IVENIX™

Exploring Real-World Performance

of IV Pumps

Authored by

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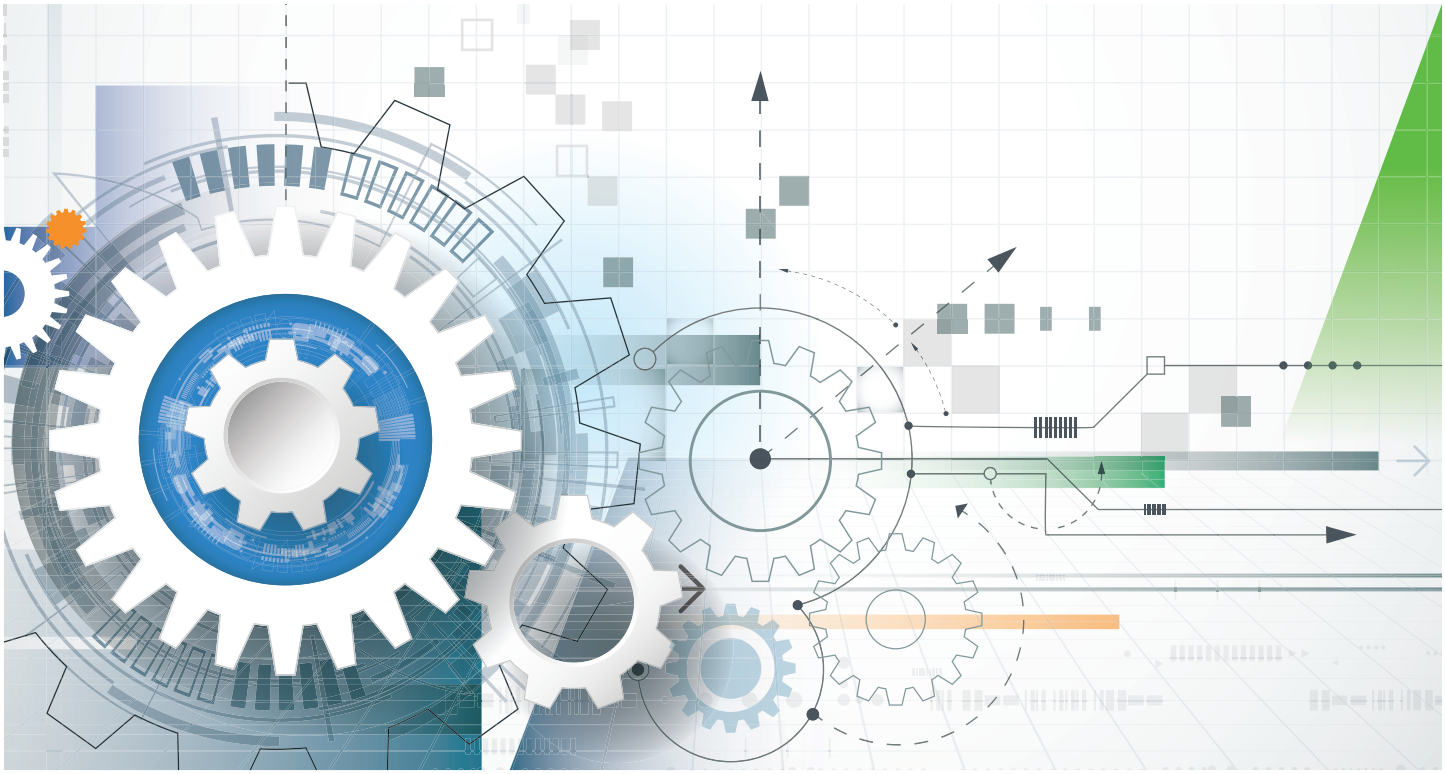

Goals

This paper investigates critical aspects of IV pump performance under real-world conditions and possible adverse clinical impacts. It introduces issues that may arise during 'secondary-mode' infusion and concludes with a vision for a new system design to significantly improve care.

The Essential Role of IV Pumps

The IV pump performs an essential role in the accurate and timely delivery of a wide range of medications for the treatment of nearly every disorder. Its mechanisms and sensors are relied upon by nurses to perform vital care with ultimate safety and effectiveness.

The average US hospital general floor/ward patient receives IV medication from two or more pumps while critical care patients may have six to as many as 40 infusion lines in use[1]. For some infusions such as oncologic and adjunct medications, the pump must provide long term flow accuracy to assure that the total volume is delivered in very close to the time expected. High accuracy is needed to achieve time scheduling and administration according to protocols and specific drug recommendations. For other medications, such as those that rapidly influence the function of the heart, lungs and neural systems, moment-by-moment stability of medication flow is critical to maintaining blood pressure and heart rate at intended levels.

