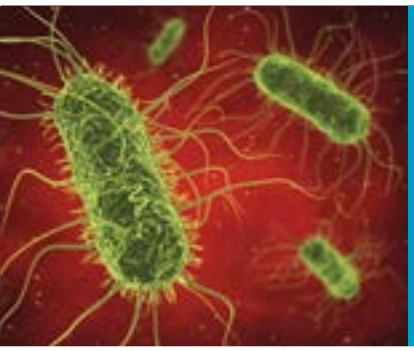

Treating CLABSI: A Clinical and Economic Challenge

A Roundtable Discussion

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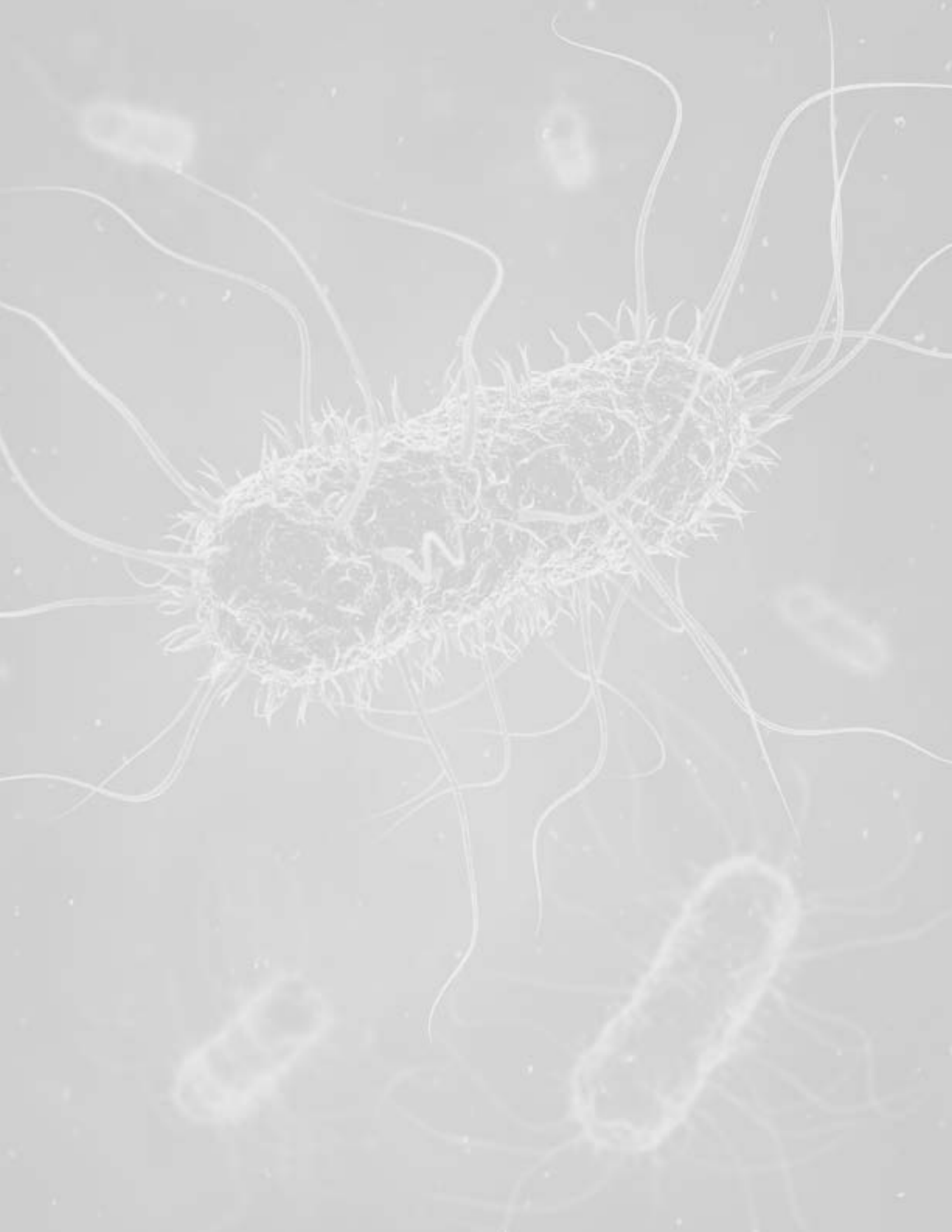

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Glossary of Terms

ALT
Antimicrobial (or antibiotic) lock therapy: the instillation of a concentrated antimicrobial solution into the catheter lumen, as a method of treating infection in central venous catheters

fistula (arteriovenous)
Surgical connection of an artery to a vein. An arteriovenous fistula causes extra pressure and extra blood to flow into the vein, making it sufficiently large and strong to provide reliable long-term vascular access

graft (arteriovenous)
A connection from an artery to a vein using a synthetic tube for long-lasting vascular access

CDAD
Clostridium difficile-associated disease

CLABSI

Central line-associated bloodstream infection

CMS
The Centers for Medicare & Medicaid Services

CRBSI
Catheter-related bloodstream infection

CVC
Central vein catheter

ICD-10
The International Classification of Diseases, Tenth Revision

IDSA
Infectious Diseases Society of America

MBI
Mucosal barrier injury

MDRO
Multidrug-resistant organism

NHSN
National Healthcare Safety Network

PICC
Peripherally inserted central venous catheter

SIRS
Systemic inflammatory response syndrome

SOC
Standard of care

TPN
Total parenteral nutrition

Introduction

In spite of best clinical practice, catheters contribute to approximately 70% of blood stream infections that occur in the ICU, or are associated with hemodialysis or cancer patients (approximately 470,000 per year).[1-3] Bacteria enter the catheter either from the skin or intraluminally through the catheter hub. Once in the catheter, bacteria tend to form a protective biofilm on the interior surface of the catheter that become resistant to most antimicrobial agents. The most frequently used maintenance flush, heparin, actually stimulates biofilm formation. Heparin is widely used as a prophylactic lock solution, in spite of the evidence that it contributes to the promotion of biofilm formation. The formation of bacterial biofilm usually precedes CRBSIs.

