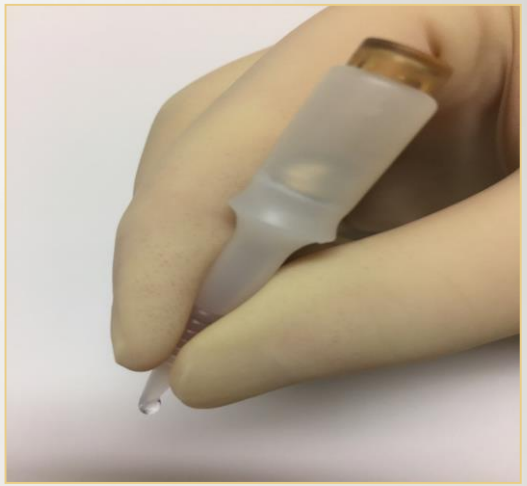
Solving Vascular Access Device Complications with Tissue Adhesive



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Disclosures/Disclaimers

- Adhezion Biomedical
- Teleflex, Inc.
- Genentech
- Brand names to provide examples of products used in the evidence presented.

Learning Objectives

- Review of vascular access device complications.
- Define the components and characteristics of tissue adhesives.
- Describe the purposes of tissue adhesives when used with VADs.
- Analyze the clinical outcomes with tissue adhesives used with VADs.

Vascular Access

- 1 – 2 Billion PIVs annually world wide
  - >300 million in the US
- Over 30 million CVC's, PICCs, Midlines

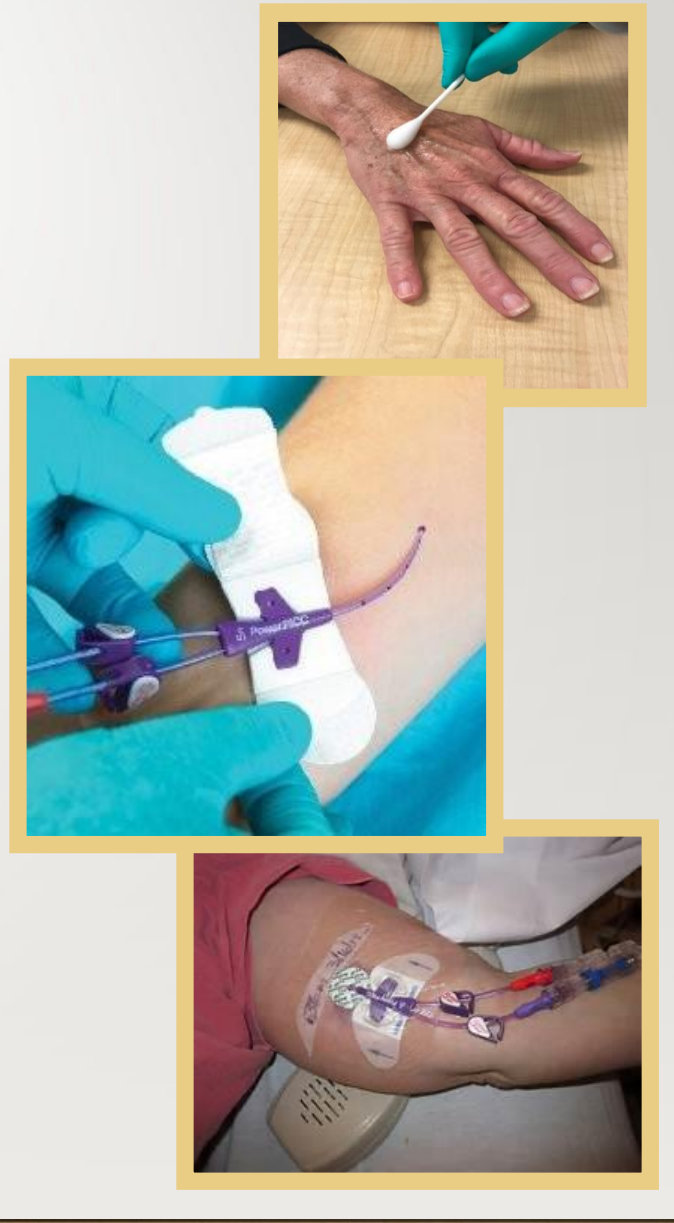
Vascular Access Devices (VAD)