Glossary of Terms

Term	Definition
administration set	A flexible tube connecting supply container to a patient cannula and providing interface to a pumping mechanism.
AFC-Adaptive Flow Control	A pump-based sensing and control system for correcting errors in flow accuracy caused by component tolerances and external influences.
compliance	The ability of the administration set and its pump element to expand or contract under pressure or vacuum.
continuity	A measure of the time between aliquots or 'shots' of flow caused by a pump.
continuous infusion	A pump delivery system where the supply container may be replaced repeatedly without interruption of the ongoing infusion.
effect-site	The tissue or organ affected by a medication, particularly short half-life drugs.
flow restriction	A region of the fluid pathway with a small radius and/or long length resulting in an elevated loss of pressure per unit of flow passing through (see the Hagen-Poiseuille equation).
half-life	The time required for the concentration of a medication to diminish by 50%.
hydrostatic pressure	Pressure in a liquid due to its density together with gravity and elevation differences in a vertical column of the liquid (see the Bernoulli equation).
mean flow rate accuracy	The capacity of a pump to infuse at the set flow rate when measured over typically one hour or more.
mm Hg (or mmHg)	A unit of liquid pressure, 1 inch of water height = 1.866 mmHg, 1 psi = 51.715 mmHg.
PD – Pharmacodynamics	The relation between drug concentration in a tissue and the response of the organ system such as blood pressure or heart rate[2].
peristaltic	A method of positive liquid displacement (propulsion) by sequential occlusion of a tube or flexible path.
PK – Pharmacokinetics	The measurement and prediction of the time course of drug distribution, metabolism and elimination[2] in the body.
positive displacement	A method for propulsion of a fluid based on changing shape of a closed chamber and valves not permitting gravity driven flow.
pump element	A portion of the administration set on which the pump acts to propel fluid at the set flow rate.
set flow rate	The flow rate (ml/h) programmed into pump.
short term flow accuracy	The ability of the pump to infuse with adequate continuity and uniformity, especially at low flow rates, when measured over periods typically from 30 seconds to 30 minutes.
shot	A measure of the pump's smallest discrete aliquot of flow defined by IEC and AAMI Standards.
stepper motor	A motor whose movements are non-continuous discrete increments.

Infusion Device Types and their Characteristics

Today the most prevalent pump design is the continuous infusion 'positive displacement' pump, which includes linear peristaltic, piston and diaphragm architectures (Figure 1). It is estimated that, in the US alone, more than 2 million of these are in use.

Displacement pumps operate, in some respects, like a conveyor belt, using a peristaltic action to move fluid at a controlled flow rate. In many situations, the pump is actually holding back the fluid against gravity much as a climber uses a rope to descend at a controlled rate. The pressure present at the inlet and outlet of the pump is the result, not the cause, of the flow passing through a flow restriction downstream plus any hydrostatic pressure. These pressures can significantly impact the pump's flow.

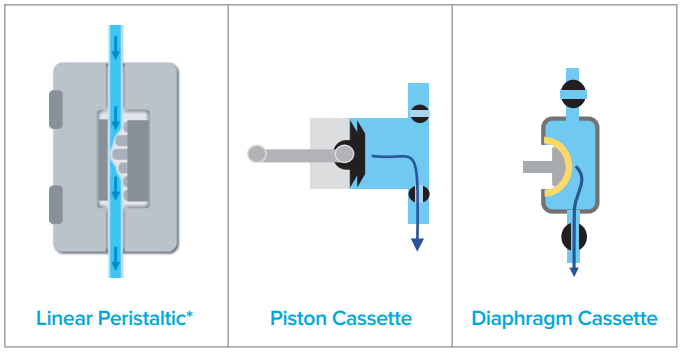

Figure 1. Three common types of displacement pump mechanisms

*Graphic courtesy Dr. Nat Sims & Chris Colvin "Drug Administration & Mixing Decisions" Massachusetts General Hospital 2018

Flow Accuracy and the Causes of Flow Rate Error

Mean Flow Rate Accuracy

Mean flow accuracy is measured over many minutes to hours of an infusion and may be affected by several factors[3,4]. First, variation in the exact dimensions of each administration set and each pump mechanism results in mean flow error. Manufacturers typically specify accuracy to be within about ± 5% under ideal conditions. Second, the portion of the administration set operated on by the pump exhibits elasticity or compliance. This compliance will permit change in the flow rate when inlet and outlet pressures vary. As shown in Figure 2, these intake and output pressures can come from a variety of sources.

