

---

HIM 1990-2015

---

2012

## Ethanol lock therapy in the treatment and prevention of catheter-related bloodstream infections

Breanna Anderson  
*University of Central Florida*



Part of the [Nursing Commons](#)

Find similar works at: <https://stars.library.ucf.edu/honorstheses1990-2015>

University of Central Florida Libraries <http://library.ucf.edu>

This Open Access is brought to you for free and open access by STARS. It has been accepted for inclusion in HIM 1990-2015 by an authorized administrator of STARS. For more information, please contact [STARS@ucf.edu](mailto:STARS@ucf.edu).

---

### Recommended Citation

Anderson, Breanna, "Ethanol lock therapy in the treatment and prevention of catheter-related bloodstream infections" (2012). *HIM 1990-2015*. 1245.

<https://stars.library.ucf.edu/honorstheses1990-2015/1245>



ETHANOL LOCK THERAPY IN THE TREATMENT AND PREVENTION OF  
CATHETER-RELATED BLOODSTREAM INFECTIONS

by

BREANNA ANDERSON

A thesis submitted in partial fulfillment of the requirements  
for the Honors in the Major Program in Nursing  
in the College of Nursing  
and in The Burnett Honors College  
at the University of Central Florida  
Orlando, Florida

Spring Term 2012

Thesis Chair: Stephen Heglund, MSN, ARNP

## ABSTRACT

Ethanol lock therapy is a novel technique that is being studied for its efficacy in eradicating catheter related bloodstream infections. A systematic review of interdisciplinary studies from CINAHL, Medline, Academic Search Premier, Biological Abstracts, and Web of Knowledge databases was performed. This meta-analysis examined the findings of thirty-five studies on ethanol lock therapy. Twenty-six of these studies compared ethanol to a placebo and nine studies performed a direct comparison of ethanol to other agents frequently used in antimicrobial lock technique. Ethanol lock therapy was shown to be effective as both a prophylactic therapy and as an active treatment in eradicating biofilms of organisms that frequently cause catheter-related blood stream infections, including *Staphylococcus epidermis*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *E. coli*, and *Candida albicans*. Ethanol has been shown to have a synergistic effect with several other antimicrobial agents. The majority of studies examined in this thesis have found that ethanol has equal or greater efficacy to several antibiotic and antimicrobial agents used in practice and should therefore be considered for the treatment of catheter-related blood stream infections.

## **DEDICATIONS**

I would like to thank my mother, Brenda, for all of her encouragement and support. Thank you for believing in me and supporting me every step of the way.

I would like to thank my father, Brian, for always supporting me and encouraging me in my endeavors.

And lastly, I would like to thank my brother, Brandon. Your optimism and sense of humor have always been an inspiration to me.

## **ACKNOWLEDGMENTS**

I would like to give immense recognition and thanks to the members of my committee for all of their support and guidance in this endeavor.

Sincere thanks to Mr. Stephen Heglund, Mrs. Charlotte Neubauer, and Dr. Otto Phanstiel for all of the time and effort you have invested in this project. I am extremely grateful for all of your wisdom and insight.

Mr. Heglund and Mrs. Neubauer, I am very blessed to have had you both as teachers. Thank you for all that you have taught me and for helping me develop a life-long interest in nursing research.

## TABLE OF CONTENTS

INTRODUCTION .....	2
PROBLEM.....	4
PURPOSE.....	7
METHOD .....	8
FINDINGS.....	9
The Effects of Various Agents on Biofilm.....	9
Choosing an Antimicrobial Lock Agent: Mechanisms of Agents Used for Lock Therapy .....	10
Mechanisms of antibiotics.....	11
Mechanism of non-antibiotic antimicrobial agents.....	13
Ethanol Comparisons .....	15
Ethanol as single agent compared to other single agents.....	15
Combinations of agents compared to ethanol as a single agent.....	17
Ethanol in combination with other agents compared to ethanol as a single agent.....	18
DISCUSSION.....	20
Indications for Clinical Use.....	21
LIMITATIONS.....	23
APPENDIX A: FLOW DIAGRAM OF THE SELECTION PROCESS .....	24
APPENDIX B: TABLE OF EVIDENCE.....	i

REFERENCES ..... 35

## INTRODUCTION

The mortality rate from catheter-related bloodstream infections is 12-25% (Srinivasan, et al., 2011). In addition to adversely affecting patient outcomes, catheter-related bloodstream infections create significant economic cost to the health care system. Treating a single catheter-related bloodstream infection ranges in cost from \$4,000 to \$80,235 (Bakke, 2010). Annually, this amounts to between \$296 million and 2.3 billion (Kim, Saunders, & Yousefzadeh, 2010). This cost will now be entirely funded by hospital organizations, since the Centers for Medicare and Medicaid will no longer reimburse catheter-related bloodstream infections as of October 2008 (Kim et al.).

There are two main courses of action that can be pursued when a patient develops a catheter-related bloodstream infection: 1) The catheter can be removed, and 2) attempts can be made to salvage the catheter. A third option, inaction, is not a valid option in clinical practice as it typically results in sepsis and the death of the patient. There is an increase in costs associated with the replacement of tunneled central lines, as a surgical procedure is needed to place the new central venous catheter. The probability of adverse outcomes increases with catheter replacement. Chemotherapy and bone marrow transplantation patients may be thrombocytopenic and require a delay before reinsertion due to impaired coagulation. Adverse outcomes and increased costs could be diminished if catheters can be salvaged (Broom et al., 2008). It is preferable to avoid removing the catheter if possible because of associated costs and limited access sites in pediatric patients (McGrath et al., 2011).

Antimicrobial lock therapy is one technique used in salvaging infected catheters.

Antimicrobial lock technique involves filling the lumen of the catheter with an antibiotic or other antimicrobial agent at a high concentration. The solution is left to dwell in the lumen of the catheter (Qu, Istivan, Daley, Rouch, & Deighton, 2009). In essence, the solution is “locked” into the central line for a certain length of time. Ethanol is a potential antimicrobial lock solution that has been shown to be effective in multiple studies. Ethanol is an antimicrobial lock solution that works by denaturing microbes on a broad-spectrum level (Sherertz, Boger, Collins, Mason, & Raad, 2006). Ethanol has a bactericidal effect on both Gram positive and Gram negative bacteria due to its action of denaturing protein (Broom et al., 2008). Sherertz et al. (2006) conclude that the chances of resistance developing are “unlikely.” This statement was supported by Opilla, Kirby, and Edmond (2007), who stated that ethanol lock therapy was unlikely to cause microbial resistance.

A double-blind randomized trial that compared the prophylactic administration of ethanol compared to heparinized saline showed the ethanol does have a significant effect in preventing catheter-related blood stream infections. This study also showed that Gram-negative bacteremia was susceptible to the effects of ethanol (Sanders et al., 2008). However, a study by Slobbe, Doorduijn, and Lungtenburg (2010) found that prophylactic ethanol lock solutions instilled for fifteen minutes daily did not have a significant effect on the reduction of catheter-related bloodstream infections. The incidence in the experimental group was 0.70 and 1.19 for the control group per 1,000 catheter days (Slobbe et al.). Ethanol instilled for longer periods of time has met greater success as a therapeutic measure. Administered in conjunction to systemic antibiotics, ethanol lock therapy was effective in catheter salvage in pediatric patients (Onland, Shin, Fustar, Rushing, & Wong, 2006). Both this study and a retrospective study of pediatric

patients with intestinal failure by Jones et al. (2010) reported no adverse side effects to ethanol lock therapy. Slobbe et al. did report some adverse effects, none of which were life-threatening. A study by Crnich, Halfmann, Crone, and Maki (2005) indicated that the integrity of the selected polyetherune and silicone catheters were not significantly altered by ethanol. Based upon their findings on ethanol's efficacy as an individual agent in lock solutions, Sherertz et al. (2006) hypothesize that a synergistic effect could be achieved by combining antibiotic lock agents with ethanol.

## **PROBLEM**

Although the incidence of catheter related bloodstream infections has decreased in the past decade, the Centers for Disease Control and Prevention (CDC) reports that it is still a significant problem. Eighteen thousand catheter-related bloodstream infections occurred in 2009 in intensive care units in the United States. Twenty-three thousand catheter-related bloodstream infections occurred in inpatient wards during the same year. From 2001 data, this amounts to approximately a 58% reduction (CDC, 2011).

