



When Minutes Matter: Rapid Infusion in Emergency Care

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Abstract

Purpose of Review This review provides historical context and an update on recent advancements in volume resuscitation for circulatory shock. Emergency department providers who manage critically ill patients with undifferentiated shock will benefit from the insights of early pioneers and an overview of newer techniques which can be used to optimize resuscitation in the first minutes of care.

Recent Findings Rapid infusion of fluids and blood products can be a life-saving intervention in the management of circulatory and hemorrhagic shock. Recent controversy over the role of fluid resuscitation in sepsis and trauma management has obscured the importance of early and rapid infusion of sufficient volume to restore circulation and improve organ perfusion. Evidence from high-quality studies demonstrates that rapid and early resuscitation improves patient outcomes.

Summary Current practice standards, guidelines, and available literature support the rapid reversal of shock as a key priority in the treatment of hypotension from traumatic and non-traumatic conditions. An improved understanding of the physiologic rationale of rapid infusion and the timing, volume, and methods of fluid delivery will help clinicians improve care for critically ill patients presenting with shock.

Clinical Case A 23-year-old male presents to the emergency department (ED) after striking a tree while riding an all-terrain vehicle. On arrival at the scene, first responders found an unconscious patient with an open skull fracture and a Glasgow coma scale score of 3. Bag-valve-mask (BVM) ventilation was initiated, and a semi-rigid cervical collar was placed prior to transport to your ED for stabilization while awaiting air transport to the nearest trauma center. You are the attending emergency medicine physician at a community ED staffed by two attending physicians, two physicians assistants, and six nurses covering 22 beds. On ED arrival, the patient has no spontaneous respiratory effort, and vital signs are as follows: pulse of 140 bpm, blood pressure of 65/30 mmHg, and oxygen saturation 85% while receiving BVM ventilation with 100% oxygen. He is bleeding profusely through a gauze dressing applied to the exposed dura. The prehospital team was unable to establish intravenous access. What are the management priorities for this patient in shock, and how should his hypotension best be addressed?

Keywords Shock · Trauma · Rapid Infusion · Fluid Resuscitation · Hypotension

Introduction

Shock is a state of inadequate tissue perfusion resulting from hypovolemia, vasodilation, or impaired cardiac function. Clinical findings of shock include altered mental status, tachycardia, tachypnea, and poor skin perfusion. While

patients with shock may initially have normal blood pressure, the development of hypotension signifies decompensated shock which is associated with increased mortality [1, 2]. This is particularly true for patients with traumatic brain injury, septic shock, and hypotension occurring during intubation or with return of spontaneous circulation after cardiac arrest [3,4,5••]. Rapid intravenous (IV) infusion of fluid or blood products is often used in these situations to restore intravascular volume, correct hypotension, improve organ perfusion, and prevent cardiovascular collapse. A variety of barriers can limit effective resuscitation, including difficult vascular access, inadequate provider resources, and technically complex or slow infusion methods.

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For the patient described in the vignette above, immediate restoration of adequate systemic arterial pressure and cerebral perfusion is critical to the patient's survival and prevention of secondary neurologic injury. Which tools are available to the emergency medical services responders who arrive on scene? What factors limit their ability to provide effective volume resuscitation, and what are the likely equipment, personnel, and clinical management challenges of a free standing or community ED? Upon arrival at a trauma center, what devices are available for the rapid infusion of needed crystalloid fluids and blood products? What is the maximal achievable flow rate through a typical peripheral IV, intraosseous (IO) access, or central venous catheter? How efficiently can these methods restore intravascular volume given the manpower, time, and expertise needed to set up and operate the devices? These are some of the many issues that the practicing clinician must consider when managing a patient with severe shock.

This paper will review the history of volume resuscitation in circulatory shock, the physiologic rationale for volume resuscitation, and the rapid infusion methods available to facilitate effective resuscitation in the earliest moments of care. For purposes of this review, "early" will refer to the rescue or "salvage" phase of resuscitation, during which adequate resuscitation can limit further organ ischemia and prevent cardiovascular collapse [6–9]. While crystalloids are the most common fluid administered in acute resuscitation, blood is preferred for patients with hemorrhagic shock, and the technologies described below may be used interchangeably with blood products or fluids [7–13].