The standard of care (SOC) in the management of CRBSI patients consists of removing the infected CVC and replacing it with a new catheter at a different vascular access site. However, in cancer and hemodialysis patients with long-term surgically implantable silicone catheters, removal of the CVC and reinsertion of a new one at a different site might be difficult, or even impossible, because of the unavailability of other accessible vascular sites and the need to maintain infusion therapy. Furthermore, critically ill patients with short-term catheters often have underlying coagulopathy, which makes reinsertion of a new CVC at a different site, in the setting of CRBSIs, risky in terms of mechanical complications, such as pneumothorax, misplacement, or arterial puncture.[2,4-7] Studies have also revealed that CRBSI patients may be associated with serious complications, including septic thrombosis, endocarditis and disseminated infection, particularly if caused by *Staphylococcus aureus* or *Candida* species. Furthermore, catheter retention in patients with CRBSIs is associated with a higher risk of relapse and poor response to antimicrobial therapy.

According to Maki et al., published in the *Mayo Clinic Proceedings* in 2006, there are approximately 250,000 CRBSIs annually in the US.[2] Subsequent to that study, estimates have ranged upwards to over 450,000 CLABSIs annually. CRBSIs are associated with a 12% to 25% mortality rate and an attributable cost of $46,000 to $65,000 per episode.[2-7]

The removal of an infected CVC and replacement of a new catheter in a different venous access site is estimated to cost between $8,000 and $10,000.

While the current IDSA guidelines recommend removal and replacement of infected catheters, they also make a recommendation for certain conditions where an antibiotic lock solution can be used to try to disinfect and salvage the catheters. Several reports have been published where ALTs were tested for their ability to salvage infected catheters.[8] The IDSA recommendation is for limited use because of the lack of adequate and well-controlled trials using ALT for treating CRBSI/CLABSI.

Studies on ALT, alone or associated with systemic antimicrobials, are often limited by the small number of patients included or by the study design (e.g., not prospective; variable methods; bacteremia not specific to catheters).[9-11] Although the data suggest that ALT can be effective in treating CRBSI/CLABSI as well as avoiding risky CVC manipulation, there have been few well-controlled studies to examine the risks and benefits of ALT for catheter salvage vs. catheter removal and replacement.[8,9,12] Currently, there are no pharmacologic agents or lock solutions approved for treating and salvaging infected catheters in patients with CRBSI/CLABSI.

Despite many advances in prevention, CLABSIs remain a significant issue for hospitals. Infections have not been eliminated with recent healthcare guidelines, institutional initiatives, and financial incentives, underscoring the need for additional intervention for the treatment of CLABSI.

This roundtable features the insights of six leading healthcare specialists on the clinical and economic challenges presented by CLABSI.

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Part 1: The Magnitude of the CLABSI Problem

The challenges presented by CLABSI include improving treatment, reducing complications, and controlling costs. What do you see as the primary clinical challenges of CLABSI?

M. Ramesh: The major challenge is the morbidity and mortality associated with CLABSIs.

S. Welbel: The primary clinical challenge is that CLABSIs increase morbidity and mortality, and as a result, increase cost. CLABSIs also increase our likelihood of multi-drug resistant organisms (MDROs), particularly *C. difficile* or *C. difficile*-associated diseases (CDADs), because we're frequently treating these patients for four to six weeks. Moreover, with prolonged antimicrobial treatment or any lengthy intubation of a lumen, we may actually lose the use of the catheter, which can be very significant for long-term cancer chemotherapy patients and dialysis patients, for example.

M. Rupp: We need to be working together to, first, understand these infections better. Second, with a better understanding of the pathogenesis of CLABSI on a molecular level, it may suggest more effective means to prevent CLABSI. Third, when a CLABSI occurs, we need to devise methods to successfully treat patients with the catheters in place and thus salvage needed CVCs.

Finally, we also need to do a better job reconciling the differences between surveillance definitions and clinical definitions of CLABSI and stop using CLABSI surveillance in a punitive manner.

> ***When a CLABSI occurs, we need to devise methods to successfully treat patients with the catheters in place and thus salvage needed CVCs.***

R. Hachem: Although I do agree that definitions and how people look at CLABSI are extremely important, the main challenge is how to best provide access lines whenever they are needed. In particular, long-term central venous catheters have become a lifeline for patients with cancer.

S. Gordon: Number one is the fact that there isn't any good treatment for CLABSI. Not any one therapy has shown efficacy in disinfecting and salvaging the infected catheter.

S. Mufti: I think it's important to also remember that it can take a day or two for the diagnosis of CLABSI, which can be a critically important delay for patients, especially those that are immunocompromised, have cancer, or are otherwise dependent on that catheter. I would even include patients who have pulmonary edema and need to have that catheter infusing a lifesaving medication 24/7.

The published annual incidence of CRBSI/CLABSI in the US ranges from 250,000 to 500,000. What factors do you feel make these estimates vary so widely?

S. Welbel: Despite the fact that it's now a CMS regulation that institutions in the US submit their CLABSI data, a big question is: who is monitoring that process? Whether I say that I have 3 CLABSIs this year or 33 this year, there's often very little monitoring of: 1) the number that we report, and 2) the definition of CLABSI that we are using (for example, how well we are sticking to the NHSN definition?)

Even among those of us who pride ourselves in being very accurate, data driven, and scientific, there's still huge heterogeneity in the reporting.

M. Ramesh: One of the biggest reasons for such variability is that institutions can be penalized by CMS for reporting CLABSIs, and therefore may be reluctant to do so.

Also, the definition of CLABSI is typically determined by CMS, and it is different from that which is used in a true clinical practice. It becomes the institution's or clinician's onus to prove that a given infection is not CLABSI, largely a result of the inconsistent CMS definition.