The treatment of catheter-related bloodstream infections with systemic antibiotics alone has several deficits. Systemic antibiotics are often ineffective in eradicating biofilm-grown bacteria, and access of the system antibiotics to the catheter lumen may be poor when systemic antibiotics alone are used. Eradicating the biofilm through systemic antibiotics alone is difficult given the multi-factorial nature of the biofilm's resistance. Planktonic organisms released by the biofilms are killed by systemic antibiotics; however, the organisms embedded in the biofilm are difficult for the systemic antibiotics to penetrate (Aslam, 2008). Catheter lock technique may be used (most often in conjunction with systemic antibiotics) to help prevent or treat catheter-related bloodstream infections. In this technique, the catheter lumen is filled with a high concentration of an antimicrobial agent during times when it is not in use (Qu et al., 2009).

A study by Polgreen, Beekmann, Diekema, and Sherertz (2010) found that only 19% of infectious disease consultants had used antimicrobial lock prophylaxis. Antimicrobial lock therapy is more common, and is often used along with systemic antibiotics in attempts to salvage catheters. Data collected in the above study found that, among infectious disease consultants using antimicrobial lock therapy, vancomycin is the most frequently used agent (Polgreen et al.).

However, Sherertz et al. (2006) compared the in vitro efficacies of various lock solutions and found vancomycin to be the least effective with a high risk of microbial resistance. This demonstrates the need for a more comprehensive comparison among lock agents.

Due to the comparatively high expense of antibiotic lock solutions and the possibility of increasing microbial resistance, other antimicrobial lock solutions would be preferable (Opilla et al., 2007). Although the Infectious Diseases Society of America has guidelines for the use of antibiotic lock solutions to treat catheter-related bloodstream infections, the routine prophylactic use of antibiotic lock solutions is currently advised against (Kim et al., 2010). However, the CDC (2011) recommends that practitioners “[u]se prophylactic antimicrobial lock solutions in patients with long term catheters who have a history of multiple catheter-related bloodstream infections despite maximal adherence to aseptic technique.” One of the concerns of the Infectious Diseases Society of America and a major contraindication to the prophylactic use of antibiotic lock solutions is the risk for microbial resistance (Casey & Elliot, 2010). A study by Venkatesh, Rong, Raad, and Versalovic (2009) cite the need for non-antibiotic measures against catheter-related bloodstream infections due to antimicrobial resistance. Ethanol is comparatively inexpensive: according to Opilla et al. (2007), the 5 milliliter ampules of 98% medical grade ethyl alcohol costs roughly \$10.00. McGrath et al. (2011) estimated the costs of an ethanol lock to be around \$16.00 (McGrath et al.) The cost of a vancomycin flush is roughly \$29.40 (Penel & Yazdanpanah, 2008).

The efficacy demonstrated in the findings of Sanders et al. (2008), Onland et al. (2006), and Jones et al. (2010), suggest that ethanol may be an efficacious agent in eradicating and preventing catheter related blood stream infections. If found to be an efficacious agent, it would be more cost effective than antibiotic lock therapy, as evidenced by the cost efficiency cited by

McGrath et al. (2011) and Opilla et al. (2007). Furthermore, the Infectious Diseases Society of America cites the risk of developing resistance as a barrier to the use of prophylactic lock therapy (Kim et al., 2010). The findings of Sherertz et al. (2006) and Opilla et al. suggest that it is unlikely that bacteria will develop a resistance to ethanol. The potential benefits of reducing antimicrobial resistance and cost effectiveness are indicative that ethanol is an agent that warrants further research in regards to its efficacy in comparison to antibiotic lock therapies currently used in practice. Ethanol lock therapy may have advantages over antibiotic lock therapy; however, the primary consideration is ethanol's efficacy in comparison to existing lock therapies in preventing catheter related blood stream infection.

## **PURPOSE**

Is ethanol lock therapy as effective as antibiotic lock solutions in the treatment and prevention of catheter-related bloodstream infections? Many other research questions arise in order to answer this question. Is ethanol effective when used as a prophylactic measure? Lastly, is ethanol most effective as a single agent or is it more efficacious when used in combination with other antimicrobial lock agents? The purpose of this thesis is to provide a comprehensive review of recent literature concerning ethanol lock therapy and its efficacy. This thesis will review studies comparing the efficacies of ethanol lock therapy to antibiotic lock therapy, and will also examine whether ethanol is more efficacious when used alone or when used in conjunction with other antimicrobial lock solutions. A comparison of the therapeutic and prophylactic efficacies of ethanol and antibiotic lock solutions is necessary to help determine if ethanol lock therapy is as effective in the treatment and prevention of catheter-related bloodstream infections and whether this technique should be used in clinical practice.

## **METHOD**

A review of literature related to central line infection reduction methods including ethanol lock and antibiotic lock therapies and their respective effects on the prevention and treatment of catheter-related bloodstream infections has been conducted. Both the therapeutic and prophylactic effects of ethanol lock therapy have been examined. The literature on antibiotic lock therapies is substantial. Therefore, the findings of this thesis consider three categories of studies. The first category compares only single agents (e.g. vancomycin, ciprofloxin, and rifampicin) to ethanol lock therapy. The second category examines the efficacy of combinations of various agents (excluding ethanol as a component) into one lock solution compared to ethanol as a single agent. The third and last category examines studies comparing the efficacy of combinations of lock agents containing compared to the efficacy of ethanol used as a single agent. Information was gathered from CINAHL, Medline, Academic Search Premier, Biological Abstracts, and Web of Knowledge databases. Articles were peer-reviewed and published in English. Restrictions were not placed on the date of publication. The studies reviewed for this thesis are interdisciplinary, including but not limited to nursing, and may be conducted in the United States or internationally.

## FINDINGS

### The Effects of Various Agents on Biofilm

A biofilm is formed when free-floating bacterial organisms (planktonic organisms) adhere to the surface of the catheter. An extracellular polysaccharide matrix is then secreted by the micro colonies of the bacteria that have begun to form. The matrix accounts for 95% of the biofilm's mass, with only 15% actually composed of living cells. Detachment of the living organisms can occur when the biofilm is overcrowded or if there is insufficient nutritional support for the biofilm. The planktonic organisms can then create new areas of colonization. The biofilm creates an environment that is more conducive to the survival of the bacteria. The first advantage is the polysaccharide matrix, which makes it difficult for antimicrobial agents to reach the bacteria and penetrate the cell wall. Free-floating organisms do not have this protection, and are therefore eradicated effectively by systemic antibiotics. The metabolism of bacteria in a biofilm also changes, giving the biofilm another defense mechanism against antibiotics. Antibiotics that affect cell wall and protein synthesis will not be as effective against organisms in a biofilm since the rate of protein and cell wall synthesis is dramatically reduced (Aslam, 2008). Another mechanism that has been hypothesized to increase the resistance of biofilms to antibiotics is the relative hypoxic environment. This environment would affect the activity of antibiotics, reducing the efficacy of the aminoglycoside class of antibiotics in particular (Stewart & Costerton, 2001). Furthermore, when the biofilm is composed of multiple organisms, the resistance of the organisms to antimicrobial agents may increase. Protective effects have been noted when *Staphylococcus epidermis* and *Candida albicans* are both part of a biofilm. The yeast

cells were more resistant to the azole family of antifungals and the efficacy of vancomycin against the bacteria was decreased due to the presence of the other organism.

Concentrations of up to 1,000-fold of antibiotics are not effective against biofilms due to these mechanisms of resistance (Aslam, 2008). Due to toxicities and adverse effects from antibiotic agents, it would not be feasible to give a patient systemic antibiotics in a concentration great enough to eradicate the biofilm. The catheter-lock technique is used in conjunction to systemic antibiotics in order to instill a high concentration of antimicrobial solution into the catheter in order to eradicate the biofilm without systemic side effects.

### **Choosing an Antimicrobial Lock Agent: Mechanisms of Agents Used for Lock Therapy**

As recommended by Berrington and Gould (2001), bactericidal agents are preferable to bacteriostatic agents for antimicrobial lock therapy. Bacteriostatic agents inhibit bacterial growth; these agents do not directly kill the cell. In contrast, cells are eradicated directly by bactericidal agents (Lehne, 2010). As stated above, biofilms are more resistant to antimicrobial agents that inhibit cell wall synthesis, as the growth rate of the biofilm is reduced in comparison to that of planktonic organisms (Donlan, 2011). In summary, an agent that can eradicate biofilms effectively must be able to function in anaerobic conditions and be able to penetrate the matrix of the biofilm.