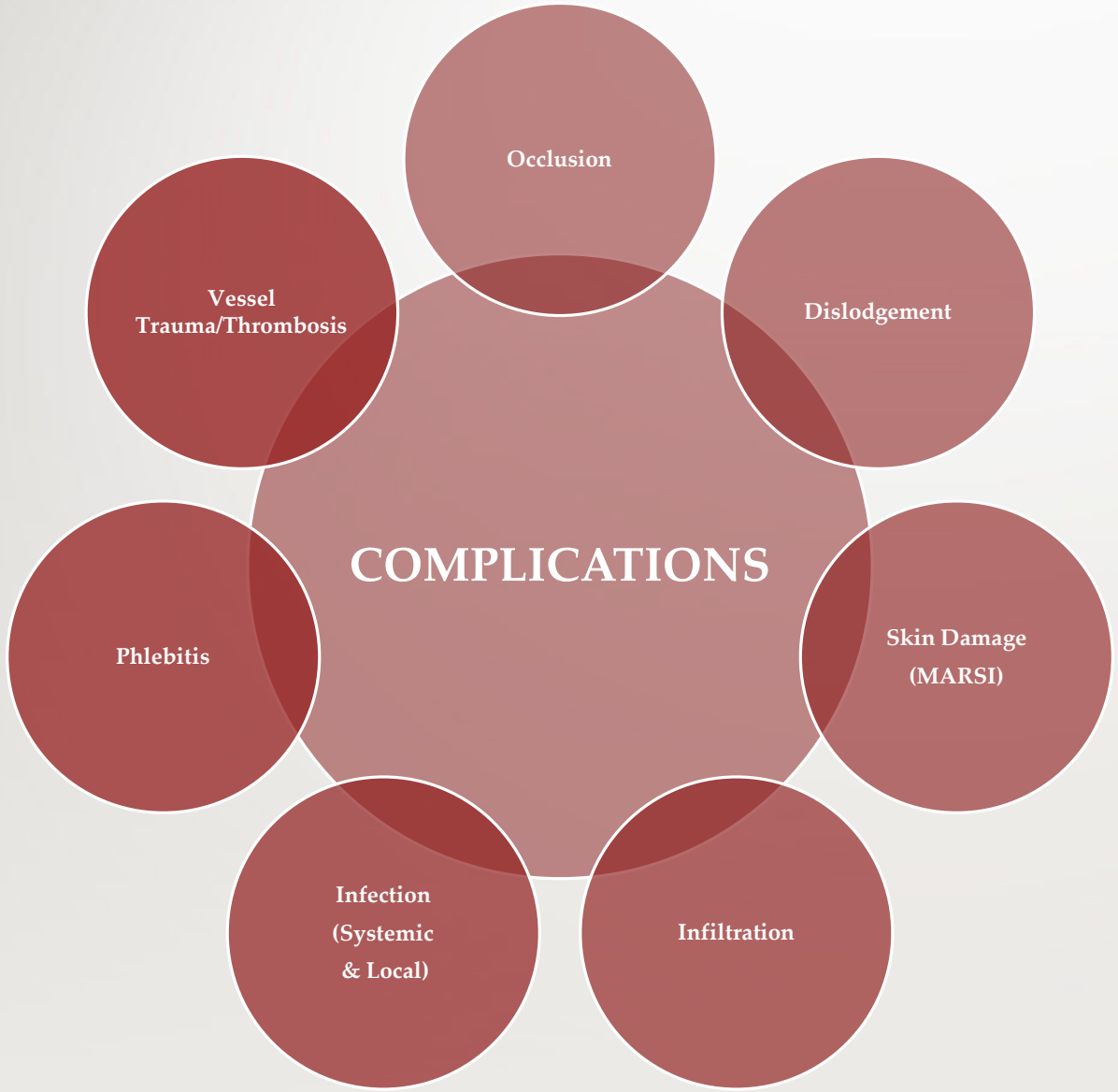
Goals & Objectives

- Protect the integrity of skin
- Protect puncture site from skin organisms
- Reduce VAD movement and dislodgment
- Reduce unplanned dressing changes