History

The first use of IV saline for the treatment of hypovolemic shock is attributed to Thomas Latta, who created a saline solution "to restore the blood to its natural state" in severely ill patients during England's 1831 Cholera epidemic [14]. When oral administration of the saline solution was ineffective for his first patient, he decided to attempt intravenous delivery. After inserting a tube into the basilic vein and injecting several ounces of saline, he observed that "she began to breath less laboriously... and began to glow with returning animation. ...the pulse became more and more distinct, fuller, slower, and firmer, and in the short space of half an hour, when six pints had been injected she expressed in a firm voice that she was free from all uneasiness, actually became jocular; her extremities were warm, and every feature bore the aspect of comfort and health." [15]. Latta administered the fluid by means of the Read's apparatus, originally designed for gastric lavage, with which he could repeatedly draw saline into a metal syringe and then deliver

it to the patient by means of an automatic ball-valve mechanism [16].

Though initial reactions from the medical community were generally favorable, Latta's discovery was a therapy ahead of its time. The proper balance of electrolytes, optimal fluid dosing, indications for use, and associated risks (e.g., sepsis and thrombophlebitis) of this innovation were not yet fully appreciated. With the end of the cholera epidemic and Latta's death in 1833, the technique was largely forgotten until reports of IV injection of saline and blood reappeared in the medical literature of the 1880s for the treatment of trauma, surgical blood loss, and most commonly, severe obstetric hemorrhage [17]. By the early 1900s, IV infusion was commonly recommended in surgical and obstetric textbooks for the treatment of severe hemorrhage [18]. During this time, devices such as the Collin's or Waller's apparatus (Fig. 1) had gained popularity. Utilizing a technique similar to that of Latta, these methods allowed rapid delivery of intravenous saline or blood with simultaneous bedside observation of pulse rate and quality, skin color, and mental status. These early practitioners demonstrated a remarkable understanding of the need for urgent treatment guided by continuous bedside monitoring of the patient's physiologic response. This approach led to the delivery of only as much fluid volume as was necessary to bring about improvement in the patient's condition.

Though it would remain poorly understood until the next century, the physiologic condition that these physicians were treating was hypovolemic shock, first described in the late 1800s as a state in which, "the heart and arteries have nothing to contract upon" [19, 20]. During the 1930s, cardiac surgery pioneer Alfred Blalock outlined the broad categories of shock as we generally understand them today, including hematogenic (hypovolemic), vasogenic (distributive), and cardiogenic shock [21]. Blalock's animal models showed that if hypotension due to hemorrhage was allowed to persist for over an hour prior to initiating volume resuscitation, the animal would not survive. If instead intravascular volume was restored quickly, the shock state and subsequent organ damage could be reversed [21, 22]. Subsequent data demonstrated that crystalloid resuscitation improved hemorrhagic shock survival when compared to blood transfusion alone [23, 24]. These findings, combined with reports of improved outcomes for injured soldiers and burn victims initially resuscitated with crystalloid, likely led to the original concept of "liberal" or "aggressive" fluid resuscitation in the care of post-surgical and trauma patients [25–27]. While whole blood was understood to be the preferred treatment for hemorrhagic shock, it was rarely available in the earliest moments of care. As a result, twentieth-century clinicians gradually became accustomed to using large volume isotonic intravenous solutions to restore and maintain adequate perfusion pressures. This shift in ideology toward a more liberal

