ASK THE QUESTION

Question: After spiking an IV fluid bag, what is the optimal time frame for it to remain spiked and stored at room temperature before it must be used or discarded?

SEARCH FOR EVIDENCE

Databases: PubMed, Scopus


Filters: English, Published last 10 years

CRITICALLY ANALYZE THE EVIDENCE

There were four studies found addressing bacterial contamination of IV fluids after they have been spiked. Two of these studies (Macias et al., 2010; Rickard et al., 2009) address the prevalence of infusate contamination in the clinical setting. Macias et al. (2010) specifically evaluated IV fluids that were admixed in nursing areas, while Rickard et al. (2009) evaluated crystalloid fluids (85% normal saline) used for 24 hours or more. Macias et al. (2010) found that GNR bacteremia associated with infusate contamination represented 7% (95% CI 5 2-11%) of all primary bloodstream infections and 11% (95% CI 5 2-22%) of all primary bloodstream infections not associated with venous catheter infection in a tertiary care hospital with a consolidated infection control program, strong support from microbiology, and an around-the-clock IV therapy nursing team. Rickard et al. (2009) compared infusate contamination prevalence in IV fluids used 24 hours or more in the acute care setting, and found that colonization (≥ 5 cfu) occurred at a rate of 0.4% (0.09 per 1000 infusion hours). The median duration of fluid bag use was not significantly different between colonized and “clean” specimens (p=0.99).

The remaining studies (Haas et al., 2017; Stedman et al., 2017) were experimental studies that evaluated bacterial growth in specific IV fluids over time. Haas et al. (2017) evaluated Lactated ringers spiked and hung in the laboratory environment, while Stedman et al. (2017) evaluated normal
saline spiked and hung in 5 busy perioperative areas (inside 4 ORs and in OR holding). Samples were collected at time of spiking, 1 hr, 2 hr, 4 hr, and 8 hr after spiking by Hass et al. (2017) and at time of spiking and for 4 hours afterward once per week for five weeks by Stedman et al. (2017). No growth was identified in any of the specimens for either of these studies.

Association for Professionals in Infection Control and Epidemiology (2016) position paper on safe injection, infusion, and medication vial practices in health care “supports the USP General Chapter 797 1-hour timeframe between preparation and initiation of administration in most clinical practice settings, but acknowledges that in certain settings this practice can be challenging to safely implement.” APIC does not support the advance preparation (the night before or many hours before administration) of IV bags or syringes. However, they do note that it is important to recognize that USP Chapter 797 standards “do not pertain to the clinical administration of CSPs to patients via application, implantation, infusion, inhalation, injection, insertion, instillation, and irrigation, which are the routes of administration.” APIC also strongly supports using an IV solution (e.g., bag or bottle) for only 1 patient and then discarding.

Association of perioperative Registered Nurses guideline for medication safety (drafted for public comment) recommends that precautions should be taken to mitigate the risk for errors during medication administration, including:

- Unused, opened irrigation or IV solutions should be discarded at the end of the procedure. [5: Benefits Balanced with Harms]
- Medications that are removed from the original package and found in a secondary container without a label should be discarded. [5: Benefits Balanced with Harms]
- Intravenous solution containers should be punctured (e.g., spiked) within 1 hour of the initiation of administration. [2: High Evidence]

The evidentiary support for this recommendation is based on the APIC and USP General Chapter 797 guidelines.

<table>
<thead>
<tr>
<th>Author/Date/ Journal</th>
<th>Purpose of Study</th>
<th>Study Design</th>
<th>Sample&amp; Setting</th>
<th>Outcomes</th>
<th>Design Limitations</th>
</tr>
</thead>
</table>
| Macias et al., 2010, American Journal of Infection Control | To determine the prevalence of infusate contamination in patients with gram-negative rods (GNR) bacteremia in a tertiary care hospital where good IV therapy practice is followed | Prospective observational | 384 matched specimens (infusate culture and blood culture) from adult patients with an IV line diagnosed with GNR bacteremia in a tertiary care hospital in Mexico City -IV infusates were admixed in nursing areas -bacteremia not related to an infection at another site -Infection control: -consolidated infection control program with 11 infusates (2.7%) grew bacteria in culture 7 infusates (2%, 95% CI 1-3%) were contaminated (i.e., grew the same bacteria as the blood culture) GNR bacteremia associated with infusate contamination represented 7% (95% CI 5 2-11%) of all primary bloodstream infections and 11% (95% CI 5 2-22%) of all primary bloodstream infections not associated with venous catheter infection | Study Limitations = None Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, survey) - Insufficient sample size - Sample not representative of patients in the population as a whole - Variables (confounders, exposures, predictors) were not described and accounted for - Outcome criteria not objective or were not applied in blind fashion - Insufficient follow-up, if applicable - For prognostic study, sample not