Vascular Access Devices (VAD)

- Current standard of practice
  - Application of skin antiseptics
    - Central – sterile technique
    - Peripheral – aseptic no touch technique
  - Puncture of skin and vein wall – **create a surgical wound**
  - Securing and stabilizing the VAD
    - Securing from movement & accidental dislodgement
  - Application of medical adhesives
    - Tape/Dressings




Occlusion
Dislodgement
Skin Damage (MARSI)
Infiltration
Infection (Systemic & Local)
Phlebitis
Vessel Trauma/Thrombosis
COMPLICATIONS

= FAILURE

Peripheral Catheter Failure

- Up to 63% failure across 8 RCTs [1]
- All study types, all causes – minimum failure 30%, maximum 95%
  - Included infiltration/extravasation, occlusion, accidental removal, phlebitis, and infection
- Dislodgement 3-10%

Helm, et. al. 2015

Peripheral IV Complications

- Phlebitis -- Incidence reports of 14.7% to 16.1%
  - Precipitated by mechanical, chemical and infectious causes
  - *Movement of the body relative to the secured catheter - Direct trauma to the intima*
- Infiltration – Most common form of failure; Incidence 15.7% to 33.8%
  - Results from erosion or penetration of the catheter through the vessel wall
  - *Even in non-joint regions, inadequate device securement can lead to catheter tip motion and consequent injury to vessel wall*

Helm, et. al. 2015

Peripheral IV Complications

- Occlusion -- Incidence of 2.5% to 32.7%
  - Device kinking
  - *Catheter migration* **(movement)** *into a dead-end position within the vessel wall without frank infiltration*
- Dislodgement -- Incidence of 3.7% to 50%
  - Study by Jackson; 3296 PIV restarts over 6 months
    - *Catheter dislodgement 50% of the failures*
  - Inadequate securement; tubing catching on clothing, etc.
  - *Current securement devices add bulk to the catheter-dressing complex and extend adhesive surface area*

Helm, et. al. 2015

Peripheral Catheter Infection

- New Systematic Review
  - PIVC-BSI = 0.18% in 85063 peripheral catheters
  - Mean of 22% (range 7%-60%) of 7860 nosocomial CRBSI
  - Mean of 38% (range 12% to 64%) S. aureus CRBSI from infected peripheral catheters [2]
- Arterial Catheters – 1.7/1000 catheter days [3]

Mermel, et al. 2017, Maki, et al. 2006

Peripheral IV Dwell Time – Clinically Indicated

- Before 2011 – Routine removal (48-96 hours)
- 2011 – *CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections*
  - No need to replace more frequently than 72-96 hours
- 2011 – Infusion Nursing Society Standards of Practice
  - Removal time-based site rotation and supported removal when clinically indicated

Report All Laboratory Confirmed BSIs??

- Hospitals in Pennsylvania required to report ALL laboratory confirmed bloodstream infections (LCBI) – not just CLABSI
  - 2011-2012 PA HAI report revealed:
    - 1890 (38%) LCBI reported had no central line
      - How many of these BSIs may have been related to a PIV?
      - 31% of these pathogens = Staphlococcus aureus

Davis, J. (2014)

Protect the PIV ~ Clinical Indication

- Staff education
- Insertion Bundle
  - Sterile Procedure
- 37% reduction in primary bacteremia
  - Combining PIV & CLABSI infections
- 19% reduction in PIV bloodstream infections
  - 11 years of surveillance data (PIV-associated bloodstream infections)

DeVries, 2016

CVAD Infections

- CRBSI
  - PICCs – 0.12 – 2.3/1000 catheter days [4,5]
    - 3.1/1000 catheter days (Ullman, Pediatrics; 2015) [6]
  - CVCs – 0.1 – 4.8/1000 catheter days [3]