According to the Centers for Disease Prevention and Control, there is a high occurrence of antibiotic resistant organisms in device-related infections (CDC, 2011). Data from 2006-2007 showed that 56% of *Staphylococcus aureus* were methicillin resistant (MRSA). Resistance of enterococci was also high, with 80% of *E. faecium* and 7% of *E. faecalis* having a resistance to vancomycin. Among organisms of *Pseudomonas aeruginosa*, 30% were resistant to ceftazodime, 17% were resistant to piperacillin, and 25% were resistant to carbapenems. The

rate of isolates resistant to carbapenems was also significant in *A.baumannii*, for which 29% of isolates were resistant, and *Klebsiella pneumoniae*, for which 10% of isolates were resistant (Hidron et al., 2008). Although there has been a decrease in the rates of catheter-related infections caused by Gram-negative organisms, the incidence of multidrug resistant Gram-negative bacteria is increasing (Hidron et al.). The antimicrobial lock solution chosen for treatment should be based on the causative organism. The most common organisms that cause catheter-related bloodstream infections are coagulase-negative staphylococci (Hidron et al.). The second most common cause of device-related infections is *Candida*. Antibiotic lock therapy is not as effective against *Candida* as it is against bacterial organisms since *Candida* is a fungal organism. Lock solutions with antifungal agents must be used in order to eradicate *Candida* (Hidron et al.). Another common organism is *Staphylococcus aureus*, which is more common among dialysis patients (Lederer, Riederlisdorf, & Schiffel, 2007). The rates of enterococcal catheter-related bloodstream infections are also increasing. According to Mermel et al. (2009) the appropriate protocol is to first obtain a culture to determine the causative organism. While the results of the culture are pending, the agents initially used should be effective against Gram negative bacilli and staphylococci. If the patient has a femoral access, the agent should be effective against *Candida* spp. After the results of the culture have been obtained, the regimen should be modified to treat the specific organism (Mermel et al.).

### **Mechanisms of antibiotics.**

According to the CDC (2011), the most common antibiotic agents currently used in antibiotic lock therapy are gentamicin, ciprofloxacin, amikacin, minocycline, cefazolin, ceftazidime, and vancomycin. Donlan (2011) indicates that fluoroquinolones, rifampin, and the macrolides are among the antibiotics that are more successful in penetrating the biofilm.

According to Lehne (2010), there are seven major classes of mechanisms through which antibiotics work. One of these, suppressing viral replication, is not of concern when considering catheter-related bloodstream infections. The remaining mechanisms of antibiotics are to inhibit cell wall synthesis (bacteriostatic or bactericidal), to disrupt the cell membrane (bacteriostatic or bactericidal), to interfere with synthesis or integrity of bacterial deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), or to disrupt specific biochemical reactions (Lehne). The macrolides are broad-spectrum, bacteriostatic inhibitors of protein synthesis (Lehne). Gentamicin and tobramycin are both aminoglycosides, which are bactericidal inhibitors of protein synthesis. However, it is important to note that aminoglycosides are effective against Gram-negative bacteria but not against most Gram-positive bacteria. In addition, anaerobes are not killed by aminoglycosides (Lehne). Lehne remarks that “[f]or that same reason, aminoglycosides are inactive against facultative bacteria when these organisms are living under anaerobic conditions” (Lehne). As previously noted, the anaerobic conditions of the biofilm may lead to resistance to aminoglycosides (Aslam, 2008). Vancomycin is bactericidal and works by inhibiting cell wall synthesis. It is not effective against gram-negative bacteria (Lehne). Ciprofloxacin is a fluoroquinolone that is bactericidal and inhibits bacterial enzymes needed for DNA replication. It is a broad spectrum agent, but it is not effective against anaerobes (Lehne). The Healthcare Infection Control Practices Committee is particularly concerned with microbial resistance to vancomycin. For this reason, it advises that only certain severe cases receive antibiotic lock therapy containing vancomycin and that it is not a routinely used agent (Donlan). However, the development of resistance is an issue of concern with all antibiotic agents (Lehne).

### **Mechanism of non-antibiotic antimicrobial agents.**

Ethanol, trisodium citrate, and taurolidine are other antiseptic, non-antibiotic agents that have been studied in antimicrobial lock therapy (CDC, 2011). Ethanol works by denaturing protein (Lehne, 2010). Due to its ability to denature protein, ethanol is effective against both Gram positive and Gram negative bacteria (Broom et al., 2008). It has a very small molecular weight and is hydrophilic, which makes penetration of the biofilm possible (Donlan, 2011).

### ***Efficacy of ethanol as an antimicrobial lock agent.***

According to Venkatesh et al. (2009), the most frequently causative organisms for catheter related blood stream infections are *Staphylococcus epidermis* and *Candida albicans*. Other studies examined for this paper examined the effects of ethanol on *Methicillin-resistant Staphylococcus aureus*, *Methicillin-sensitive Staphylococcus aureus*, *Methicillin resistant Staphylococcus epidermis*, *Psuedomonas aeruginosa*, *E. coli*, *Klebsiella pneumonia*, and *Staphyloccocous epidermis*.

An *in vitro* study by Henry-Stanley, Shepherd, Wells, and Hess (2009), tested the efficacy of ethanol against *Staphylococcus aureus* growing within silastic catheters. The biofilms were grown *in vitro* for 48 hours using a nutrient source to imitate a clinical setting. The catheter segments were then placed in 70% ethanol. The segments were placed in the ethanol for times varying from five minutes to twenty-four hours, but there was not a significant difference in results secondary to immersion time. Initial cultures showed that there were no viable bacteria. The catheter segments were then reattached to the growth medium for 24 hours to test for regrowth. No regrowth occurred in the ethanol treated segments. Another study by Chambers, Peddie, and Pithe (2006) showed that exposure to 70% ethanol killed planktonic organisms in seconds. However, longer dwell times (the amount of time the solution is left in the lumen of the

catheter) were needed to eradicate established biofilms. A four hour exposure to 70% ethanol eradicated all viable cells in *in vitro* biofilms of *Staphylococcus aureus* (strain ATCC 25923 and three clinical isolates), *Staphylococcus epidermis* (strain ATCC 49134 and three clinical isolates), *E. coli* (strain ATCC 25922 and three isolates), *Pseudomonas aeruginosa* (strain ATCC 27853 and four clinical isolates), *Klebsiella pneumonia* (three clinical isolates), and *Candida albicans* (four clinical isolates). After the cultures were allowed to incubate for 40 hours, there was regrowth of *Candida albicans* after 1-2 hours of exposure to the ethanol lock. However, there was no regrowth after a four hour dwell time (Chambers et al.). Certain isolates of *Klebsiella pneumonia* and *P. aeruginosa* also required a four hour dwell time to completely prevent regrowth. All other organisms noted above did not have any regrowth after a one hour dwell time. A one hour dwell time effectively eradicated all of the organisms in the study and prevented regrowth for biofilms that were incubated for 16 hours (Chambers et al.).

Ethanol lock therapy appears to be tolerated well by patients, and has been used successfully in pediatric populations. One retrospective study examined ethanol lock therapy (a 70% concentration) instilled into a central venous catheter as a single agent used in conjunction with systemic antibiotics for short-term therapy less than or equal to three days (McGrath et al., 2011). The rate of success in eradicating the catheter related blood stream infections was 86% with a 78% rate of central line retention and salvage. This study estimated that the eradication rate using systemic antibiotics alone would be 50% (McGrath et al.). Several other studies examining the effects of ethanol lock therapy in comparison to a placebo and in clinical practice are included in Table 1.

## Ethanol Comparisons

### Ethanol as single agent compared to other single agents.

An in vitro study by Qu et al. (2009) found that six strains of coagulase-negative staphylococci were more effectively eradicated by ethanol than by oxacillin, gentamicin, vancomycin, ciprofloxacin, or rifampin. The minimal effective concentration needed for biofilm eradication was compared. All cells were killed by ethanol at a 20% concentration. Gentamicin was the only antibiotic to eradicate the biofilm cells of two strains overnight at a comparatively high concentration of 10,000 mcg/ml<sup>-1</sup>. Oxacillin and vancomycin (both at concentrations of 5,000 mcg/ml<sup>-1</sup>) did not completely kill the cells of the biofilm after an overnight exposure. At a full 24 hours of exposure, all isolates were sterilized by rifampicin and ciprofloxacin. However, the concentration of these agents needed to achieve sterilization was comparatively high, ranging from 32-128 mcg/ml<sup>-1</sup> for ciprofloxacin and 256-512 mcg/ml<sup>-1</sup> for rifampicin. The minimal effective concentration for ethanol against all six strains was consistently 20% and was completely eradicated isolates within 4 hours (Qu et al.).