GRADE CRITERIA (See Appendix A)

Lower Quality Rating if:
- High risk of bias (When design limitations for one or more criteria impact the quality of studies sufficiently enough to lower confidence in the estimate of effect)
- Studies inconsistent (When there are differences in the direction of the effect, populations, interventions or outcomes between studies)
- Studies are indirect

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strong support from microbiology
-IV administration set included a primary system for continuous infusion and a secondary “piggyback” system for intermittent infusions (changed every 72hr)
-30 nurses dedicated to providing IV therapy care 24/7

Excluded patients where the administration set was changed after the blood culture was collected

Infusate specimen (1.5 mL) collected from the injection port of the secondary system after disinfection with 70% alcohol
-obtained average of 27.2 hr after blood culture
-cultures with ≥10CFU/mL considered +
-infusate contamination confirmed by the growth of the same organism in both infusate and blood

-estimated # of cultured infusates needed to diagnose 1 bacteremia associated with infusate contamination was 55

defined at common point in course of disease/condition
- For diagnostic study, gold standard not applied to all patients
- For diagnostic study, no independent, blind comparison between index test and gold standard

(Your PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)

- Studies are imprecise
  (When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)
- Publication Bias
  (e.g. pharmaceutical company sponsors study on effectiveness of drug)

Increase Quality Rating if:
- Large effect
  (When the relative risk of association between two factors is large or very large)
- Dose response
  (When the dose-response relationship increases the confidence than an effect is real and substantial)
- Plausible confounders
  (When plausible residual confounding is directly impacting the magnitude of effect)

Level of evidence for studies as a whole:
- High

Rickard et al., 2009, Journal of Clinical Nursing

To examine the level of microbial colonization in IV fluids after 24 hours of use in an acute care setting and to determine the necessity of changing infusate bags on a time-related basis

Cross-sectional

264 infusate specimens from crystalloid fluids (85% normal saline) used for 24 hours or more at a single teaching hospital in Australia
-control specimens (sealed, unused IV bags; n=261)
-over 18 months
-77% discontinued by 48 hr; 100% by 185 hr

7 infusate specimens (2.7%) used for 24 hours or more revealed some bacterial growth
-colonization (≥5 cfu) occurred at a rate of 0.4% (0.09 per 1000 infusion hours)
-median duration of fluid bag use was not significantly different between colonized and “clean” specimens (p=0.99)
-patients with colonized specimens were younger

Study Limitations = None

Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, survey)
- Insufficient sample size
- Sample not representative of patients in the population as a whole
- Variables (confounders, exposures, predictors) were not described and accounted for
- Outcome criteria not objective or
<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Study Type</th>
<th>Methods</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haas et al., 2017, <em>American Journal of Infection Control</em></td>
<td>To determine if spiking an IV bag of Lactated Ringers (LR) produces bacterial growth in the IV fluid over time</td>
<td>Experimental</td>
<td>80 infusate specimens - samples collected at 5 intervals: at time of spiking, 1, 2, 4 and 8 hours after spiking - 8 sham samples (4 contaminated with e.coli [sham +]; 4 sterile irrigant saline [sham -]) LR was used because it most closely approximated a normal daily anesthesia department routine - samples obtained by a certified registered nurse anesthetist - specimen collection included: standard hand hygiene, donned non-sterile gloves and then spiked IV bag (50-60mL)</td>
<td>Infusate specimens: there was no growth in any of the IV samples at any of the times tested at either 24 or 48 hours after plating</td>
<td>Study Limitations = None</td>
</tr>
<tr>
<td>Stedman et al., 2017, <em>Anesthesia and Analgesia</em></td>
<td>To determine whether there was an increased</td>
<td>Experimental</td>
<td>125 normal saline samples collected at spiking and hourly for 4 hours</td>
<td>No growth was identified in any of the specimens related to the 125 samples (95% CI, mean 38.3 yr vs 63.6 yr; p&lt;0.001) 18 control infusate specimens (6.9%) revealed some bacterial growth - colonization (&gt; 5 cfu) occurred at a rate of 3%</td>
<td>Study Limitations = None</td>
</tr>
</tbody>
</table>

Moderate
Low
Very Low
infection risk within 4 hours of spiking an IV fluid bag

hours weekly for 5 weeks at a hospital in New York
- IV administration sets were spiked and hung in 5 busy perioperative areas (inside 4 ORs and in OR holding) once a week
- samples were cultured in 2 mediums for aerobic and anaerobic growth (total of 250 specimens)
- multiple surgical specialties