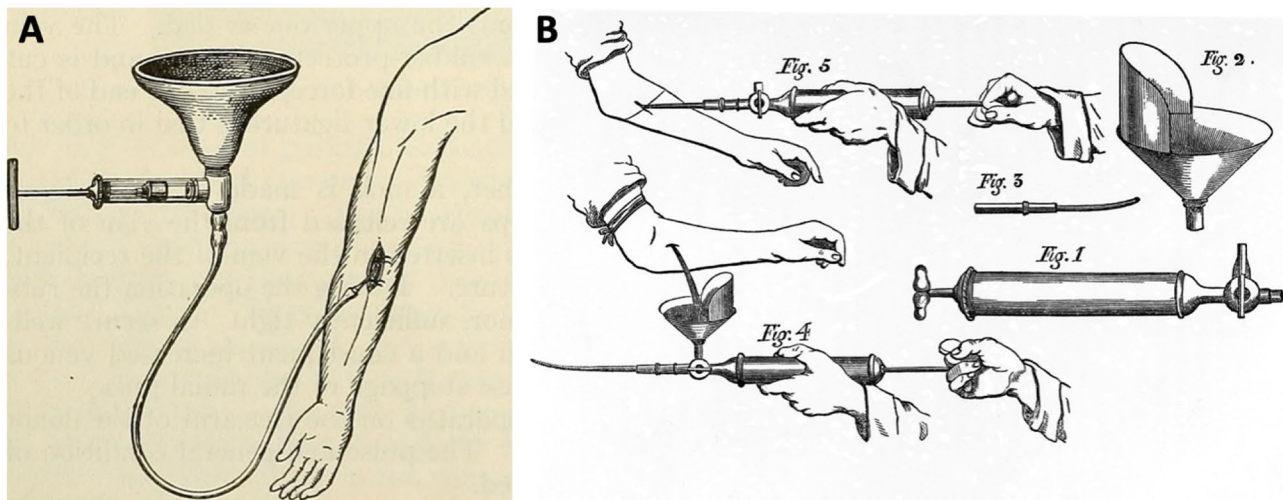


Fig. 1 A Collin's apparatus, DaCosta *Modern Surgery*, p 399–400; B Waller's apparatus. Creative Commons License: Waller's transfusion apparatus, nineteenth century. Wellcome M0010139.jpg

crystalloid resuscitation strategy overlooked the concerns raised by early researchers regarding the hidden dangers of indiscriminate large volume resuscitation [28, 29].

Physiologic Rationale for Rapid Infusion

The classic Frank-Starling curve (Fig. 2) helps to explain how volume resuscitation may benefit patients in shock, many of whom are in the preload-dependent area of the curve. For hypovolemic patients, and even those early in the course of cardiogenic shock, augmentation of intravascular volume on the preload-dependent portion of the curve

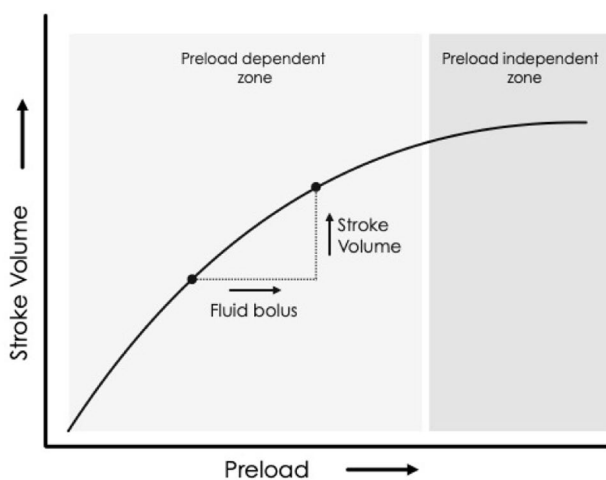


Fig. 2 A modification of the Frank-Starling curve

will result in increased ventricular filling and subsequent improvement in stroke volume, cardiac output, and blood pressure [7,30••,31••,32•]. After this point, additional volume given in the preload-independent zone will raise left ventricular end-diastolic pressure (LVEDP), potentially leading to increased pulmonary hydrostatic pressures, elevated central venous pressure (CVP) and resultant tissue edema [33].

It should be emphasized that the “classic” Frank-Starling curve omits many complex and interwoven physiologic determinants of preload and cardiac output. We now understand that CVP and right atrial pressures are not the only determinants of cardiac output [34]. However, in the profoundly shocked patient with hypotension and other markers of impaired perfusion, a low right atrial filling pressure indicates that timely infusion of crystalloid, colloid, or blood will likely improve blood pressure and global perfusion. Reduced right atrial filling pressure and low CVP can be readily assessed using point of care ultrasonography. The appearance of a thin or collapsing inferior vena cava (IVC) indicates that the patient with shock will tolerate, and likely benefit from, an initial fluid bolus [35, 36]. When objective measures such as IVC ultrasound are not available, an increased blood pressure following a small but rapid fluid bolus is likely the best indicator of volume responsiveness [37•].