Maki, et al. 2006, Raiy et al. 2010, Kang et al. 2017, Ulllman et al. 2015

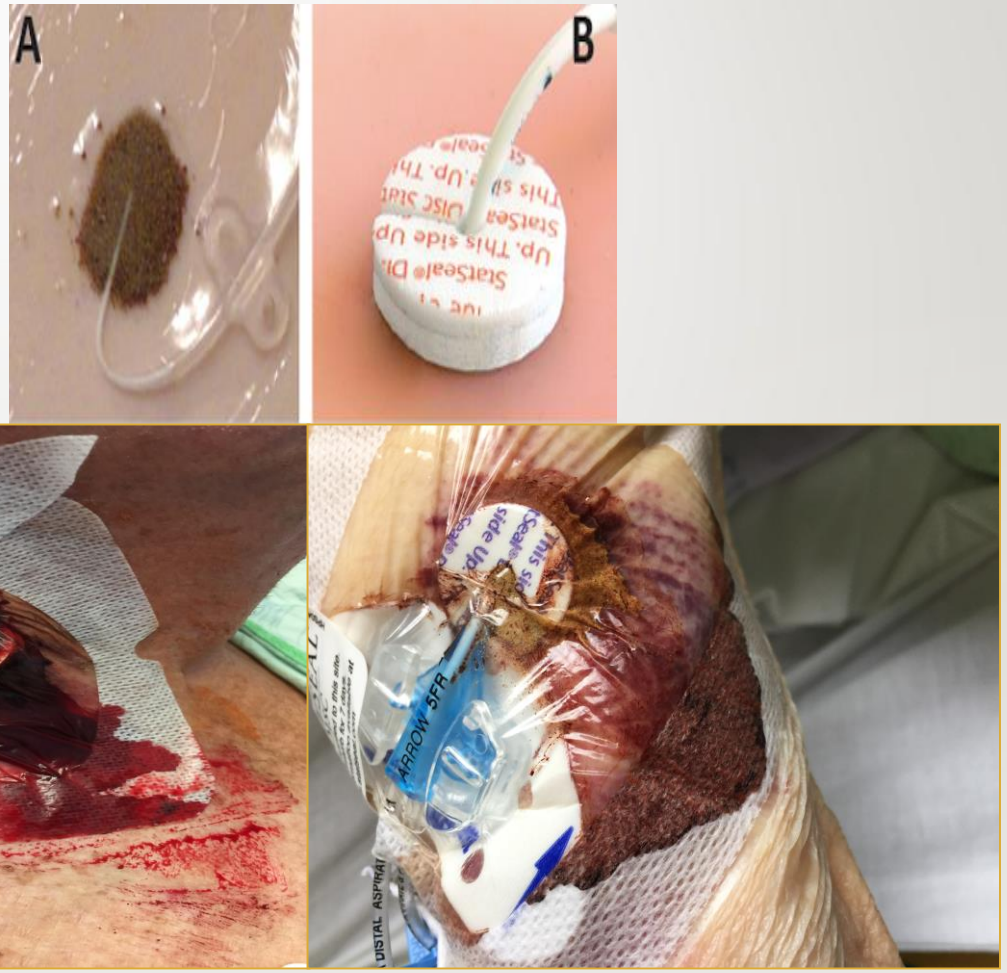
Central Line Complications

- Oozing/blood leakage at insertion site
  - Non-routine dressing changes are common: Average 22.8%
  - 43% of respondents have > 25% Early Dressing Changes (AVA 2017 survey)
  - 7 – 24.7% Oozing and 3.8% leaking [6]
  - 0.6% major bleeding; 2.8 – 5.4% minor bleeding [7]

Lueng et al. 2011, Vinson et al. 2014

Hemostatic Agents

- D-Stat
- Surgicel
- StatSeal



Central Line Complications

- Accidental Withdrawal
  - 4.2% [8]

Qui et al. 2014

CHG Allergy

Tissue Adhesive

- Can adding tissue adhesive to our toolbox make a difference in these outcomes?
- What is tissue adhesive?
  - Glue - cyanoacrylate, (CA) a liquid monomer [9]
    - Polymerizes when exposed to moisture present in air, liquid, or tissue
    - Exothermic process – releases energy when the molecules come together
      - May release a small amount of heat