At our institution, we perform blood cultures through the catheter, and we evaluate every patient with central lines. If we suspect CLABSI, we double check; we look through the chart, and we examine the patient to make sure it is truly CLABSI. We try to document everything correctly for reporting purposes.

I would say the true nationwide annual incidence is probably somewhere in the 400,000 range.

> ***One of the biggest reasons for such variability is that institutions can be penalized by CMS for reporting CLABSIs, and therefore may be reluctant to do so.***

R. Hachem: I agree with the estimate of 400,000. These numbers vary because providers look at CLABSI in different ways.

The bottom line is that there may be no perfect way to report these infections.

M. Rupp: I think that there is such pressure on organizations and individuals to get institutional CLABSI rates reduced, that the current published rates of CLABSI are not as reliable as they need to be.

Due to the financial and reputational penalties that hospitals are subjected to, personnel are pressured to reduce CLABSI rates even if it means bending the rules and not applying the surveillance definitions accurately. Without stringent data validation, I have much less faith in the current published rates of infection. Many institutions are claiming zero CLABSIs for long periods of time in very complex groups of patients – I think that's just not possible to achieve.

> ***I think that there is such pressure on organizations and individuals to get institutional CLABSI rates reduced, that the current published rates of CLABSI are not as reliable as they need to be.***

Based on your experience, what do you feel is the true incidence of CLABSI, and why?

S. Welbel: The CLABSI rate is probably about 0.5-1 per 1,000 catheter-days.

S. Mufti: I feel that the incidence is higher than has been reported. For example, if a patient has a catheter that's been in for six months and it becomes infected, you give them antibiotics. The infection may go away, and we think it may be related to pneumonia, or maybe it's related to something else, and the infection does not get reported as a CLABSI.

M. Rupp: If all preventive measures are in place, even with very sick and complex patients, it is possible to achieve an institutional CRBSI rate in the neighborhood of 0.5 per 1,000 catheter-days. Even with that level of prevention, with the large number of CVC days that we have in the US, we would still have several hundred thousand episodes of CRBSI per year. Thus, we probably have more infections than are reported. You'll notice, I use the term CRBSI instead of CLABSI. CLABSI is a surveillance definition and by design is highly sensitive but not as highly specific. Patients can meet the definition of CLABSI but not truly have bacteremia due to an infected CVC – in other words, the bacteremia is due to infection at another site but the illness still satisfies the definition for CLABSI. At present, in our institution, about half of what we report to CMS as a CLABSI would not be classified as a CRBSI. I think it is very important for hospital administrators, third-party payers, and governmental agencies to understand the important differences between CLABSI and CRBSI, and be more realistic about "zero CLABSI targets".

R. Hachem: For the US overall, the rate is between 1 and 2 episodes of CLABSI per 1,000 catheter-days. (Zimlichman 2013) And that varies from institution to institution. For example, our incidence is the lowest in the US – between 0.5 and 1. Despite the rigorous and tested infection control and monitoring systems that we have in place at MD Anderson, CLABSIs cannot be entirely eliminated.

> ***Despite the rigorous and tested infection control and monitoring systems that we have in place at MD Anderson, CLABSIs cannot be entirely eliminated.***

To what extent do you feel CLABSI is underreported? What do you feel are the reasons for this?

M. Rupp: I think CLABSI is indeed underreported at some institutions. As I have already stated, the primary problem lies in the variability of the definitions, surveillance methods, oversight, and reporting of CLABSIs.

One of the other things that I've become fond of saying with regard to the application of the CLABSI surveillance definition is that the hospital that cares for very ill and complex patients and reports zero healthcare-associated infections for any length of time is akin to the man who lives in a luxury home, has a yacht, drives a luxury automobile, and wears a lot of bling, but declares zero income. These facilities should be ripe for an audit.

The perception that all of these infections are 100% preventable is not realistic, based on our current level of knowledge and current preventive practices.

> ***The primary problem lies in the variability of the definitions, surveillance methods, oversight, and reporting of CLABSIs.***

S. Gordon: Let's say a patient who has a dialysis catheter comes in from home because of a fever. If their blood tests positive for infection on admission, that's not something that's reportable, even though the patient has a bacteremia and, more likely than not, it's due to the catheter.

We have five different hospitals in Portland, so a patient can have a dialysis catheter placed in an outpatient clinic, then come to our facility with an infection. I don't report that because the catheter is not something that we've put in.

CLABSI is underreported because we don't *have* to report it. To a large degree, not having to report it means you're not going to report it. And there's the financial benefit of not having a whole lot of CLABSIs attributed to your system or to your hospital. This is basically a reimbursement issue involving Medicare/Medicaid and GMSNs, so it's to our advantage not to have any infections on our record.

S. Welbel: I believe the primary reason for underreporting is financial – not getting reimbursed.

What is the impact of variable definitions, variable coding, and variability in CLABSI surveillance practices from institution to institution?

S. Gordon: If you actually have an infection rate that's on the high side, there are a lot of people who spend a lot of time trying to legitimately attribute these infections to something else, whether it's a contaminated specimen or a remote site that caused the problem. There's just a plethora of resources dedicated to that, because nobody at a hospital wants to have a bad quality metric reported.

S. Mufti: A lot of times institutions don't know, or aren't sure, that it's a catheter-related infection. They may feel there's no 100% guarantee that a patient's infection is catheter-related—perhaps this patient has pneumonia. They take the catheter out, treat the pneumonia, the patient gets better, and it's not reported as a CLABSI.

S. Welbel: What gets reported depends on the source from which one is getting the data. There are a ton of codes for these infections, especially with our new coding system. Results will depend on how the institution codes the infection, and who pulls that data. With ICD-10, there are a lot more codes. It's just important to know what you're looking at.

