Infection Control and Extracorporeal Life Support

Introduction

In 2008, the leadership of ELSO (the Extracorporeal Life Support Organization) recognized concerning trends and unanswered questions from its membership concerning numerous issues focusing on the diagnosis and treatment of infections in patients on extracorporeal support, in addition to extremely variable practices in antibiotic prophylaxis, use of pre-primed circuits, and a general lack of recommendations in these practices from infectious disease colleagues and the ELSO organization. While general guidelines for many aspects of the management of ECMO have been established and posted by ELSO on its website, specific information and recommendations about infection control remained sparse. In response to this, the steering committee established the "ELSO Infectious Disease Task Force" which was composed of experts in both ECMO care and in adult and pediatric infectious disease. The prestigious group represented 8 specialties, 16 ECMO institutions and 4 countries (Table 1). The group was presented with a list of tasks and goals which included:

1) a thorough review of the ELSO database to define the incidence of infection, the offending organisms;

2) completion a survey of active ELSO centers to establish common practices in infection prevention and control;

3) an extensive literature review to establish and support evidence based recommendations by the group;

4) conducting studies of pre-primed circuits to establish any infectious risk to this common practice;

5) conducting antibiotic binding studies of both the silicon and polymethylpentene oxygenators;

6) recommendations for additions to the current ELSO data collection to improve future studies and quality reviews in infection control; AND

7) Return to the committee and the ELSO membership specific recommendations for best practices in ECMO infection prevention, diagnosis and treatment.

Over a period of about 2 years, the task force worked in smaller groups to accomplish the initial tasks, including several organizational conference calls, and then met in Chicago to discuss, debate, and finalize the group's recommendations. This chapter is the summary of the work of the task force, and the resultant recommendations.

Infections on ECMO – Incidence and Etiology

As an initial step in the ID task force's process, several of its members made a thorough review of the current data to evaluate and outline the incidence of infection, the most common offending organisms, route of infection and impact on outcomes in order to not only define the problem, but also to help guide the infectious disease experts in making their recommendations.   The results of the database analysis have been reanalyzed and subsequently published separately, but the original findings and recommendations will be summarized here to

explain the basic principles as they were used to make the subsequent recommendations, as well as summarizing the results of the published expanded analysis.

Initially data was collected from the ELSO database from the years 2001 to 2008 and analyzed with multiple models in respect to ECMO group (neonates, pediatric and adult), Indication (Respiratory, Cardiac, ECPR), mode of ECMO (VA, VV, combinations, etc.) as well as time on ECMO, organisms reported, etc. The incidence of infections in all groups was reported as overall percentage of patients with infections, along with number of infections reported per 1000 days of ECMO support (#/K-days).   The overall infection rate in all groups was 11.5% and 15 infections / 1000 ECMO days. As might be expected, the lowest incidence was in the neonatal group at 7.9% or 9.9/K-days and highest in the adult ECMO group with 20.6% or 29.7/K-days.   Reported infections were also highest in the ECPR group at 23.6/K-days, and these incidences were relatively stable across the 7 year period examined.

The data also suggested that in all patients with reported modes of support, the infection rates were highest in the VV Double Lumen catheter group with an incidence of 20.5/K-days, more than VA, VV with two cannulas, VA-V, and other combinations. However, it must be noted that the actual highest rate was 26.6/K-days in the "other" group, which led the group to conclude that there is no data to truly support any actual increased risk with VV DL support, but rather the quality of the data collected was too poor to make any conclusions in this area.

In examining the length of ECMO runs (days on ECMO) in "infected" versus "non-infected" patients, the runs were far longer in the "infected" groups in all age groups and categories. Specifically in all groups, infection rates increased from 6% (17/K-days) for patients on one week or less, 15% (15/K-days) in patients on support from 8-14 days, and up to 29% (13/K-days) in patients on ECMO for over 2 weeks (>14 days). This was most true in the adult patients on support over 14 days who had an infection incidence of 53%, but the odds ratio was increased in all groups on over 1 week, and as much as 3-4 times higher for runs over 2 weeks in younger patients and 6 times higher in adults. This relationship between the risk of infection and length of support, as well as increased mortality with infection has been demonstrated in many previous studies as well in neonates[2] pediatric patients[3], and adults[4,5] and specifically in cardiac patients[6]. Only one small study of neonates did not demonstrate an increased mortality in infected patients on ECMO support[7]. However because the database did not previously collect dates of positive cultures, the available data does not delineate is whether the longer run led to higher risks of infections, or the reverse, that patients who are either placed on ECMO for complications of infections already present, or who developed infections early in their course, leading to sicker patients and longer ECMO runs. While this question will hopefully be answered with the proposed modifications to data collection, there is still likely some validity to the general connection with infections and longer ECMO runs.