Rapid Infusion Methods

Though rapid delivery of fluid or blood products is commonly recommended for the urgent reversal of shock, little attention has traditionally been paid to *how* rapid

infusion should be accomplished, and no consensus opinion exists on the optimal volume or rate of infusion [38, 39]. For example, well-known emergency medicine and critical care texts recommend an initial 1000 mL delivered over 5–20 min for patients with shock [39, 40]. The European Society of Intensive Care Medicine suggests 500 mL be given in under 30 min [41], while the International Fluid Academy advocates a bolus 4 mL/kg over 10 min [42]. The American College of Critical Care Medicine Guideline for pediatric septic shock and the Pediatric Advanced Life Support Manual both suggest 20 mL/kg as few as 5 min [43, 44]. Finally, the Advanced Trauma Life Support (ATLS) guidelines historically recommended an initial 2 L infusion of crystalloid for patients presenting in shock. More recent editions of ATLS have reduced the recommended volume to 1–2 L in the 9th and 1 L the 10th edition, reflecting the increasing priority of blood products over crystalloid in traumatic shock [45, 46]. No specific flow rates or infusion methods are mentioned in the ATLS guidelines.

Most texts and guidelines rightly note that the initial bolus should be followed by an immediate assessment of blood pressure and other markers of perfusion to determine whether additional infusion is required. It is important to note here that *rapid* infusion does not necessarily imply *large volume* infusion. In most clinical scenarios, severe hypotension can be reversed by the immediate delivery of a relatively small volume of fluid, for example 500 mL in adult or 20 mL/kg in a child. Especially for non-traumatic shock, a volume over 2 L in adults (or 40–60 mL/kg in a child) is rarely required for immediate stabilization. Of course, much larger volumes of blood products may ultimately be required for patients experiencing severe hemorrhage.

Regardless of the precise rate of infusion, the goal should be rapid restoration of adequate blood pressure and perfusion. Nineteenth-century medical pioneers, constrained by the difficulties inherent in establishing vascular access and the lack of available and suitable fluids or blood products, were compelled to deliver fluid rapidly in small, discrete doses by means of a syringe and stopcock. Through constant bedside vigilance, they determined when the patient's condition had sufficiently improved and then provided no further fluid boluses. The approach to severe shock in the ED today should be guided by this same principle.

Infusion Pumps

Intravenous infusion pumps are now commonly used for the delivery of fluid in acute care settings. Unfortunately, these devices provide a maximum flow rate of 1000 mL/h and

are therefore too slow to rapidly correct acute hypotension during the salvage phase of resuscitation. Paradoxically, the ubiquitous presence of automated infusion pumps has enabled a hands-off resuscitation approach that has likely played a significant role in the development of the adverse effects of fluid accumulation in hospitalized patients.

Gravity

While gravity infusion is commonly used for fluid resuscitation, providers must recognize that fluid flow is highly dependent upon luminal diameter (i.e., IV gauge), tubing length, and the position of the patient's extremity. One liter of saline suspended 100 cm above the patient will flow at a rate of approximately 50 mL/min through a 20 G catheter, requiring at least 20 min for delivery of the full liter [47, 48]. According to Poiseuille's law, larger bore catheters of shorter length will improve the rate of fluid flow. Therefore, one of the most effective methods of improving infusion rate is to place the shortest and largest gauge intravascular catheter possible. This is the basis of the frequent recommendations to immediately establish two large-bore (14–16 gauge) IV lines in patients with shock and to prioritize larger-gauge short peripheral catheters over longer central venous lines [49, 50]. Unfortunately, this is not always easily accomplished, and in fact, one large study found that 22 G and 20 G catheters are the most commonly used sizes in emergency and inpatient settings [51]. As shown in Fig. 3, gravity flow through standard-gauge catheters is too slow to provide rapid resuscitation. It is also important to note that commonly used needleless Luer connectors add additional resistance and thereby further decrease the flow rate [52]. While intraosseous (IO) catheters are frequently used in the ED for emergent vascular access, the flow rates through this route can be as slow as 10–60 mL/min [53, 54].