*Staphylococcus aureus*, *Staphylococcus epidermis*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *Candida albicans* were more effectively eradicated by a 60% ethanol solution than by a 46.7% trisodium citrate solution (Balestrino et al., 2009). Trisodium citrate is not an agent that is currently recommended against for clinical use per the CDC as of 2011. Although it has shown to be efficacious in lowering the rate of catheter-related bloodstream infections, life-threatening hypocalcemia, cardiac dysrhythmias, and death can occur if it is infused too rapidly (CDC, 2011). Systemic side effects of ethanol lock therapy noted in clinical practice have included dizziness, lightheadedness, and nausea (Dannenber, Blerbach, Rothe, Beer, & Korholz, 2003).

An in vitro study by Venkatesh et al. (2009) compared ethanol (12.5%) to Ethylenediaminetetraacetic acid (EDTA), *N*-acetylcysteine, and talactoferrin. The results of the study indicated ethanol was also the most efficacious of the four agents in reducing the biomass of *S. epidermis* (strain ATCC 55133). All four agents significantly reduced a polymicrobial film consisting of *S. epidermis* (strain ATCC 55133) and *Candida albicans* (strain ATCC 32354); for this biofilm, ethanol was the least efficacious of the four agents. Ethanol was the only agent of the four listed above to significantly reduce *Candida albicans* (strain ATCC 32354) in polymicrobial biofilms as compared to the control.

The in-vitro study by Chaudhury, Rangineni, and Venkatramana (2012) used eight isolates of methicillin resistant staphylococci from colonized central venous catheters. Gentamicin, ciprofloxacin, and vancomycin were each used in varying concentrations of 1,5, and 10 mg/mL and compared to ethanol in concentrations of 20%, 40%, and 80%. All of the isolates were eradicated by the 40% ethanol solution within one hour. The isolates were not eradicated by the gentamicin, ciprofloxacin, or vancomycin within a period of 24 hours.

According to the Infectious Disease Society of America, the efficacy rates of antibiotic lock therapy vary. The efficacy rate was roughly 77 % in 21 open studies of antibiotic lock therapy (Mermel et al., 2009). This is only a rough estimate, however, as the results will depend upon the conditions in which the study is conducted. The most difficult organisms to treat with antibiotic lock therapy are *Candida albicans*, a fungal infection, and *Staphylococcus aureus*. One study reports only a 50% success rate in treating *S. aureus* with antibiotic lock therapy (Mermel et al.). While there is some variance among studies, the efficacy of ethanol in treating existing infection is usually comparable to antibiotic lock solutions or higher. Onland et al. (2006) found a success rate of 88%, Cober et al. (2011) had a success rate of 73%, McGrath et al. (2011)

showed an efficacy rate of 86%, and Valentine's (2011) study in pediatric patients sterilized 92% of the catheters.

Ethanol as a single agent shows significant promise, but further research is needed in regard to the optimal concentration and dwell time. A concentration of 70% ethanol is the most efficacious for topical antiseptics, which efficacy declines when concentrations over 70% are used topically (Lehne, 2010). Further research is needed to see if ethanol instilled as a lock solution follows these findings. In the *in vitro* study by Venkatesh et al. (2009), the authors speculate that a concentration of ethanol >12.5 % may be more efficacious. The indications of Dannenberg, et al. (2003), were that concentrations of ethanol used in clinical practice should be over 40%. Most of the studies examined used ethanol in a concentration of 70% or lower. It appears that a 100% concentration of ethanol may not be suitable for clinical use. One letter to the editor citing use of 100% ethanol in three patients found that the high concentration caused precipitation and occlusion of the line, necessitating removal (Laird, Soutar, & Butcher, 2005). Catheter occlusion was noted in two other studies reviewed in this paper. Two catheters became occluded in a study by Wales, et al. (2011). However, the number of catheter replacements decreased from  $5.6 \pm 4.1$  per 1000 catheter days to  $0.3 \pm 0.2$  per 1000 catheter days. A study by Kayton et al. (2010) was discontinued after three of the catheters became occluded. This may be due in part to the overnight dwell time. Further research is needed to determine the optimal dwell time and concentration of ethanol lock therapy, particularly when it is used prophylactically long term.

### **Combinations of agents compared to ethanol as a single agent.**

The *in vitro* study by Qu et al. (2009) also examined the efficacy of combinations of antibiotics compared to ethanol. The combinations of antibiotics that were effective in

preventing regrowth of various strains of *S. epidermis* were gentamicin and rifampicin in a concentration of 16:4 mcg/ml<sup>-1</sup> (effective against one strain); gentamicin, vancomycin and rifampicin in a concentration of 16:32:4 mcg/ml<sup>-1</sup> (effective against one strain); and gentamicin, ciprofloxacin, and rifampicin in a concentration of 16:4:4 mcg/ml<sup>-1</sup> (effective against one strain). The study also compared ethanol to single antibiotic lock agents, and found that a concentration of 20% ethanol was found to be the minimal concentration efficacious against all six strains.

Sherertz et al. (2006) compared the efficacy of ethanol, minocycline-edetate calcium disodium (MEDTA), and taurolidine polyvinylpyrrolidone against rifampin, ciprofloxacin, vancomycin, and minocycline. In this study, ethanol was used as a single agent and compared to antibiotic agents used both individually and in combination with one another. *S. aureus* was more effectively eradicated by ethanol (3.6-3.9 log units of killing at 2 and 4 hours) compared to all other single and combination lock agents.

#### **Ethanol in combination with other agents compared to ethanol as a single agent.**

Current studies indicate that ethanol may have a synergistic effect with antibiotics and chelating agents such as ethylenediaminetetraacetic acid (EDTA) and trisodium citrate. A study examining biofilm growth in vitro showed the regrowth of *methicillin-resistant staphylococcus aureus* (MRSA) and *C. parapsilosis* was not completely prevented by 25% ethanol. However, MRSA and *C. parapsilosis* organisms were completely eradicated and did not regrow after exposure to a low concentration of ethanol (25%) used in conjunction with EDTA and minocycline. This triple combination was found to be more effective than a combination of minocycline and EDTA, minocycline in combination with 25% ethanol, EDTA in conjunction with 25% ethanol, or 25% ethanol as a single agent (Raad, Hanna, Dvorak, Chaiban, & Hachem,

2007). The concentration of ethanol was comparatively low, and more research is needed to see if the effects of a higher concentration may yield different results. However, it appears that low concentrations of ethanol may have a synergistic effect when used with minocycline and EDTA (Raad et al.). According to an in vitro study by Takla, Zelenitsky, and Vercainge (2007), one hour of exposure to a 30% ethanol, and 4% trisodium citrate lock solution also resulted in eradication of MRSA, MSSA, MRSE, *P. aeruginosa* and *E. coli*. Nett, Guite, Ringeisen, Holoyda, and Andres (2008) found that ethanol had a synergistic effect with fluconazole in eradicating *Candida albicans*.

Ethanol may have a synergistic effect with antibiotics. In the in vitro study conducted by Venkatesh et al. (2009), ethanol has been shown to have a synergistic effect with nafcillin and vancomycin in reducing three strains of *S. epidermis*. Synergistic effects between ethanol and amphotericin B and ethanol combined with fluconazole were also noted in reducing the biomass of two strains of *Candida albicans* (Venkatesh et al.).