In the subsequent reanalysis, the time period was extended to a decade, from 1998-2008, during which 20,741 cases were entered, including 2,418 infections, for an overall reate of (11.7%)[1]. As with the preliminary study, the incidence of

infection was highest in the adult group, and lower in the pediatric and neonatal groups (30.6 versus 20.8 and 10.1 per 1000 ECMO days).   In the expanded population, infections were highest in the VA mode of support, however this difference may be related to frequency of use of VV in the later years of the study.   Also as in the preliminary study, the infection rates were highest in patients supported over 14 days (30.3%) versus those on support for less than 7 days (6.1%).   Similarly patients with infections were older, had longer runs, required ventilation longer post-ECMO and had higher mortality

When the subcommittee examined the specific organisms reported in the database, it did not adequately separate source of infection (blood, urine, sputum, etc.). However in looking at the reported organisms, it was still felt by the group consensus, that the pattern would be helpful in directing future empiric therapy for patients on ECMO, particularly those with suspected life-threatening sepsis.

In the neonatal group, by far the largest number of reported infections involved coagulase negative staphylococcus. In the pediatric and adult group other organisms were also more commonly cultured including pseudomonas, staph aureus, and candida albicans, at varying incidences. Overall the most common organisms that were found and that therefore are recommended to be covered with empiric therapy include coagulase negative staph, pseudomonas aeruginosa, staph aureus and candida albicans.   In addition smaller numbers of enterobacter, Klebsiella, enterococcus and E.coli species were also reported.   In the published reanalysis, the overall incidence of specific organisms in all groups

was coagulase negative staphylococci (15.9%), Candida species (12.7%) and Pseudomonas (10.5%).

The mortality in all patients on ECMO with reported infections ranged from 56-68%, with the highest odds ratio for mortality in the neonatal groups (2.5-2.8). It is the recommendation of the task force that ECMO teams take this data into consideration in choosing empiric antibiotics for patients on ECMO with suspected or presumed infections. In addition, because of the somewhat surprising high incidence of candida in these patients, and the high mortality in those patients who do get infected, it is the strong recommendation of the task force ID experts, that clinicians raise their index of suspicion for yeast in significantly ill patients suspected to have sepsis on ECMO and lower their threshold for antifungal treatment in these patients.

In the process of analyzing the ELSO data with regards to infections in patients on ECMO, the task force did find many limitations in the data including not having dates or sources for cultures, not being able to clearly distinguish infection and colonization for reported resistant organisms, not collecting data about high risk conditions such as open chests and open abdomens, and recognizing the presence of inaccurate and/or insufficient reporting of some other data points (mode of ECMO e.g.). However, the overall incidence and mortality information is still felt to be of significance in making recommendations and in clinical decision making until more specific and accurate data can be collected. In summary, this information includes: an increasing incidence of infection with increasing age; increased incidence of infection with length of the ECMO run at one week, and beyond two weeks;

increased odds ration of death with the presence of infection on ECMO; and a predominance of infections with coagulase negative staph, pseudomonas aeruginosa, staph aureus and candida albicans.

Circuit Management

The task force reviewed many of the common practices in an attempt to identify areas of potential improvement and reduction in contamination of the circuit, particularly with the increased length of support noted in an expanding adult population on ECMO. Based on known risk factors and general principles of infection control, and more recent data about prep solutions, IV connections, central IV access, etc. the task force has outlined the following basic guidelines:

A) In general, it is recommended that the ECMO circuit be cared for like a protected central line used for hyperalimentation, such that "breaking" the line unnecessarily is strongly discouraged. This will make contamination of the circuit much less likely. Obviously blood gases from the circuit for calibration of monitoring technology is at times necessary, however routine sampling from the circuit when patient sites (e.g. arterial lines) are available is strongly discouraged.