> ***Results will depend on how the institution codes the infection, and who pulls that data. With ICD-10, there are a lot more codes.***

M. Rupp: Clearly, it is in everyone's best interest to have accurate and reliable surveillance data. Thus, we need to have better definitions that more clearly parallel our clinical definitions and clinical experience. For example, there is an abundance of data to indicate that the blood culture, "Differential Time to Positivity", is a useful clinical tool to diagnose whether a catheter is the source of bacteremia. However, this criterion is not utilized in the current CLABSI definition. As I mentioned previously, in my best clinical judgement, about half of the patients with CLABSIs that we report to CMS don't actually have bacteremia due to their CVC. However, we play by the rules and dutifully report these infections as CLABSIs. I wish all institutions were as honest and transparent.

We clearly need improved definitions that we can rely upon. We also need data that is validated so that we don't have doubts about the legitimacy of the surveillance system data.

> ***We clearly need improved definitions that we can rely upon. We also need data that is validated so that we don't have doubts about the legitimacy of the surveillance system data.***

M. Ramesh: The impact of such variability is definitely negative, because currently no one is stating very clearly what to do or what not to do in terms of reporting CLABSIs.

Institutions think what they're doing is correct. There is fear – a lot of fear – of being penalized by CMS because the infection rate directly impacts the amount of money that is reimbursed. In many cases, the easiest solution becomes simply to avoid reporting of many CLABSIs.

R. Hachem: Variable definitions are a big factor contributing to unreliable surveillance data. A sticking point is often the inclusion or exclusion of mucosal barrier injury in these definitions of CLABSI. If you include MBI as part of the CLABSI definition, the rate will be higher. If you exclude MBI, the rate will be lower.

The published cost of CLABSI ranges from about $46,000 to a high of $65,000 per episode. What factors do you feel make these estimates vary so widely? What would be your estimate of the true financial burden of CLABSI?

S. Welbel: Total cost depends largely on the data that one puts into the model. Are we looking at service costs? Healthcare worker hourly costs vary widely. Even just for supplies and medications, the range of costs at an institution is enormous.

We also need to factor in how institutions look at their costs – are they looking at the cost that they're charging the patients? Are they looking at their purchasing costs?

M. Rupp: No one argues that CLABSIs are enormously expensive; and that patients who are bacteremic due to infected IV catheters stay in the hospital an average of a week longer than they might otherwise. And when you talk about somebody staying in the hospital a week, you're talking about tens of thousands of dollars.

R. Hachem: I am thinking the total average cost for a CLABSI episode would be in the area of $50,000. You could even go higher. The patient who has a complicated line-related infection and develops septic thrombosis may be hospitalized for a month, for example. Because of that complication and extended hospitalization, costs could reach up to $100,000.

S. Mufti: Let's say the diagnosis is slightly delayed due to a catheter infection in somebody who's compromised, and their infection now becomes sepsis. The patient goes into organ failure and, due to the delay, there's a cascade of things that can occur. Costs can vary widely based on the type of catheter, the type of patient, and the clinical setting.

> ***Costs can vary widely based on the type of catheter, the type of patient, and the clinical setting.***

M. Ramesh: The type of patient/disease you are managing might be one of the reasons for variable costs. If a patient develops a *C. difficile* infection, that nearly doubles the cost for the hospitalization. If someone were admitted for a condition and happens to develop a CLABSI, I would venture that means at least a 20% additional cost for that hospitalization because of the increased length of stay and patient management needs.

How does reimbursement affect the financial burden of CLABSI?

S. Welbel: Obviously, reimbursement is critical for the hospitals if they're not getting reimbursed because an infection is reported as hospital-acquired. With healthcare-associated infections, the financial burden falls on the hospital or facility, for the most part.

M. Rupp: The cost penalties that accrue to hospitals when they report a CLABSI rate higher than the arbitrary target, and the additional costs that are associated with that CLABSI that are not reimbursed through third-party payers, add to the financial burden of hospitals. Similarly, patients bear additional costs – whether in terms of morbidity/mortality or economic cost.

S. Mufti: Cost is becoming a big issue, as hospitals are not being reimbursed for catheter infections. That means that they have an incentive to prevent these infections as much as possible. But sometimes they're unpreventable, and it becomes a major issue where you're shifting a lot of the financial burden onto a hospital, to the point where it becomes a loss for certain

institutions—if a catheter-based infection occurs and you're not reimbursed to take care of it, money is lost.

Even if the staff does everything 100% right, and the patient does everything right, they are still not going to get reimbursed for a hospital-acquired CLABSI. It's almost unfair that something like this happens, because we all are trying to do the best for our patients. Yet these catheter-related infections occur and everyone gets a penalty.

> ***Cost is becoming a big issue, as hospitals are not being reimbursed for catheter infections. That means that they have an incentive to prevent these infections as much as possible.***

S. Gordon: It's important to note that the treatment itself is not going to vary because of reimbursement. That is because we're going to end up paying for the CLABSI anyway, and we're not going to be able to charge the patient for it, so we're going to treat it properly – however we have to.

Please comment on the interrelationships between underreporting of infections, reimbursement, and hospital ratings.

S. Welbel: I think there's a lot of incentive to underreport. Certain states issue a report card that is made public for every hospital. Anything that is reportable to CMS goes on that report card. A prospective patient can then say: "Well, I saw how many surgical-site infections or bloodstream infections were reported for that hospital, and I don't want to go to there."

M. Rupp: The problem is that hospitals are being compared to one another based upon CLABSI rates as well as a variety of other parameters, sometimes with very little in the way of risk stratification between institutions or validation of surveillance data. In addition, I am aware of hospitals that have become creative with "cost shifting" – for example, extensively using midline catheters, as they are not classified as CVCs (and thus infected midlines are not counted as CLABSIs), or using "virtual unit designations" to take patients out of reported surveillance data.

M. Ramesh: Hospitals are rated based on the incidence of certain infections. Less CLABSI produces better ratings, which in turn is supposed to reflect on the quality of any hospital. The rating is valid only if all hospitals report correctly.

S. Gordon: In addition to the problem of not being reimbursed for your costs, the very reporting of a CLABSI might carry the stigma that you're the reason that the CLABSI happened, either through a lack of care, or negligence somewhere along the line. There can be advantages to not having to report these things. It all has to do with how it makes your hospital look.