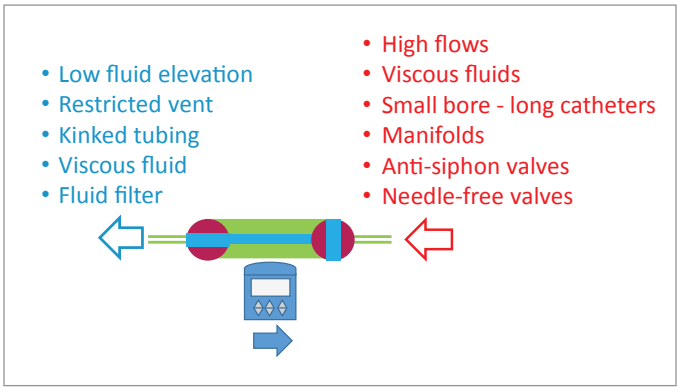

Figure 2. Typical sources of varying intake and outlet pressures

Pumps are typically calibrated with manufacturer-specified nominal intake and outlet pressures. If the intake pressure is below this nominal, the chamber will fill slightly less than intended, resulting in a reduced mean flow rate. Similarly, the output pressure is typically assumed to be zero during calibration, though this is rarely the case in practice. As a result, a positive outlet pressure can cause some fluid to be sequestered into the administration set's pump region as the flow cycle completes. Then, when the next pumping cycle begins, this excess fluid flows upstream back into the container resulting in reduction of mean flow.

Effect of Intake Pressure

Mean flow typically is reduced by about 1% for every 15 mmHg the intake pressure falls. This reduction of intake pressure may be due to the fluid level in the container falling, by a lack of adequate container venting or by kinking of the administration set. When filters are used in an administration set's drip chamber, the filter will typically clog over time, causing a vacuum

to form at the pump's inlet. Likewise, if a pump is used for the withdrawal of fluids from an extracorporeal circuit, it may cause as much as 200 mmHg vacuum[3] to form at the pump's inlet. In many cases, alarms for detection of these upstream pressure restrictions may not trigger until as much as 250 to 300 mmHg vacuum is present, resulting in a significant undetected flow reduction.

Effect of Outlet Pressure

Elevated outlet pressure can reduce flow by 0.55 to 3% per psi depending on the pump and set design. Since outlet pressure may reach 10 psi or more during normal operation without an occlusion alarm, this condition also can go undetected and result in a significant flow error.

Concurrent Intake and Outlet Pressure Effects

In clinical use, both intake and outlet pressures can simultaneously depart from nominal values. When combined, these may add to cause large positive or negative variation as illustrated by Jenkins findings shown in Table 1. Figure 3 shows that the additive effects may introduce negative mean flow errors of as much as 30% in some pump designs.

Linear Peristaltic silicone tube (0.2 ml)		OUT mmHg		
		-100	0	100
IN mmHg	-100	0%	-11%	-13%
	0	3%	4%	-12%
	100	12%	9%	7%
Average Intake Sensitivity			**8.6% / 100 mmHg**	
Average Output Sensitivity			**-5.4% / 100 mmHg**	

Table 1. Mean flow error and sensitivity of flow to intake and outlet pressures for a linear peristaltic pump using silicone tubing[3]

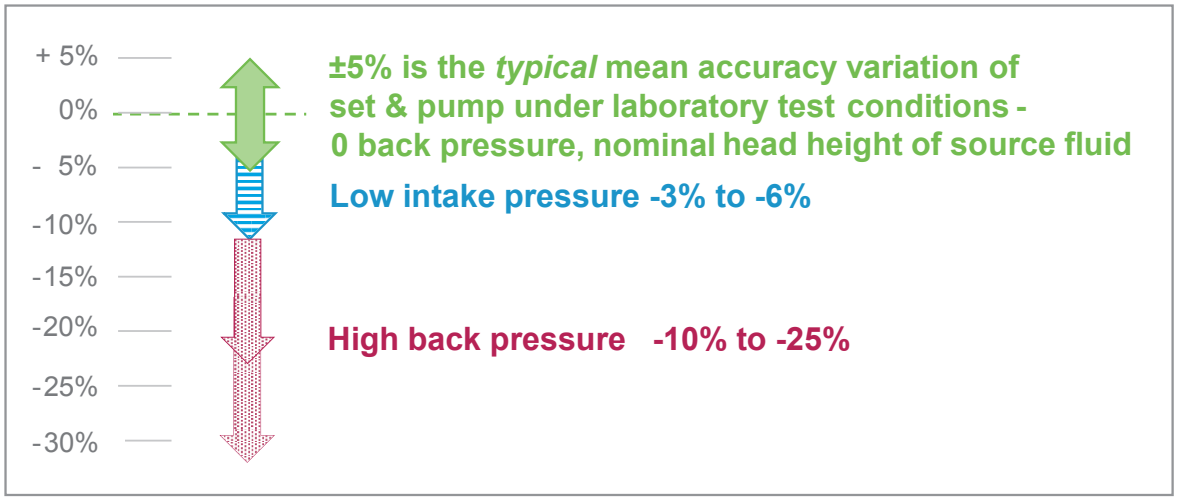

Figure 3. Additive effects on total flow rate error caused by materials, devices and external pressures

Causes of Short Term Flow Rate Variation

Displacement pumps repeatedly fill and then dispense fluid to the patient. This often results in temporary slowing or stopping of flow during each filling cycle. Peristaltic displacement pumps produce additional fluctuations with the motion of each pumping finger. These two effects are shown in Figure 4 for a peristaltic pump with a silicone segment operating at 10 mL/h[4]. The refill slowing occurs at 36 second intervals, indicating that the volume pumped each cycle is about 100 microliters.