B) The use of needleless hubs is strongly encouraged for all connection and access sites in the circuit including connections to stopcock access ports. These are not only better from a user safety perspective, but are much more reliably sterilized with prep solutions than stopcock Leur-Lock ports.

C) The prep solution of choice is chlorhexidine, rather than alcohol or betadine.

D) It is recommended that only continuous infusions be administered to the circuit, to minimize "breaking" the sterility of the lines. These may include heparin, vasopressors, inotropes, narcotics and sedation which will allow dosing changes without disconnecting and reconnecting the lines on a regular basis. Initial connection of these lines to the circuit and changing of old lines should follow the strictest sterile techniques with chlorhexidine prep and use of the needleless hubs.

E) Intermittent Drug and electrolyte boluses should be administered to the patient whenever appropriate access is possible to avoid unnecessary "breaks" to the circuit.

F) Because of the increased risk of contamination of the blood in patients who are on extracorporeal support, an earnest attempt should be made to avoid pairing the care of ECMO patients with other patients with highly resistant organisms or with grossly contaminated wounds or serious infections, or having such patients immediately adjacent to patients on ECMO.

G) As always, frequent hand washing and easy access to cleansing solutions are essential for bedside personnel handling circuit access, sampling, line connections, etc.

Antibiotic Prophylaxis

In the Task Force survey of ELSO centers current practices, there was a tremendous variety in use of prophylactic antibiotics intended to prevent

infection the patient or contamination of the circuit. Practices varied from multidrug therapy for the entire ECMO run, to selective gram positive coverage, to the absence of antibiotic use beyond surgical prophylaxis for cannulation.   In addition, there are no randomized trials examining this issue, and in fact, construction of such a trial would be extraordinarily complex because of the multiple potential sources of infection and contamination, and the potential long duration of ECMO support.   While there are two studies which recommend avoiding use of prophylactic antibiotics beyond 24 hours[3,8], neither article specifically address the topic in the study, nor supported their conclusion with data.   Because of this, the task force relied heavily on the available data regarding the use of antibiotics in the prevention of infection, and the expert opinions of our ID colleagues. Despite many of us on the task force having managed ECMO for many years with routine antibiotic use, none of us could defend the practice beyond a "sense" that we needed to protect the circuit and patient from contamination simply because of its extracorporeal nature.   After extensive literature reviews and discussion, it was the unanimous opinion of the infectious disease experts, and the subsequent conclusion and recommendation of the task force that there is no data to support the routine use of continued antibiotics for patients on ECMO support, simply for prophylaxis, without specific culture or physiologic evidence of ongoing infection, and in fact, the common practice of continuous "prophylactic" antibiotics, may likely only increase the risk of resistant strains, as well as potential yeast overgrowth which as previously stated was an unexpected finding in the database review. The recommendation to avoid the routine use of antibiotic prophylaxis for patients on extracorporeal support does NOT necessarily apply to cardiac

patients with transthoracic cannulation through open chests, a group of patients with documented increase risk of infection, specifically mediastinitis[3,6,7]. The use of antibiotics in this group is based on the clinical judgment of the cardiac surgeons along with their ID colleagues, and based on multiple factors including the length of time the chest has been open, the circumstances under which it was opened (left open in OR versus opened urgently in ICU), the patient's overall immune and nutritional status, and the perceived risk of contamination of the open wound, as well as any pre-existing infections or skin conditions (e.g. MRSA contamination).

Prophylactic antibiotics for the actual cannulation procedure should follow standard principles of surgical prophylaxis, and a single dose, or at the most 24 hours of coverage can be justified with either open or percutaneous cannulation techniques. Additional doses beyond the procedure are not supported by any literature.

Because of the increased incidence and high mortality in ECMO patients with fungal infections, the task force recommends "cautious, but aggressive" use of antifungal prophylaxis in patients deemed to be at particularly high risk (e.g. prolonged open chest on multi-drug antibiotic therapy, or significantly immunocompromised patients).