## DISCUSSION

The purpose of this review was to compare the efficacies of ethanol lock therapy to agents currently used for antimicrobial lock therapy and prophylaxis. The major finding of this paper is that ethanol is as effective or more effective than the majority of antibiotic lock solutions currently used to treat catheter-related bloodstream infections. Studies have shown that ethanol lock therapy is effective in eradicating biofilms of organisms that frequently cause catheter-related bloodstream infections, including *Staphylococcus epidermis*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *E. coli*, and *Candida albicans* (Chambers et al., 2006). Ethanol also has a synergistic effect with other antimicrobial agents. A low concentration of ethanol used in conjunction with other agents has been shown to be effective against antibiotic resistant organisms such as MRSA (Raad et al., 2007). The cost of ethanol lock therapy is significantly lower than antibiotic lock therapy, and ethanol lock therapy is generally well tolerated by patients. Few side effects occurred systemically, and were limited to non-life threatening side effects including nausea, taste of alcohol, and dizziness. Ethanol also has been shown to have a synergistic effect when combined with antibiotics and antifungals in a lock solution. When used prophylactically in patients experiencing recurring catheter-related bloodstream infections, ethanol lock therapy has been shown to significantly lower the rate of infection and the number of catheter replacements

The use of ethanol lock therapy appears relatively safe for clinical practice. Long-term ethanol lock therapy does not appear to significantly alter the structure of silicone catheters, but studies have indicated that it may alter the structure of polyurethane catheters. Many antibiotic lock solutions will precipitate if the concentration is above the recommended level (Mermel et

al., 2009) and the same phenomenon has been noted for ethanol lock therapy (Laird et al., 2005). Catheter occlusion was noted in three studies reviewed in this paper. Catheter occlusion was not noted when ethanol (in concentrations of 70% or less) was used short-term to treat active infections, but appears more likely when high concentrations (over 70%) of ethanol are used or during long-term prophylactic therapy. Further research is needed to determine the optimal dwell time and concentration of ethanol lock therapy. Clinical studies are needed to establish the safest and most effective guidelines for both ethanol lock prophylaxis and for ethanol lock therapy for the treatment of active infections. Another area where further research is needed concerns ethanol combined with anticoagulants. The CDC (2011) states that antibiotic locks are usually combined with an anticoagulant such as heparin or EDTA. None of the studies presented in this paper examined the use of ethanol combined with an anticoagulant in a clinical or *in vivo* setting. The combination of EDTA and ethanol appears to be promising. EDTA has anticoagulant properties (CDC) and has been shown to synergistically enhance the effects of ethanol (Raad et al., 2007). Lastly, additional research on the sensitivity to various organisms to ethanol is needed.

### **Indications for Clinical Use**

Ethanol is an agent that has been shown to be effective in treating existing catheter-related bloodstream infections in conjunction with systemic antibiotics. It has been shown to have equal or greater efficacy to several antibiotic and antimicrobial agents used in practice and should be considered as an agent for the treatment of catheter-related bloodstream infections. It is effective when used as a single agent or when used in combination with other antimicrobial agents. Clinical studies have shown that prophylactic ethanol lock therapy is effective in reducing the rates of infection and catheter removal. Although the Infectious Diseases Society of

America currently does not recommend routine prophylactic lock therapy using any agent, ethanol lock prophylaxis may be of consideration in patients who have recurring catheter-related bloodstream infections. It is recommended that cultures be obtained before beginning ethanol lock therapy in order to determine that the causative organism is sensitive to ethanol. According to the recommendations of the Infectious Diseases Society of America, 70% ethanol may be considered for a mixed culture of Gram positive and Gram negative organisms (Mermel et al., 2009).

## **LIMITATIONS**

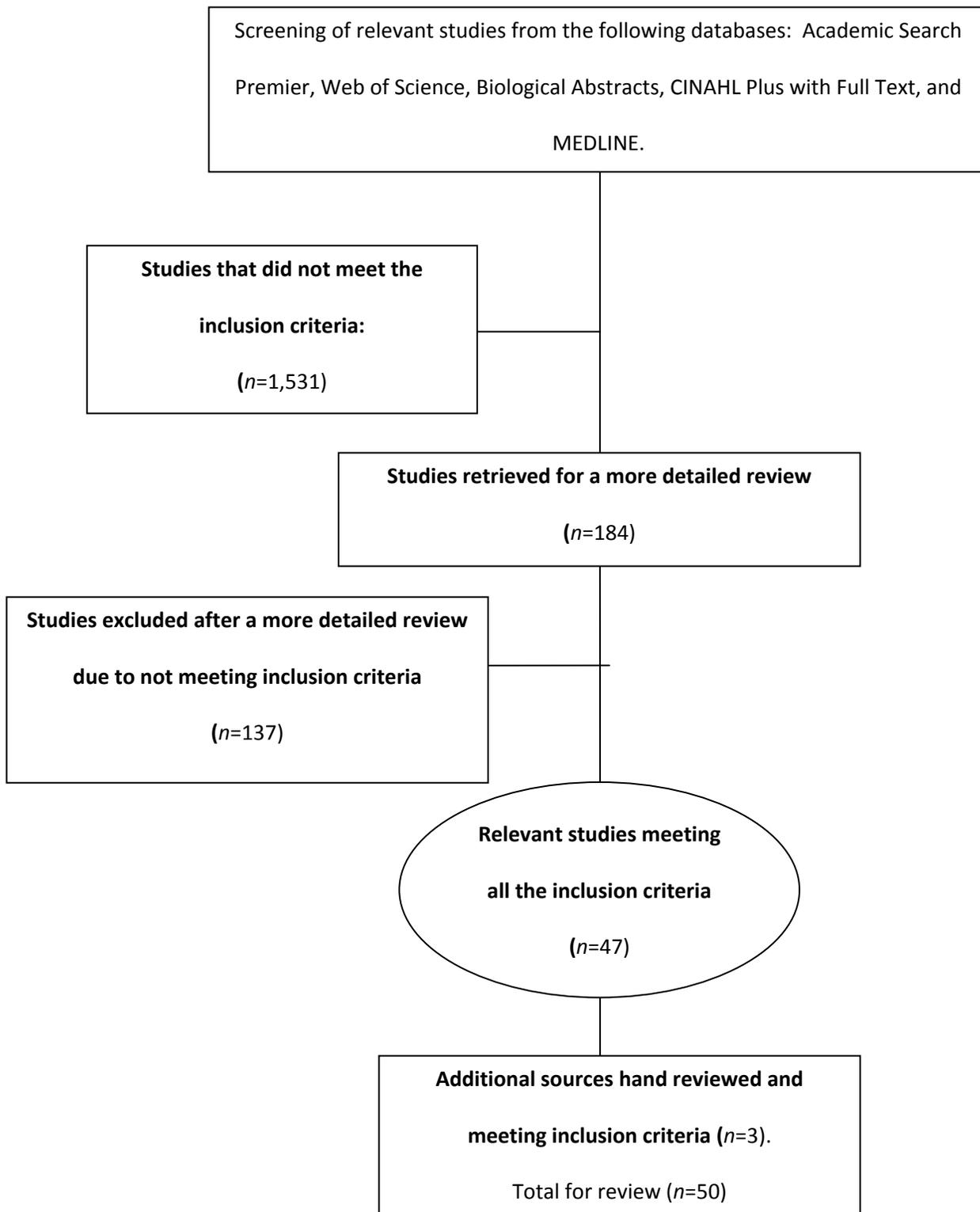
The limitations of this study include the lack of extensive research comparing ethanol lock therapy to existing lock solutions. Although there were numerous studies comparing ethanol to a placebo such as heparinized saline, there were only a few studies comparing ethanol to antibiotic or other antimicrobial lock agents currently used in clinical practice. Among the studies found and cited throughout this review, the concentration of ethanol and antimicrobial lock solutions varied with each study. Limitations for clinical practice include the lack of data concerning the optimal concentration and dwell time. There is currently very little data comparing combinations of antibiotic and antimicrobial lock therapies to ethanol as a single agent. Culturing the organism before beginning ethanol lock therapy is necessary. There are currently no evidenced-based guidelines for practitioners regarding the susceptibility of various organisms to ethanol. The studies cited in this paper provide a starting point, but further research is needed to determine guidelines for the use of ethanol lock therapy in clinical practice.

## **APPENDIX A: FLOW DIAGRAM OF THE SELECTION PROCESS**

## FLOW DIAGRAM OF THE STUDY SELECTION PROCESS

Key search terms: catheter\*, ethanol\*

Inclusion criteria: English only, peer-reviewed, full-text only. No restrictions placed on date of publication



## **APPENDIX B: TABLE OF EVIDENCE**

## TABLE OF EVIDENCE

Inclusion criteria: English only, peer-reviewed, full-text only. No restrictions placed on date of publication. Includes the search terms: catheter\* and ethanol\*

Exclusion criteria: Articles not meeting the inclusion criteria listed above or pertaining to the use of ethanol in central venous lines for uses other than catheter-related bloodstream infections (i.e. prevention of occlusion).