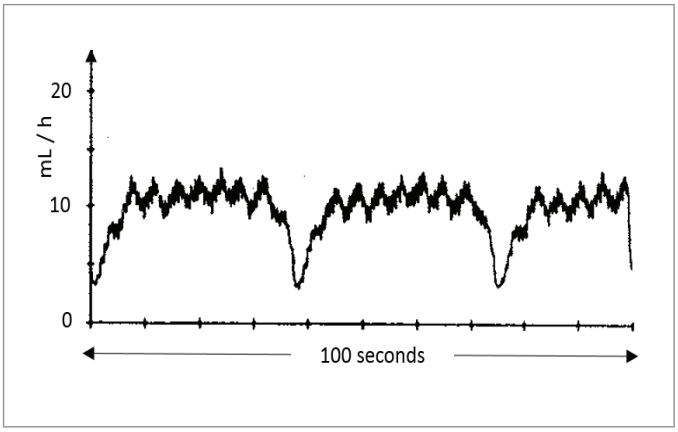

Figure 4. Cyclic Flow pattern of a continuous peristaltic pump[4]

During each delivery cycle, the motion of the driving element, such as peristaltic fingers, is typically controlled by a stepper-type motor, producing discrete movements or steps. The resulting flow is described as a shot in IEC Standard 60601-2-24 and others. Figure 5 shows a conceptual stepper motor rotating in a discrete manner, resulting in shots of fluid being dispensed.

The flow patterns produced by stepper motor driven pumps can be characterized by two key parameters: Continuity and Uniformity. Continuity refers to the time gap between shots of flow, while Uniformity describes the equivalence of the volume produced by each shot. Flow rate naturally affects these properties. At slower flow rates, Continuity will suffer since the shots must be spaced further apart to reduce the mean flow rate.

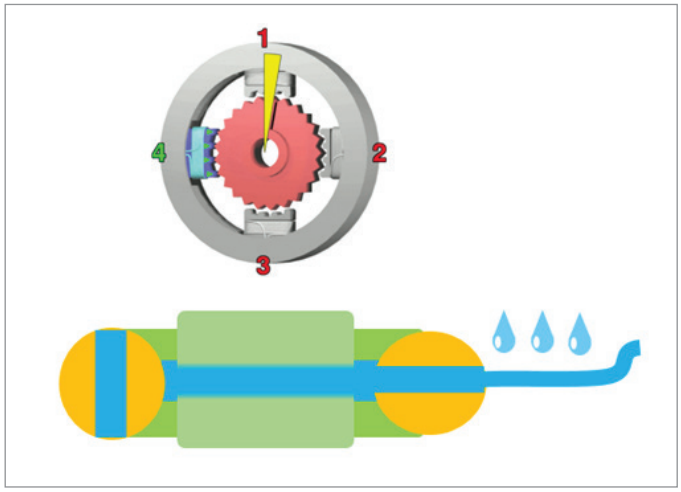

Figure 5. Stepper motor induced pulsatile flow *shots*

As shown in Figure 6, it is important that both the Continuity and Uniformity of the flow pattern are suitable for the flow rate and drug dynamics. For rapid-acting drugs, more than a few seconds between flow shots can allow the potency to diminish. In a similar manner a significant variation of the shot volume may introduce periodic wave-like changes in the drug potency as well[5,6,7].

Stability of flow can be impacted by both intake and outlet pressures acting on a compliant pump element. For example, if the intake pressure is abnormally low, then when the chamber outlet is opened for delivery, a reflux of fluid from the patient may occur as the elastic pump element expands.

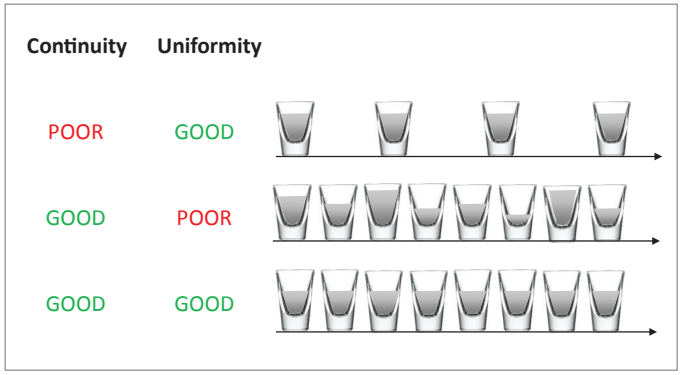

Figure 6. Continuity and Uniformity of Flow

This fluid reflux can result in significant interruption of delivery since blood enters the cannula and must be re-infused before medication flows into the vein. Positive output pressure may create a similar reflux as it expands the pumping element when the outlet valve opens. Similarly, a significant negative output pressure, such as caused by pump elevation, may introduce a small unintended bolus at the beginning of each pump cycle as it causes deformation of the pumping element.