Januchowski et al. 2014

CA'S HAVE BECOME MORE COMPLEX… AND MORE VERSATILE

POLYMER LENGTH

methyl-CA

1 carbon chain

Industrial plastic bonding

- Permabond® 910

ethyl-CA

2 carbon chain

Consumer glues

- SuperGlue®
- Krazy® Glue

n-butyl-CA

4 carbon chain

Earliest topical medical adhesives, embolization and veterinary use

- Indermil® tissue adhesive
- Histoacryl® topical skin adhesive
- LiquiBand® topical skin adhesive

2-octyl-CA

8 carbon chain

Newer CA formulations exhibit more characteristics that are important to clinicians and patients

- SURGISEAL® topical skin adhesive
- Dermabond® topical skin adhesive
- DERMA+FLEX QS adhesive

Tissue Adhesive

- N-butyl-cyanoacrylate (BCA)*
  - Quick drying
  - Rigid/Brittle
  - More cytotoxic
  - Stronger thermal reaction
  - Requires minimum 24 hours before fully water resistant
- 2-octyl-cyanoacrylate (OCA)*
  - Longer drying time
  - Higher tensile strength & more flexible
  - Less cytotoxic
  - Reduced thermal reaction
  - Immediately water-resistant

*Adhezion Biomedical, Internal Testing

Tissue Adhesive

- Antimicrobial activity of different cyanoacrylate formulations
  - First generation products
    - Most were effective against gram positive bacteria
  - Second generation products (2-octyl and octyl blends)
    - Most are effective against gram positive
    - ***Two of newer formulations; published data demonstrating broad-spectrum activity against Gram Positive, Gram Negative, Yeast, and Fungi***[10,11]

Prince et al. 2017

Tissue Adhesive

Tissue Adhesive – Uses with VADs

- Early in vitro testing demonstrated suitability of tissue adhesive for VADs [12]
- 4 purposes identified
  - Enhanced securement of VADs
  - Wound closure by a protective barrier
  - Minimizes oozing at puncture site
  - Infection prevention by immobilizing and killing bacteria

Simonova et al. 2012

Types of Dressings*

Standard polyurethane (SPU)	Bordered polyurethane	Sutureless securement (SSD)	Integrated securement (ISD)
			

* For illustration purposes only

TA Effectiveness – in vitro study

1. Chemical compatibility TA & TA removal agents
   - Overall tensile strength was not reduced
2. Pull out strength TA versus current dressings and control
   - TA outperformed standard polyurethane & bordered polyurethane dressings
3. Microbiological qualities of TA against current dressing methods

Simonova et al. 2012

Microbiological results

		18 Hours		72 Hours	
		Beneath Device	Around Device	Entry Point	IVC Tract
S. aureus	TA	-	+	-	-
	(2) Dressings	+	+	+	+
S. epi	TA	-	+	-	-
	(2) Dressings	+	+	+	+

Simonova et al. 2012

Tissue Adhesive – Current Evidence

- Peripheral IV catheters
- Peripheral arterial catheters
- Central venous access devices
- Epidural catheters

Tissue Adhesive – Peripheral IV Catheters

- 4 arm pilot randomized trial in adults on medical-surgical units [13]
  - Catheter failure, premature removal due to complication

	Standard polyurethane (SPU) control group	Bordered polyurethane	Sutureless securement (SSD) + SPU	TA + SPU
Number	21	20	23	21
# failed	8	5	5	3
Failure rate	6.92	3.82	3.14	2.40
Adverse Events	0	0	0	4

Marsh, N., et al. 2015.

Tissue Adhesive – Peripheral IV Catheters

- 2 arm randomized trial in adult emergency patients [14]
  - Assessed failure at 48 hours, modes of failure

	BPU + tape	TA + BPU + tape
Number	190	179
Failure No (%)	52 (27%)	31 (17%)
Dislodgement	26 (14%)	13 (7%)
Phlebitis	9 (5%)	6 (3%)
Occlusion	20 (11%)	15 (8%)

Bugden, S., et al., *2016*

Tissue Adhesive – Peripheral IV Catheters

- ***Dressings and securements for the prevention of peripheral intravenous catheter failure in adults (SAVE): a pragmatic, randomised controlled, superiority trial***

- Published in the Lancet; July 2018
- Two facilities; 1 ½ years; March 2013 – September 2014
- Large randomized trial; Over 1800 patients