Prevention of Systemic Infections

In addition to proper care of the circuit, many aspects of patient care technique and maneuvers can be used to prevent and avoid the development of systemic infections in patients while on ECMO support. The following recommendations

from the task force are specifically designed to help prevent such nosocomial infections.

A) Standard guidelines to prevent ventilator associated pneumonia including elevation of the head of the bed, oral prophylaxis, medical treatment of reflux as indicated, etc. should be strictly followed while on ECMO if at all possible.   Appropriate pulmonary toilet, suctioning and bronchoscopy should be used liberally as indicated. Each of these has been shown to be able to be performed safely, and avoidance of such procedures out of concerns for bleeding in the heparinized patient are not felt to be justified by the task force, and likely will increase the risk of VAP.   Similarly early tracheostomy should be considered in non-pediatric patients who are likely to require ECMO more than a few days, to improve pulmonary toilet, reduce the potential for GI contamination from reflux as well as reduce sedation requirements, allowing the patients to be more awake, and even generate a cough to help clear the airway.

B) Oral and GI decontamination protocols should be strongly considered and used when appropriate.

C) Whenever possible, early and complete enteral nutrition should be used to help maintain the gut mucosa, prevent translocation, and also help avoid the use of hyperalimentation and its inherent risks of infection while on ECMO. If enteral feeding is not possible, and hyperalimentation must be used, it is preferential to administer it directly to the patient in a clean dedicated line, rather than to the circuit because of the high glucose concentration and risk of infection. In the case of limited patient central access where the hyperalimentation must be given into the circuit, a

dedicated site should be used without mixing of other infusions, and it should be cleaned with strict sterile technique and changed daily.

D) It is recommended that all unnecessary lines, access and devices be removed once the patient is stable on ECMO support to minimize the risk of sepsis. Peripheral IV's should be used for intermittent boluses of drugs and blood products whenever they are available. The removal of unnecessary central access including long standing umbilical lines is NOT contraindicated because of anticoagulation. The task force felt strongly that the risk of infection and its inherent morbidity and potential mortality far exceeded the risk of bleeding from carefully removing an unused or unnecessary central line. On the other hand, the task force recognizes that some patients, particularly children, may have limited peripheral access availability, especially early in the course when peripheral edema is a significant issue. In these cases when central access is required, strict sterile technique is essential in changing and accessing the lines.   In patients who may have need for specific pressure monitoring (Swan-Ganz catheter for pulmonary hypertension e.g.) when ECMO is to be discontinued or trialed off, it is recommended that existing lines be removed upon placement on ECMO, or soon thereafter, and then fresh clean lines be inserted when they are required at or near the end of the ECMO course.   Again, careful technique in the hands of skilled physicians make the risk of insertion of these lines reasonably low even in patient who are mildly anticoagulated for ECMO, and certainly do not outweigh the infection risk of an indwelling cardiac line for several weeks while on support.

E) The insertion of indwelling long term IV access (tunneled or cuffed catheters) while on ECMO is discouraged due to the risk of hematoma formation and subsequent infection. Additionally, it is recommended that a low threshold be maintained for removing such long term access and that the lines be removed if there is any suspicion that they might be contaminated.

Diagnosis of Infections on ECMO

The diagnosis of infection and sepsis can be painfully obvious in the presence of pus and wound infections, but can also be challenging at times in the ICU setting, particularly in patients on extracorporeal support. In some patients the exposure of the blood to the foreign surfaces of the circuit can in and of itself generate an inflammatory response that can rival the sepsis itself. In addition to that source of confusion, much of the difficulty in diagnosing infection and sepsis is the loss of many of the usual markers for systemic infection that are relied upon in the intensive care environment. For example, let's look at fever. The sudden rise in a patient's temperature in the ICU to levels above 102 degrees is a common and reliable sign that there has been at least some significant stimulus to the inflammatory response, if not some form of infection. However when the blood is removed from the body and circulated in large bore tubing surrounded by ambient room temperature, it tends to cool very quickly, and without intervention, significant, even profound, hypothermia can result. To prevent this problem the blood taken into the ECMO circuit is warmed back to normothermia prior to reinfusion. However as a down side to this artificial homeostasis, patients who have significant inflammatory response including