Clinical Impact

The potential clinical impact of deviations in performance of any infusion device inevitably depends on the medication being delivered as well as the condition of the patient. Practical factors such as scheduling of therapy may also result in unplanned deviation in the pump's performance. Nonetheless, minimization of both mean and short term flow errors is essential to eliminate the uncertainties and complications of intravenous infusion delivery. Some of the potential impacts of each type of error are discussed next.

Clinical Impact of Mean Flow Rate Error

The most obvious impact of mean flow rate error is a discrepancy between the programmed volume to be infused and the actual fluid infused. For example, if a bag contains 1000 mL, the nurse may program the pump to deliver this amount and then either stop or go to a keep vein open (KVO or KOR) flow rate. However, if the pump is running 10% slower than intended, it will indicate that all the fluid had been infused even though 100 mL of the medication remains in the bag. To complete the infusion requires reprogramming, delaying therapy and introducing difficult-to-resolve discrepancies in the patient's infusion record.

Delay in completion may have irrecoverable impact on patient scheduling in settings such as day-oncology clinics. Even a 10% under-infusion of a planned two hour treatment would run 12 minutes longer than scheduled, not counting reprogramming. This added time could add up through multiple patients, risking that the last patient of the day would not be able to receive their scheduled infusion.

When infusions occur over longer periods, the impact of even modest mean flow rate errors can have severe consequences. Consider the 24 hour oncologic infusion illustrated in Figure 7, with the pump running 10% slow – a readily possible situation – this infusion would require 144 extra minutes to complete. Alternately, had the infusion been stopped as scheduled, the patient would have received 10% less medication than intended.

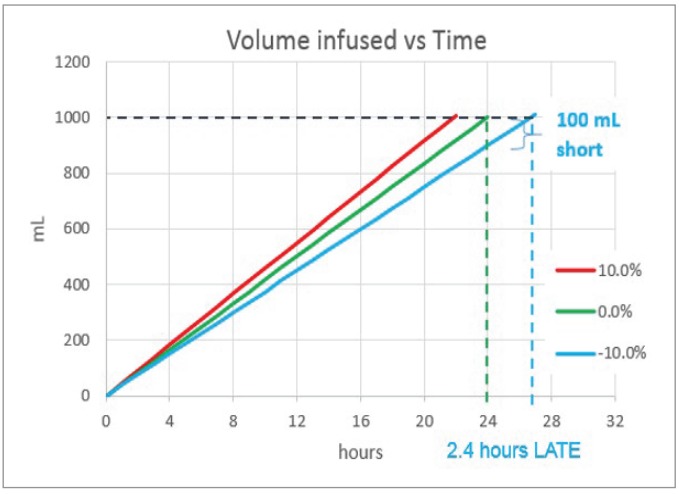

Figure 7. Time course of infusion with ideal and ±10% mean flow rate error

Short Term Flow Rate Variability

A significant percentage of drugs given in anesthesia and critical care are used for control of heart rate, blood pressure and anesthetic state. These have very rapid response times determined by their pharmacokinetics (PK)[4,5,6,7,8]. Their properties are described in terms of half-life, onset and decay time and similar parameters indicating how quickly the drug's concentration in the blood or effect-site organ varies as the incoming flow changes. These medications, when given via a peripheral cannula such as in the hand or arm, experience mixing and transport delay through the peripheral vasculature. However, when given by central catheters directly into the heart, they produce an even more rapid effect. The change to the patient's cardiovascular state is further affected by the shape of the pharmacodynamic (PD) dose-response curve for a given medication. At some effect-site concentrations, a small change can result in a large response, while at other effect-site concentrations this behavior is less pronounced[2].

When the instantaneous flow from a pump fluctuates while delivering short half-life medications, stability of the patient's vital signs can be disrupted as shown in Figure 8[9]. Many of these medications are delivered at very slow flow rates producing a flow cycle many minutes in duration. These slow flow changes allow the effect-site concentration to 'track' with the pump's variation[10].

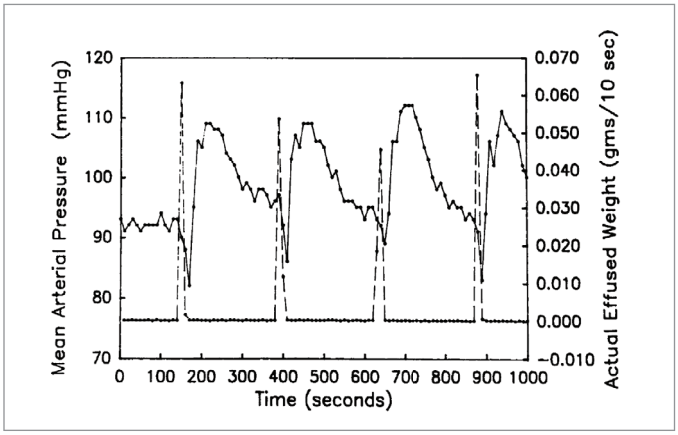

Figure 8. In vivo variation of mean blood pressure with pulsatile flow of epinephrine[9]

Multiple infusions via a Common Tubing

Variation of flow into the vein may be compounded when multiple medications pass through a common tubing ('dead-volume') as is done frequently in critical care and surgery[11,12,13] (Figure 9). The disruption of flow of one drug impacts all the others. Finally, infusion devices may be used to deliver a carrier fluid to which other medications are added at various points in a complex tubing network. Variation in flow of the carrier inevitably impacts the time delivery of all medications entering its flow stream.