> ***In addition to the problem of not being reimbursed for your costs, the very reporting of a CLABSI might carry the stigma that you're the reason that the CLABSI happened, either through a lack of care, or negligence somewhere along the line.***

S. Mufti: The one thing that's very obvious is that all the hospitals and institutions get rated by their infection and complication rates. They all want to get high ratings that get published in *U.S. News & World Report* and elsewhere. And it becomes a matter of reputation.

Moreover, the administrators frequently get bonuses based on their rankings, and the hospitals get ranked by various media.

R. Hachem: In addition to a reluctance to report a high incidence rate, a limited number of infection control officers can often become overwhelmed and unable to adequately assume the reporting task, particularly if the hospital has a huge patient population.

What are the other important financial issues surrounding CLABSI?

M. Rupp: Because patients who experience a CLABSI stay in the hospital a week longer than they otherwise would, we need to think about all of the adverse events that happen to people, despite our very best efforts, simply because they're in the hospital for that extra week. For example, drug toxicity, falls, pressure sores, other hospital-acquired infections, and, because they are on antibiotics to treat the CLABSI, the emergence of antibiotic resistance, *C. difficile* colitis, and antibiotic allergic reactions.

R. Hachem: Extended hospitalization is a huge financial factor. When you have a line-related infection, the major variable is how long the patient is going to remain hospitalized due to this complication. That time can vary from a couple of days to a month or more, depending largely on what kind of complication is involved, and what kind of biofilm is forming.

> ***Extended hospitalization is a huge financial factor. When you have a line-related infection, the major variable is how long the patient is going to remain hospitalized due to this complication.***

S. Mufti: In addition, the patient's primary care provider may need to consult the infectious disease specialist or the interventional radiologist, all of which escalates costs. These costs, plus the costs of X-rays, the culture, etc. are all costs that can be associated with the infected CVC that many don't immediately consider.

Part 2: Challenges Associated with the Treatment of CLABSI

Current IDSA Guidelines strongly recommend removing and replacing infected CVCs. What is your experience with this broad recommendation in your institution?

R. Hachem: Such a broad recommendation is a problem nearly everywhere, because, at the first sign of an infection in a patient who has a catheter in place, the initial reaction is typically to remove the line. And line removal adds to a patient's treatment burden and financial burden, and is not always necessary. It is important to verify that you are dealing with a true line-related infection, and to identify the pathogen causing the infection before removing the catheter.

M. Rupp: For patients with non-tunneled CVCs, it's a pretty tried and true approach that the catheter comes out, and usually it can be relatively easily replaced. This approach gets rid of the nidus of infection quite quickly.

Where it becomes trickier is in patients who have very limited vascular access or who have tunneled or implanted vascular access devices. Obviously, patients with implanted devices – ports, and tunneled CVCs – have a need for ongoing, long-term vascular access. We're talking about dialysis patients, patients on chronic total parenteral nutrition (TPN) because of conditions of their gastrointestinal tract, and people who are going to need recurrent therapy because of underlying tumors.

All these people are very dependent upon ready access to their vascular system through their catheters. Simply pulling infected catheters is a very unsatisfactory solution to the problem because those patients will continue to require long-term vascular access. This goes back to the question of how to salvage CVCs and treat infected catheters without having to remove them.

> ***All these people are very dependent upon ready access to their vascular system through their catheters. Simply pulling infected catheters is a very unsatisfactory solution to the problem because those patients will continue to require long-term vascular access.***

S. Mufti: One of the things that we worry about is catheter replacement in hemodialysis patients, who are reliant on access for their life. I will tell you we've had many patients over the years who have died because they no longer have IV access for hemodialysis.

And we've had patients where we've had to come up with some very, very creative ways to provide their hemodialysis. For example, we once had to put a catheter into a patient's liver – their hepatic vein – so that we could get a dialysis catheter into the right side of their heart.

M. Ramesh: What the guidelines recommend is to remove the catheter, be line free, and replace the catheter at a different site. In my patient population (immunocompromised hosts), preserving the line is often essential. I don't typically have the luxury of removing and replacing lines easily.

S. Gordon: I think there are some physicians who are reluctant to remove and replace as the first treatment, and will instead try antibiotic locks or ethanol locks. They're really trying to save the line, often because they want to save that patient's vasculature.

S. Welbel: What the latest guidelines say is that unless it's *Staph aureus*, or *Pseudomonas* (or fungi or mycobacteria), or if the patient has sepsis, thrombophlebitis, endocarditis or blood stream infection after 72 hours of antibiotics, you can certainly try to salvage those long-term catheters with antibiotic lock therapy; however, IDSA recommendations tend to be conservative and very evidence-based, and there's not a lot of data on antibiotic locks. As we're seeing more data, the recommendations should become more positive.

When is it not possible to follow these guidelines?

S. Mufti: Sometimes we cannot follow the criteria in those guidelines because of comorbid conditions. For example, if we have a morbidly obese patient whose body habitus will not allow a catheter to be well managed in the groin region, or even in the back because it just can't be accessed, you're probably going to change it over a wire instead of taking it out and replacing it in another spot, thereby not following the criteria for remove and replace found in the guidelines.

R. Hachem: It's not possible to follow those guidelines when you have no vascular access or a very sick patient, particularly one with profound thrombocytopenia. In those cases, the line cannot be removed; otherwise, patients may have severe bleeding resulting in death. Overall, these guidelines need to be brought into reality and tightened up. The real world can be very different from those guidelines.

> ***It's not possible to follow those guidelines when you have no vascular access or a very sick patient, particularly one with profound thrombocytopenia.***

M. Rupp: Despite the fact that there are tens of thousands of patients with bacteremia due to infected intravascular catheters, this condition has not been studied adequately to answer questions such as: How long do we need to treat? Can we treat with the catheters in place? What's the best method to treat with the catheter in place? In which patients do we really need to remove the catheter? Most of the guidance that we follow is based upon the wisdom of clinicians who treat a lot of patients, but the guidance is certainly not based on empiric data from randomized, prospective trials. And that's just a real weakness right now – a gap in our knowledge base.

