Intraosseous Vascular Access

A Guide for Healthcare Professionals

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Preface

My first exposure to intraosseous (IO) vascular access was as a trauma surgery resident working in a busy urban Level I trauma center. My mentor, Dr. Thomas Knuth, had a wealth of military experience and had become familiar with IO cannulation techniques during his military service. I was surprised by the lack of civilian experience with this technique but immediately grasped the value of this somewhat unorthodox approach to vascular access. Under Dr. Knuth's tutelage, I first studied a cohort of trauma patients in 2008, who received the proximal humerus approach to IO vascular access, and found that this technique was not only invaluable but also incredibly safe and effective. Over the last 15 years, I have seen the growth of this approach in the civilian world and have personally witnessed the potential of IO infusion to salvage the resuscitation of patients who cannot receive direct venous access rapidly enough to achieve clinical stabilization.

Although explorations of therapeutic IO cannulation have been underway for more than a century, much of the early research into this modality is squirreled away in obscure journals, some of which are no longer in print. Even recent data can be hard to find, leading to a somewhat disjointed view of this approach in many modern reviews on the topic. Our goal with this "primer" is to present the modern clinician with at least a scoping review of relevant knowledge in a cohesive and cogent manner. Despite the extensive growth of the IO approach in the prehospital and emergency medicine environments, consideration of the IO technique remains underutilized in the clinical arena. We believe that lack of familiarity and education with this modality is a key factor contributing to this phenomenon and hope to improve upon this situation through a targeted discussion on several fundamental aspects of the technique.

As an emergency medicine physician, I am haunted by the memory of patients who suffered intolerable delays in vascular access due to inaccessible peripheral veins. This is never a problem when IO cannulation is considered in the vascular access algorithm, but providers must be comfortable with IO cannulation and competent in the use of this technique for its potential to be fully realized. When we published our primer, "Emergent Vascular Access," in 2021, only a single chapter was dedicated to IO access. After publishing that "primer," it became obvious that an entire book was needed to describe the many nuances of the IO technique. This book is the result of that unanswered need for improved awareness of the risks and benefits of the IO approach to indirect venous access.

Modern patients can expect to live longer with chronic diseases than ever before due largely to recent diagnostic and therapeutic advances that prolong life by reducing the risk of emergent complications. But chronic diseases lead to recurrent hospitalizations and other acute care events, ultimately requiring repeated direct venous access attempts. Each direct venous access attempt (successful or failed) carries with it the potential for venous injury or other traumatic effects that can render future attempts at venous cannulation at that site more difficult or even impossible. Patients carry these scars of previous venous injury with them into future care events, eventually leading many patients with chronic illness toward a state of difficult venous access that may overwhelm the ability of providers to safely and efficiently establish therapeutic venous access during an emergency. Thus, as we get better at keeping people with chronic illness alive, we are likely to experience an increasing threat of difficult or impossible direct venous access. Alternative routes for providing fluids and medications to critically ill patients are needed to combat this threat, and I believe that indirect routes of venous access such as the IO approach will become increasingly important to future generations of clinicians and patients.

This book is dedicated to the emergency care provider who has attempted or at least considered the need for direct venous access but has found that direct methods for venous access are not adequate or feasible. Recognition that IO access is an available option is a crucial step toward improving the care of our emergency patients under austere conditions where direct venous access is not assured. It is our hope that a better understanding of this approach will yield better outcomes for patients with difficult venous access, both now and far into the future.

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A History of Intraosseous Vascular Access

1

Jacob Dougherty and James H. Paxton

History of Intraosseous Vascular Access

The earliest reference to studies of the intraosseous (IO) circulation can be traced back to **Franz Müller** (1871–1945), of Humboldt University (Berlin, Germany), at the turn of the twentieth century. In animal studies, Müller observed that blood taken directly from the nutrient vein of the canine tibia was identical in its composition to blood drawn from other parts of the animal [1]. Around the same time, the first bone marrow samples from living patients were obtained independently by two physician-scientists, Italian hematologist **Giuseppe Pianese** (1864–1933) at the Anatomical-Pathological Institute of Naples and German hematologist **Alfred Wolff-Eisner** (1877–1948) of Berlin, circa 1903, in an effort to diagnose parasitic infections [2, 3]. While none of these early scientists developed a technique for IO infusion, their groundbreaking work would stimulate interest across the globe in studying the bone marrow and its blood supply.