Articles	Design	Findings
McGrath et al., 2011	Retrospective review	Seventy percent ethanol was instilled for 4 to 25 hour dwell times with systemic antimicrobials. This study involved 59 pediatric patients (ages 2 months to 19 years). There was an 86% eradication rate for catheter-related bloodstream infections and a central line retention rate of 78%. The ethanol lock therapy was tolerated well. This study has a 95% confidence interval.
Bijo et al., 2011	Retrospective study	This retrospective study examined 31 adult patients receiving home parenteral nutrition from January 2006 to August 2009. Between parenteral nutrition infusion cycles, the central venous catheter was locked with 70% ethanol. Admissions for catheter-related bloodstream infections dropped from 273 prior to ethanol lock therapy to 47 post-ethanol lock therapy. The rate of catheter-related admissions was 10.1 per 1,000 catheter days prior to ethanol lock therapy and 2.9 per 1,000 catheter days after ethanol lock therapy. No side effects or complications were reported.
Blackwood, Klein, Willers, Mody, Teitebaum, & Cober, 2011	Case study	Ethanol lock therapy and systemic antifungals were used for successful treatment of three consecutive cases of catheter-related bloodstream infection caused by <i>Candida</i> spp.
Chambers, Pithie, Gallagher, Liu, Charles, & Seaward,	Animal trial	A double-blind animal trial was conducted using a cross over design. The sheep were catheterized twice, and for both times the

2007		central venous lines were inoculated with <i>S. epidermis</i> . One catheter was treated with ethanol (70% and water), and the control was heparinized normal saline. There were eight days between placement of the first and second central lines. After a three hour lock period, sterilization was achieved in 9 of 11 catheters using ethanol lock therapy, and in 0 of 11 catheters using heparinized saline.
Ackoundou-N'guessan et al., 2006	Case study	A 60% ethanol lock solution was started on day 24 of a catheter-related bloodstream infection of a 70 year old female with sepsis. The causative organism was methicillin-resistant <i>Staphylococcus aureus</i> . Previous treatment with vancomycin and gentamycin were unsuccessful and resulted in the removal of the catheter on day 18. The catheter was changed again on day 22 due to sepsis and catheter dysfunction. The third catheter on day 24 was locked with 60% ethanol. All subsequent blood cultures were sterile. Lock technique was stopped on day 53 with no adverse effects or catheter dysfunction.
Crnich, Halfmann, Crone, & Maki, 2005	In vitro study	Polyetherurethane and silicone catheters were locked with a 70% ethanol solution for approximately 10 weeks. Their integrity was then compared to a control group of the same catheters that were left empty and were not filled with a lock solution. There was not a statistically significant difference in force at break between the ethanol-filled catheters and the control group. There were slight differences in elasticity and slight swelling of the walls of the polyethurethane occurred when locked with the ethanol solution for 10 weeks. These measures were not affected in the silicone catheters.
Genu et al., 2007	In vitro study	This in vitro study examined the effects of

		<p>ethanol on the mechanical properties of silicone catheters. For fifteen days, catheters were locked with 0.9% sodium chloride, 95% ethanol, and 60% ethanol. The catheters immersed in 95% ethanol were examined using scanning electron microscopy and did not have any damage to the surfaces of the catheter. Silicone was released from the catheter into the solution. In contrast, the 60% ethanol did not have any silicone released into the solution and was comparable to the normal saline regardless of exposure time.</p>
<p>Raad, Hanna, Dvorak, Chaiban, &amp; Hachem, 2007</p>	<p>In vitro comparison of the efficacy of 25% ethanol, minocycline, EDTA, and combinations of the above agents.</p>	<p>Ethanol may have a synergistic effect with minocycline and EDTA. The most efficacious agent in completely preventing regrowth of MRSA and <i>C. parapsilosis</i> was a triple combination of minocycline, EDTA, and 25% ethanol.</p>
<p>Maharaj, Zelenitsky, &amp; Vercaigne, 2008</p>	<p>In vitro study</p>	<p>All isolates of <i>Candida albicans</i> were eradicated within an hour exposure to a combination of 30% ethanol and 4% trisodium citrate.</p>
<p>Cober, Kovacevich, &amp; Teitelbaum, 2011</p>	<p>Retrospective study</p>	<p>This study examined the effects of long-term prophylaxis using ethanol lock therapy in pediatric patients. Out of 15 patients, 73% remained infection free. The rate of catheter repair was elevated after initiation of ethanol lock therapy. The rate of BSI per 1,000 catheter days was initially 8.0 and was 1.3 after ELT. Noted side effects included one incidence of thrombosis, difficulty withdrawing blood, and increased need for repair of the device.</p>
<p>Heng, et al., 2011</p>	<p>Controlled non-</p>	<p>This study noted an increase of 2-13% in catheter dysfunction during short-term ethanol</p>

	crossover cohort study	lock therapy with tunneled silicon catheters. Removal of the catheter was not necessary for any of the 30 patients. Efficiency of dialysis was not decreased.
Kayton et al., 2010	Clinical trial	A prophylactic 70% ethanol lock solution was administered overnight to 12 pediatric patients. This study was discontinued after three of the catheters became occluded.
Sanders, et al. 2011	Clinical trial	This clinical trial conducted in Australia examined the prophylactic use of a 70% ethanol lock. Blood stream infections occurred in 9% of the group receiving ethanol lock therapy and in 37% of the control group receiving heparinized saline.
Shenep, et al., 2011	In vitro study	Seventy percent ethanol showed the greatest antimicrobial activity within the shortest incubation periods when compared to heparin with preservative parabens or 0.9% benzyl alcohol. The organisms used in the study were <i>Candida albicans</i> , <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Bacillus cereus</i> , and <i>Staphylococcus epidermis</i> .
Slobbe et al., 2010	Clinical trial	This study examined the prophylactic effect of ethanol lock therapy. Patients were either prophylactically given ethanol lock therapy or a placebo. The rate of infection for patients who received the ethanol locks prophylactically for fifteen minutes daily was 0.70 per 1,000 catheter days. The authors conclude that there was a non-significant reduction of 41%. For the control group, the rate of infection was 1.19 per 1,000 catheter days. Side effects in the experimental group included one episode of syncope, taste of ethanol, and facial flushing. One catheter in the experimental group was removed due to rupture of one of the lumens.

Sherertz, Boger, Collins, Mason, & Raad, 2006	In vitro study	Ethanol as a single agent was superior in eliminating <i>Staphylococcus aureus</i> organisms in 2-4 hours.
Valentine, 2011	Retrospective study	This study in pediatric patients aged 77 days through 20 years. Twenty-six central venous catheters were treated using a 70% ethanol lock. Sterilization was achieved in 92% of catheters. Single doses of ethanol lock therapy were used in 13 of the catheter-related bloodstream infections, and multiple doses were required for the other infections.
Broom et al., 2008	Retrospective study	This study examined the efficacy of 70% ethanol lock therapy in conjunction with systemic antibiotics. The mean catheter retention rate was 47 days and the median was 36 days in 15 out of 17 patients. The only side effect noted was a patient described tasting alcohol.
Qu, Istivan, Daley, Rouch, & Deighton, 2009	Clinical in vitro trial	Ethanol was more effective in eradicating coagulase-negative staphylococci than oxacillin, gentamicin, vancomycin, ciprofloxacin, and rifampin.
Laird, Soutar, & Butcher, 2005.	Letter to the editor, clinical use	Use of 100% ethanol for 24 hrs. in 3 cases of catheter related blood stream infections in a Scottish hospital led to line precipitation and occlusion leading to removal of the catheter.
Takla, Zelenitsky, & Vercainge, 2007	In vitro trial	One hour of exposure to a 30% ethanol, and 4% trisodium citrate lock solution resulted in eradication of MRSA, MSSA, MRSE, P. aeruginosa and E. coli.
Bell, Jayaraman, & Vercaigne, 2006	In vitro study	A 30% ethanol and 4% trisodium citrate solution was locked into catheters for 9 days at 37 degrees Celsius. Less force was needed to break the catheter that had been filled with the ethanol and trisodium citrate solution than the catheters filled with trisodium citrate or

		heparin. Elongation at break was also less for the ethanol and trisodium filled catheters. The ethanol and trisodium catheter After 9 weeks, 11.5 kg of force could be applied to the ethanol and trisodium citrate locked catheter and the ability to stretch after locking was to 22 times the original length.
Jones et al., 2010	Retrospective review	The retrospective review examined the prophylactic use of 70% ethanol lock therapy three times a week in pediatric patients receiving parenteral nutrition. The rate of infection prior to initiation was 9.9 per 1,000 catheter days. During ethanol lock therapy, the rate of infection was 2.1 per 1,000 catheter days. The study's population was 23 patients.
Balestrino et al., 2009	In vitro study	This trial compared 46.7% trisodium citrate to a 60% ethanol. The organisms used in the comparison were <i>Staphylococcus aureus</i> , <i>S. epidermis</i> , <i>Klebsiella pneumonia</i> , <i>Pseudomonas aeruginosa</i> , and <i>Candida albicans</i> . TSC had a significant bactericidal effect but did not fully eradicate any sessile organisms of the above bacteria. Twenty-four hour exposure to TSC resulted in the eradication of <i>P. aeruginosa</i> . A 20-minute exposure to ethanol (60%) resulted in eradication in all of the above planktonic organisms.
Rajpurkar et al., 2009	Case studies of three patients with hemophilia A undergoing ethanol lock therapy.	Three cases of hemophilia A patients with catheter-related bloodstream infections resistant to vancomycin were treated using ethanol lock therapy. The infections were eradicated in all three patients with no noted side effects.
Mouw, Chessman, Leshner, & Tagge, 2008	Retrospective review	This study examined the prophylactic use of ethanol lock therapy in ten children with short bowel syndrome who were receiving home parenteral nutrition. Seventy percent ethanol