pyrogens, whose bodies are trying to mount a febrile response, can't do so completely because of the circuit. The temperature of the blood that without ECMO, would be slowly climbing, now cools down when exposed to the ambient air while coursing through the ECMO circuit, and then just prior to re-entering the body, it is warmed back to normal (or what we set as "normal" based on the water bath temperature). Unfortunately there is no mechanism currently to monitor the "amount" of rewarming required, and we do not routinely measure the blood temperature of the venous limb of the circuit. In fact, with the high blood flows on ECMO it is unlikely we would notice a significant rise in the venous blood temperature even in patients mounting significant "febrile" responses.   These circumstances make it very difficult, though not impossible, to mount a true fever while on significant ECMO support.   Patients being actively weaned from VA support for example, where a relatively small percentage of their blood volume is running through the circuit, can certainly mount a fever.   With all this in mind, patients who are able to generate fevers of as little as 101 or greater while on "full-flow" ECMO are likely to be having extremely strong inflammatory responses, and should be checked very carefully for other signs of infection and treated appropriately.   As a corollary, it is not uncommon to have patients spike fevers soon after coming off ECMO support, and this can frequently be the result of an ongoing inflammatory response that has been "hidden" by the ECMO support and the above described phenomena, rather than a "new" infectious process.

The interpretation of laboratory data is also hindered by the presence and systemic effect of the ECMO circuit.   The reliability of leukocytosis and leucopenia is poor at best, particularly in the early ECMO course where WBC's

are known to be activated by the foreign surfaces and potentially stick to these sites, particularly in the oxygenator, depending on the patient's particular response to the circuit. White counts may fall significantly low early in the course, or late as the oxygenator and other components become "old" and begin consuming products. Conversely, in some patients the initial response to the circuit may cause general demargination and significant elevation of the WBC count. Because of this, general high or low white counts are difficult to interpret in the absence of other findings. This is not to say that a sudden rise in the WBC count in an otherwise stable patient who has been supported for many days on ECMO should be ignored, particularly if accompanied by a significant bandemia, but rather one has to be careful not to over-interpret moderate rise and falls of the WBC count during the ECMO course. While no prospective studies have been completed, a formal retrospective analysis in neonates which specifically looked at the benefit of WBC counts, absolute neutrophil counts, and the immature/total ratio, could demonstrate no predictive value of nosocomial infections in patients on ECMO[9].

Similarly thrombocytopenia is very common as a result of platelet activation by the circuit and adherence to its many components. In fact it is the rare patient that does NOT have a significant drop in platelets and require intermittent platelet transfusion during the ECMO course. As an aside, care must be taken not to over-diagnose this as heparin-induced-thrombocytopenia as well.

Because the individual patient's inflammatory response to the ECMO circuit is as variable and unpredictable as their response to different infectious agents, the use of inflammatory markers such as C-Reactive Protein and sedimentation

rates are also fairly unreliable as a sign of infection, particularly when first obtained with some suspicion of infection. If these markers were known to be normal or mildly elevated in a stable patient on ECMO, and then a dramatic rise was documented when evaluated as part of a suspicion of infection, their usefulness may be increased, however any benefit from the routine monitoring of these markers has not been adequately documented to justify the cost, at least to date.

With the increase in mortality in patients who develop ventilator associated pneumonia in the ICU, it would be most beneficial to diagnose and treat this as early as possible. This can usually be done with a simple CXR. However, in the early course on ECMO, this becomes impossible since the CXR is most frequently completely opacified with the inflammatory changes seen on ECMO and ventilator "rest" settings. Thus without a useable CXR, close observation of the quantity and quality of the sputum aspirated from the airway becomes essential, including liberal bronchoscopy to examine the airways, clean them out, and get appropriate samples for cultures to guide therapy.