Pressure Infusion

Application of a pressure cuff to the bag of crystalloid or blood is commonly used to increase infusion speed. However, this method may not substantially increase flow compared to gravity infusion and requires continuous re-inflation of the cuff to maintain flow since applied pressure quickly diminishes as fluid volume decreases. A pressure cuff inflated to 300 mmHg will increase flow rate through a 20 G catheter to approximately 100 mL/min, whereas rates of 250 mL/min and higher can be achieved with larger-gauge catheters if pressure is continuously maintained (Fig. 3) [55]. Unfortunately, it may not be possible to establish a large-bore peripheral IV access for many patients who present in shock. Additionally, the amount of time required to set up the IV access, maintain constant pressure, and perform bag changes during the chaotic and resource-limited clinical setting is often underestimated [56]. Furthermore,

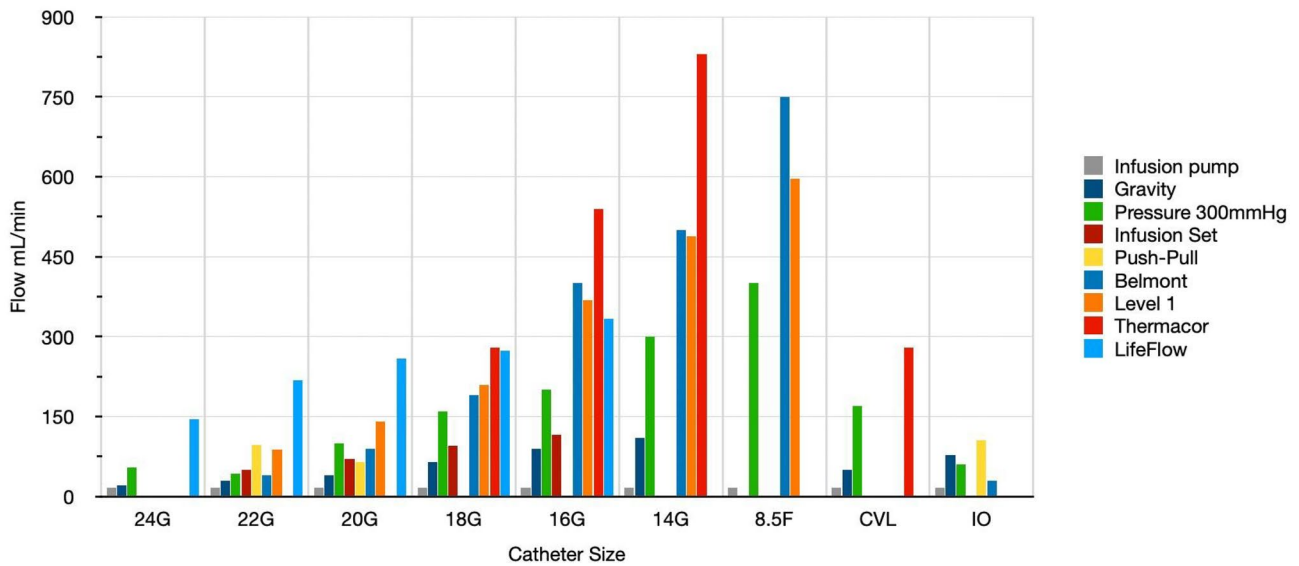
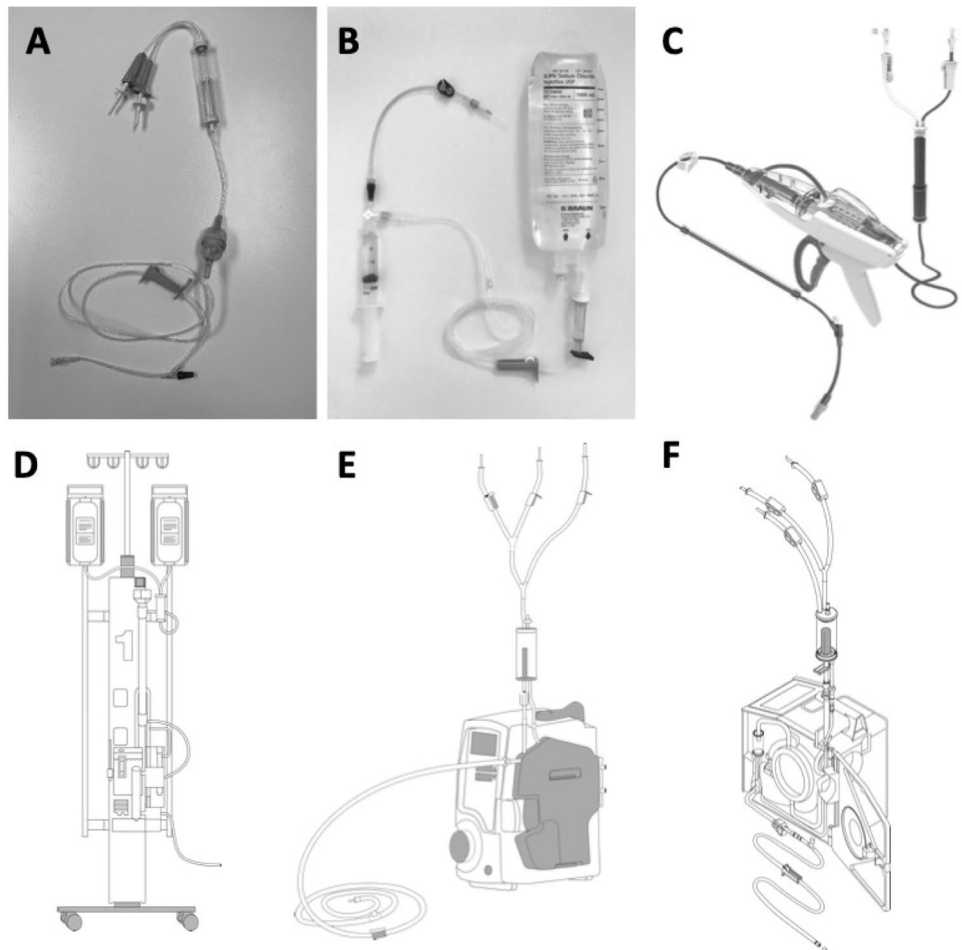


