing home, or having hemodialysis, then it probably makes sense to give cefazolin plus vancomycin to those patients.

The new prophylaxis guidelines, which were published just earlier this month, and which are a joint effort of the American Society for Health System Pharmacists, the Surgical Infection Society, the Infectious Disease Society of America, and the Society for Healthcare Epidemiology of America, recommends that for patients at risk for MRSA to use both vancomycin and cefazolin for prophylaxis.

So if you are going to screen, who should you screen?Does it depend on patient characteristics?Possible characteristics that might lead you to do screening are patients who are obese, patients above a certain age -- 45, 50, 60, hard to know.I personally define old age as anybody older than me.Patients with diabetes are at higher risk.Patients with immune suppression are probably at higher risk.So other areas would be patients with any history of prior colonization or any prior infection; patients receiving dialysis; patients with open wounds; patients with any history of IV drug use; recently in the hospital, although how recent is unclear; recently in a long-term care facility, again, the duration is not clear; those who received antibiotics let's say within the last 30 days.Perhaps there are other risk factors.This is an area that could use more research.

Specific procedure, certainly anybody getting a median sternotomy or arthroplasty or implantation of other prosthetic device is at risk for really serious consequences with any Staph infection, and the risk to these patients comes primarily from the skin where the Staph live.So that makes sense.Are there other procedures that should be screened?Possibly, again, an area where more research should be done. What site do you screen?The most common site that is screened is nares, and that is the most common location for Staph colonization, but it is very clear that there are a certain proportion of patients who have Staph in their throat and negative cultures in the nose.Other areas that commonly have Staph, if it's present, are the axilla and perineum, and definitely open wounds.The way I do it for my patients if I'm going to screen them is I take a sterile swab and do first the throat and then use the same swab to do nares in order to save on processing in the microbiology lab.And then if there are open wounds, I swab them separately.

For what organisms do you screen?I think it's a tremendous mistake if we focus only on MRSA, which is sort of what the tabloid press and some people would seem to have us do.Sensitive Staph cause infections just as bad as MRSA, and the risk of infection is reduced just as effectively by a decolonization for sensitive Staph as for resistant Staph.

Should we be culturing for other multi-drug-resistant organisms such as acinetobacter or other organisms of that sort, Klebsiella and so on with multiple resistant organisms.There is no coherent information on

this at this time and I can't make any solid recommendations, but I would welcome additional research in this area.

How do you screen?PCR gets you your information much more rapidly but also costs more.Specialized agars can be used.Other techniques may be coming down the road.How early should you screen?Well, the study from the "British Journal of Surgery" in orthopedic patients shows clearly that if you screen and decolonize and then wait a month or more for operation that you probably have not done your patients much good.On the other hand, if you screen only an hour before operation, you can't do anything with the information.So the logistics of screening, especially in the U.S. where our patients typically show up only a couple of hours before operation and may have had their preoperative workup done in the surgeon's office separate from the institution where the operation will be performed, can become daunting.

Is there a level of MRSA in the community that should lead to screening all patients, if so, what percent of patients should this be, or should it be the proportion of Staph aureus that are MRSA in the entire community?I think it makes more sense to say, "What proportion of the infections detected in your hospital are MRSA," but even there, nobody agrees on what that percentage should be to lead to different policies.Is it cost-effective to screen?Screen all, treat positives, screen as many as you can, treat positives.And those you can't screen, treat everyone, don't bother to screen.These analyses have not been done in enough detail for us to understand what the most cost-effective approach is.

Should we worry about resistance to mupirocin and/or chlorhexidine?In New Zealand, a number of years ago, when mupirocin was an over-the-counter drug, they developed such extensive resistance to mupirocin that it essentially became useless.In the study I cited earlier from Geneva, they found dramatic reduction in the effect of mupirocin after they had been using it intensively for 12 years.So I think this is something we need to worry about and a reason, if you're using mupirocin, to screen and treat only patients who are positive rather than to try to treat everyone.

I'll close with a fascinating bit of information which at this stage is very preliminary.But Michael Phillips at NYU here in New York City did a study, which was presented in abstract form at Infectious Disease Week this past October in San Diego.Dr. Phillips randomized patients having spine operations or arthroplasty operations to get mupirocin preoperatively, or to get a povidone-iodine nasal swab in the pre-op holding area shortly before the operation was done.Their preliminary results actually showed that there was a significantly lower rate of infection in patients who got povidone-iodine shortly before operation compared to those who were using mupirocin prior to coming into the hospital.This is an intriguing result, and I look to more detailed information when Dr. Phillips gets these data published, and hope that other institutions will study this similarly.

So with that, I will conclude my remarks by observing that if you are going to pay attention to Staph I urge you to pay attention to both sensitive and resistant Staph.And if you have a MRSA problem, I urge you to use both vancomycin and cefazolin for your patients in order to give them optimum prophylaxis both for resistant and sensitive Staphylococcus aureus.

Thank you very much for your attention and I hope that you all have a good day and that you see decreasing Staph aureus infection rates in your patients.Thanks, again.