M. Ramesh: In most cases that I deal with, we will usually attempt to preserve these lines. In a dialysis patient who has exhausted all access sites, we will keep the line in if possible. Similarly, in immunocompromised hosts with low platelets or bleeding tendencies, we tend to preserve lines as much as possible. Removing the lines in those cases causes more morbidity.

My goal when it comes to catheter-related infection is preservation of the line. In my patient population, it is particularly important to preserve the line, and for that reason we are more open to newer management strategies.

> ***My goal when it comes to catheter-related infection is preservation of the line.***

Can you discuss the risks of remove and replace and your experience with those risks?

R. Hachem: The risk of removal and replacement can be considerable. It is associated with mechanical complications, such as failure of insertion, misplacement, pneumothorax, and bleeding. In someone with no other vascular access, it's a major risk, because you can put the patient in a life-threatening situation.

> ***The risk of removal and replacement can be considerable. It is associated with mechanical complications, such as failure of insertion, misplacement, pneumothorax, and bleeding.***

S. Welbel: The risks really have to do with the replacing. In most patients, there's little risk in removing, because we're getting rid of a prosthetic device which doesn't have its own blood flow, but it does have a biofilm, which is coated with microorganisms, so we always prefer to get the line out…but there are risks.

Because we have to cannulate another vessel, or place another central line, there are all the various mechanical risks associated with inserting a central line, depending on where one puts the line – if it's in the neck, there could be a pneumothorax.

Other potential complications include bleeding, thrombosis, and loss of a vessel. For anybody who is going to require long-term parenteral feeding or medication, including dialysis patients, cancer chemotherapy patients, and patients who have short gut syndrome, the loss of another major vessel can be detrimental.

M. Ramesh: I agree that removing the lines is the easy part. When there's no further access for reinsertion, that can add significant morbidity. Particularly in patients where you are removing a dialysis or Hickman catheter, the risky aspect is lack of further access.

S. Gordon: Anytime you place a central line, there's a risk. I'm aware of catheters where the tips have been placed too far into the atrium, and the patient came back within a month with palpitations, requiring a new catheter.

M. Rupp: Remove and replace is obviously associated with a variety of complications. Thromboembolic events are a possibility, and we always worry about air embolism in these patients, for example.

In patients with intravascular catheters in place for cancer chemotherapy, infections often occur when their health is seriously compromised – they're sometimes profoundly neutropenic or pancytopenic, and lack sufficient platelets. Accordingly, there's a great concern for bleeding complications when catheters are removed.

In addition, there are complications associated with replacing the catheter. Every time you do a procedure around these great vessels there is the potential to cause injury to surrounding structures. You may inadvertently cannulate an artery rather than a vein, resulting in bleeding or hematoma formation.

Because you are operating in close proximity to the lungs, if you aren't using ultrasound guidance, or don't have an experienced operator, a pneumothorax can result.

There was a time when we used to change catheters routinely over guidewires in order to try to prevent infections. And what we found was this: any time that you're manipulating these catheters, you're actually subjecting the patient to greater risk of infection.

Probably the greatest risk of introducing infection is during the catheter insertion process. There are many steps involved, and if you're not doing all those steps

appropriately (disinfecting the skin, using good aseptic technique, putting on appropriate dressings, etc.), the patient is again at risk of infection, and that shouldn't be underestimated.

S. Mufti: In addition, every time we do a new replace procedure, there's more radiation involved for everyone. Because we have to check placement with X-rays, both my technologist and I get radiated. There's also a cumulative radiation dose for patients, and we sometimes overlook the radiation cost in catheter manipulations, placements and replacements.

People can develop all kinds of coagulopathies, especially cancer patients, who can get DVTs from catheters. In addition, the more you manipulate that catheter, the greater the chance that you're going to injure the vein and produce a clot, particularly in the cancer population, and in patients with sickle-cell anemia.

What do you feel are the most serious complications of CVC removal and replacement, and why? How often do these complications occur?

S. Gordon: Depending on the device and the skill level of the operator, serious complications could include substantial blood loss, a pneumothorax from a lung puncture, rare instances of nerve injuries, and then the infection itself, of course. Those would be the big four complications.

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M. Rupp: I feel it is important to distinguish the most *common* complications from the most *serious* ones. Some rare, but tragic, complications that I've seen include patients who develop an air embolism, with resultant central nervous system insults, due to removal of a catheter. The most common complication from catheter removal that I've noted is bleeding. Clearly, catheter insertion is associated with occasional complications such as pneumothorax, bleeding, and nerve damage.

S. Welbel: Some patients end up in the ICU, not necessarily for their line placement, but definitely due to the morbidity of the infection. Particularly if it's a gram-negative or a gram-positive, a toxin-producing organism, patients can become hypotensive, develop SIRS, or wind up in the ICU for *Staph aureus*, even endocarditis.

M. Ramesh: The most serious complication would be pneumothorax from putting the line in the chest. The second would be bleeding, which is less likely to occur if ultrasound guidance is used.

I probably would estimate bleeding to occur in under 5% of cases. Pneumothorax, to a large degree, depends on the experience and proficiency of the operator. It occurs less frequently than in the past, as we now have ultrasound to guide us.

R. Hachem: I agree. The most serious complications are pneumothorax and bleeding, especially when you have a patient with a low platelet count. We are lucky that neither are very common, occurring in less than 1% of cases, I would estimate.

S. Mufti: Another thing that I wanted to say about catheters, costs, and complications is septic emboli that can occur when an infection starts out at the catheter tip.

When that catheter is used more and more, you're spreading that infection to other parts of the body, particularly if you have a venous, dialysis, or chemotherapy catheter. Now you may be sending the infection into the lungs as you use that catheter.

How are these procedures complicated by the general health of the patients?

S. Mufti: More medical problems translate to more time and more expense all around. Catheters are essential in many sick patients – in chemotherapy, hemodialysis, pulmonary hypertension, and transplants, just to name a few. And these patients are at the greatest risk. Many have tumors, lymphoma or leukemia, are immunocompromised, and/or have coagulopathy issues. Hemodialysis patients require indwelling catheters basically forever, which can create more problems.

M. Rupp: Taking out a catheter and replacing it is frequently a very undesirable and complicating factor in patient care. The last thing you want to do for your sick patient in the ICU is to have to deal with a catheter infection. ICU patients can have fever from a large number of potential causes – both infectious and non-infectious.

Trying to determine the source of fever is a major, and often expensive, venture. Certainly, part of the cost equation is the number of diagnostic tests that might be required in order to establish the catheter as the cause of fever.

It's tricky, because in very ill patients you do not have the luxury of time, and you're doing everything all at once to define the problem.

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S. Welbel: There are patients for whom we just don't have any place to put the new line, especially those short-gut folks, cancer chemotherapy patients, and some dialysis patients who have lost all of their appropriate vessels.

M. Ramesh: If the patient is too sick – for example, in the ICU and/or hypotensive – we prefer not to remove the inserted line, as it is in continuous use. Sometimes, the patient is even too sick to be transported to get a tunnel catheter exchanged by IR. Inserting a PICC line at the bedside could be an option, but even that carries some morbidity. Other conditions that could make removal and replacement more difficult include excessive anasarca and lack of available vascular space.

The estimated cost to "remove and replace" CVCs has ranged from $8,000 to $10,000. What would be your estimate of the true cost of a remove and replace at your institution?

R. Hachem: I would estimate that the direct procedural cost would comprise most of a $10,000 total cost. Indirect costs should be under $5,000.

S. Welbel: One must look at the extra days spent in the hospital, and break that down by things like type of bed – regular, ICU, etc., the procedure itself, and the cost of the drug. Also consider other factors such as days of missed work, even mental distress and life quality measures. All of these factors likely come to an overall cost of about $7,200 for remove and replace.

How important is the ability to salvage an infected catheter for the following patients: solid tumor cancer, lymphoma, leukemia, hemodialysis?

S. Welbel: It's difficult to generalize because we are frequently unsure for how long some solid tumor cancer patients are going to require chemo – some solid tumors are treated with peripheral IVs rather than a port. For patients who do need long-term chronic parenteral therapy – whether it's parenteral feeding, parenteral cancer chemotherapy, or parenteral antibiotics – salvaging a catheter is very important, particularly in cancer chemotherapy patients, because they can be neutropenic.

The two most important patient types requiring line salvage are probably the leukemia and the hemodialysis patients.

For the most part, hemodialysis patients are going to require dialysis for life, frequently don't have a fistula or a graft, and typically have a limited number of vessels.

M. Rupp: The cases where it's just imperative that we develop better ways of salvaging catheters are those patients who are going to need their vascular access over the long haul. The obvious one on that list would be the dialysis patient. A group that I would add would be those requiring TPN.

Another group would be our hematogenous malignancy patients – particularly during any period in which they are being treated with cytotoxic chemotherapy or undergoing bone marrow transplantation – it's absolutely imperative that we have vascular access.

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S. Gordon: It is particularly important to salvage dialysis catheters. Dialysis catheters are going to be left in until the patient dies or the patient gets a fistula or graft. If the fistula or graft doesn't take, then they're going to have a catheter reinserted.

S. Mufti: It could take many weeks to several months for a fistula to mature in a hemodialysis patient before it can be used. In the meantime, almost all dialysis patients will start out with catheters.

Please comment on the challenges associated with different patients and disease stage impact on catheter salvage vs. remove and replace.

M. Rupp: The stage of disease is very important. The leukemia patient who is in the throes of a preparative regimen for bone marrow transplant is at an incredibly tenuous and vulnerable place – they are pancytopenic, and they're going to be in that state for several weeks. It's absolutely crucial that they have a line. It's absolutely the worst time for the line to get infected.

In addition, the person who is on TPN for short-gut syndrome, who is waiting for a small bowel transplant, may be dependent upon ongoing parenteral nutrition for months, if not years. The problem is that over time, with recurrent line placements and repeated infections or thrombosis, these patients have sclerosis and scarring of the vessels, and may have extremely limited anatomic locations for vascular access. This is another group of patients where absolutely the worst thing that can happen is to lose that vital vascular catheter. We are then faced with the question: "How am I going to get vascular access to keep this person alive and functional?"

> ***Over time, with recurrent line placements and repeated infections or thrombosis, these patients have sclerosis and scarring of the vessels, and may have extremely limited anatomic locations for vascular access.***

S. Gordon: A catheter salvage issue can occur because there are just X number of veins available. For example, in a renal patient or dialysis patient you have right jugular, left jugular, and both femoral veins. After that, you really don't have a lot of options for a catheter.

S. Welbel: In cancer chemotherapy patients it's all the things that we've already mentioned. A lot of it has to do with their bleeding times and their thrombocytopenia – it's difficult to put another line in, or they just don't have a place to put it.

R. Hachem: Particularly challenging are the leukemia and transplant patient populations, who may be profoundly thrombocytopenic for a long time. As a result, catheter removal and replacement are associated with high morbidity and mortality.

In order to salvage infected catheters, investigators have proposed antibiotic lock therapy (ALT). Currently-available ALT is generally considered to be of somewhat limited utility in the management of CLABSI. What factors in your view contribute to that perception?

S. Gordon: The primary reason is the lack of definitive studies that show the effectiveness of one ALT compared to the other.

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S. Welbel: The thing with ALT is that there have been few good prospective studies. We haven't seen large, double-blinded, high-quality trials. There have been a number of meta-analyses now, and many case studies, but they're just not as robust as we would like. But I think we're getting there.

M. Ramesh: The problem with antibiotic lock therapy is that we don't have great randomized trials. Many of the published studies enrolled only a small number of patients, and some employed various combinations, making definitive efficacy and safety conclusions difficult.