Fig. 3 Pressure-flow relationship of various vascular access devices [48, 53, 67–60]

life-threatening air embolism can occur if all air has not been removed from the IV fluid container prior to infusion [57–59].

Other methods for improving flow, such as manually squeezing or kneeling on the fluid container or applying a

Fig. 4 Rapid infusion devices: **A** Hospira® Blood Infusion Set; **B** “push-pull” syringe and stopcock set; **C** LifeFlow®; and powered rapid infusers with warming capacity: **D** Smiths Medical Level 1® H-1200; **E** Smisson-Carlledge Biomedical TheraCor® 1200; **F** the Belmont® Rapid Infuser RI-2. (Adapted from Belmont Medical Technologies, Smiths Medical, and Smisson-Carlledge product information brochures. LifeFlow image courtesy of 410 Medical.)



manual blood pressure cuff, do not appreciably increase flow when compared to gravity infusion [55]. Blood infusion sets with an in-line bulb are used intra-operatively and in one study were shown to deliver fluid faster than a pressure bag through a 16G IV (Fig. 4A) [60].

Manual syringe infusion, often referred to as the “push–pull” technique, is used for rapid infusion in anesthesia, pediatric critical care, and military trauma care [61–63]. This method may be particularly useful in urgent situations when large-bore IV access and mechanical rapid infusers are not available. Typically, a 10–60-mL syringe is connected by a 3-way stopcock, which allows fluid to be repeatedly withdrawn from the fluid reservoir and then administered to the patient (Fig. 4B). See Fig. 3 for representative flow rates. Interestingly, this technique is almost identical to devices used by the early pioneers in its function and requirement for bedside attentiveness. Disadvantages of the manual syringe infusion method include the need for two-handed operation, user distraction and fatigue, errors such as inadvertently withdrawing blood from the patient, and the risk of nosocomial infection through repeated contamination of the exposed syringe plunger [64, 65, 66].