Building on Müller's research, **Cecil Kent Drinker** (1888–1956), a professor of physiology at Harvard University Medical School (Cambridge, Massachusetts), noted the extensive vascular network that existed within the canine tibia and suggested that substances injected into the tibial bone marrow could be taken up and distributed into the central circulation [4]. Although Drinker was an anatomist and physiologist, his early publications were among the first in the English-language literature to propose the potential therapeutic use of intraosseous infusion. Drinker published his report on maintaining circulation through the tibia of an anesthetized dog in 1916, including a proposed method for perfusing the bone marrow, as illustrated in Fig. 1.1 [4]. Drinker's technique involved exposure of the nutrient artery of

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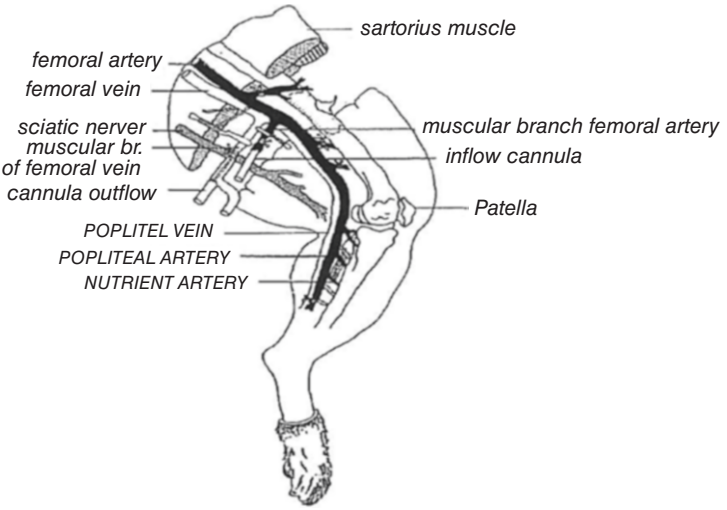

Fig. 1.1 Drinker's original sketch of his technique for studying intraosseous blood flow [5]

Fig. 1.2 Cecil K. Drinker *(Image courtesy of Harvard T.H. Chan School of Public Health. © 2023 The President and Fellows of Harvard College. All rights reserved.)* [6]

the tibia following ligation of the popliteal artery branches. Cannulation of the popliteal artery was performed, and study solution was then shunted through the cannula into the tibial nutrient artery, with the aid of a thigh tourniquet [5]. Drinker's experiments, in which he injected various substances into the live canine tibia to observe their movement and removal from the marrow, demonstrated that infused substances were subsequently distributed into the central circulation [5]. A photograph of Drinker examining his work can be seen in Fig. 1.2.

Perhaps inspired by the early work of Drinker and others, **Charles A. Doan** (1896–1990), a medical student at Johns Hopkins University (Baltimore, Maryland), similarly explored the role of bone marrow in the circulation of adult pigeons [7]. While attempting to deliver ink, mercury, and saline into the pigeon's circulation through intraosseous infusion, Doan found that infusion pressures near 130 mm were

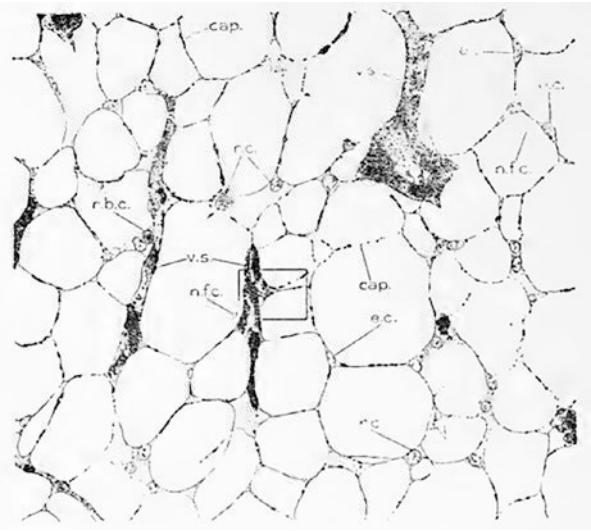

Fig. 1.3 Doan's original sketch of the intraosseous capillary system [7]

required, but pressures above that level led frequently to tissue injury. In his 1922 publication, Doan reported that a well-defined and extensive network of capillary beds existed to drain the marrow space of adult pigeons. Although much of the hematopoietically active marrow had been replaced with fatty tissue in adult subjects, he speculated that these channels were "functionally dormant" and might be activated to drain the marrow space in times of urgent need [7]. Doan's original sketch of the capillary is illustrated in Fig. 1.3, with endothelial cells (ECs), reticular cells (RCs), nuclei of fat cells (NFCs), red blood cells (RBCs), capillaries (CAPs), and venous sinusoids (VSs). The interstitial capillaries can be surrounding the nuclei of fat cells and communicate with the larger venous sinusoids, with carbon granules distributed via injection scattered throughout the capillaries. A photograph of Doan is provided in Fig. 1.4.