Due to all the diagnostic limitations described above, the suspicion and diagnosis of infections and sepsis in patients on ECMO requires close monitoring of specific clinical observations such as pyuria, purulent secretions at bronchoscopy, or drainage of pus from an open wound, as well as recongnition of changes in the general clinical condition and signs of poor perfusion or inadequate oxygen delivery as manifested by increasing lactate levels, decreasing urine output, metabolic acidosis, rise in the hepatic transaminases, and the general state of the patient's hemodynamics. This can at times be

exceedingly challenging in patients who have been in shock prior to support, and who may have little to no urine output, have baseline elevated transaminases, and even have hepatic dysfunction with the inability to metabolize lactate, so that determining if the rise in lactate is from increased production or from decreased breakdown, or a combination of the two, can be extremely difficult. In these patients a significant decrease in overall perfusion, without the help of the other usual diagnostic signs, must be met with aggressive work-up for sepsis, and appropriate antibiotic coverage. However it remains extremely important in the patient's survival, that an exhaustive search for the source of infection be found and appropriately treated. Antibiotics alone are unlikely to adequately treat an undiscovered and undrained intra-abdominal abscess for example, and the underlying ARDS will not likely resolve as long as the abscess remains intact. The discovery of such "hidden" infections, such as intra-abdominal abscesses, require a high index of suspicion and a willingness to undergo appropriate diagnostic and therapeutic procedures, frequently outside of the ICU.   Since it has been clearly established that safe in-hospital transport of patients on ECMO is very feasible given sufficient care and personnel, it is extremely important to not let excessive and often overstated concerns about the risks of transporting a patient on ECMO prevent the proper diagnosis and treatment of a significant infection.   Similarly methods and protocols have been established to safely perform many surgical procedures on patients on ECMO, so that failure to treat a known infection or abscess that requires surgical intervention should be avoided. While it is recognized that the risk of surgery on ECMO is elevated above that of the non-heparinized patient, the task force strongly urges sufficiently aggressive approaches to these

patients as the morbidity and mortality in patients on ECMO with undiagnosed and untreated infections exceeds all reports of risks and complications from appropriately managed transports and surgical procedures.   This approach includes the liberal use of diagnostic tests such as CT scans and bronchoscopy, and the aggressive re-exploration of wounds and body cavities that are at risk for infection, late perforations, abscess formations, etc.

The task force also examined a fairly common use of "routine" blood cultures as well as other "surveillance" cultures of urine and sputum.   Despite this being a fairly common practice among ECMO programs, there is no supporting evidence that there is any benefit to this practice, and likely only a source of unnecessary expense. Several retrospective studies have examined this question and the majority could not demonstrate any benefit to this practice. One study recommended daily cultures beginning on the 10th day of support, due to the documented increased risk of infection late in the ECMO course[9]. Another group could find no benefit to daily blood cultures, but suggested routine tracheal cultures beyond the 5th day of support might help guide future antibiotic therapy[10].   Still a third group recommended the continued practice of obtaining daily blood cultures, despite their own data that found no predictors of blood stream infections, nor proven benefit on mortality or outcome with the practice[8].   Given the data at hand and the significant cost of obtaining cultures, the task force recommends that blood, urine and tracheal cultures be obtained from patients on ECMO only when there is a significant clinical suspicion of localized or systemic infection, and that routine collection of blood, respiratory or urine cultures is not supported by any evidence, even late in an ECMO course, in the absence of clinical signs or suspicion of infection.

Treatment of Infections on ECMO

The recommendations of the ELSO ID task force can be summarized into the following statements and recommendations:

A) There are no specific antibiotic recommendations for patients on ECMO. As previously stated, the use of prophylactic antibiotics is unsupported and therefore discouraged.

B) Treatment of documented infections should follow the same principles as with patients not on ECMO support. While additional detail should be paid to the volume of distribution and selecting the appropriate dosage, monitoring of levels, etc. the specific choice of antibiotic is unrelated to the presence of the ECMO circuit unless a silicon membrane is in use. Several older papers as well as a recent pharmacologic study have documented well the propensity of some drugs, particularly lipophilic substances, to be sequestered within the membrane[11,12,13]. However with the more recent use of polymethyl pentene oxygenators, and the planned discontinuation of silicon oxygenators, it is recommended that standard doses of the majority of commonly used antibiotics be used, and levels monitored as appropriate.