Rapid Infusers

Mechanical rapid infusers are considered to be the fastest method for intravenous fluid delivery and can achieve rates of close to 1000 mL/min (Fig. 3). The first of these devices, the Rapid Infusion System (RIS) (Haemonetics Corp., Braintree, MA), was developed in the 1980s for use during liver transplantation but is no longer commercially available [72]. It was capable of flow rates as high as 1200 mL/min by means of an electronically controlled roller pump, with safety mechanisms to detect air and limit infusion pressure. During early use for trauma resuscitation in major trauma centers, it was found to be effective for correcting hypotension and preventing hypothermia during massive transfusion through large-bore (14 G, 8.5 F) catheters [73]. Subsequent data showed that patients treated with RIS received an average of 9700 mL of fluid and blood products during their resuscitation and that mortality in these patients was higher compared to similar patients who had conventional fluid and blood delivery [72]. This mortality difference was attributed to over-aggressive volume resuscitation resulting in excessive crystalloid volume, electrolyte and pH imbalance, dilutional coagulopathy, and marked third spaced fluid [74].

Three rapid infusion devices with improved safety features were subsequently developed and are commercially available in the USA, including the Level 1® H-1200, the Belmont® Rapid Infuser (RI-2), and the ThermaCor® 1200 Rapid Infuser (Fig. 4). To achieve faster flow, the Level 1 pressurizes the chamber around the fluid reservoir, while the Belmont and ThermaCor use roller pump mechanisms

similar to the RIS. The Level 1 warms by countercurrent circulation of warm water around the infusion tubing, while the Belmont and ThermaCor pass the blood or fluid past metallic heating elements. Each device limits infusion pressure to approximately 300 mmHg and will slow or stop flow if resistance causes pressure to rise above this level. Mechanisms are included to detect air in the infusion line and prevent further flow until air is removed. Each device is also designed to vent the small volume of “outgassed” air that arises from the fluid during warming.

The most significant disadvantages of rapid infusers are their cost, complexity, and requirement for frequent staff training. Prices range from \$8,000 to \$39,000 for the infusion devices, with disposable components costing \$100–250 per patient. Their size, weight, and dependence on AC power make these devices difficult to use during pre-hospital and in-hospital transport. In the ED and operating rooms (ORs), staff training and familiarity are essential, yet competency may be difficult to achieve. In one study of preparedness among anesthesia personnel with responsibility for using a rapid infuser, no participant was able to successfully complete a written proficiency test or assemble the device correctly [75]. Lastly, mechanical rapid infusers may not work as effectively through smaller IV catheters, and they appear to function poorly with IO access due to slow delivery rate and the frequent high-pressure alarms generated [53]. These devices may be best suited for the acute resuscitation of patients with severe hemorrhagic shock who require large volumes of warmed blood products in busy trauma centers or ORs where they are used regularly and where large-bore vascular access is readily available.

One emerging solution is LifeFlow®, a novel handheld, single-use rapid infusion device (Fig. 4C). This device operates by manual compression of a handle that actuates a syringe to deliver fluid to the patient, then automatically refills through an automatic check valve when the trigger is released. This device includes a mechanism to prevent inadvertent entrainment of air and distensible infusion tubing that smooths flow and limits infusion pressure transmitted to the vascular catheter. The LifeFlow is capable of infusing fluids and blood products at over 250 mL/min through a variety of access devices, and early reports have described its use in a variety of settings and patient populations [76–80].

Can Rapid Infusion Cause Harm?

One potential concern with rapid infusion devices is subcutaneous extravasation due to catheter dislodgement, a complication also known to occur with standard infusion pumps. Risk of extravasation may be increased when the vascular access site is not continuously monitored for

patency, with larger-bore catheters that may damage the vessel wall upon insertion, or when the device is used for delivery of large volumes of fluid over many hours or days [81, 82]. In one study of 8.5 F peripheral rapid infusion catheters, the reported rate of extravasation was approximately 1.7% with no evidence of permanent injury [83]. This contrasts with a 23% infiltration rate for peripheral IVs used for other purposes, and a complication rate for central venous catheters (CVCs) as high as 45% [83, 84]. The prolonged dwell times associated with peripheral IVs increase the risk of phlebitis or dislodgement leading to catheter failure and infiltration, whereas complications of CVCs are more likely due to vascular injury, thrombosis, and nosocomial infection. Interestingly, with CT contrast infusion devices which generate pressures of 300 psi (approximately 15,000 mmHg) and flows as high as 8 mL/s, IV cannula disruption and extravasation are infrequently reported. In one study of over 40,000 patients, contrast extravasation occurred in 0.3% of cases [85].