Rickard CM, et al. 2018

Tissue Adhesive – Peripheral IV Catheters

	Standard polyurethane (SPU) - control	Bordered polyurethane	Sutureless securement (SSD) + SPU	TA + SPU	
Number	454	454	453	446	
% Failure: Total Failure	43%	40%	41%	38%	> 2 - 5%
% Failure: Pre-Protocol Analysis	34%	35%	34%	**26%**	**> 8 - 9%**
Failure rate/100 PIV days	18.3	19.6	15.9	**12.7**	**> 3 - 7**
% due to Occlusion	22%	19%	23%	**16%**	**> 3 - 7%**
Dislodgement/100 PIV days	3.5	3.5	3.0	2.5	> 0.5 - 1

Pilot Trial with Tissue Adhesive on PIVs

	Control Group	Study Group
Range of Dwell Time	4h 9min – 164h 1min	5h 32min – 329h 26 min
Average Dwell Time	35 hours	73.2 hours
Number of Patients	N=35	N=25
Age Range	24d – 24.4years	2.5 months – 20.2years
Complications	16 (46%)	8 (32%)
Leaking	5	4
Phlebitis	0	1
Occlusion	3	2
Infiltration	4	1
Pulled out by patient	4	0

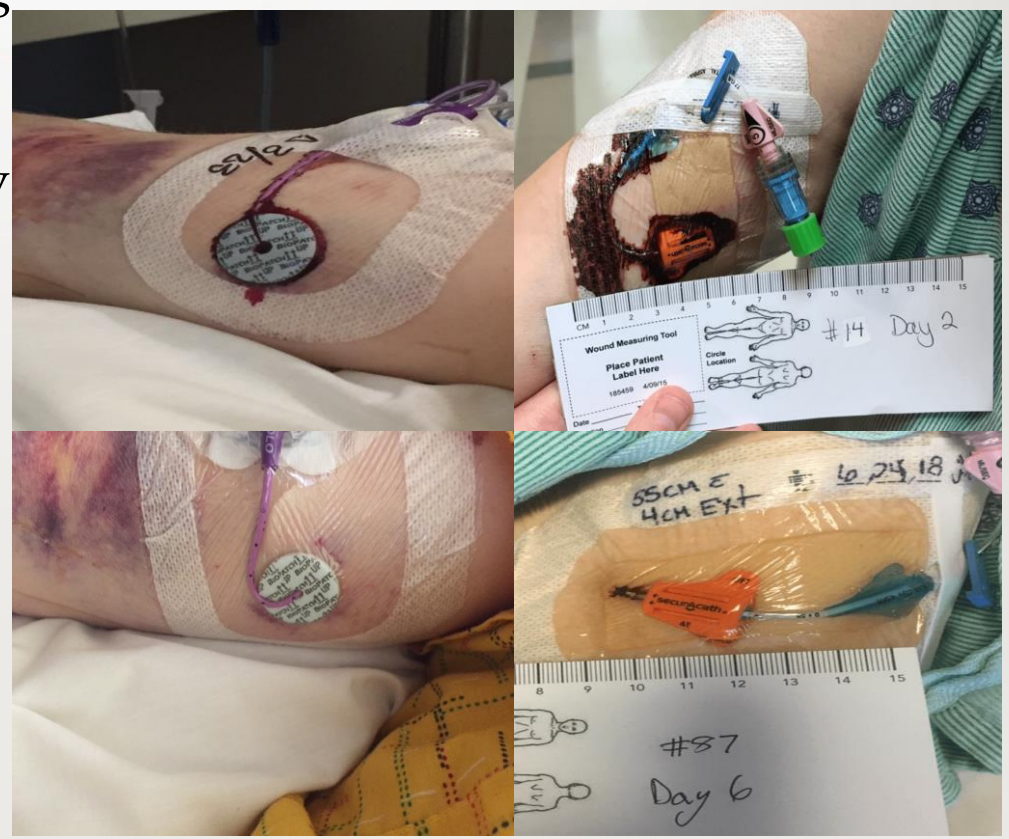
Presented with permission from D. Doellman, Cincinnati Children's Hospital

