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Leaving More Than Your Fingerprint on the Intravenous Line: A Prospective Study on Propofol Anesthesia and Implications of Stopcock Contamination

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Abstract

Introduction—Acute care handling of IV stopcocks during anesthesia and surgery may result in contaminated IV tubing sets. In the context of widespread propofol use, a nutrient-rich hypnotic drug, we hypothesized that propofol anesthesia increases bacterial contamination of IV stopcocks and may compromise safety of IV tubing sets when continued to be used after propofol anesthesia.

Methods—We conducted an *in vitro* trial by collecting IV tubing sets at the time of patient discharge from same-day ambulatory procedures performed with and without propofol anesthesia. These extension sets were then held at room temperature for 6, 24, or 48 hours. We cultured 50 samples at each interval for both cohorts. Quantitative cultures were done by aspirating the IV stopcock dead space and plating the aspirate on blood agar for colony count and speciation.

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Results—Positive bacterial counts were recovered from 17.3% of propofol anesthesia stopcocks (26/150) and 18.6% of non-propofol stopcocks (28/150). At 6 hours, the average bacterial counts from stopcocks with visible residual propofol was 44 colony forming units (CFU)/mL, compared to 41 CFU/mL with no visible residual propofol and 37 CFU/mL in non-propofol anesthesia stopcocks. There was a 100-fold increase in bacterial number in contaminated stopcock dead spaces at 48 hours after propofol anesthesia. This difference remained significant when comparing positive counts from stopcocks with no visible residual propofol and non-propofol anesthesia (p-value=0.034).

Conclusion—There is a covert incidence and degree of IV stopcock bacterial contamination during anesthesia which is aggravated by propofol anesthetic. Propofol anesthesia may increase risk for postoperative infection because of bacterial growth in IV stopcock dead spaces.

Introduction

Propofol is widely used for both inpatient and outpatient anesthesia. Because propofol is highly hydrophobic, it is manufactured in a nutrient-rich emulsion called Intralipid that is white in appearance, containing soy bean oil, egg phospholipids, and glycerin. Shortly after propofol was introduced, investigators found its clinical use problematic because of microbial contamination. The Food and Drug Administration mandated addition of antimicrobial preservative, but the complication of infection persisted.^{1–2} Investigators found that the improper handling of opened vials and re-use of syringes resulted in logarithmic growth at 6 hours, even in the presence of ethylenediaminetetraacetic acid (EDTA).^{3–4} Thus, manufacturers' directions for use include discarding propofol after 6 hours of opening the vial or filling the syringe.^a For continuous IV infusions, manufacturers recommend discarding tubing and any unused portion of propofol after 12 hours.^b

Loftus et al. found that microorganisms from anesthesia providers' hands and equipment commonly serve as significant sources for IV stopcock contamination associated with anesthesia delivery.^{5–6} However, these studies were limited to the intraoperative period only and did not investigate whether the use of nutrient-rich medications such as propofol increased contagion levels postoperatively.

Newly opened IV sets are sterile upon removal from packaging, but quickly become at risk for bacterial contamination during anesthesia through repetitive interactions in the course of medication delivery with improper handling. The incidence of propofol syringe contamination in the operating room and intensive care unit (ICU) has been reported to be 4.8 to 6%.^{7–9} Additional studies have shown contamination to be evident in 8 to 11% of syringes, even when propofol is drawn up according to the manufacturer's guidelines.^{10–11} Despite these known acute care contamination rates, the longer term risk of IV stopcock bacterial contamination after routine propofol anesthesia remains unexamined.

While IV tubing sets remain connected to patients after propofol anesthesia, dead spaces may harbor growing bacterial contaminants, even in the absence of visible residual propofol.

^aNovaplius. Propofol injectable emulsion, USP. 451192A/Revised: October 2009

^bAstraZeneca. Diprivan 1%, package insert 235003. Revised: August 2005

We hypothesized bacterial growth occurring in these dead spaces could be detected by sampling the IV stopcock after propofol anesthesia and is a potential indicator for contamination in the IV stopcock. Prior work *in vitro* by Fukada and Ozaki showed that methicillin-resistant *Staphylococcus aureus* (MRSA) survived and grew in the dead space of IV stopcocks regardless of whether or not the propofol formulation contained EDTA or had a continuous acetate Ringer's solution flow rate of 50 mL/hr for 24 hours after propofol anesthesia.¹²

We sought to examine IV extension tubing stopcocks quantitatively for presence of aerobic bacteria after ambulatory procedures with or without propofol anesthesia. The primary aim was to determine if propofol increased the presence of bacterial contaminants at 48 hours. Our secondary aim was to examine if after propofol anesthesia administration, bacterial contamination (colony forming units [CFU]/mL) in IV stopcock dead spaces increased, regardless of whether residual propofol was visible.