		<p>was instilled daily for 4 to 14 hours. Five patients had an initial period without prophylactic ethanol lock therapy. The incidence of infection during this time was 11.15 per 1,000 catheter days. When these patients were placed on prophylactic ethanol lock therapy, the incidence of infection was 2.06 per 1,000 catheter days. Five patients received ethanol locker therapy throughout their treatment, and had an infection rate of 1.85 per 1,000 catheter days. No adverse effects were noted.</p>
<p>Onland, Shin, Fustar, Rushing, &amp; Wing-Yen, 2006</p>	<p>Retrospective review</p>	<p>Seventy percent ethanol was used in 40 pediatric patients. Clearance of the organism was achieved in 88% of the treated episodes. Treatment was successful in 94% of monomicrobial isolates and in 75% of polymicrobial isolates.</p>
<p>Opila, Kirby, &amp; Edmond, 2007</p>	<p>Retrospective review</p>	<p>This study examined the incidence of catheter-related bloodstream infections in nine patients with recurring infections before and during prophylactic ethanol lock therapy (25-70% with a dwell time between 2-4 hours). The rate of catheter changes prior to initiating therapy was 7.0 per 1,000 days. After prophylactic ethanol lock therapy, this sample of patients experienced 0.3 catheter changes per 1,000 days. The incidence of infection was 8.3 per 1,000 catheter days prior to initiating therapy and 2.7 per 1,000 catheter days in this sample of nine patients. Transient dizziness and nausea were the only noted side effects.</p>
<p>Pomplun, Johnson, Johnston, &amp; Kolesar, 2007</p>	<p>In vitro study</p>	<p>This study examined the stability of 50% ethanol stored in syringes at room temperature, unprotected from light. A concentration of 47.08% was the mean for all samples older than 28 days. According to the author's interpretation, the findings of this study indicate</p>

		that a stability period of 28 days is typical of 50% ethanol stored at room temperature.
Wales et al., 2011	Retrospective review	This study compared the rates of catheter-related bloodstream infection in 10 pediatric patients dependent on parenteral nutrition before and after receiving prophylactic ethanol lock therapy. The rate prior to ethanol lock therapy was 5.6 per 1,000 catheter days, and 0.3 per 1,000 catheter days after receiving ethanol lock prophylaxis (70% ethanol). Two of the catheters were removed due to thrombosis. “Central venous catheter replacements also decreased from $5.6 \pm 4.1$ per 1000 catheter days to $0.3 \pm 0.2$ per 1000 catheter days after ethanol lock therapy” (Wales et al., 2011).

## REFERENCES

- Ackoundou-N'guessan, C., Heng, A., Guenu, S., Charbonne, F., Traore, O., Detiex, P., & Souweine, B. (2006). Ethanol lock solution as an adjunct treatment for preventing recurrent catheter-related sepsis—first case report in a dialysis setting. *Nephrology Dialysis Transplantation*, *21*(11), 3339-3340.
- Aslam, S. (2008). Effect of antibacterials on biofilms. *American Journal of Infection Control*, *36*(10), 175.
- Bakke, C.K. (2010). Clinical and cost effectiveness of guidelines to prevent intravascular catheter-related infections in patients on hemodialysis. *Nephrology Nursing Journal*, *37*(6), 601-162.
- Balestrino, D., Souweine, B., Charbonnel, N., Lautrette, A., Aumeran, C., Traore, O., & Forestier, C. (2009). Eradication of microorganisms embedded in biofilm by an ethanol-based catheter lock solution. *Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association – European Renal Association*, *24*(10), 3204-3209.
- Berrington, A., & Gould, F. (2001). Use of antibiotic locks to treat colonized central venous catheters. *Journal of Antimicrobial Chemotherapy*, *48*(5), 597-603.
- Blackwood, R., Klein, C., Micel, L., Willers, M., Mody, R., Teitelbaum, D., & Cober, M. (2011). Ethanol locks therapy for resolution of fungal catheter infections. *Pediatric Infectious Disease Journal* *30*(12), 1105-1107.

- Bowen, A., & Carapetis, J. (2011). Advances in the diagnosis and management of central venous access device infections in children. *Advances in Experimental Medicine and Biology*, 697, 91-106.
- Broom, J., Woods, M., Allworth, A., McCarthy, J., Faoagali, J., Macdonald, S., & Pithie, A. (2008). Ethanol lock therapy to treat tunneled central venous catheter-associated blood stream infections: Results from a prospective trial. *Scandinavian Journal of Infectious Diseases*, 40(5), 399-406.
- Carlson, R., & Patterson, T. (2010). A pioneer approach to preventing central venous catheter infections. *Critical Care Medicine*, 38(11), 2255-2257.
- Casey, A., & Elliot, T. (2010). Prevention of central venous catheter-related infection: Update. *British Journal of Nursing*, 19(2), 78-87.
- Chambers, S., Peddie, B., & Pithie, A. (2006). Ethanol disinfection of plastic-adherent micro-organisms. *Journal of Hospital Infection*, 63(2), 193-196.
- Chambers, S., Pithie, A., Gallagher, K., Liu, T., Charles, C., & Seaward, L. (2007). A prospective double-blind randomized trial comparing intraluminal ethanol with heparinized saline for the prevention of catheter-related bloodstream infection in immunosuppressed haematology patients. *Journal of Antimicrobial Chemotherapy*, 62(4), 809-809.
- Chaudhury, A., Rangineni, J., & Venkatramana, B. (2012). Catheter lock technique: In vitro efficacy of ethanol for eradication of methicillin resistant *Staphylococcal* biofilm compared to other agents. *FEMS Immunology and Medical Microbiology*. Advance online publication. doi:10.1111/j.1574-695X.2012.00950.x

- Crnich, C.J., Halfmann, J.A., Crone, W.C., & Maik, D.G. (2005). The effects of prolonged ethanol exposure on the mechanical properties of polyurethane and silicone catheters used for intravascular access. *Infection Control and Hospital Epidemiology* 26(8), 708-714.
- Cober, M., Kovacevich, D., & Teitelbaum, D. (2011). Ethanol-lock therapy for the prevention of central venous access device infections in pediatric patients with intestinal failure. *Journal of Parenteral and Enteral Nutrition*, (35)1, 67-73.
- Dannenberg, C., Bierbach, U., Rothe, A., Beer, J., Korholz, D. (2003). Ethanol-lock technique in the treatment of bloodstream infections in pediatric oncology patients with broviac catheter. *Journal of Pediatric Hematology/Oncology*, 25(8), 616-621.
- Donlan, R. (2011). Biofilm elimination on intravascular catheters: Important considerations for the infectious disease practitioner. *Clinical Infectious Diseases*, 52(8), 1038-1045
- Genu, S., Heng, A., Charbonne, F., Galmier, M., Charles, F., Deteix, P., Souweine, B., & Lartigue, C. (2007). Mass spectrometry and scanning electron microscopy study of silicone tunneled dialysis catheter integrity after an exposure of 15 days to 60% ethanol solution. *Rapid Communication in Mass Spectrometry*, 21(2), 229-236.
- Henry-Stanley, M., Shepherd, M., Wells, C., & Hess, D. (2009) Selected factors affecting *Staphylococcus aureus* within silastic catheters. *Journal of Surgical Research*, 161(2), 202-208.
- Heng, A., Abdekader, M., Diaconita, M., Nony, A., Guerraoui, A., Cailot, N., & Souweine, B. (2011). Impact of short term use of interdialytic 60% ethanol lock solution on tunneled silicone catheter dysfunction. *Clinical Nephrology*, 75(6), 534-541.