Financial Impact

- Insert 100,000 PIVs annually
  - Cost @ $30 = $3,000,000
- Adding Tissue Adhesive to PIV Protocol
  - Approximately $5
- 15% Improvement = $25,000 savings
  - 85,000 PIVs annually
  - $35 x 85,000 catheters = $2,975,000

Tissue Adhesive – Reduced Dressing Changes

- 3 Posters 2018 AVA Scientific Meeting
  - Decreased early dressing changes
    - Reduced bleeding
  - Saved estimated $40,000 annually



Tissue Adhesive - Tunnelled CVADs in Pediatrics

- 4 arm, 2 centre pilot RCT [16]
- Primary outcome: CVAD failure
- Compared:
  1. Bordered polyurethane (BPU) dressing + suture
  2. Sutureless securement device (SSD) + suture + BPU
  3. Tissue adhesive (TA - at exit wound and under catheter bifurcation) + BPU
  4. Integrated securement-dressings (ISD) + suture

Ullman, AJ., et al. 2017

Tissue Adhesive - Tunnelled CVADs in Pediatrics

Results

- Lower non-routine dressing changes
- High staff approval on application
- High parental satisfaction on removal but not staff satisfaction

	ISD+ suture n=12	SSD+suture +BPU n=13	BPU+suture (control) n=11	TA+ BPU n=12
CVAD failure	2 (17%)	1 (8%)	0	0
Complications	1 (8%)	2 (15%)	0	0
Adverse skin event*	2 (17%)	1 (8%)	2 (18%)	0
Non-routine dressing	10	25	17	4

*rash, blister, itchiness

Tissue Adhesive – All CVADs

- Pittiruti, M., et al. Cyanoacrylate Glue and Central Venous Access Device Insertion [18]
- Poster – AVA 2016 Scientific Meeting
  - 513 non-tunneled PICCs and CICCs
  - 114 tunneled PICCs, CICCs, and FICCs
  - 802 implanted ports
- 100% effective in prevention of post-insertion bleeding
- **10 fold reduction in CRBSI**

Pittiruit, et al. AVA Scientific Meeting 2016

Tissue Adhesive in CR-BSI Prevention Bundle

- Added elements to their existing CR-BSI Prevention Bundle[19]
  - US pre-puncture evaluation (RcCeVA)
  - Tunneled the exit site
  - Sealed exit site with tissue adhesive at the time of insertion
    - **No CHG sponge dressing at time of insertion; added at 1st dressing change**
  - Consistent use of transparent dressings
  - Simulation based training program for all inserters