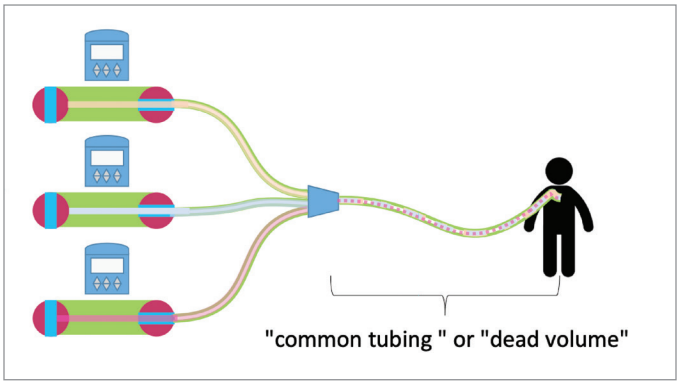

Figure 9. Simultaneous infusion of multiple medications through a common tube space ("dead-volume") poses risks of unrecognized interactions between pump flows.

Secondary Mode Delivery

While not a type of pump per se, the so called 'secondary mode', sometimes known as piggyback delivery, is used extensively in the United States. secondary mode permits automated delivery of the fluid container contents without the need for the nurse to return to the bedside or disturb the patient with alerts. Pumps require a special mode and administration sets to carry out this delivery. Unfortunately, the most frequently used method – check valve/elevation – is beset by pitfalls and common errors.

Below the check valve/elevation method and some of its challenges are reviewed.

Secondary mode permits the clinician to temporarily interrupt flow of a primary medication to deliver fluid from a 'secondary' medication container (see Figure 10a). The primary line has an access port just upstream of the pump and a one-way check-valve. The clinician must lower the primary container causing the check-valve to close due to greater net pressure from the higher secondary fluid. The valve should remain closed until the secondary fluid level falls near that of the primary, when ideally the primary flow resumes automatically as shown in Figure 10b.

The pump provides a secondary mode of operation permitting programming of both a secondary flow rate and secondary volume-to-infuse. Importantly, the pump does not control the actual volume delivered from the secondary container. Setting the secondary volume-to-infuse establishes only the time period during which the secondary flow rate is applied.

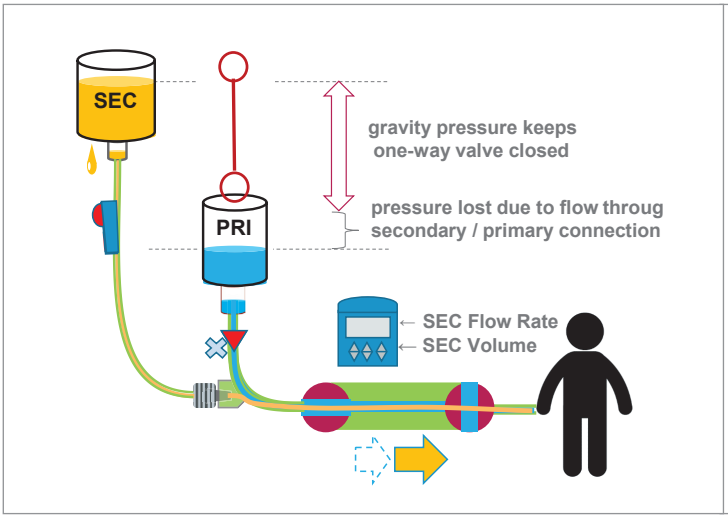

Figure 10a. Initial conditions of a secondary

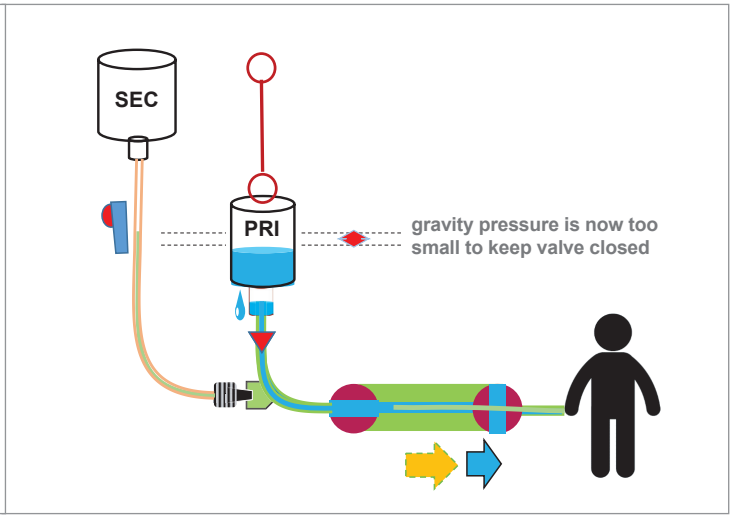

Figure 10b. Completed secondary delivery

Complications of Check Valve Secondary Infusion

The following are common unexpected pump behaviors during a secondary infusion.