This pioneering work by Drinker and Doan laid the framework for subsequent experiments involving human subjects and clearly inspired other scientists to explore the use of intraosseous infusion for therapeutic purposes. German physician **Paul Carly Seyfarth** (1890–1950) of the University of Leipzig investigated the use of sternal trephination for the diagnosis of malaria [9] and brought this technique with him as director of the German Alexander Hospital in St. Petersburg (Russia) from 1922 to 1923. A Russian physician, **Mikhael Innokent'evich Arinkin** (1876–1948) of the nearby Military Medical Academy at Leningrad, adopted Seyfarth's technique using a spinal needle for the diagnosis of various hematological disorders as well as typhus and tuberculosis in 1922 [10].

Arnold R. Josefson (1870–1946), a Swedish internist and pathologist by training, had already become very well known for his work in the diagnosis and treatment of a variety of endocrinologic and hematological disorders. In the early 1930s, Josefson began to explore the possibility of infusing campolon (liver extract) into the sternum and manubrium of human patients as an alternative to intravenous injection in the treatment of pernicious anemia. His report of these experiments in

Fig. 1.4 Charles A. Doan *(from library.osu.edu, licensed under CC-BY 4.0)* [8]

1934 included a claim that intraosseous infusion of this substance was equally effective as intravenous infusion and much simpler to perform. Josefson deemed the IO method superior as a result of less frequent injections being needed when compared to other common routes of infusion [11].

Although Josefson is generally considered to be the first clinician to treat a human patient with intraosseous infusion, his work built on the efforts of Seyfarth, Arinkin, and a host of other European hematologists who pioneered sternal and tibial IO access for diagnostic bone marrow sampling. Italian physician **Giovanni Ghedini** (1877–1959) at the University of Padua (Italy) published the first report of a bone marrow biopsy technique for use in live human subjects in 1908, building on the work of mid-nineteenth-century physicians **Charles-Philippe Robin** (1821–1885) and **Rudolf Albert von Kölliker** (1817–1905), who had described a similar approach for the sampling of cadaveric specimens [12]. Although Ghedini endorsed the tibial bone as a site for marrow sampling, the sternum was generally preferred by Seyfarth and most other investigators. Another early clinician who expanded upon Ghedini's work was the American physician **Francis Weld Peabody** (1881–1927) of Harvard Medical School (Boston, Massachusetts), whose research focused on bone marrow changes with pernicious anemia [12].

Within a few years of Josefson's report, other clinician-scientists began reporting on their own experiences with sternal IO infusion. By 1937, French scientists were

Fig. 1.5 Leandro M. Tocantins. *(Image courtesy of Thomas Jefferson University, Philadelphia. © 2023 Thomas Jefferson University. All rights reserved.)* [16]

experimenting with IO infusion of drugs, bacteria, air emboli, and various radiopaque substances in guinea pigs and human subjects [13–15]. In 1940, hematologist **Leandro M. Tocantins** (1901–1963) at the Jefferson Medical College and Hospital (Philadelphia, Pennsylvania) published his first of many reports on the use of sternal IO injection in the treatment of patients suffering from "acute failure of the peripheral circulation" (i.e., shock) (Fig. 1.5). Tocantins' subsequent work with **James F. O'Neill**, a surgeon at the Wake Forest Bowman Gray School of Medicine (Winston-Salem, North Carolina), and internist **Alison H. Price**, a recent graduate of Jefferson Medical College, emphasized the importance of this technique, describing the bone marrow as a superior route of infusion in the setting of hypotension and hypovolemia for both pediatric and adult subjects [17–20]. He found that blood, dextrose, and dye infused into the human sternum or rabbit tibia were absorbed just as quickly as with intravenous infusion, with emergent IO infusion of dextrose capable of rapidly correcting dangerous levels of hypoglycemia [21].

Tocantins' study of the sternal site for IO infusion revealed that the pediatric sternum (especially in infants) appeared to be relatively undeveloped and generally unsuitable for IO infusion. Figure 1.6 demonstrates the path of a solution following injection into the manubrium, with the solution rapidly traveling to the internal mammary veins.