Each IV administration set was assembled following standard hand hygiene and donning non-sterile gloves
- IV bag removed and hung on IV pole; tubing opened and uncoiled
- spike inserted into administration port and time of spiking noted on the data sheet
- IV set up primed with 30-40mL normal saline, tubing coiled and hung on IV pole (end cap not replaced)

Sterile specimen cups used to collect 10mL infusate and refrigerated

0.063)

- Insufficient sample size
- Sample not representative of patients in the population as a whole
- Variables (confounders, exposures, predictors) were not described
- Representation of the clinical environment unclear
- Representation of the decision-making environment unclear

REFERENCES
### Appendix A: GRADE criteria for rating a body of evidence on an intervention

Developed by the GRADE Working Group

#### Grades and interpretations:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>Low</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td>Very low</td>
<td>Any estimate of effect is very uncertain.</td>
</tr>
</tbody>
</table>

#### Type of evidence and starting level

<table>
<thead>
<tr>
<th>Evidence Type</th>
<th>Starting Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized trial</td>
<td>High</td>
</tr>
<tr>
<td>Observational study</td>
<td>Low</td>
</tr>
<tr>
<td>Any other evidence</td>
<td>Very low</td>
</tr>
</tbody>
</table>

#### Criteria for increasing or decreasing level

**Reductions**
- Study quality has serious (−1) or very serious (−2) problems
- Important inconsistency in evidence (−1)
- Directness is somewhat (−1) or seriously (−2) uncertain
- Sparse or imprecise data (−1)
- Reporting bias highly probable (−1)

**Increases**
- Evidence of association† strong (+1) or very strong (+2)
- Dose-response gradient evident (+1)
- All plausible confounders would reduce the effect (+1)

†Strong association defined as significant relative risk (RR 2-5 or 0.5-0.2) based on consistent evidence from two or more studies with no plausible confounders;

Very strong association defined as significant relative risk (RR >5 or <0.2) based on direct evidence with no threats to validity
Appendix B. Trustworthy Guideline rating scale

The University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

1. Transparency

<table>
<thead>
<tr>
<th>A</th>
<th>Guideline development methods are fully disclosed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Guideline development methods are partially disclosed.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline development methods are not disclosed.</td>
</tr>
</tbody>
</table>

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:
- Who wrote the initial draft
- How the committee voted on or otherwise approved recommendations

Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest

| A          | Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or |

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other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members).

<p>| | |</p>
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<thead>
<tr>
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<tbody>
<tr>
<td><strong>B</strong></td>
<td>Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.</td>
</tr>
<tr>
<td><strong>C</strong></td>
<td>Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.</td>
</tr>
<tr>
<td><strong>NR</strong></td>
<td>Guideline does not report on potential conflict of interests.</td>
</tr>
</tbody>
</table>

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything, this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. **Guideline development group**

<p>| | |</p>
<table>
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<tr>
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</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>Guideline development group includes one of the above, but not both.</td>
</tr>
<tr>
<td><strong>C</strong></td>
<td>Guideline developers all from one specialty or organization, and no methodologists.</td>
</tr>
<tr>
<td><strong>NR</strong></td>
<td>Affiliations of guideline developers not reported</td>
</tr>
</tbody>
</table>

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

4. **Systematic review**

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>A</strong></td>
<td>Guideline includes a systematic review of the evidence or links to a current review.</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>Guideline is based on a review which may or may not meet systematic review criteria.</td>
</tr>
<tr>
<td><strong>C</strong></td>
<td>Guideline is not based on a review of the evidence.</td>
</tr>
</tbody>
</table>

In order to qualify as a systematic review, the review must do all of the following:
- Describe itself as systematic or report search strategies using multiple databases
- Define the scope of the review (including key questions and the applicable population)
- Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.

Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. **Grading the supporting evidence**

<p>| | |</p>
<table>
<thead>
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<th></th>
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</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>Specific supporting evidence (or lack thereof) for each recommendation is cited and graded</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded.</td>
</tr>
</tbody>
</table>
6. Recommendations

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form.</td>
</tr>
<tr>
<td>B</td>
<td>Either one or the other of the above criteria is met.</td>
</tr>
<tr>
<td>C</td>
<td>Neither of the above criteria are met</td>
</tr>
</tbody>
</table>

In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.

7. External review

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline was made available to external groups for review.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline was reviewed by members of the sponsoring body only.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline was not externally reviewed.</td>
</tr>
<tr>
<td>NR</td>
<td>No external review process is described.</td>
</tr>
</tbody>
</table>

8. Updating and currency of guideline

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline is current and an expiration date or update process is specified.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline is current but no expiration date or update process is specified.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline is outdated.</td>
</tr>
</tbody>
</table>

A guideline is considered current if it is within the developers’ stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst’s discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated.