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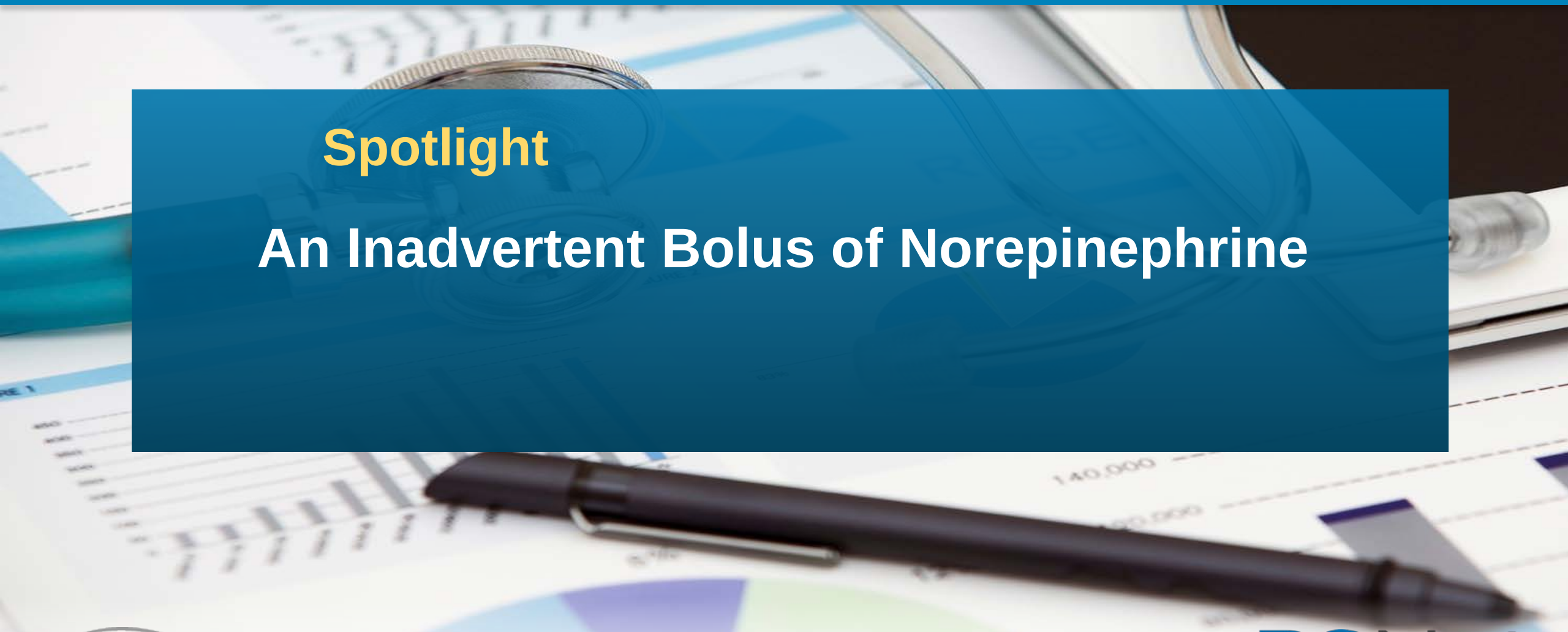


## Spotlight

# An Inadvertent Bolus of Norepinephrine

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

PSNet
PATIENT SAFETY NETWORK

# Source and Credits

- This presentation is based on the May 2021 AHRQ WebM&M Spotlight Case
  - See the full article at https://psnet.ahrq.gov/webmm
  - CME credit is available
- Commentary by: Sarina Fazio, PhD, RN, Emma Blackmon, PhD, RN, Amy Doroy, PhD, RN, Ai Nhat Vu, and Paul MacDowell, PharmD
- AHRQ WebM&M Editors in Chief: Patrick Romano, MD, MPH and Debra Bakerjian, PhD, APRN, RN
  - Spotlight Editors: Ulfat Shaikh, MD, and Patricia Poole, PharmD
  - Managing Editor: Meghan Weyrich, MPH

# Objectives

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

- Explain general approaches for treating hypotension in the ICU.
- Recognize risks associated with vasopressor (norepinephrine) administration.
- Identify the most frequent types of IV medication errors in the ICU.
- Describe best practices for co-administration of multiple IV infusions.

# AN INADVERTENT BOLUS OF NOREPINEPHRINE

A case describing intravenous infusion errors in intensive care unit settings and best practices for co-administration of multiple intravenous infusions

# Case Details

- 64-year-old woman admitted for aortic valve replacement and aortic aneurysm repair
- Following surgery, she experienced intermittent episodes of hypotension, for which she was given intravenous (IV) fluid boluses and vasopressor support
  - She received IV norepinephrine at a rate of 0.5 - 6 mcg/minute until 21:00 on postoperative day 1

# Case Details

- At 08:00 on postoperative day 2, the patient's blood pressure was 98/59 mmHg and a 250 mL fluid bolus was ordered
  - The fluid bag was attached to the IV line that had the vasopressor at a Y-site and the bolus was initiated
  - The patient developed diaphoresis, tachycardia to 114 bpm, and hypertension with an apex value of 271/161 mmHg
  - Once the inadvertent bolus was recognized, the vasopressor infusion was immediately stopped
  - In total, the patient received approximately 4.5 mL (or 160 micrograms) of norepinephrine infused over 15 minutes

# Case Details

- The patient was then closely monitored, and her hemodynamic parameters returned to baseline approximately 15 minutes later
  - However, the patient had ongoing hypotension in the hours following the inadvertent bolus of norepinephrine with a nadir of 54 / 38 mmHg, again requiring vasopressor administration and additional fluid boluses
- The next day, the patient's blood pressure stabilized, and she was transferred to a stepdown unit, and later discharged home
  - While the incident caused only temporary and minor harm to the patient, it was a cause of significant stress and anxiety throughout the rest of her hospital stay and persisted after her discharge

# AN INADVERTENT BOLUS OF NOREPINEPHRINE

## THE COMMENTARY

By Sarina Fazio, PhD, RN, Emma Blackmon, PhD, RN, Amy Doroy, PhD, RN, Ai Nhat Vu, and Paul MacDowell, PharmD

# ICU Hypotension

# ICU Hypotension (1)

- Hypotension following cardiac surgery may result from a variety of factors, such as hypovolemia, pump failure due to heart failure or shock, or maldistribution of blood flow due to septic shock
- Severe, systemic vasodilation can occur in 5-25 % of patients following cardiac surgery, resulting in postoperative hypotension despite a normal or increased cardiac index
- Most patients with vasodilatory shock respond to hemodynamic-guided IV fluid therapy and/or low-dose vasopressor agents, such as norepinephrine or vasopressin

# ICU Hypotension (2)

- Expected mean arterial pressure (MAP) values in the postoperative period are between 60-90 mmHg
  - Vasopressors are indicated for a MAP < 60 mmHg, a decrease in systolic blood pressure > 30 mmHg from baseline, or when there is risk of end-organ dysfunction due to hypotension
  - Prior to initiation of vasopressor therapy, patients should be assessed for hypovolemia which should be corrected with intravascular volume resuscitation. However, for patients with pulmonary edema due to heart failure or acute respiratory distress syndrome, fluids may be cautiously withheld and/or administered in smaller quantities to assess for fluid responsiveness and prevent fluid overload

# Vasopressor Administration & Monitoring

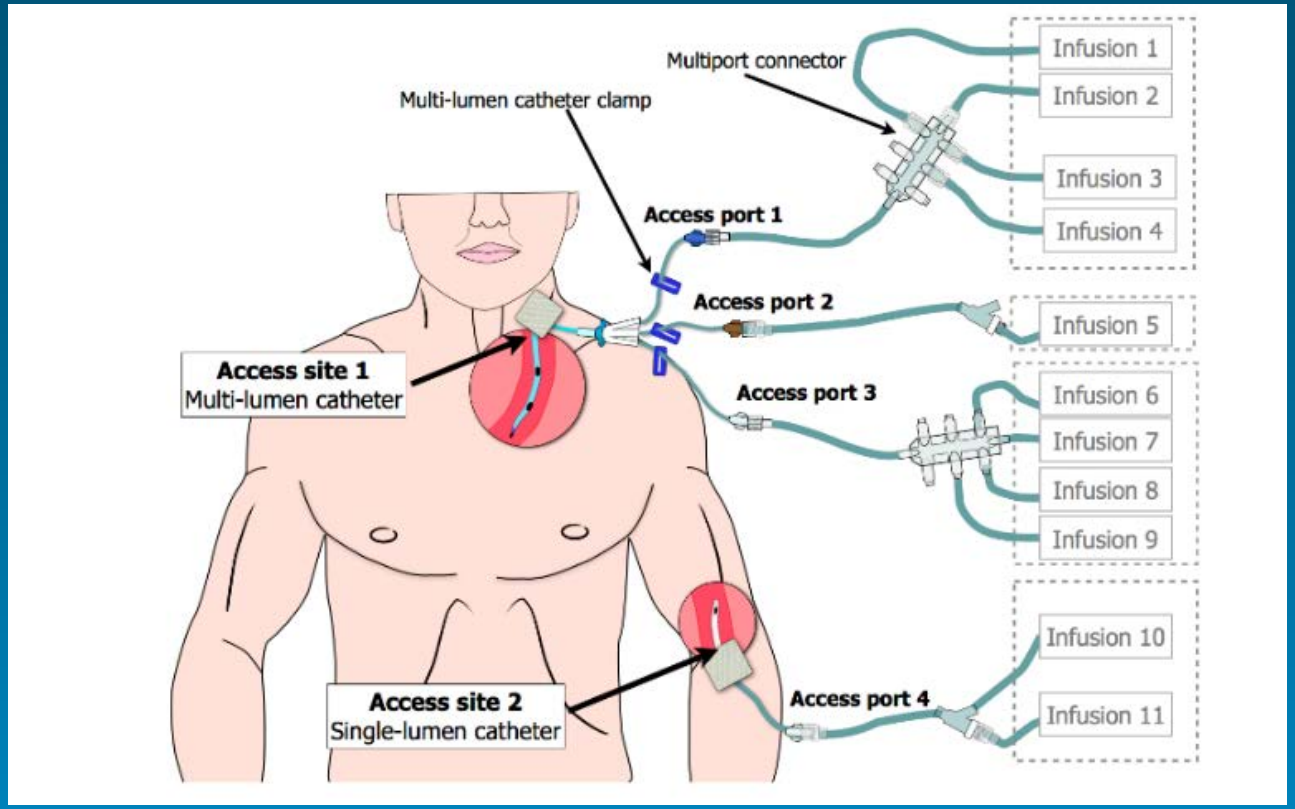
# Vasopressor Administration & Monitoring (1)

- Vasopressors are drugs that induce vasoconstriction and elevate MAP; they are most safety administered intravenously through a central venous catheter
- Despite their life-sustaining benefit, vasopressors and inotropic agents have the potential (at high doses and with prolonged use) to cause serious complications, such as cardiac arrhythmias, myocardial ischemia, peripheral vascular insufficiency and peripheral ischemia

# Vasopressor Administration & Monitoring (2)

- Vasopressor administration requires admission to an ICU and continuous cardiac and blood pressure monitoring by an interprofessional team. Infusions are typically titrated by ICU nurses based on provider orders regarding clinical endpoints and hemodynamic goals, such as blood pressure (MAP) and end-organ perfusion, that may differ based on clinical condition

Multiple IV Infusion Setup

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# Vasopressor Administration & Monitoring (3)

- Norepinephrine is the preferred, first-line vasopressor for the treatment of septic and distributive shock
  - Produces vasoconstriction and increases contractility by stimulating alpha and $beta_1$ adrenergic receptors
  - Rapid onset of action, with 5 minutes to peak serum steady-state and mean half-life elimination of 2.4 minutes
  - Can be administered using weight-based or non-weight-based dosing

# Vasopressor Administration & Monitoring (3)

- Dosing and titration parameters may vary across institutions and clinical pathologies
- Examples of initial dosing and dose ranges administered using weight-based or non-weight-based dosing:

**Table 1: Norepinephrine Dosing**

| | Initial Dose | Typical Dosage Range |
|---|---|---|
| **Weight-based Dosing** | 0.05-0.15 mcg/kg/minute | 0.05 to 0.4 mcg/kg/minute |
| **Non-weight-based Dosing** | 5-15 mcg/minute | 5 to 30 mcg/minute |

# ICU Medication Errors Associated with IV Infusions

# ICU Medication Errors Associated with IV Infusions (1)

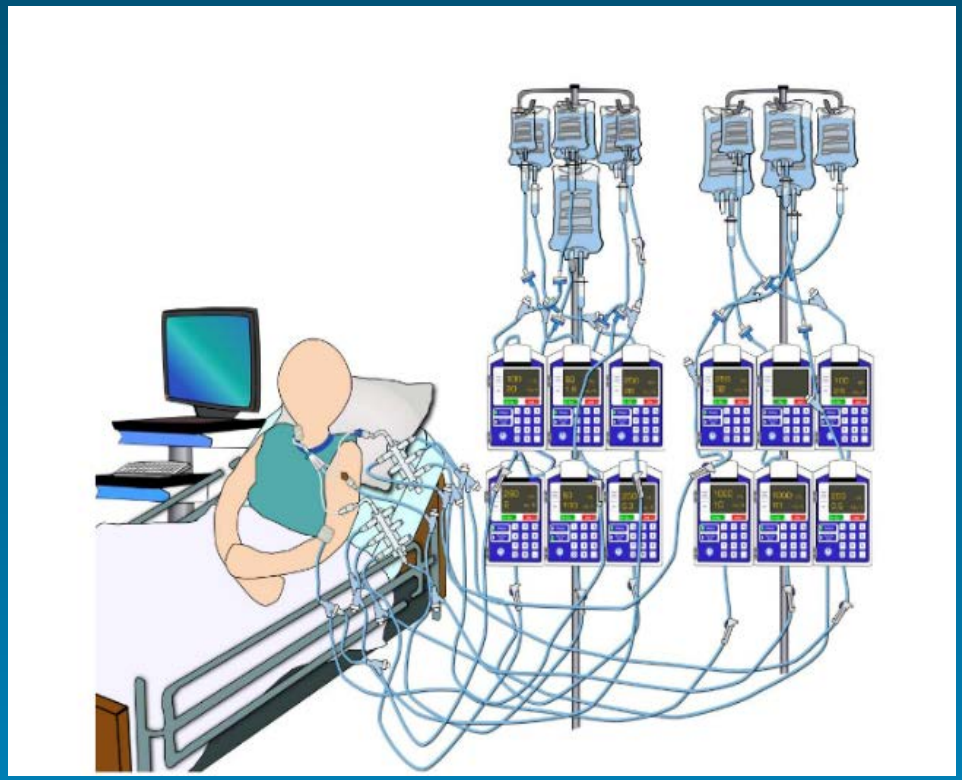
- IV medication administration is an integral component of treating ICU patients
- The complex process (can require up to 200 steps from prescription to administration), high patient acuity and treatment complexity makes ICU medication administration particularly error-prone
  - Additional factors such as a high number of infusions, administration of high-alert medications, and rapid bolus infusions further increase the likelihood of an IV medication error taking place and a subsequent adverse drug event
  - The Institute for Safe Medication Practices (ISMP) reports that that 56% of medication errors are associated with IV medications
  - Medication administration accounts for approximately 66% of ICU medication errors

# ICU Medication Errors Associated with IV Infusions (2)

## Rate or IV Line Mix-Ups

- In the ICU setting, where patients commonly receive multiple IV infusions, IV line or rate mix-ups are common errors that can be attributed to a number of factors including a variety of medication administration routes, difficulties in visually distinguishing between lines, and inadequate medication reconciliation handoffs
- While there are many types of IV infusion mix-up errors, these types of errors commonly result in medication dosing errors and incorrect amounts of fluid volume delivered to the patient

Multiple IV Infusion Administration



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# ICU Medication Errors Associated with IV Infusions (3)

## Errors Associated with Secondary Infusions

- Secondary (“piggyback”) infusions are IV infusions that are attached to the primary continuous IV infusion and hung above the primary infusion bag to deliver intermittent, scheduled medications, such as antibiotics and electrolytes
- Medication errors associated with secondary infusions arise from their complex setup process and include but are not limited to ***wrong Y-site connection***, failure to open the catheter clamp, inappropriate height differential between the primary and secondary infusion bags, and programming errors

# ICU Medication Errors Associated with IV Infusions (4)

## Errors Associated with Norepinephrine

- Norepinephrine (and other adrenergic agonists) can cause significant patient harm if used in error
- The earliest report the authors of this commentary could find of an inadvertent over-infusion of norepinephrine related to a pump programming error that resulted in cardiac arrest and the patient's subsequent death was published in 2015
- Given the complexities of dosing and titration when administering norepinephrine, additional research is necessary to identify and examine the effects of risk reduction strategies on patient outcomes

# Best Practices in Management of Multiple IV Infusions

# Best Practices in Management of Multiple IV Infusions (1)

- The potential risks associated with administration of multiple IV infusions in the ICU setting are increasingly recognized
- In 2010, the Association for the Advancement of Medical Instrumentation and the U.S. FDA issued a call to action to improve the management of multiple IV infusions
- Best practices include:
  - Utilization of smart pumps.
  - Standardized dosing
  - IV infusion setup
  - Line labeling
  - Management of continuous primary infusions
  - Titratable, intermittent, low-dose infusions

# Best Practices in Management of Multiple IV Infusions (2)

## Smart Pumps

- The use of smart pumps with ‘dose error reduction software’ is becoming more prevalent as a method to reduce the risk of errors associated with IV infusions and pump programming
- In addition to comprising a drug library, smart pump software is programmed with individual medication parameters (acceptable prescribed rate, concentration, and dosing limits)
- Smart pumps can mitigate errors associated with incorrect programming of IV infusions but do not target risks associated with setting up and co-administration of multiple IV infusions
  - *The medication error in the case was related to the physical maintenance of the patient’s IV infusions, an underappreciated area of concern that lacks a technological, smart pump prevention solution*

# Best Practices in Management of Multiple IV Infusions (3)

## Standardized Dosing

- Variations in how ICU nurses manage vasoactive medications can contribute to medication errors, patient harm and nurse anxiety
  - Systematic review found that ICU nurses aligned their choices of dosing units with the preferences of the patients' primary medical team; surgical teams are known to favor weight-based doses while medical teams prefer non-weight-based units

# Best Practices in Management of Multiple IV Infusions (4)

## Standardized Dosing (cont.)

- Conversion to a single method of dosing (e.g., weight-based dosing) and standardizing vasopressor infusion concentrations across care areas and provider services may prevent medication administration errors
  - However, if an order to change norepinephrine concentration occurs during medication administration, implementing effective communication or an alerting system is an important additional step to take to ensure smart pump programming updates are reflected and medication/tubing is exchanged properly

# Best Practices in Management of Multiple IV Infusions (5)

## IV Infusion Setup

- Setting up multiple, continuous IV infusions is a common nursing task when caring for a critically ill patient in the ICU.
- Each additional IV infusion can increase the likelihood of an error occurring due to increasing demands associated with
  - Physically managing multiple infusions with limited access points, and
  - Cognitively managing multiple medication orders and titration parameters

# Best Practices in Management of Multiple IV Infusions (6)

## IV Infusion Setup (cont.)

- Research has shown that setting up multiple infusions in parallel, when either initiating IV therapy or changing medications and their tubing, has led to errors related to IV tubing, pumps, drug orders and mixed-up labels
  - To decrease the chance of error when setting up multiple IV infusions, each IV infusion should be set up one at a time and as completely as possible before moving on to the next infusion
  - Clinicians should “trace” infusions from top to bottom, or from the administration bag, through the pump, and to the patient, before making any new connections or disconnections, when adjusting any existing medication rates, and during communication handoffs.

# Best Practices in Management of Multiple IV Infusions (7)

## Line Labeling

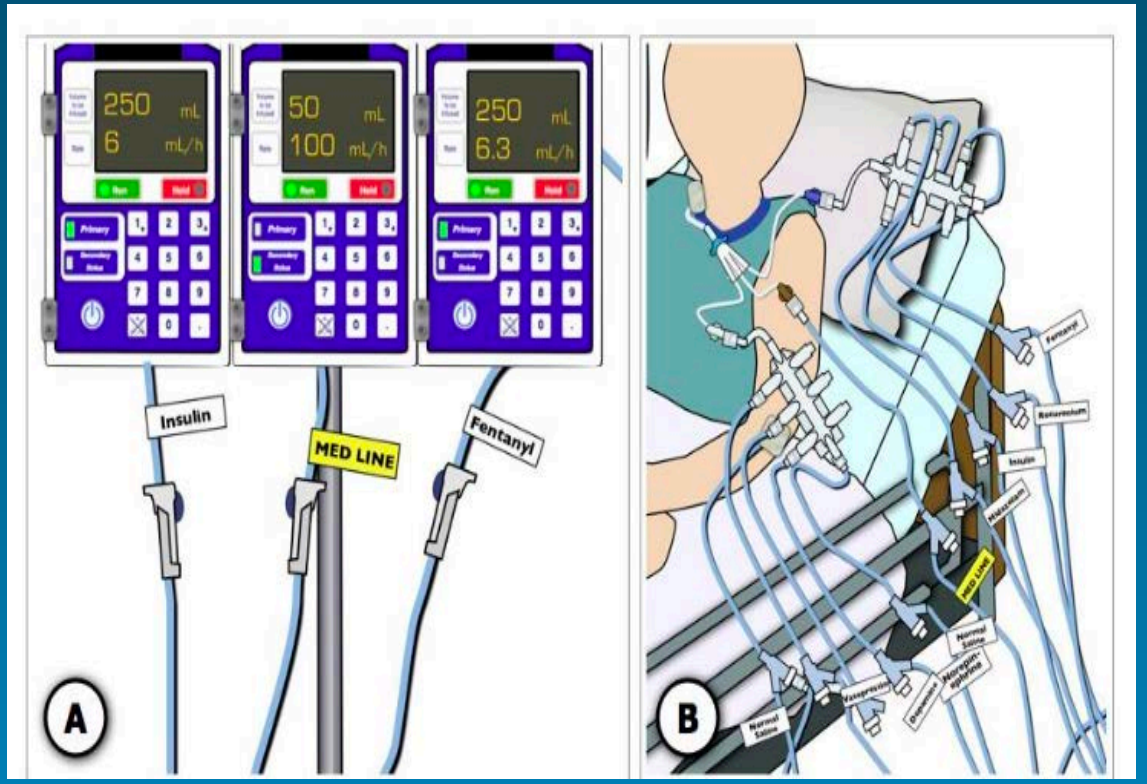
- Solutions to improve accurate identification of IV infusions when multiple infusions are being administered include color-coded tubing, pre-printed or handwritten adhesive labels, infusion organizers, pump displays, and light-linking systems
- Findings from a high-fidelity critical care simulation study suggest that line labels/organizers increase infusion identification accuracy and efficiency

# Best Practices in Management of Multiple IV Infusions (8)

## Line Labeling (cont.)

- Requires standardization in labelling practices to decrease troublesome variation.
- ISMP supports (1) use of black and white medication labels (with the exception of the emergency medication or “stat” line label) to promote careful reading to differentiate between infusions and (2) placement of labels in two standard locations, below the smart pump and near the distal end of the tubing
- Line labeling should not be the sole means used to identify medication infusions; the labels should support clinicians in facilitating line tracing

Labeling Multiple IV Infusions

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# Best Practices in Management of Multiple IV Infusions (9)

## Management of Continuous Primary Infusions: Dedicated Lines

- High-alert, continuous medications should be administered as a primary infusion (on its own ***dedicated line***) without any attachment of a secondary/piggyback infusion
  - Attachment of a secondary infusion may result in transition of a continuous medication to an intermittent one and delivery of inconsistent doses and rates outside of what is intended for medication delivery
  - Vasopressors such as norepinephrine should be administered through a dedicated IV line or administered concurrently with other compatible medications though a Y-site multi-port connector when vascular access is limited.

# Best Practices in Management of Multiple IV Infusions (10)

## Management of Continuous Primary Infusions: Extension Sets

- To administer continuous medications through a dedicated IV line, Y-site or multi-port connectors/IV ***extension sets*** are used to simultaneously deliver IV medications
- Back-check valves, which prevent backflow of medication due to differences in pressure in an IV infusion line, should also be used to prevent errors associated with administering multiple IV infusions into the same access point
- There are no standard guidelines for setting up multiple primary continuous IV infusions and multi-port connectors, especially for life-sustaining therapies that cannot be interrupted without causing hemodynamic instability
  - Standardization of IV tubing and extension equipment across an institution may help to validate and implement best practices
  - Further research is necessary to understand practice variation in setting up, flushing, and exchanging multi-port connectors

# Best Practices in Management of Multiple IV Infusions (11)

## Management of Continuous Primary Infusions: IV Bolus

- Bolus infusions should be administered through a dedicated emergency medication ("stat") IV line and a single vascular access port to avoid Y-site incompatibility and inadvertent rapid infusion of other medications
  - Ideally, bolus infusions should not be co-administered with additional medications or attached on a primary IV tubing side port
  - In situations with limited vascular access, co-administration may occur during the process of establishing IV access for medication and fluid administration
  - In cases where IV push medication is prescribed, the ISMP suggests administering IV push medications through a dedicated IV infusion line, through the port closest to the patient, unless contraindicated or inaccessible for use, such as during a sterile procedure

# Best Practices in Management of Multiple IV Infusions (12)

## Titratable, Intermittent, Low-Dose Infusions

- Patients can have periods of time when they are receiving very low and intermittent doses, until their MAP is consistently > 60 mmHg.
  - In these cases, the nurse may decide to keep the IV infusion attached to the central venous catheter to reduce the risk of central-line-associated blood stream infection (CLABSI).
- In contrast, for patients with labile blood pressure, when vasopressors are being titrated on and off according to medication titration orders, the nurse may disconnect the IV tubing from the patient's central venous catheter port but leave the bag/tubing present and hanging in the room in case the patient requires restarting the vasopressor due to a subsequent drop in blood pressure.
  - However, once the medication order is discontinued, removing intravenous bags and tubing from the patient comprises current best practices.

# Best Practices in Management of Multiple IV Infusions (13)

## Additional Considerations

- Additional considerations clinicians must account for in “real-world” settings given the nature and complexity of caring for critically ill patients in the ICU setting include:
  - Additional risk of infection (e.g., CLABSI) when connecting and disconnecting IV infusions from central venous catheter access ports,
  - Limited availability of vascular access coupled with co-administration of many infusions (e.g., >10) with different compatibilities,
  - The fact that technology does not solve all the problems with IV administration, human factors must be considered as well, and
  - The COVID-19 pandemic, which has led to changes in: the IV supply chain, nurse-to-patient ratios, and handoff communication practices and independent medication checks to decrease virus exposure and PPE waste.

# TAKE HOME POINTS

# Take-Home Points (1)

- The most common types of errors associated with administration of multiple IV infusions in the ICU include: rate or line mix-ups, secondary or Y-site infusion-associated errors, and bolus administration.
- Recommendations for reducing risks of errors associated with co-administration of multiple IV infusions include:
  1. Utilize a single dosing strategy, either weight or non-weight based
  2. Setup IV infusions completely and one at a time
  3. Trace or walk the lines often and when any change in medication administration or line management occurs
  4. Label lines in a standardized fashion
  5. Administer high-alert medications as primary infusions
  6. Utilize infusion sets with back-check valves and multi-port extension sets
  7. Administer bolus infusions through a primary and isolated/dedicated single access point
  8. Disconnect and remove all medications/tubing that are no longer ordered

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