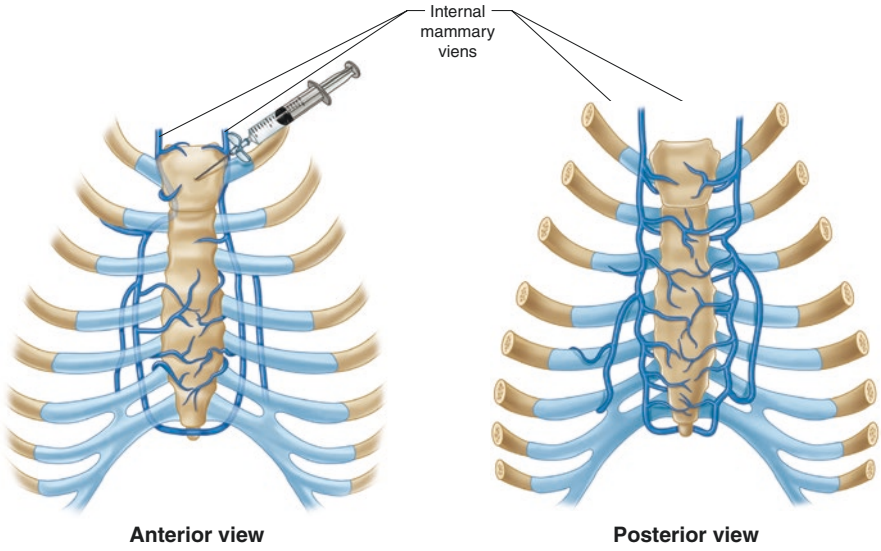

Fig. 1.6 Tocantins' sternal infusion approach, including relevant venous anatomy [18]

Fig. 1.7 Tocantins' push-pull system for IO infusion [18]

Tocantins' push-pull infusion system (Fig. 1.7) called for the infusate to be first placed into a flask, with tubing including a two-way stopcock placed between the flask and the needle. After closing the infusion tubing system to the sternum, the fluid was drawn from the flask into the syringe. The stopcock was then turned to close the flask tubing system, and the syringe contents were injected through the

sternal tubing into the patient's sternum. This process could be repeated without requiring disconnection of the syringe from the infusion tubing, greatly improving the efficiency of high-volume IO fluid infusions [17, 18].

Tocantins was among the first clinician-investigators to propose the use of the proximal tibia (preferred) or distal femur (as a secondary site) for pediatric IO infusions, and he also reported satisfactory results with the proximal humerus site decades before this site was commonly used [19]. Tocantins was also one of the first to develop his own IO device, later known as the "Tocantins needle," which was manufactured by the George P. Pilling and Son company (Philadelphia, 1900–1960) [22]. This needle was described as a "needle with a wide wing top, having a ball guard which slides along the shaft to fix the needle after it is in place, another indwelling needle for marrow aspiration, a stylet, and a curved adapter" [22]. The Tocantins needle was manufactured in four different lengths.

Around the same time, several Spanish- and German-language reports were published extolling the virtues of intraosseous infusion [23–32]. During the late 1930s, German hematologist **Norbert Henning** (1896–1985) began studying the use of IO infusion at the University of Leipzig [25–27]. Although his multiple German-language publications were relatively unreferenced in American medical circles, Henning was a vocal advocate for the use of IO infusion as an alternative to intravenous infusion [27]. Henning also developed his own biopsy needle, which included a side hole for irrigation of the marrow space and graduated centimeter depth markings ringing the cannula [25, 28]. His studies of sternal blood flow revealed that substances injected into the sternum were transmitted to the central circulation via the internal thoracic and brachiocephalic veins with a speed and efficacy comparable to intravenous injection [26]. This led him to announce his findings at the annual meeting of the German Society of Internal Medicine in May 1940, several months before Tocantins published his groundbreaking article [26]. While Tocantins strongly discouraged the IO infusion of hypertonic saline and glucose-containing solutions due to the risk of extravasation with resultant soft tissue necrosis, Henning showed that these substances could also be safely administered, and he was a pioneer in the infusion of blood products through the IO route [29, 30]. Though largely neglected in the English-language IO literature, Henning's work undoubtedly influenced the use of IO technology by other European practitioners much as Tocantins influenced those in the United States and England. Two German surgeon-scientists, **Joseph Korth** (1907) at the University Clinic of Leipzig and **Werner Lamprecht** (1900–1970) of Osnabrück, developed their own eponymous IO catheters that were widely used within the German-speaking world during the 1940s [25, 31, 32].