Methods

This was a prospective cohort study of IV extension tubing stopcock dead space (see Figure 1) culturing after propofol and non-propofol anesthesia. The study was conducted with approval and waiver of informed patient consent from the University of Florida, College of Medicine, IRB, application #48-2011. There is no linkable identification of IV extension sets to patient or provider. We reviewed the anesthetic record at time of extension tubing collection to confirm propofol administration and absence of other nutrient-rich infusions such as blood products, platelets, or total parenteral nutrition. The study was blinded to all anesthesia and nursing care providers and absent of all patient identifiers. There were at least 10 different blinded providers in each arm of the study (propofol and non-propofol), respectively.

Over a 30 consecutive work-day period, IV stopcock extension sets were collected after propofol (same-day ambulatory surgery) and non-propofol anesthesia (mainly methohexital, administered for cataract extraction and electroconvulsive therapy). Propofol used throughout this study contained preservative EDTA (63323-270-25, APP Pharmaceutical, Schaumburg, IL). All tubing sets in this study included stopcock extension (MX5996, Smith Medical, Dublin, OH). We collected the IV stopcock extension sets after they were removed from patients at the time when the IV sets are typically discarded.

Collected IV tubing was stored at room temperature (20 °C) with the roller clamp closed and all IV fluid remaining in the tubing. The tubing was coiled and protected in a biohazard bag for the duration of the holding time. The stopcock was covered with a sterile cap (R2000, B. Braun, Allentown, PA) and stored in a clean, room temperature environment with individual packaging.

The stopcock dead space from both propofol and non-propofol IV extension sets was sampled at 6, 24, or 48 hours after surgery for a total of 50 samples at each interval. Individual extension sets recovered from propofol and non-propofol anesthesia were

randomized to different holding times. The study was designed to identify differences in bacterial contamination after anesthesia.

Because bacterial growth in propofol is slow at room temperature (beginning after a dormant period of 6 hours) we began our quantitative cultures at 6 hours for baseline values. Each IV extension set stopcock was sampled only once. We adhered to standard precautions for handling of all IV tubing, containers were clearly marked with biohazard labels, and no sharps were included in sample collections.

Bacteremia has been understood to result from catheter colonization at as few as 15 CFU/mL.¹³ When blood drawn for quantitative culture from the catheter luminal hub or from peripheral venipuncture contains 4 to 10 times more than 15 CFU/mL, a catheter-related bloodstream infection is confirmed.¹⁴ Thus, we considered any IV stopcock dead space bacterial counts above 120 CFU/mL as a significant bacterial burden. Considering the dynamic nature of bacteria's natural system, we selected an effect size of 50 CFU/mL to ensure an adequate difference at lower counts. Our sample size calculations determined we needed 50 samples in each group with a large standard deviation of 200, along with type I error of 0.05 and type II error of 0.2.

All IV stopcock dead spaces were cultured in an aseptic environment by removal of the cap and using a sterile micropipette (02-707-135, Fisherbrand, Stephens City, VA) to aspirate the residual volume from the dead space. After tarring a sheep blood agar plate (R01198, Remel, Lenexa, KS) on a 3-digit scale (PE160, Mettler, Toledo, OH), each aspirate aliquot was spread on individual agar plates for culture (aspirates ranged from 25 to 200 micrograms). Weight in micrograms of aspirate aliquots was noted for quantitative culture calculation. Aspirated volumes were balanced equally with sterile buffer dilution (D699, Hardy Diagnostics, Santa Maria, CA) to a total of 250 micrograms for equal dispersion of all aliquots across the agar surface by one-time use of sterile inoculating loop (R641820, Fisherbrand, Stephens City, VA). Laboratory control blanks were also performed with each culture run by inoculating sterile blood agar with 250 micrograms sterile dilution buffer and blanks were handled in the same fashion as study samples. Any sample runs with bacteria found on laboratory blanks were invalidated and not included in the study. A total of 320 samples were collected, but 20 samples were discarded due to contaminant colonies on laboratory blanks from that set, leaving a total of 300 samples with 150 in each group (propofol and non-propofol), respectively.

We incubated all blood agar plates at 37°C for 48 hours (630D, Fisherbrand Isotemp, Stephens City, VA) with CFU per mL calculated by total colonies present (Figure 2) divided by weight in micrograms multiplied by 1000 to get CFU/mL (correction factor 1000 mcg/mL ~density of water) according to standard laboratory methods.¹⁵ Colony morphology was noted and pure isolates were submitted for speciation via bioMérieux (Vitek 2, Durham, NC). In the decade before mainstream propofol use, clinical studies indicated a low level of IV fluid contamination of 11% yielding microbial contaminants;¹⁶ other studies identified contamination rates as high as 32%.¹⁷

We collected data using an Excel spreadsheet (version 2010, Microsoft, Redmond, WA) and analyzed them with SAS version 9.2 (SAS Institute, Cary, NC). We hypothesized that propofol increases the presence of bacterial contaminants at 48 hours. We modeled the number of bacteria using the administration of propofol anesthesia or non-propofol anesthesia as the explanatory variable by negative binomial regression due to overdispersion, because the variance was greater than the mean.

Our secondary hypothesis required testing whether post-propofol anesthesia bacterial contamination (CFU/mL) in IV stopcock dead spaces increased over time compared to post-non-propofol anesthesia; we wanted to discern if there were any significant differences in positive bacteria counts regardless of whether or not residual propofol was visible. All positive bacteria counts were compared using negative binomial regression with grouping variable (visible propofol, nonvisible propofol, non-propofol group) as the explanatory variable at each interval. Observed counts in average CFU/ mL per group and holding times are listed in Table 1, Figures 3 and 4. An additional log-linear mixed model with grouping variable with three levels, time variable with 3 levels (6 hrs, 24 hrs, and 48 hours), and time and group interaction were included in the model as fixed effects. Sample id was included as a random effect to account for correlation among measurements from the same sample at different intervals. Post hoc multiple comparisons were performed using Tukey-Kramer method. Diagnostic plots were reviewed to assure validity of the models. Kruskal-Wallis test was used to confirm the differences in counts among the three groups.

Results

Positive bacterial cultures were recovered from 17.3% of propofol anesthesia stopcocks (26/150) and 18.6% of non-propofol anesthesia stopcocks (28/150). Growth of all samples per respective holding times was averaged in CFU/mL plus 1 standard deviation (18) with subset averages from only positive samples also analyzed (Table 1). At 6 hours, we observed average values for visible propofol in the dead space at 44 CFU/mL and no visible propofol in the stopcock dead space from propofol-receiving patients and non-propofol-receiving patients at 41 CFU/mL and 37 CFU/mL, respectively. At 24 and 48 hours, the incidence of positive bacterial cultures remained unchanged (Table 1), but differences in average bacterial counts were readily apparent (Figures 3 and 4). When comparing all samples, average bacterial counts at 48 hours for propofol and non-propofol groups were 472 CFU/ml and 4 CFU/mL, respectively. When comparing only positive samples at 48 hours, averages from the visible propofol group were 5066 CFU/mL, compared to the non-visible propofol group at 831 CFU/ml and non-propofol group at 30 CFU/mL. There was no evidence of significant differences among the three groups according to the negative binomial regression model or the Kruskal-Wallis test at 6 hours, although there were significant differences among the groups using both methods at 24 and 48 hours (Table 2).

Log-linear mixed model analysis performed to compare visible propofol, nonvisible propofol, and non-propofol groups showed that group and time were significant predictors of the number of bacteria (p-values of 0.0005 and 0.006, respectively), although there was no strong evidence of significant interaction between group and time (p=0.09). Multiple comparison tests using the Tukey-Kramer method showed that there were no significant

differences among groups at 6 hours ($p=0.99$), but number of bacteria was significantly higher for the visible propofol group than the nonvisible group ($p=0.03$) and the non-propofol group at 24 hours ($p=0.0008$). Similarly, number of bacteria observed in the visible propofol group was significantly higher than in the nonvisible propofol and non-propofol groups at 48 hours (p -values of 0.01 and 0.0003, respectively). Table 3 shows p -values for differences in bacteria count in visible-propofol, no-visible-propofol and non-propofol groups at each time point obtained using mixed-model analysis along with estimates for differences and 95% confidence intervals on log-scale. Median and 95% confidence intervals for the ratio of number of bacteria comparing pairs of groups are reported as well.

A representative set of colonies from each holding interval was submitted for speciation (Table 4). Review of microorganisms indicated that sources were most likely skin flora and environmental fomites. The bulk of bacteria recovered were gram-positive cocci at varying levels of CFU/mL. Densities of slower growing bacteria, such as *Micrococcus* and *Kocuria*, had only moderate growth after propofol anesthesia compared to higher yields of *Staphylococcus*, *Acinetobacter*, and *Pseudomonas* after propofol anesthesia. The concentration of Intralipid varied widely and was not evaluated in this study; we noted presence or absence of visible propofol in the IV extension set stopcock dead space of patients known to have received propofol via those stopcocks.

Discussion

In our study, we held IV stopcocks in isolation after removal from patients and measured bacterial contaminants up to 48 hours later. At our institution IV tubing sets are changed every 96 hours from time of initial use, except for propofol infusion sets (changed every 24 hours) and total parenteral nutrition sets (changed every 48 hours). In many hospitals, IV tubings are changed immediately after anesthesia in postoperative care units (PACU), but this is not a patient safety standard. Considering the average patient who receives anesthesia, we wanted to determine if IV stopcock contamination in the operative period posed subsequent risk if nutrient-rich medications were used during anesthesia. These data are most significant for patients who will continue to have their associated IV connections in place after anesthesia, especially those with longer-term access at central lines and peripherally inserted central catheters. We isolated IV tubing sets after same-day surgery to limit possible contamination from subsequent hub interactions to specifically address contamination associated with anesthesia. It is local routine practice to have one IV stopcock extension used for all injections.

We measured positive bacterial cultures in 16–20% of IV stopcocks after propofol anesthesia, compared to 12–32% after non-propofol anesthesia, which is consistent with previous studies that reported ranges of 11–32%.^{16–17} Importantly, our study found a significant difference in bacterial density over time in the IV extension stopcocks after propofol anesthesia compared to non-propofol anesthesia, as seen in the growth curve up to 48 hours (Figure 3). It is unknown how many IV sets collected were from ambulatory patients remaining in the PACU beyond the average discharge time of less than 90 minutes (cursory review of PACU stays overall at these locations during the study period indicated

this number to be less than 10%). This *in vitro* trial after routine anesthesia allowed comparison of bacterial growth over time after propofol and non-propofol anesthesia without confounders from subsequent hub use for medication delivery. However, this study does not directly measure the actual bacterial burden experienced by patients in the context of an in-hospital setting.

The numbers of hub interactions were not recorded intraoperatively, nor were they noted postoperatively, because this study was blinded to all care providers in order not to detract from usual practices. Regardless of degree of acute care IV access handling and length of procedure, the incidence of contaminated stopcocks between propofol anesthesia and non-propofol anesthesia was similar. Positive cultures were recovered from IV stopcocks at a rate of 17.3% after propofol anesthesia (26/150) and 18.6% after non-propofol anesthesia (28/150). This may be biased due to an uninvestigated equivalent number of hub interactions during ambulatory anesthesia or directly observed vigilance of hand hygiene between anesthesia providers. It is expected that ambulatory anesthesia procedures require a much different degree of acute care IV access handling than main operating room procedures, and consequently have different (less) potential for contamination. Yet baseline quantitative cultures at 6 hours yielded equivalent average bacterial counts from stopcocks with visible propofol (44 CFU/mL), compared to 41 CFU/mL in those stopcocks with no visible residual propofol, and 37 CFU/mL in stopcocks after non-propofol anesthesia. The fact that there was no detected difference at time 6 hours may have been due to small sample size and skewness with corresponding large confidence intervals.

It is important to note that preservative-containing propofol was used throughout this study and could have reduced contamination within the first 6 hours. Surgery duration for ambulatory procedures in which propofol was used ranged from 1 to 2 hours, with more than one dozen hub interactions compared to less than half an hour for the non-propofol group, where the total number of drugs administered ranged from 2 to 6 with less than a dozen hub interactions in total. This difference may render the former an inappropriate control group considering the varying degrees of acute care IV handling, but the incidence of contamination and average baseline counts were similar among all groups at 6 hours. The fact that the IV sets in this study had no other nutrient-rich infusions (i.e., blood products, platelets, and total parenteral nutrition) supports the hypothesis that propofol alone can contribute to increased bacterial counts and to the risk of iatrogenic infection after propofol anesthesia.

Recent “Scrub the Hub” campaigns¹⁸ encourage anesthesiologists to follow best-practice guidelines for disinfection of IV hubs with isopropyl alcohol before syringe or infusion tubing connection. A direct relationship between scrub duration and stopcock decontamination by residual fluorescent powder has been demonstrated.¹⁹ Preventing stopcock contamination by improving hand hygiene compliance rates among anesthesia providers is also a clear goal. Real-time observations in the operating room by Loftus et al. showed that contamination by anesthesia providers’ hands persists and serves as a significant source of stopcock set contamination.⁵ We should continue to emphasize intraoperative hand hygiene both before and during patient care, but also consider postoperative decontamination strategies. With opportunities to use needleless hubs, this

may require further investigation to determine efficacy of routine disinfection before handling every injection site in the operating room. Notwithstanding a 3- to 5-second swabbing of 70% alcohol pledget, Menyhay and Maki found needleless Luer-activated connectors remained heavily contaminated by downstream quantitative cultures on the intraluminal side.²⁰

Our IV tubing sets also contained needle-free injection ports at various points. But to ensure no interference with usual practices, hub interactions were not monitored nor did we did trace whether the stopcock was the only possible access site for propofol delivery. There were, however, stopcocks with visible residual propofol, clearly identifying the propofol site of delivery. In comparison, Fukada and Ozaki evaluated three venous access systems and growth of MRSA-contaminated propofol containing EDTA over 24 hours:¹² one system with very little dead space (Planecta) versus a standard three-way stopcock (TOP) and a three-way stopcock plus needle-free adaptor (Interlink). They observed residual amounts of propofol in all three types of dead spaces and detected MRSA growth in all three systems at 6 hours, with logarithmic growth at 24 hours in the stopcocks.

Visible residual propofol in the stopcock was evident in multiple samples: 13 stopcocks with visible residual propofol had positive bacterial growth, and 14 had no detected growth. Considered alone, this observation yields an alarming 48% incidence of bacterial contamination when propofol remains visible in the IV stopcock dead space.

We acknowledge our study's approach is limited to the small sample volumes aspirated from the IV extension set's stopcock dead space. Yet, our results reinforce prior observations of bacterial transmission intraoperatively and, specifically, they identify the key role that propofol plays in enhancing bacterial amplification after IV extension set stopcock contamination after anesthesia.

Our study is limited to only the IV stopcock dead space and does not allow us to assess total bacterial burden in IV tubing after propofol anesthesia.

Our high *Pseudomonas* count was also observed by Crichton in a study of Intralipid with intentional bacterial seeding with *Serratia*, *Pseudomonas*, and *Klebsiella*, where confluent growth at 48 hours was recorded.¹⁷ Considering this bacterial burden and the outcomes of critically ill patients, Haddad et al. showed the use of preservative-free propofol as having an association with increased risk of ICU-acquired infection and with ICU-acquired severe sepsis and septic shock.²¹

Other microbial analyses of Intralipid without preservative found that bacterial growth occurred as early as 6 hours after incubation and was at levels of clinical concern within the first 12 hours, about 103–104 CFU/mL.²² It is possible that residual propofol in IV tubing after anesthesia may have diluted preservative and bacterial growth becomes easier. Interestingly, the spectrum of microorganisms recovered in our study is similar to that found by Loftus et al., whose perioperative surveillance found hand contaminants in 49–100% of anesthesia providers, including *Micrococcus*, *Staphylococcus*, and gram negative bacteria.⁶

The fact that adherence to Surgical Care Improvement Project measures alone is not obviously associated with a significantly lower probability of postoperative infection²³ suggests there are other perioperative sources yet to be addressed. Many patients receive propofol via an IV stopcock access point during the course of an anesthetic. Previous work by Langevin et al. showed deliberate infection of *Staphylococcus aureus* was recovered from rabbit kidneys regardless if bacterial suspensions were injected IV with Intralipid or followed after Intralipid with saline injection.³ These findings support our hypothesis that bacterial contaminants in the IV stopcock and other dead space in the IV tubing may thrive after propofol anesthesia and suggest that inadvertent injection may become a significant stress to a vulnerable patient.