Delayed Completion

High flow rates above 200 ml/h may result in a pressure loss through the secondary line and/or container. Loss of secondary pressure can result in some of the primary fluid infusing simultaneously. This so-called 'sympathetic flow' results in delayed completion of the secondary fluid as shown in Figure 11.

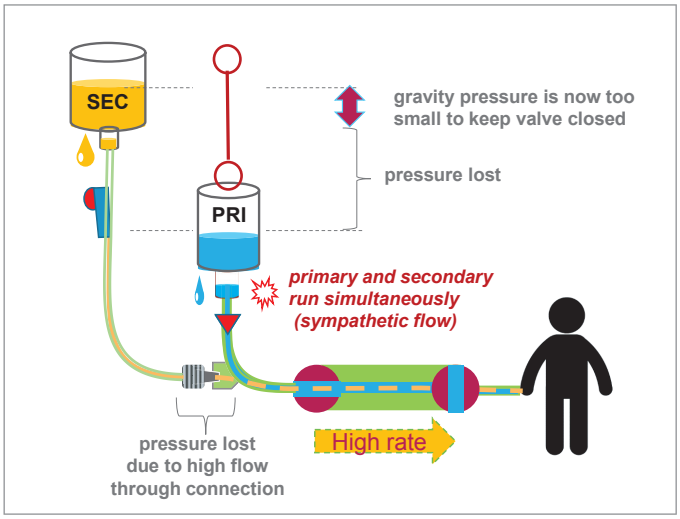

Figure 11. Delayed completion of secondary due to sympathetic flow caused by inadequate secondary pressure

Failure to Deliver Secondary

If the nurse fails to open the roller clamp on the secondary tubing, which is used to manage priming, the secondary fluid does not infuse. A clear, un-delivered secondary fluid, possibly in a small container, may go unnoticed and never be administered.

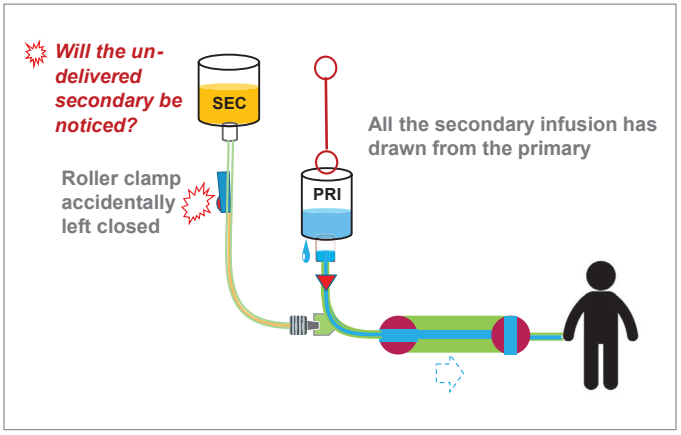

Figure 12. Failure to deliver secondary fluid due to un-noticed closed roller clamp

Unintended Over-Infusion of Secondary Fluid

A clinician may erroneously believe that programming the secondary mode volume-to-infuse will limit the amount infused from the secondary container. In reality, all of the secondary container fluid will be delivered, though possibly some at the primary flow rate. If more fluid than intended is in the container, an overdose will occur. Rare errors of this kind have been responsible for patient mortality.