The infusion of blood can be associated with potential complications, including but not limited to hemolysis, hyperkalemia, hypocalcemia, transfusion reactions, and transfusion-related acute lung injury (TRALI). Older packed red blood cells (PRBCs) are known to be less stable and more susceptible to hemolysis resulting in the rise of serum potassium levels. The use of fresh (< 7 day old) PRBCs or fresh whole blood minimizes this hemolysis risk. Citrated blood products may bind extracellular calcium during transfusion and cause acute hypocalcemia, leading to myocardial depression. The risk of both complications increases with the volume of blood transfused, and therefore, attentiveness to measurement of potassium and ionized calcium values is important. Small-gauge catheters may also produce excess hemolysis by increasing turbulent flow. For this reason, at least one anesthesia society has recommended that blood be infused only through catheters larger than 23 G [86]. Lastly, pressurized rapid infusion of platelets, either as concentrates or within whole blood, has the potential to cause platelet injury. While pressurized infusion of fresh whole blood by rapid infusion methods modestly reduces platelet count, platelet activation and overall hemostatic function of the blood may actually be enhanced through rapid infusion [87].

Perhaps the biggest concern with the concept of rapid infusion is volume overload [88–90]. Although excess fluid accumulation is known to be harmful [91, 92], the adverse effects of fluid arise largely from the use of large volumes of fluid given over the course of a patient's hospitalization rather than the volume administered during the early minutes of resuscitative care [93,94•]. In fact, adequate fluid therapy in the early moments of care may actually reduce the patient's overall fluid requirement and prevent the complications of large-volume resuscitation

[30••,31••,37•,95,96•,97,98]. In one of the few recent studies examining the speed of fluid delivery in the early management of septic shock, the highest rates of infusion were associated with faster shock reversal and lower mortality [96].

Conclusions

Rapid infusion of crystalloid and/or blood products can be a life-saving intervention for patients with acute circulatory failure and remains first-line treatment for the acute resuscitation of patients with shock [7–11]. The patient in the vignette above presented to the ED with hemorrhagic shock, respiratory failure, traumatic brain injury, and a possible spinal cord injury. Reversal of shock was the immediate management priority since every minute of hypotension increases the risk of permanent neurologic sequelae and places the patient at significant risk of peri-intubation cardiac arrest. With no pre-existing vascular access at the time of ED arrival, immediate establishment of IV or IO access was required. Without a mechanical rapid infuser or whole blood, a manual method of rapid infusion was required to begin to restore intravascular volume while preparing for intubation. While fresh whole blood or O-negative PRBCs would be preferred for this patient, crystalloid solutions may be the only fluid immediately available.

In this case, a humeral head IO catheter was placed and 1000 mL of lactated Ringer's solution were rapidly infused with a manual rapid infusion technique, resulting in improvement of the blood pressure to 85/40 mmHg and potentially preventing peri-intubation cardiac arrest. Two units of emergency release O-negative PRBCs were subsequently transfused by the same method after placement of an 18 G IV. The patient's blood pressure stabilized at 110/60 mmHg, and he was transferred for operative care while temporary hemorrhage control was achieved using direct pressure. He subsequently achieved a full neurologic recovery.

For this patient, the ability to rapidly restore circulating volume and reverse hypotension proved critical to his successful outcome. Emergency care providers should be aware of the multiple techniques available for providing volume resuscitation in situations where minutes truly matter. Large mechanical rapid infusion devices can work well in centers where they are regularly used and when adequate vascular access is immediately available. In other settings, such as austere environments, during prehospital transport, and in community emergency departments, methods such as a pressure bag, syringe and stopcock, or a handheld rapid infuser may be the only options, especially when only smaller-gauge IVs or IO access are available. Regardless of the infusion method selected, emergency providers should follow the

guidance of early medical pioneers who recognized that rapid resuscitation must be accompanied by continuous attention to the patient's response after each dose of fluid or blood that is delivered.

Compliance with Ethical Standards

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Conflicts of interest Mark Piehl is Chief Medical Officer and a Director of 410 Medical, a shareholder in the company, and an inventor of the LifeFlow device.

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- 64% of initially hypotensive patients are fluid responsive, including patients with CHF; the biggest predictor of fluid-refractoriness is delayed initiation of fluid therapy.**
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