The incidence and quantity of IV tubing bacterial contamination after exposure to propofol with preservative is well known through *in vitro* studies. Microbial contamination in IV stopcock dead spaces after routine anesthesia has been studied previously, but not in regards to propofol compared to non-propofol anesthesia. We hypothesized bacterial amplification occurs in IV stopcock dead spaces after propofol anesthesia even when there is no visible residual propofol. Identification of this risk suggests the need for a standard of care to remove (or replace) the IV tubing sets after propofol anesthesia. This *in vitro* study does not directly correlate to IV catheters remaining *in situ* for 48 hours postoperatively. However, this study is important from a patient safety standpoint because it indicates a continued need for improved hand hygiene skills in anesthesia providers; it also suggests, given the data on bacterial growth after 6 hours, that removal (or exchanging) of IV extension sets after propofol anesthesia may warrant a new standard of care.

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References

1. Bennett SN, McNeil MM, Bland LA, Arduino JM, Villarino ME, Perrotta DM, Burwen DR, Weibel SF, Pegues DA, Stroud L, Zeitz PS, Jarvis WR. Postoperative infections traced to contamination of an intravenous anesthetic, propofol. *N Engl J Med*. 1995; 333:147–54. [PubMed: 7791816]
2. Muller AE, Huisman I, Roos PJ, Rietveld AP, Klein J, Harbers JB, Dorresteijn JJ, van Steenberghe JE, Vos MC. Outbreak of severe sepsis due to contaminated propofol: lessons to learn. *J Hosp Infect*. 2010; 76:225–30. [PubMed: 20692067]
3. Langevin PB, Gravenstein N, Doyle TJ, Roberts SA, Skinner S, Langevin SO, Gulig PA. Growth of *Staphylococcus aureus* in Diprivan and intralipid: implications on the pathogenesis of infections. *Anesthesiology*. 1999; 91:1394–400. [PubMed: 10551591]
4. Sosis MB, Braverman B. Growth of *Staphylococcus aureus* in four intravenous anesthetics. *Anesth Analg*. 1993; 77:766–8. [PubMed: 8214662]
5. Loftus RW, Koff MD, Burchman CC, Schwartzman JD, Thorum V, Read ME, Wood TA, Beach ML. Transmission of pathogenic bacterial organisms in the anesthesia work area. *Anesthesiology*. 2008; 109:399–407. [PubMed: 18719437]