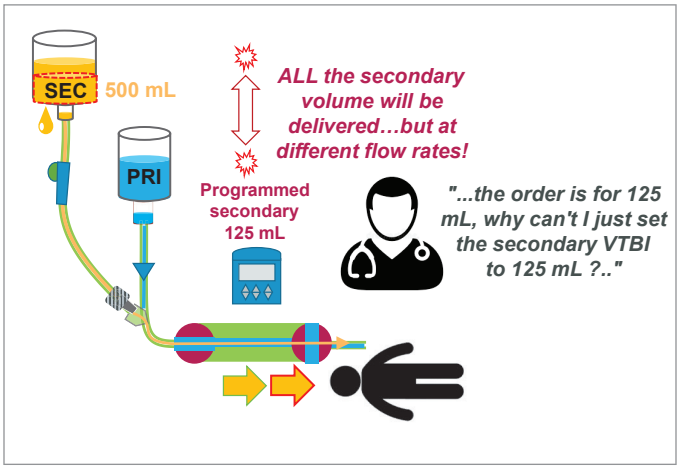

Figure 13. Accidental over-delivery of secondary container contents

Unintended Flows Due to Priming Volume

Priming volume (aka 'dead space') of the delivery tubing may result in unintended delivery of the secondary fluid at the primary rate. At the conclusion of the pump's secondary delivery, the pump flow rate transitions to the primary rate. As shown in Figure 14, approximately 20 mL of secondary medication remains in the tubing from the upper port to the patient connection. This fluid will be delivered at the primary rate, which, if lower than the intended secondary rate, will result in prolonged completion and possibly failure to achieve the desired therapeutic effect. Conversely if the primary rate is higher than the intended secondary rate, an undesired peak level of the medication may occur.

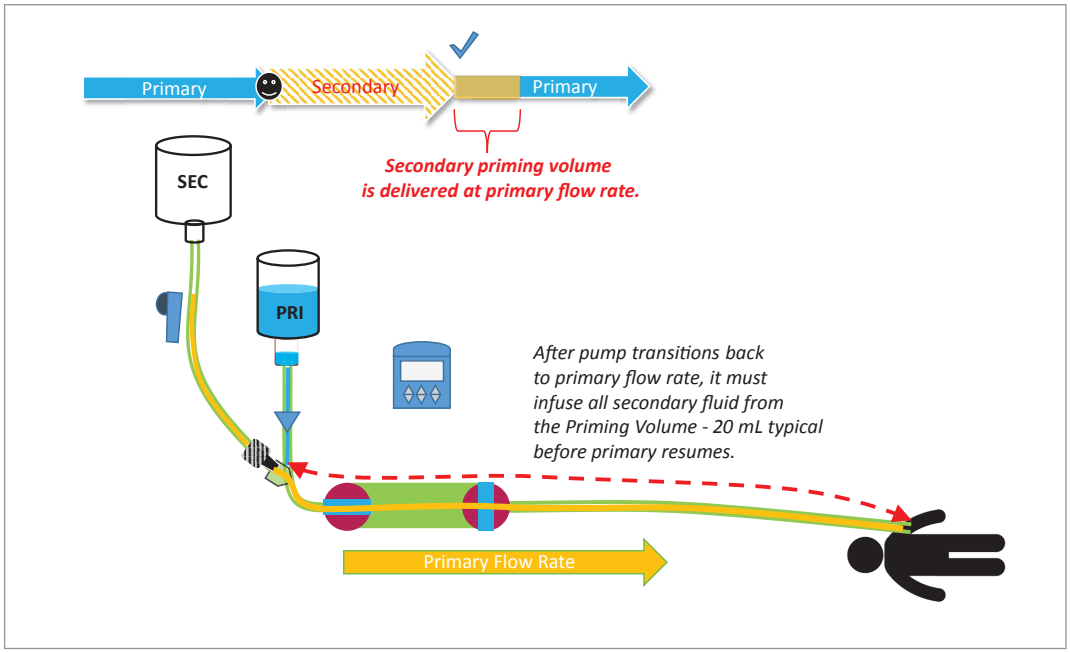

Figure 14. Unintended delivery of secondary fluid at primary flow rate

A New Approach to Infusion

After exploring some of the often hidden limitations of current-day infusion pumps, the need is clear for a new infusion design able to more effectively meet the clinician's requirements.

Flow accuracy of current pumps is susceptible to a multitude of influences because these pumps have no means to sense the actual infusion flow rate. To address this, a new pump design will provide high accuracy in mean flow by precisely sensing and correcting flow errors. An algorithm known as Adaptive Flow Control (AFC) will negate the effects of intake and output pressures, temperature, viscosity and other unavoidable real world influences.

Figure 15. Ivenix Large Volume Pump

A new pump design will also avoid the issues of inadequate short-term fl ow stability by providing both continuous and uniform fl ow. The AFC design smooths the fl ow at any infusion rate providing an uninterrupted and consistent delivery similar to a gravity infusion while maintaining high mean accuracy and the ability to infuse against high pressures independent of fl uid properties.

The numerous complications of secondary-mode infusion using container bag elevation must be addressed by providing a more reliable and easy-to-use system, avoiding the complexities and risks of the elevation/check valve approach. Key to this design is a cassette with a second intake port that can be programmatically controlled (see Figure 15).

Conclusion

While current-day IV pumps provide important improvements over manual gravity/flow restrictor methods of the past, numerous problems remain. These pumps often exhibit unrecognized variation of both long- and short-term flow due to administration set variation and compliance interacting with external pressures. Short term flow variations can disrupt cardiovascular stability, particularly at the low flow rates needed for children.

An ideal infusion pump will achieve high mean and short-term flow accuracy over the full range of clinical operating conditions. When these advances to the mechanics of infusion are combined with "smart" programming features such as dose error reduction and auto-programming software, infusion devices will become truly "intelligent" partners in the delivery of care.

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