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# Combating CLABSI: Preventing Central Line Infections and Other Central Lines Challenges

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October 9, 2015

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## OBJECTIVES

At the conclusion of this educational activity, participants should be able to:

1. Identify evidence based practices for CLABSI prevention
2. Discuss the approach to the patient with central line occlusion

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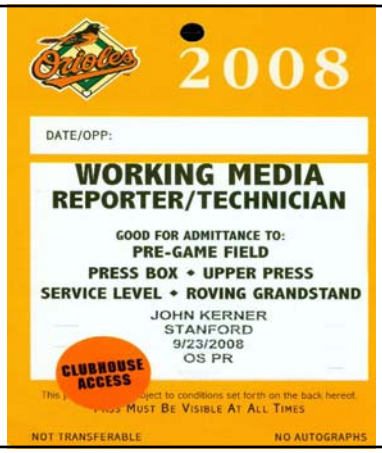

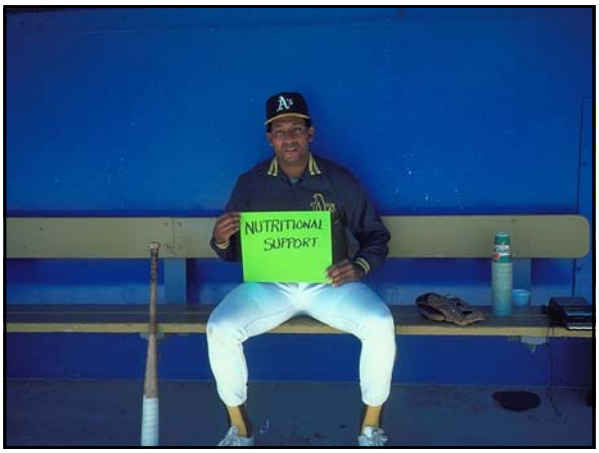


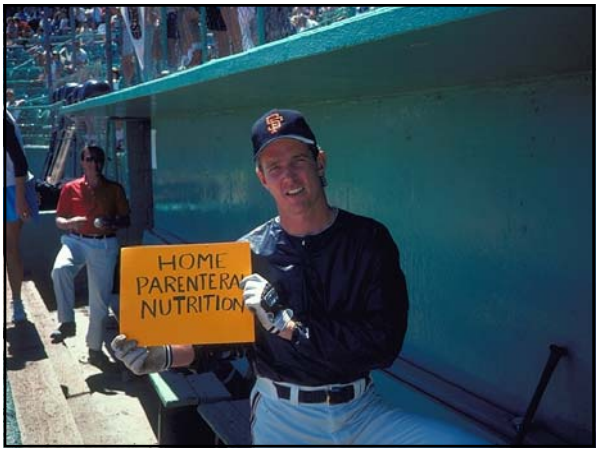


## CATHETER-RELATED OCCLUSION*

- Thrombotic 58%
- Nonthrombotic or Mechanical 42%
- Episodes/Catheter year 0.071+

*Stephens L. C. et al: JPEN 19:75, 1995
+Lyn Howard, Gastroenterology 124:1651, 2003.

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## CAUSES OF CATHETER OCCLUSION

- Clot or thrombus
- Fibrin deposition
- Fat deposition
- Calcium-phosphorus precipitation
- Drug precipitation

Mechanical Causes

- Kinking of the catheter
- Catheter tip against venous wall
- Excessively tight suture

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## NON-THROMBOTIC CAUSES OF CVC OCCLUSION*

1. Kinked catheter
2. Retaining suture too tight
3. Catheter clamped – slide or roller clamps left closed or partially closed
4. Catheter pinched+

*J Grant, JPEN 26:S21, 2002 (Coram HPEN Workshop)
+E.A. Krzywde, J Intraven Nurs 22(6S) S11, 1999.

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## NON-THROMBOTIC CAUSES OF CVC OCCLUSION (continued)

+Pinch-Off Syndrome – blood return is only obtained when patient's arm, on the same side as the catheter insertion site, is raised parallel to the shoulder. This indicates the catheter is compressed between the clavicle and the first rib. Pinch-Off Syndrome can lead to catheter fracture and embolism – remove catheter and place a new one lateral to the midclavicular line.

+ EA Krzywde, J Intraven Nurs 22(6S) S11, 1999.