6. Loftus RW, Muffly MK, Brown JR, Beach ML, Koff MD, Corwin HL, Surgenor SD, Kirkland KB, Yeager MP. Hand contamination of anesthesia providers is an important risk factor for intraoperative bacterial transmission. *Anesth Analg*. 2011; 112:98–105. [PubMed: 20686007]
7. Webb SA, Robert B, Breheny FX, Golledge CL, Cameron PD, van Heerden PV. Contamination of propofol infusions in the intensive care unit: incidence and clinical significance. *Anaesth Intensive Care*. 1998; 26:162–4. [PubMed: 9564394]
8. Farrington M, McGinnes J, Matthews I, Park GR. Do infusions of midazolam and propofol pose an infection risk to critically ill patients? *Br J Anaesth*. 1994; 72:415–7. [PubMed: 8155442]
9. Bach A, Motsch J, Schmidt H, Böttiger BW, Böhler H, Martin E, Sonntag HG. In-use contamination of propofol. A clinical study. *Eur J Anaesthesiol*. 1997; 14:178–83. [PubMed: 9088817]
10. Magee L, Godsiff L, Matthews I, Farrington M, Park GR. Anaesthetic drugs and bacterial contamination. *Eur J Anaesthesiol*. 1995; 12(Suppl):41–3. [PubMed: 7535692]
11. Lessard MR, Trepanier CA, Gourdeau M, Denault PH. A microbiological study of the contamination of the syringes used in anaesthesia practice. *Can J Anaesth*. 1988; 35:567–9. [PubMed: 3203452]
12. Fukada T, Ozaki M. Microbial growth in propofol formulations with disodium EDTA and the influence of venous access system dead space. *Anaesthesia*. 2007; 62:575–580. [PubMed: 17506735]
13. Chatzinikolaou, I.; Hanna, H.; Darouiche, R.; Samonis, G.; Tarrand, J.; Raad, I. The value of quantitative blood cultures collected through central venous catheters in establishing the diagnosis of bloodstream infections: a prospective study [abstract D-1698]. Paper presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy; Chicago IL. September 14–17, 2003;
14. Hanna R, Raad II. Diagnosis of catheter-related bloodstream infection. *Curr Infect Dis Rep*. 20005; 7(6):413–9. [PubMed: 16225778]
15. Greenberg, AE.; Clescerl, LS.; Eaton, AD. Standard methods for examination of water and wastewater. 20. Baltimore: American Public Health Association; 1998. p. 921
16. Maki DG, Anderson RL, Shulman JA. In-use contamination of intravenous infusion fluid. *Appl Microbiol*. 1974; 28:778–84. [PubMed: 4613269]
17. Crichton EP. Infusion fluids and culture media. *Am J Clin Pathol*. 1973; 59:199–202. [PubMed: 4631583]
18. Munoz-Price LS, Dezfulian C, Wyckoff M, Lenchus JD, Rosalsky M, Birnbach DJ, Arheart KL. Effectiveness of stepwise interventions targeted to decrease central catheter-associated bloodstream infections. *Crit Care Med*. 2012; 40:1464–1469. [PubMed: 22511128]
19. Lockman JL, Heitmiller ES, Ascenzi JA, Berkowitz I. Scrub the Hub! Catheter needleless port decontamination. *Anesth*. 2011; 114:958.
20. Menyhay SZ, Maki DG. Disinfection of needleless catheter connectors and access ports with alcohol may not prevent microbial entry: The promise of a novel antiseptic-barrier cap. *Infect Control Hosp Epidemiol*. 2006; 27:23–7. [PubMed: 16418982]
21. Haddad S, Tamim H, Memish Z, Arabi Y. Association of preservative-free propofol use and outcome in critically ill patients. *Am J Infect Control*. 2011; 39:141–7. [PubMed: 20888671]
22. Melly MA, Meng HC, Schaffner W. Microbial growth of lipid emulsions used in parenteral nutrition. *Arch Surg*. 1975; 110:1479–81. [PubMed: 982]
23. Stulberg JJ, Delaney CP, Neuhauser DV, Aron DC, Fu P, Koroukian SM. Adherence to surgical care improvement project measures and the association with postoperative infections. *JAMA*. 2011; 303:2479–85. [PubMed: 20571014]

Figure 1.
Visible white propofol (arrow) in IV extension set stopcock dead space after routine anesthesia care.

Figure 2.

Cultures of IV extension set stopcock aspirates at 24 hours postoperatively. Plate (A) is from stopcock with visible residual propofol totaling 188 colonies (7,230 CFU/mL). Plate (B) is from non-propofol anesthesia stopcock totaling 4 colonies (60 CFU/mL). CFU – colony forming units.

Figure 3. Growth of all samples in average colony forming unit/mL at respective holding times plus 1 standard deviation (18).

Figure 4.

All samples with (+) bacterial growth in average colony forming unit/mL at respective holding times plus 1 standard deviation (1σ).

Table 1

Average colony forming units per mL (CFU/mL) from IV extension set stopcock dead spaces held at room temperature after both propofol and non-propofol anesthesia

Hold times	Propofol		Non-propofol	
<u>6 hours</u>				(12%)
Samples (+) bacteria per total	8/50	(16%)	6/50	
Average (all samples) CFU/mL +1 δ	7 + 22	(n = 50)	4 + 14	(n = 50)
Average only (+) bacteria CFU/mL + 1 δ	43 + 41	(n = 8)	37 + 21	(n = 6)
<u>24 hours</u>				
Samples (+) bacteria per total	10/50	(20%)	16/50	(32%)
Average (all samples) CFU/mL +1 δ	278 + 1131	(n = 50)	31 + 96	(n = 50)
Average only (+) bacteria CFU/mL + 1 δ	1526 + 2387	(n = 10)	94 + 154	(n = 16)
<u>48 hours</u>				
Samples + bacteria per total	8/50	(16%)	6/50	(12%)
Average (all samples) CFU/mL +1 δ	472 + 2017	(n = 50)	4 + 11	(n = 50)
Average only (+) bacteria CFU/mL + 1 δ	2949 + 4487	(n = 8)	30 + 12	(n = 6)

Table 2

Mean and medians of number of bacteria reported with their 95% confidence intervals along with p-values comparing number of bacteria among visible propofol, no visible propofol and non-propofol groups at each time point.

Hold times	Mean/Median (95% Confidence Intervals)				p-values	
	Non-propofol	Propofol	Propofol		Kruskal-Wallis	Negative Binomial Regression
			Visible Propofol	Nonvisible Propofol		
6 hours					0.85	0.8
Mean (95% CI)	37 (14, 59)	43 (9, 77)	44 (0, 106)	42 (0, 118)		
Median (95% CI)	29 (14, 65)	24 (17, 114)	33 (11, 100)	18 (17, 114)		
24 hours					0.04	0.02
Mean (95% CI)	95 (13, 177)	1390 (0, 3029)	2361 (0, 6045)	418 (0, 1418)		
Median (95% CI)	42 (32, 74)	146 (38, 2968)	1400 (42, 7231)	53 (19, 1857)		
48 hours					0.03	0.0002
Mean (95% CI)	30 (18, 43)	2949 (0, 6700)	5066 (0, 14131)	831 (0, 3374)		
Median (95% CI)	29 (15, 45)	133 (24, 10000)	5091 (83, 10000)	45 (8, 3228)		

CI=confidence interval

Table 3

Differences in bacteria count on log-scale among visible propofol, no visible propofol and non-propofol groups at each time point obtained using mixed model analysis.

Hold times	Groups Compared	Mean Difference (log scale)	Standard Error (log scale)	p-value	95% CI for difference (log scale)	95% CI for ratio of medians (anti-log scale)
6	Visible propofol vs. nonvisible propofol	0.16	1.02	0.87	(-1.9, 2.2)	1.2 (0.2, 9.1)
	Visible propofol vs. non-propofol	0.02	0.93	0.98	(-1.8, 1.9)	1 (0.2, 6.6)
	Nonvisible propofol vs. non-propofol	-0.14	0.93	0.88	(-2, 1.7)	0.9 (0.1, 5.6)
24	Visible propofol vs. nonvisible propofol	2.02	0.91	0.03	(0.2, 3.8)	7.5 (1.2, 46.9)
	Visible propofol vs. non-propofol	2.65	0.74	0.0008	(1.2, 4.1)	14.1 (3.2, 62)
	Nonvisible propofol vs. non-propofol	0.63	0.74	0.40	(-0.9, 2.1)	1.9 (0.4, 8.2)
48	Visible propofol vs. nonvisible propofol	2.64	1.02	0.01	(0.6, 4.7)	14.1 (1.8, 108.7)
	Visible propofol vs. non-propofol	3.67	0.93	0.0003	(1.8, 5.5)	39.1 (6, 253.2)
	Nonvisible propofol vs. non-propofol	1.02	0.93	0.28	(-0.8, 2.9)	2.8 (0.4, 18)

Microorganism concentrations found in IV extension set stopcock dead spaces after propofol and non-propofol anesthesia at respective holding times.

Table 4

Propofol	CFU/mL	Non-propofol	CFU/mL
6 hours			
Staph epidermidis	18	Staph warneri	14
Acinetobacter	18	Staph cohnii	65
Micrococcus	46	Micrococcus	61
Kocuria	69	Kocuria	14
24 hours			
Staph hominis	269	Dermacoccus	51
Micrococcus	115	Micrococcus	33
Acinetobacter	6846	Kocuria	79
Staph Epidermidis	2968	Strep sanguinis	41
48 hours			
Pseudomonas oryz	> 10,000	Staph lentus	31
Micrococcus	83	Micrococcus	45
Kocuria	182	Kocuria	15

CFU = colony forming units