M. Rupp: ALT is not standardized, and institutions have come up with what we like to call "home brew". Because there is not an FDA-approved standardized approach to ALT, some have had to depend on what's in the literature, or what other organizations are doing. They then try to work with their pharmacists to come up with some sort of concoction of antibiotics. Sometimes the concentrations are poorly defined.

In order for ALT to work, it has to be in the lumen of the catheter for a period of time – this minimum time period is also undefined. Unfortunately, in ill patients who need continuous access, it may be difficult or impossible to lock the catheter and allow it to stay idle for several hours. The optimum lock solution would work very quickly and would not need to be indwelling for a long period.

This is another great example of a real gap in our knowledge base – what is the best lock solution and what is the minimum dwell time to be effective?

What do you feel is the role of ALT in patients with a history of multiple CLABSIs?

S. Welbel: I think the main benefit is that many of those patients are out of vessels, making something like ALT a necessity.

M. Rupp: Because people with multiple CLABSIs are frequently getting down to very limited vascular access, ALT becomes increasingly attractive as an option for prophylaxis.

R. Hachem: When you have somebody with multiple episodes of CLABSI, having to change the line very frequently is problematic, and sooner or later you may run out of vascular access. And we have many patients like that right now. There are some who will develop a *Staph aureus* infection every time you insert a new line. This is where ALT is greatly needed.

M. Ramesh: We are in immediate need of an effective, FDA-approved, ALT that we can use on a routine basis.

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Summary

Incidence and Burden of CLABSIs

CLABSIs are a widespread and serious medical problem, occurring at a rate of nearly 400,000 each year in the US alone.

Studies have also revealed that catheter-related bloodstream infections may be associated with serious complications, including septic thrombosis, endocarditis and disseminated infection. Catheter retention in such patients, moreover, is associated with a higher risk of relapse and poor response to antimicrobial therapy.

Catheter-related bloodstream infections are also associated with a 12% to 25% mortality rate and an attributable cost of $46,000 to $65,000 per episode.

Variability in Reporting the Scope and Costs of CLABSIs

The true scope of CLABSI is difficult to quantify, and its incidence is very likely underreported. There are multiple reasons for the wide ranges that have been published for the incidence and cost of CLABSIs, including the following:

- Definitions, surveillance practices, oversight, and cost assessments of CLABSIs vary widely among institutions
- There are numerous disincentives for accurate reporting of CLABSIs
- There is considerable pressure on organizations and individuals to reduce institutional CLABSI rates, to the point that the current published rates of CLABSIs are not as reliable as they need to be

Although some individuals in the healthcare systems may not be as attentive to accurate reporting of these infections as they could be, it should be noted that most institutions are making considerable efforts to ensure that all such reporting is complete and accurate.

Our panelists agree that disincentives for complete and accurate infection reporting do exist, but the primary problem lies with the variable or unclear definitions from overseeing bodies (which may be subject to individual interpretation), and heterogeneous reporting or monitoring requirements and practices among institutions.

Reducing the Incidence of CLABSIs

The institutions represented by our panelists employ the best infection control specialists and systems anywhere, yet even they are hard pressed to reduce their CLABSI rates below 1 episode/1,000 catheter-days. All continue to strive towards what is felt to be the minimal attainable incidence of CLABSI – 0.5 episodes/1,000 catheter-days – but virtually none are there yet.

The panelists are in agreement that, even with improved prevention techniques, CLABSIs will continue to be a serious and widespread medical challenge for the foreseeable future.

Clinical Challenges Involving Catheter Removal and Replacement

Although it is considered to be the standard of care for CLABSIs, removal of the central vein catheter and reinsertion of a new one at a different site might be difficult, or even impossible, in patients with long-term surgically implantable silicone catheters.

Furthermore, critically ill patients often have underlying coagulopathy, which makes reinsertion of a new CVC at a different site risky in terms of mechanical complications, such as pneumothorax, misplacement, or arterial puncture.

Salvaging the existing catheter is essential – or at the very least, far preferable to remove and replace – when faced with the following clinical conditions:

- **No vascular access**
- **A very sick patient** (e.g., ICU, hypotensive, thrombocytopenic)
- **Need for long-term chronic parenteral therapy**
- **Acute leukemia or lymphoma**
- **Other comorbid conditions such as gross obesity**

Morbidities and Costs of Remove and Replace

There are a number of morbidities as well as significant costs associated with remove and replace. Every time there is a procedure around major vessels, there is the potential to cause injury to surrounding structures, bleeding or hematoma. There is also considerable discomfort to the patient caused by the procedure itself.

When a catheter continues to be used, a CLABSI can spread to other parts of the body, particularly with a venous, dialysis, or chemotherapy catheter.

Individuals can develop a variety of coagulopathies, especially cancer patients, who can get DVTs from catheters. In addition, the more that a catheter is manipulated, the greater the chances of a vein injury or a clot.

Serious complications could include substantial blood loss, a pneumothorax from a lung puncture, and rare instances of nerve injuries.

Particularly challenging are the leukemia and transplant patient populations, who may be profoundly thrombocytopenic for a long time. As a result, the chances of the catheter being a source of morbidity and mortality are high.

The panelists agree that taking out a catheter and replacing it is frequently an unneeded and very undesirable and complicating factor in patient care.

The Promising Role of Antimicrobial Lock Therapy (ALT)

Antimicrobial lock therapy involves the instillation of a concentrated antimicrobial solution into the catheter lumen, as a method of eradicating organisms in biofilm settings and salvaging the catheters. In many types of patients and a variety of clinical situations, salvaging an infected CVC is essential.

Moreover, in patients with a history of multiple episodes of CLABSI, frequently having to change the line is problematic, and sooner or later those individuals may run out of vascular access. There are others who will develop a *Staph aureus* infection every time a new line is inserted.

The panelists concur that these are areas where ALT is greatly needed.

The panelists note that effective ALT would become a standard of care in central vein catheterization, and would fill a significant unmet need.

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