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## CAUSES AND MANAGEMENT OF CATHETER OCCLUSION

| Cause | Management |
|---|---|
| • Clot or thrombus | • t-PA (Alteplase) |
| • Fat deposition | • 70% ethanol |
| • Calcium-phosphorus deposition | • 0.1 N Hydrochloric acid |
| • Drug precipitation | • 0.1 N Hydrochloric acid or 0.1 N NaOH |

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## WHAT IS ALTEPLASE?

- Genetically engineered human tissue-plasminogen activator
- Generic = alteplase (t-PA)
- Plasma half-life: 5 minutes (hepatic clearance)
- Tradename
  - 2 mg – Cathflo™ Activase ®
    - Catheter clearance
  - 50, 100 mg – Activase ®
    - Acute MI, acute stroke, pulmonary embolism


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## CATHFLO ACTIVASE PEDIATRIC STUDY (CAPS)

- Determine catheter efficacy at 30 and 120 minutes
- Determine rates of SAE that occur within 48 hours of treatment

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## PATIENT CHARACTERISTICS

- Total Enrolled 321
- Treated subjects 310
- Subjects <2 years 55
- Subjects ≥2 years 255
- Gender 174 M;136 F
- Age (mean,SD) 7.2 years (5.1)
  Range (years) 0.04 to 18.3
- Weight (mean, SD) 30.3 kg (23.1)
  Range (kg) 2.2 to 107

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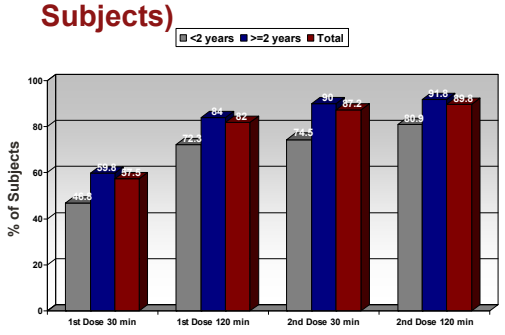
## CUMULATIVE RESTORATION RATES (Efficacy-Evaluable Subjects)




## CONCLUSION

- Cathflo™ Activase® is safe in both patients <2 years of age as well as the general pediatric population <17 years of age.
- No ICH, Major Hemorrhage, Thrombosis, or Embolic Events observed.
- Incidence of protocol defined sepsis similar to that seen in COOL-2.
- High rate of efficacy similar to that seen in COOL-1 and COOL-2.

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## OCCLUSION SECONDARY TO FAT DEPOSITION ("WAXY" BUILD-UP OF LIPIDS ON THE INTERNAL CATHETER)

- Werlin (JPEN 19:416, 1995) – In Pediatrics: up to 3 mL EtOH (max. 0.55 mL/kg); 10 of 26 occlusions were secondary to lipid.

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## CALCIUM-PHOSPHATE OR DRUG PRECIPITATION IN CHILDREN

- Up to 3 mL of 0.1N HCl (up to 1 mL. in infants between 1 and 3 kg.)
  - Tb syringes containing 0.5 ml connected to catheter hub and gentle push-pull motion applied to syringe plunger. If catheter did not clear, treatment remains in the line up to 1 hr; then aspirate
    - Werlin: JPEN 19:416, 1995 (mineral deposits n=3; medication ppts n=13)
    - Breaux: J Ped Surg 22:829, 1987 (Ca-Phos ppt. n=7)
- Shulman JPEN 12: 509, 1988 – 0.2-1.0 mL HCl cleared 4/4 catheters
  a) Ca-Phos ppts. (2)
  b) Amikacin, piperacillin, vancomycin, heparin ppt.
  c) Etoposide ppt.

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## DRUG PRECIPITATE

- ACIDIC DRUGS
  (e.g., Vancomycin, Etoposide)
  Tx. With 0.1N HCl
- BASIC DRUGS
  (e.g., ticarcillin, oxacillin, heparin, phenytoin, imipenem)
  Tx. With sodium bicarbonate 1mEq/mL or 0.1N NaOH

Reed T, Phillips S: Management of central venous catheter occlusions and repairs. J Intraven Nurs 19:289, 1996.

Hadaway LC: Major thrombotic and non-thrombotic complications. J Intraven Nurs 21(55)S 143, 1998.

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*Clinical Observations*

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**Efficacy and Safety of Using L-cysteine as a Catheter-Clearing Agent for Nonthrombotic Occlusions of Central Venous Catheters in Children**

Vinita B. Pai, MS, PharmD[1,2]; and Steven Plogsted, BS, PharmD, BCNSP, CNSC[3,4]

Nutrition in Clinical Practice
Volume 29 Number 5
October 2014 636-638

DOI: 10.1177/0884533614539177
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- Compounding and storing of 0.1N HCl is now more complex due to USP <797> guidelines for sterile compounding – an alternative is needed
- L-cysteine pH 1 - 2.5
- CVC occlusion resolved in 10 of 16 episodes in 13pts.
- Dose: no more than 2mL (100mg; 50mg/mL)
- 2 that could not be cleared were from phenytoin admin. (has a basic pKa)

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## CLABSIs

- CLABSI rates for inpatient pediatric units
  - 0.5-1.9 per 1,000 catheter days
- CLABSI rates among pediatric IF
  - 8.0-10.2 per 1,000 catheter days
  - Proposed reasons
    - Relative immune-deficient state
    - Poor intestinal motility
    - Reduced barrier function
    - Frequency of line access/Line colonization

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## CLABSIs IN CHILDREN WITH INTESTINAL FAILURE

- Children with intestinal failure (IF) depend on central venous catheters (CVC) for total parenteral nutrition (TPN), placing them at high risk for central-line associated bloodstream infections (CLABSI)
- Number of CLABSIs correlate with mortality and clinical outcome
- Unlike successful CLABSI reductions in other high-risk pediatric patients, children with IF continue to have high CLABSIs rates:

**8 - 26.4 CLA-BSI/1,000 catheter days**

Emedo, *JPGAN* 2010; Schalamon, *Clin Gastro* 2003; Squires, *J Peds* 2012Cole, *J Peds*, 2010; Edwards , Jones, *J Peds Surg* 2010; Mouw *J Peds Surg* 2008; Onder, *Peds Transpl* 2007; Cober , *JPEN* 2011; Wales , *J Ped Surg*, 2011; Pieroni, *Nutrition Clin Prac*, 2013

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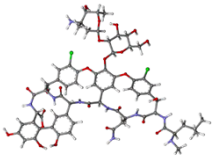
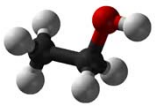
## LOCKING SOLUTIONS



- Antimicrobial locking solutions
  - Expensive
  - Encourage resistant organisms

- Ethanol
  - Cheap
  - Antimicrobial
    - Kills bacteria, fungi, and viruses
  - Penetrates biofilms



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## ETHANOL'S ANTIMICROBIAL EFFECTS

- S. aureus and S. pyogenes are killed by 10 sec exposure to 60-95% EtOH
- P. aeruginosa, E. coli, and S. marcescens are killed by 10 sec exposure to 40-100% EtOH
- More time with EtOH ≥ 40% is needed to inhibit bacterial growth in established biofilms

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## EtOH AND PLASTIC-ADHERENT MICROORGANISMS

- Biofilm incubated for 40 hr
- Exposed to EtOH in varying concentrations for 8 hr
- Bactericidal effect from 30% to 90%
- No growth after 4, 6, or 24 hr of exposure to 70% EtOH

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## ELT - PRINCIPLES

- Ethanol concentrations above 40% required to inhibit bacterial growth in established biofilms
- Use 70% ethanol lock
  - Needed for at least 2 hrs to kill established biofilms

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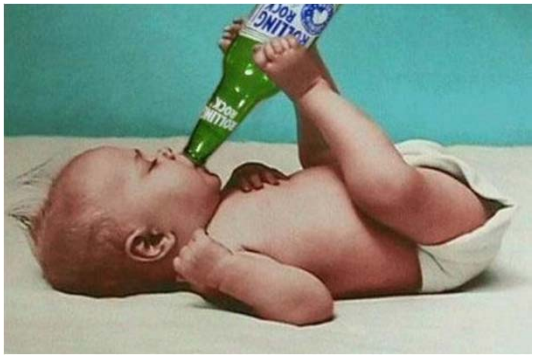

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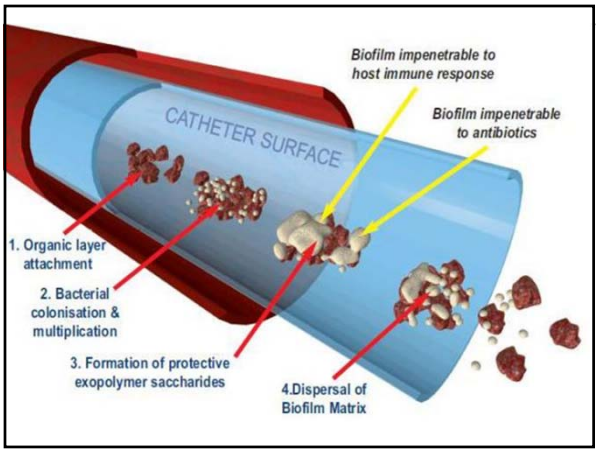

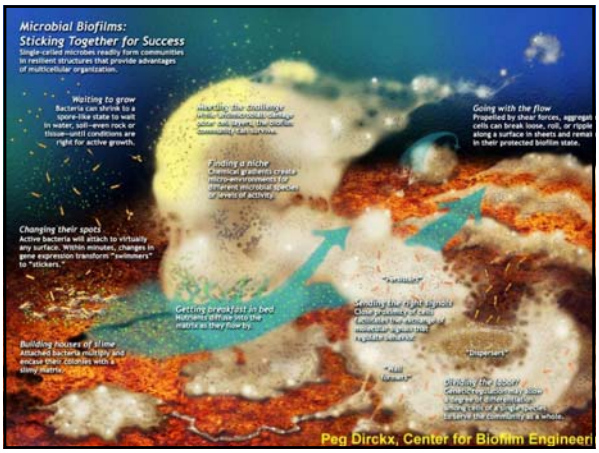


## ETHANOL LOCK

- Ethanol is bactericidal and fungicidal
  - Nonspecifically denatures cell membrane proteins
- Inhibit bacterial growth and penetrates bacterial biofilm within the line
- Improves clearance of line infection
- May save the line from replacement

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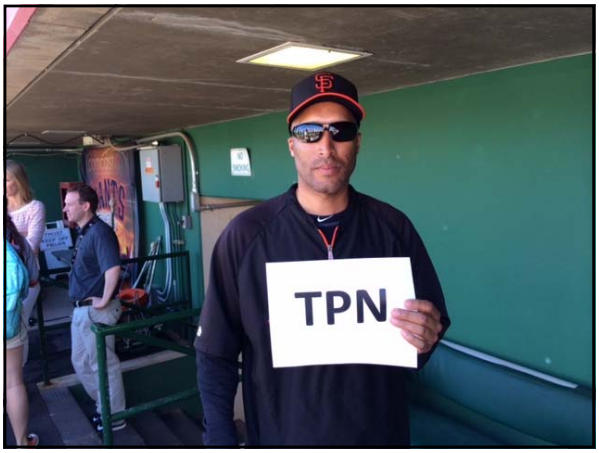

## ETHANOL-LOCK FOR CATHETER SALVAGE

- 40 children/51 CVC-related infections
- EtOH 70%: 0.8 – 1.4 mL for 12-24 hr, then withdrawn
- Catheters removed: 0

Onland W, et al. Arch Pedaitr Adolesc Med. 2005; 160: 1049-1053.

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## ETHANOL-LOCK FOR CATHETER SALVAGE

- After EtOH withdrawn, isotonic saline flush
- Repeat EtOH for 5 consecutive days
- Separate peripheral line for IV Abx.
- With double lumen catheters
  ethanol into 1 lumen for 24 hrs.,
  while the other lumen used for infusion
- Both lumens were alternately treated for 10 days

Onland W, et al. Arch Pedaitr Adolesc Med. 2005; 160: 1049-1053.

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## ETHANOL-LOCK FOR CATHETER SALVAGE

- Relapse: 12%
- 75% of polymicrobial isolates: no recurrence
- 94% of monomicrobial isolates successfully treated
- The treatments of 2 yeast isolates were also successful

Onland W, et al. Arch Pedaitr Adolesc Med. 2005; 160: 1049-1053.

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## ETHANOL LOCK

- Inexpensive, Readily available
- Bactericidal properties
  - 40% EtoH will inhibit bacterial growth in established biofilm[1]
  - 70% EtoH with 4 hr dwell time leaves no viable plastic-adherent bacteria or fungi[2]
- Protein denaturation
- No known resistance
- Limited experience in children with IF

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1 Sisson et al, 1996
2 Chambers et al, 2006

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**Ethanol lock therapy to reduce the incidence of catheter-related bloodstream infections in home parenteral nutrition patients with intestinal failure: preliminary experience**☆ Journal of Pediatric Surgery (2011) **46**, 951–956

Paul W. Wales[a,b,*], Christina Kosar[a], Megan Carricato[a,c], Nicole de Silva[a,b], Karen Lang[a], Yaron Avitzur[a,c]

- 70% ethanol solution prepared by outpatient pharmacy in pre-loaded syringes
- >5 Kg with silicone CVC or PICC
- Parents instill ethanol solution at completion of PN cycle
- Minimum dwell time of 4 hours
- Solution flushed prior to re-starting PN
- Volumes vary based on CVC device (usually 1-1.5cc)

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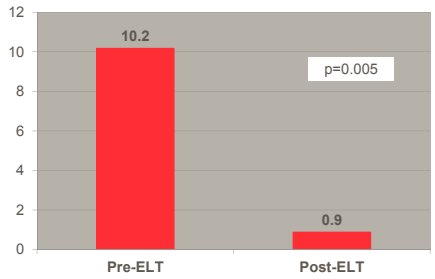
## TOTAL CRBSI PRE AND POST ETHANOL LOCK THERAPY

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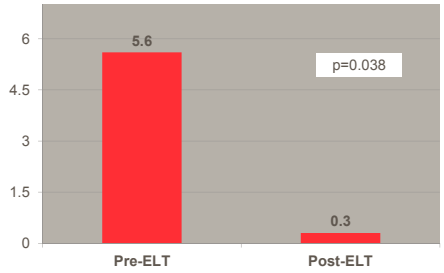
## CVC REPLACEMENTS PRE- AND POST-EtoH LOCK THERAPY

Per 1000 Catheter days

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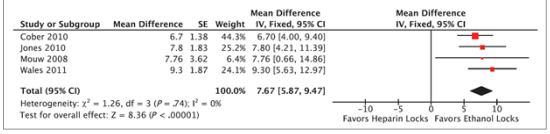
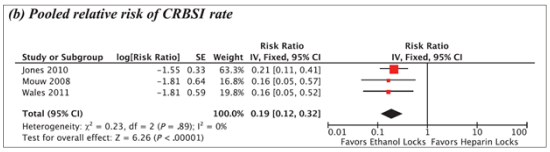
## RESULTS: META-ANALYSIS

*(a) Pooled mean difference of CRBSI rate*




*(b) Pooled relative risk of CRBSI rate*

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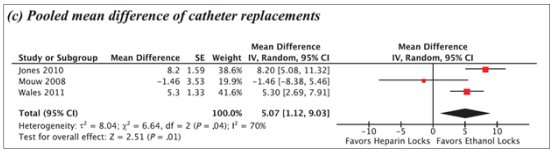
## RESULTS: META-ANALYSIS

*(c) Pooled mean difference of catheter replacements*




*(d) Pooled relative risk of catheter replacements*

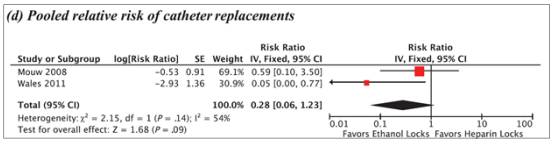



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**Table 1. Ethanol Lock Therapy in Intestinal Failure**

| Author | Year | N | Pediatric or Adult | Catheter-Related Bloodstream Infections Rate[a] Pre-ELT | Post-ELT | No. of Days/Wk | Dwell Time, h | Ethanol Concentration, % |
|---|---|---|---|---|---|---|---|---|
| Opilla et al[61,b] | 2007 | 9 | Adult | 8.3 | 2.7 | 1-7 | 2-4 | 25-70 |
| Mouw et al[59] | 2008 | 5 | Pediatric | 11.5 | 2.1 | 7 | 4-14 | 70 |
| Jones et al[60] | 2010 | 23 | Pediatric | 9.9 | 2.1 | 3 | ≥ 4 | 70 |
| Cober et al[62] | 2011 | 15 | Pediatric | 8.0 | 1.3 | 7 | ≥ 2 | 70 |
| Wales et al[63] | 2011 | 10 | Pediatric | 10.2 | 0.9 | 7 | ≥ 4 | 70 |
| Pieroni et al[64] | 2011 | 13 | Pediatric | 14 | 2.8 | 1 | 2 | 70 |

ELT, ethanol lock therapy.
[a]Per 1000 catheter days.
[b]Included home parenteral nutrition patients, not exclusively short bowel or intestinal failure.

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## ETHANOL LOCK DATA

*Clinical Research*

aspen

**Evaluation of Ethanol Lock Therapy in Pediatric Patients on Long-Term Parenteral Nutrition**

Kevin P. Pieroni, MD[1]; Colleen Nespor, RN[2]; Marisa Ng, PharmD[2]; Manuel Garcia, MD[1]; Melissa Hurwitz, MD[1]; William E. Berquist, MD[1]; and John A. Kerner Jr., MD[1,2]

Nutrition in Clinical Practice
Volume 28 Number 2
April 2013 226-231

DOI: 10.1177/0884533612468009
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- 73% Reduction in CABSI's
- 77% Reduction in line replacements

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## RESULTS: ADVERSE EVENTS

| Source | Adverse Events (reported selectively for EL) |
|---|---|
| Mouw, 2008 | No adverse events reported by parents or health care providers<br>1/10 CVC-related thrombus<br>1/10 two episodes of culture negative disseminated intravascular coagulations (full recovery without ICU admission)<br>1/10 Loss of line integrity |
| Jones, 2010 | No adverse events |
| Cober, 2010 | 1/15 deep vein thrombosis in the same leg as CVC<br>3/15 families complained temporarily the difficulty of withdrawing the solution<br>7/15 patients had twenty catheter leakages or disruptions (non-significantly different when compared to the control) |
| Wales, 2011 | 2/10 CVC-related thrombus |

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*The Pediatric Infectious Disease Journal* • Volume 32, Number 3, March 2013

## ECHINOCANDIN AND ETHANOL LOCK THERAPY TREATMENT OF FUNGAL CATHETER INFECTIONS

*Kevin P. Pieroni, MD,* Colleen Nespor, RN,† Robert L. Poole, PharmD,†‡ John A. Kerner Jr., MD,*† and William E. Berquist, MD**

**Abstract:** Ethanol lock therapy has been implemented to prevent infections of central venous catheters as well as to treat infections. Fungal catheter-associated blood stream infections are historically more difficult to treat and have required removal of central venous catheters. We report the largest case series to date, successfully treating 5 of 7 fungal catheter-associated blood stream infections with ethanol lock therapy and systemic echinocandin administration.

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*Case Report*

aspen

**Central Venous Catheter Thrombosis Associated With 70% Ethanol Locks in Pediatric Intestinal Failure Patients on Home Parenteral Nutrition: A Case Series**

Journal of Parenteral and Enteral Nutrition
Volume 36 Number 3
May 2012 358-360
© 2012 American Society for Parenteral and Enteral Nutrition
DOI: 10.1177/0148607111414713
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**Theodoric Wong[1,2,3]; Vanessa Clifford[2]; Zoë McCallum[1,3]; Helen Shalley[1]; Megan Peterkin[1]; Georgia Paxton, MPH, FRACP[1,2]; and Julie E. Bines[1,2,3]**

## Effects of 70% Ethanol Locks on Rates of Central Line Infection, Thrombosis, Breakage, and Replacement in Pediatric Intestinal Failure

*[*]Maisam Abu-El-Haija, [†]Jonathan Schultz, and [‡]Riad M. Rahhal*

(*JPGN* 2014;58: 703–708)

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## ETHANOL LOCK EFFICACY AND ASSOCIATED COMPLICATIONS IN CHILDRENS WITH INTESTINAL FAILURE

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Cincinnati Children's

Mezoff JPEN 2015

**Coauthors**: Lin Fei, PhD; Misty Troutt, MS, MBA; Kim Klotz, RN, MSN, CRNI; Samuel A. Kocoshis, MD; and Conrad R. Cole, MD, MPH, MSc

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## CCHMC ELT METHOD

- Determine ELT priming volume
- Educate caregiver
- Schedule dwell time
  - >2hrs up to length of window (12hrs)

1. Flush w/ NS
2. Instill priming volume of **70% Ethanol**
3. Dwell (no access to CVC)
4. Withdrawal with small flash of blood
5. Flush line with >5 mL NS
6. Resume use

| Tunneled Catheter | Priming Volume |
|---|---|
| **Bard** | |
| 2.7 Fr | 0.15 mL |
| 4.2 Fr | 0.3 mL |
| 6.6 Fr | 0.7 mL |
| 7.0 Fr DL Red | 0.8 mL |
| 7.0 Fr DL White | 0.6 mL |
| **Cook** | |
| 3 Fr | 0.3 mL |
| 5 Fr | 0.3 mL |
| 4 Fr DL White | 0.2 mL |
| 4 Fr DL Blue | 0.1 mL |
| 5 Fr DL White | 0.2 mL |
| 5 Fr DL Blue | 0.2 mL |

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## DEMOGRAPHICS OF STUDY PARTICIPANTS

| Demographic Category | | Number |
|---|---|---|
| Number of Patients | | 30 |
| Median Patient Age (Range) | | rs (1-20 years) |
| Sex | | 15 |
| | | 15 |
| Etiology | | 11 |
| | | 6 |
| | | 1 |
| | Metabolic | 3 |
| | Post-multivisceral transplant | 9 |
| | **Total Line Days** | 23,202 |
| Line Type | Tunneled Central Venous Catheter | 87 |
| | Peripherally Inserted Central Catheter | 61 |
| | Port | 8 |

Total Line Days
•Off ELT 8,865 days (median 210)
•On ELT 14,337 days (median 296)

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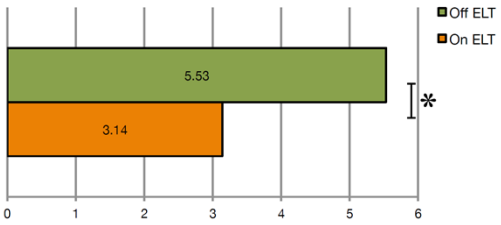
## BLOOD STREAM INFECTIONS




*Difference significant (p<0.013) by Poisson regression modeling

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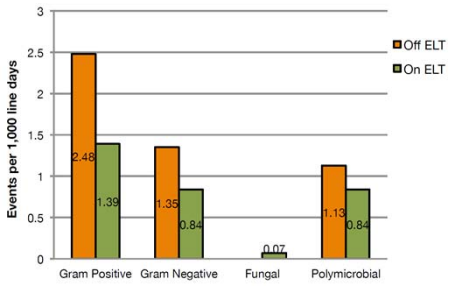
## INFECTING ORGANISMS RECOVERED BY BLOOD CULTURE

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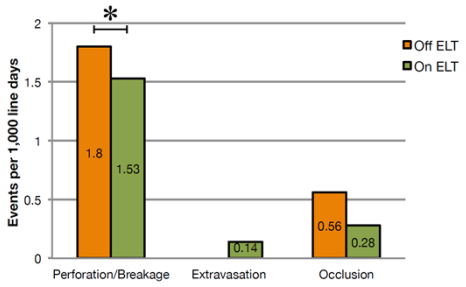
## CENTRAL LINE COMPLICATIONS




**Difference significant (p<0.006) by zero-inflated Poisson regression modeling*

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## CONCLUSIONS

ELT is a **SAFE** and **EFFECTIVE** method for reducing CLABSIs in the pediatric IF population.

- **CLABSI rates are *reduced* with ELT (p<0.013)**
- **Central line perforations or breaks are *reduced* with ELT (p=0.006)**
- **Central line occlusion rates trended *downward* with ELT (p=0.056)**
- **Low rates are possible with fastidious line care**

*Future Directions:*

- Be able to distinguish translocation from line infections
- Determine how antibiotic exposure changes the ability to grow
- ***Create a collaborative improvement network***

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## CLABSI REDUCTIONS IN CHILDREN WITH INTESTINAL FAILURE THROUGH IMPLEMENTATION OF A PREVENTION BUNDLE: BROADENING QI INTIATIVES FROM THE HOSPITAL TO THE HOME

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Nationwide Children's | The Ohio State University College of Medicine

JAMA Pediatrics 2015; 169:324-331.



## QI INITIATIVE

Goal: To evaluate whether implementation of a CLABSI prevention bundle that included the use of ethanol lock prophylaxis (ELP) in both the hospital and home settings could reduce total CLABSI rates in pediatric patients with IF.

Key driver specific aim: **Decrease the CLABSI rate in children with IF by 50%** by April 30, 2012 **and sustain** through December 31, 2013.

Secondary aims: safety assessments

- Central line replacement for any reason
- Central line repairs
- Number of hospitalizations



## INCLUSION CRITERIA

- Child with intestinal failure
  - weight ≥ 5 kg
  - clinically stable
  - requiring the CVC for at least 1 month
- Functional, silicone-based central venous catheter (CVC)
- No allergy to alteplase
- Not receiving citrate or metronidazole
- Parents were willing and able to comply with ELP in the home

## BEST-PRACTICE CLABSI PREVENTION BUNDLE COMPONENTS

- Hospital QI bundles
- Daily dressing/site assessments
- Weekly sterile dressing changes
- Use of two, 15 second alcohol scrub/dry to the CVC hub with each line entry
- Use of alcohol impregnated disinfection caps
- Daily 70% ethanol lock prophylaxis (ELP)
- Clinical practice guideline

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## FIRST ELP PROCEDURE

- Performed in hospital or clinic by CVC nurse
- CVC is functional and volume was determined
  - child < 15 kg = 0.1 mL + CVC volume
  - child ≥ 15 kg: = 0.2 mL + CVC volume (max 3 mL)
- Instillation of alteplase for at least 2 hours
- Instilling the 70% ethanol as a lock
- Confirming parents were competent with the procedure

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## DAILY ELP

- 70% ELP was performed daily
  - Lumens were alternated daily in patients with double lumen CVCs
- Heparin was removed from all TPN and medication orders
- Individualized plan, minimizing catheter entry and longest ethanol dwell time
  - Ethanol dwell: 2 – 24 hours
- Ethanol was removed at the end of the dwell and flushed with 5-10 mL of saline

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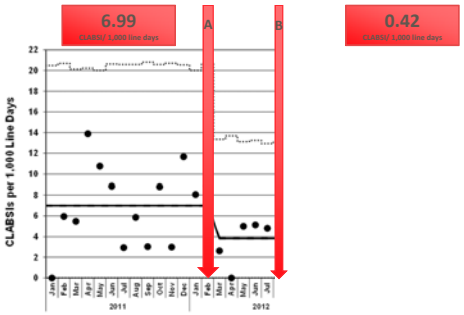
## POST-CLABSI BUNDLE + ELP IMPLEMENTATION




A: ELP offered to patients with history of ≥ 2 CLABSI; B: ELP offered to all eligible patients

Monthly Compliance — Baseline Mean(s) — Baseline Periods ····· Control Limits

## OTHER OUTCOMES

| CLABSI (number) | Pre ELP | Post ELP |
|---|---|---|
| CLABSI rates (CLABSI/1,000 catheter days) | 7.01 | 0.64 |
| Total number of CLABSIs | 34 | 3 |
| Single organism | 22 | 2 |
| Gram positive | 11 | 2 |
| Gram negative | 11 | 0 |
| Polymicrobial | 12 | 1 |
| Bacteria + Candida | 3 | 0 |
| Mixed bacterial | 5 | 1 |
| HA-CLABSI | 1 | 1 |

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## SAFETY ASSESSMENTS

- N=14 patients in whom ELP was used daily for ≥ 3months

| | Pre ELP | Post ELP | p-value* | |
|---|---|---|---|---|
| CLABSI rates (CLABSI/1,000 catheter days) | 7.01 | 0.64 | < 0.001 | |
| # catheter occlusions | 0 [0-1] | 0 [0-3] | 0.25 | |
| # use of tPA or cysteine | 3 [0-9] | 2 [0-5] | 0.23 | |
| # line repairs | 0 [1-7] | 1 [0-3] | 0.22 | |
| # central line insertions | 3 [0-6] | 0 [0-2] | 0.001 | ★ |
| # hospitalizations | 3.5 [0-20] | 3.5 [1-9] | 0.33 | |
| Duration of hospitalization (days) | 66 [5-177] | 12 [1-231] | 0.13 | |
| # hospitalizations for fever + CLABSI | 2 [0-9] | 0 [0-2] | 0.003 | ★ |

median [ranges]

*Wilcoxon matched-pairs sign rank

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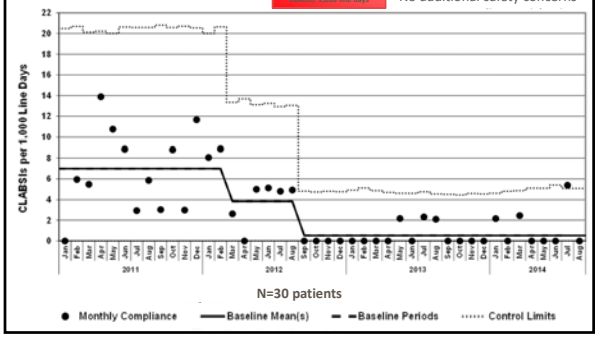
## CURRENT OVERALL CLABSI RATES IN IF PATIENTS

0.68
CLABSI/ 1,000 line days

No additional safety concerns




## SUMMARY

A best-practice CLABSI prevention bundle with ethanol lock prophylaxis in pediatric intestinal failure patients:

- Was **successfully implemented** in both the **hospital and home settings**,
- Led to a **statistically significant reduction in CLABSI rates**,
- CLABSI rate **reduction was sustainable**,
- **No significant increase in adverse events** attributable to daily 70% ethanol lock prophylaxis

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