- Hidron, A., Edwards, J., Patel, J., Horan, T., Sievert, D., & Pollock, D. (2008). NHSN annual update: Antimicrobial resistant pathogens associated with healthcare-acquired infections (HAIs) reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006-7. *Infection Control Hospital Epidemiology*, 29, 996-1011.
- John, B., Khan, M., Speerhas, R., Rhoda, K., Hamilton, C., Dechicco, R., Lopez, R., Steiger, E., & Kirby, D. (2011). *Ethanol lock therapy in reducing catheter-related bloodstream infections in adult home parenteral nutrition patients: Results of a retrospective study*. Manuscript submitted for publication.
- Jones, B., Hull, M., Richardson, D., Zurakowski, D., Gura, K., Fitzgibbons, S., & Jaksic, T. (2010). Efficacy of ethanol locks in reducing central venous catheter infections in pediatric patients with intestinal failure. *Journal of Pediatric Surgery*, 45(6), 1287-1293.
- Kayton, M., Garmey, E., Ishill, N., Cheung, N., Kushner, B., Kramer, K., & La Quaglia, M. (2010). Preliminary results of a phase I trial of prophylactic ethanol-lock administration to prevent mediport catheter-related bloodstream infections. *Journal of Pediatric Surgery*, 45(10), 1961-1966.
- Kim, E., Saunders, P., & Yousefzadeh, N. (2010). Usefulness of anti-infective lock solutions for catheter-related bloodstream infections. *Mount Sinai Journal of Medicine* (77)5, 549-558.
- Laird, J., Soutar, R., & Butcher, I. (2005). Complications of the ethanol-lock technique in the treatment of central venous catheter sepsis. *Journal of Infection*, 51(4), 338.
- Lederer, S., Riedelsdorf, G., & Schiffl, H. (2007). Nasal carriage of methicillin-resistant *Staphylococcus aureus*: The prevalence, patients at risk and the effect of elimination on outcomes among out clinic haemodialysis patients. *European Journal of Medical Research*, 12, 284-288.

- Lehne, R. (2010). *Pharmacology for nursing care*. St. Louis, MO: Elsevier.
- Maharaj, A.R., Zelenitsky, S.A., & Vercaigne, L.M. (2008). Effect of an ethanol/trisodium citrate hemodialysis catheter locking solution on isolates of *Candida albicans*. *Hemodialysis International*, 12(3), 342-347. doi: 10.1111/j.1542-4758.2008.00279.x
- Mermel, L., Allon, M., Bouza, E., Craven, D., Flynn, P., O'Grady, N., Raad, I., Rijnders, B., Sherertz, R., & Warren, D. (2009). Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection. 2009 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*, 49(1), 1-45.
- McGrath, E., Salloum, R., Chen, X., Jiang, Y., Boldt-MacDonald, K., Becker, C., Chu, R., & Ang, J. (2011). Short-dwell ethanol lock therapy in children is associated with increased clearance of central line-associated infections. *Clinical Pediatrics* 50(10), 943-951.
- Nett, J., Guite, K., Ringeisen, A., Holoyda, K., & Andres, D. (2008). Reduced biocide susceptibility in *Candida albicans* biofilms. *Antimicrobial Agents and Chemotherapy*, 52(9), 3411-3413.
- Centers for Disease Prevention and Control, Healthcare Infection Control Practices Advisory Committee. (2011). *Guidelines for the prevention of intravascular catheter-related infections, 2011*. Retrieved from <http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf>
- Onland, W., Shin, C., Fustar, S., Rushing, T., & Wong, W. (2006). Ethanol-lock technique for persistent bacteremia of long-term intravascular devices in pediatric patients. *Archives of Pediatrics & Adolescent Medicine*, 160(10), 1049-1053.
- Opilla, M.T., Kirby, D.F., & Edmond, M.B. (2007). Use of ethanol lock therapy to reduce the incidence of catheter-related bloodstream infections in home parenteral nutrition patients.

*Journal of Parenteral and Enteral Nutrition*, 31(4), 302-305.

doi:10.1177/0148607107031004302.

- Penel, N., & Yazdanpanah, Y. (2008). Vancomycin flush as antibiotic prophylaxis for early catheter-related infections: A cost-effective analysis. *Supportive Care in Cancer*, (17)3, 285-293.
- Polgreen, P.M., Beekmann, S.E., Diekema, D.J., & Sherertz, R.J. (2010). Wide variability in the use of antimicrobial lock therapy and prophylaxis among infectious diseases consultants. *Infection Control and Hospital Epidemiology* 31(5), 554-557.
- Qu, Y., Istivan, T.S., Daley, A.J., Rouch, D.A., & Deighton, M.A. (2009). Comparison of various antimicrobial agents as catheter lock solutions: Preference for ethanol in eradication of coagulase-negative staphylococcal biofilms. *Journal of Medical Microbiology*, 58(4), 442-450.
- Raad, I., Hanna, H., Dvorak, T., Chaliban, G., & Hachem, R. (2007) Optimal antimicrobial catheter lock solution, using different combinations of micocycline, EDTA, and 25-percent ethanol, rapidly eradicates organisms embedded in biofilm. *Antimicrobial Agents and Chemotherapy* 51(1), 78-83.
- Rajpurkar, M., Boldt-Macdonald, K., McLenon, R., Callaghan, M., Chitlur, M., Lusher, J., & Becker, C. (2009). Ethanol lock therapy for the treatment of catheter-related infections in haemophilia patients. *Haemophilia: The Official Journal of the World Federation of Hemophilia*, 15(6), 1267-1271.
- Sanders, J., Pithie, A., Ganly, P., Lois, S., Wilson, R., Merriman, E., Loudon, G., Judkins, R., & Chambers, S. (2008). A prospective double-blind randomized trial comparing intraluminal ethanol with heparinized saline for the prevention of catheter-associated

- bloodstream infection in immunosuppressed haematology patients. *The Journal of Antimicrobial Chemotherapy*, 62(4), 809-815.
- Shenep, L., et al. (2011). Efficacy of intravascular catheter lock solutions containing preservatives in the prevention of microbial colonization. *Journal of Hospital Infection* 79(4), 317-322.
- Sherertz, R.J., Boger, M.S., Collins, C.A., Mason, L., & Raad, I.I. (2006). Comparative in vitro efficacies of various catheter lock solutions. *Antimicrobial Agents and Chemotherapy*, 50(5), 1865-1868.
- Slobbe, L., Doorduijn, J.K., & Lungtenburg, P.J. (2010). Prevention of catheter-related bacteremia with a daily ethanol lock in patients with tunneled catheters: A randomized, placebo-controlled trial. *PLoS One* 5(5). doi:10.1371/journal.pone.0010840
- Srinivasan, A., Wise, M., Bell, M., Cardo, D., Edwards, J., Fridkin, S., Jernigan, J., Kallen, A., McDonald, L.C., Patel, P.R., & Pollock, D. (2011). Vital signs: Central line-associated blood stream infections – United States, 2001, 2008, and 2009. *Morbidity and Mortality Weekly Report*, 60(8).
- Stewart, P., & Costerton, J. (2001). Antibiotic resistance of bacteria in biofilms. *Lancet*, 358, 135-138.
- Takla, T., Zelenitsky, S., & Vercaigne, L. (2007). Effect of ethanol trisodium citrate lock on microorganisms causing hemodialysis catheter-related infections. *The Journal of Vascular Access*, 8(4), 262-267.
- Vercaigne, L., Talka, T., & Raghavan, J. (2010). Long-term effect of an ethanol/sodium citrate locking solution on the mechanical properties of hemodialysis catheters. *The Journal of Vascular Access*, 11(1), 12-16.

- Valentine, K. (2011). Ethanol lock therapy for catheter-associated blood stream infections in a pediatric intensive care unit. *Pediatric Critical Care Medicine, 12*(6), 292-296.
- Venkatesh, M., Rong, L., Raad, I., & Versalovic, J. (2009). Novel synergistic antibiofilm combinations for salvage of infected catheters. *Journal of Medical Microbiology, 58*(7).
- Wales, P., Kosar, C., Carricato, M., de Silvia, N., Lang, K., & Avitzur, Y. (2011). Ethanol lock therapy to reduce the incidence of catheter-related bloodstream infections in home parenteral nutrition patients with intestinal failure: A preliminary experience. *Journal of Pediatric Surgery, 46*(5), 951-956.