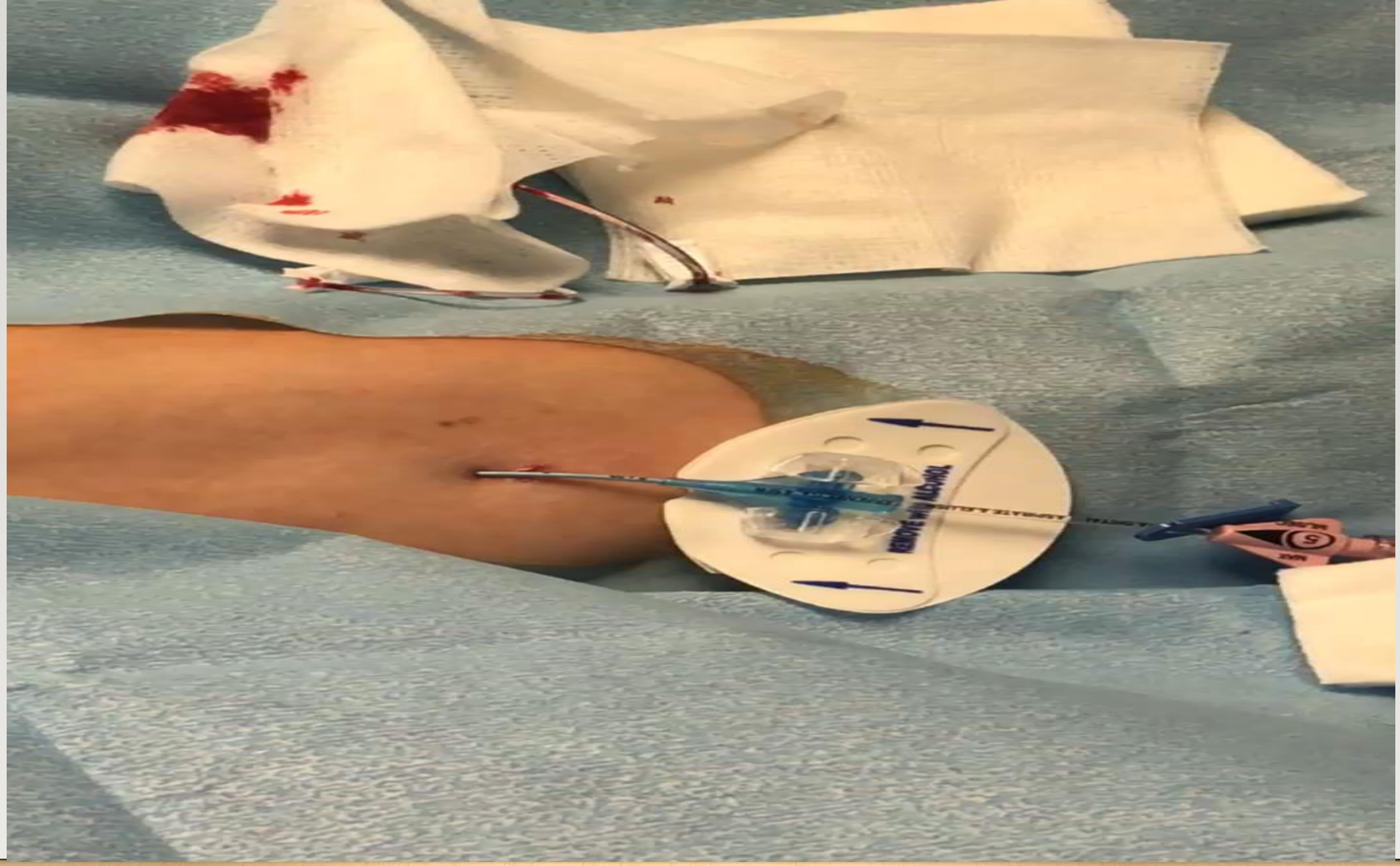
Biacucci, et al. 2017

Tissue Adhesive in CR-BSI Prevention Bundle

- Conducted in a PICU from June 2009 – June 2014
- 1150 catheter days; 648 in the study group and 503 in the control
- **CR-BSI rate dropped from 15/1000 catheter days to 1.5/1000 catheter days**
- 2.2 day longer dwell
- Comments in conclusion about tissue adhesive;
  - **"… sealing the exit site.. reduces risk of extraluminal contamination … and reduces bleeding at puncture site and prevents the "in and out" motion may reduce local damage to the endothelium and reduce risk of thrombosis."**

Video courtesy of Rebecca Stevens

Videos courtesy of Matt Ostroff/St. Joseph's Medical Center



Videos courtesy of Matt Ostroff/St. Joseph's Medical Center

Reapplication for long-term use

- Currently not well studied
- Some reports of build up on catheter tubing

Impact on Catheter Materials

- Published in JVA in 2017
- Lab study
- 12 PICC Brands
  - 11 polyurethane
  - 1 silicone
- Evaluated at 4, 8, and 12 weeks
- No changes in materials observed

Di Puccio, et al. 2017

Adhesive removal

- Commercially available adhesive removers are capable of loosening cyanoacrylate quickly
  - PDI
  - Uni-solve
  - Remove
  - Detachol
- Active ingredients:
  - Paraffin
  - Petrolatum
  - D-Limonene
  - Propanol
  - Esters of IPA

Take Home Message

- Tissue adhesive benefits
  - Enhanced catheter securement
  - Seal around puncture site
    - Decrease contamination of site
    - Reduced oozing/leaking from puncture site
  - Studies demonstrate feasibility of the concept and suggests reduction of complications
- Large studies are in progress
- Promoting skin integrity and reducing VAD complications is critical aspect of patient care with any type of VAD

Thank You for Your Attention

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