C) Empiric therapy that is started prior to the initiation of ECMO for suspected or presumed infection should be continued until the pre-ECMO cultures return negative, and then discontinued exactly as if the patient was not on ECMO. If a decision was made based on clinical criteria to complete a specific course of 7-10 days for example, then that course should be continued and completed unless additional information

becomes available that contradicts the original presumptive diagnosis and plan.

D) For presumed sepsis in patients on ECMO, choice of empiric therapy should strongly consider data obtained by the ELSO database as outlined earlier in this chapter, specifically recognizing that in this population of patients the most common organisms grown from the blood include coagulase negative staphylococcus, Pseudomonas, Staph aureus, and Candida albicans, giving extra consideration to fungal therapy in high risk patients because of the high mortality noted in patients on ECMO with fungal infections.

E) Persistently positive blood cultures or clinical sepsis despite what should be appropriate antibiotictherapy based on cultures, etc. should lead to additional investigation for "hidden" abscesses, and to consideration of changing out the entire ECMO circuit that might have become colonized during the infection.

Pre-primed Circuits

In order to provide rapid access to ECMO support in emergency situations, some centers have kept circuits constructed and filled with saline so that the limiting step in the process is vascular access and cannulation rather than waiting on a circuit to be put together and primed.   This process has been questioned by other centers on a basis of infection risk and potential contamination of the circuit. Some centers have turned to their infectious disease colleagues for guidance and in turn have been told this practice is unsafe beyond 4 or 8 hours, however it appears that this has been primarily based on data related to open

IV fluids, medications, etc.   So while there may be some non-ID concerns about keeping some oxygenators "wet" for prolonged periods of time, there has been no published data on the safety of this practice from an infection standpoint. On the other hand, a few centers had reported to ELSO that they had performed some cultures on pre-primed circuits at periods up to one month with negative results, supporting the idea that the practice may be reasonable safe. The primary argument was that a saline primed circuit that was constructed sterilely and which contained NO substrates for bacterial growth (i.e. glucose or proteins) would be unlikely to grow bacteria within the circuit over time unless it was somehow subsequently contaminated, etc. In order to address this question, the task force had three of its members participating centers prime several size circuits and perform cultures at various intervals up to 30 days. The usual sterile technique was used in constructing and priming the circuits with crystalloid based non-glucose solutions. All cultures from all circuits at all three centers were negative for any bacterial growth.   In addition, one center evaluated the effect of several practice changes on their incidence of infection. These changes included staff education, the use of electively pre-primed circuits, and a shift from open chest to neck cannulation for cardiac support. With these changes they demonstrated an overall reduction in serious infection from 29.3 to 20.1/1000 ECMO days[3]. While not definitive, this does suggest a "cleaner" electively primed circuit may be less likely to be contaminated than one constructed and/or primed in an emergency situation, possibly with less experienced personnel.   Based on these results and the experience at several experienced ECMO centers the task force concluded that strictly from an infection perspective, it is safe to maintain pre-primed circuits for up to 30 days,

and possibly beyond 30 days, if: 1) the circuit is constructed and primed using standard sterile techniques and 2) the prime is electrolyte solution based, and no glucose containing solutions or albumin are used within the prime.

Unanswered Questions and Goals for the Future

The task force learned many things from the review of the database, including the fact that we need to collect more specific data. Specifically it is recommended that the ELSO database work to collect data on culture sites and culture dates to help define pre-existing infections from infections occurring on ECMO, particularly when it comes to resistant organisms (MRSA and VRE). It is currently not possible to distinguish patients colonized with these organisms, even prior to their becoming ill, and those who became colonized in the hospital while on ECMO, and those who were truly infected with these resistant organisms.   Work also needs to be done to clarify the mode of ECMO support (better definitions provided), and to record when patients had open chests and open abdomens, and for how long. Additional data regarding severity of illness scores would also help with data analysis and outcomes.

The task force also concluded that further studies would be beneficial to define the pharmacokinetics of additional antibiotics. Research to try and define the role of inflammatory markers, including searching for new markers to assist in the identification of infection in this population would also be extremely beneficial.

Finally, the task force hopes that with implementation of its recommendations, a future study can demonstrate reduction in the rates of nosocomial infections, and perhaps lower mortality in those with sepsis.

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