Emanuel M. Papper (1915–2002), while an anesthesiology resident at Bellevue Hospital (New York, New York) during the early 1940s, built on Tocantins' work by demonstrating that an injection of macasol solution (containing a combination of magnesium and calcium salts) infused at the human sternum was absorbed only slightly less quickly than the same compound injected into the antecubital vein of seven adult subjects (Fig. 1.8) [34]. He discovered similar comparable results with a range of different infusates, reporting that some drugs appeared to be absorbed more quickly from the IO space than others [22]. In fact, 2% sodium cyanide appeared to

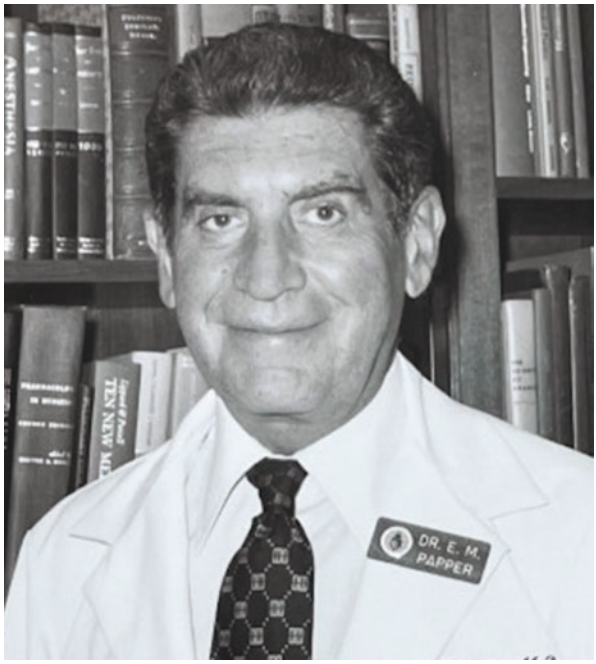

Fig. 1.8 Emanuel M. Papper. (*Image courtesy of the University of Miami Louis Calder Memorial Library collection. © 2023 University of Miami Louis Calder Memorial Library. All rights reserved.*) [33]

be absorbed more quickly from the sternal IO space than from peripheral veins [22]. Papper published his initial findings in 1942 (the same year that he finished residency), along with his mentor, **Emery A. Rovenstine** (1895–1960), then Chair of Anesthesiology at Bellevue. While he acknowledged the utility of the Tocantins needle, Papper suggested that a "wide-bore [Becton-Dickinson] Luer-Lok type (1.5 mm in diameter) sternal needle with accurately ground stylets" was more than adequate [22]. Papper's needle of choice featured a 3 cm long shaft (exclusive of the hub) for adults, with a short (4 mm) bevel and a sharp point and cutting edges [22].

Although intraosseous access had its origins in civilian medicine, the potential benefits of this approach on the battlefield were readily evident. Papper himself was a Major (1942–1946) in the Army Medical Corps and appears to have been a major advocate for the use of IO access to treat injured soldiers during the war. One very-high-profile case of IO infusion involved a Boeing B-29 Superfortress aircraft gunner from Detroit, Michigan, named **Romeo Rendina**. While flying a mission over Nagoya, Japan, on 18 February 1945, an explosive shell penetrated Rendina's aircraft and exploded in his lap. More than 100 shell fragments ripped through his right hand, right arm, and left leg, causing significant blood loss and necessitating immediate vascular access to treat hypovolemic shock [35]. After multiple failed peripheral IV attempts, crew members ultimately inserted a sternal IO device and infused 150 mL of plasma (and morphine) through the sternal IO catheter while Rendina was being transported to a military hospital. This successful resuscitation brought national attention to the use of the IO route for combat resuscitation and appears to be the first documented use of a sternal IO catheter by a medical first responder,

although Rendina was only one of many soldiers who benefited from IO infusion during the war [35]. From 1939 to 1945, an estimated 4000 intraosseous infusions were performed on injured Allied soldiers and civilians in the military arena.

As Rendina's case demonstrated, wartime conditions made the establishment of direct peripheral venous access challenging and central venous access was not yet commonplace. British surgeon **Henry Hamilton Bailey** (1894–1961) described situations of extreme hypovolemia, poor lighting conditions ("blackout"), and the chaos of battle in his rationale for proposing IO access as first-line therapy for injured soldiers during wartime [36]. Bailey had served in the British Royal Navy during World War I and experienced these difficulties in caring for injured soldiers first-hand. At the time, stainless steel hypodermic needles were still being used for peripheral venous cannulation and were especially prone to dislodgement and/or iatrogenic vascular injury. Bailey reportedly used a trocar needle with winged handle designed by Whilen Brothers of England to treat patients during the London Blitz (1940–1941).

Penicillin was only just becoming available during the mid-1940s, and ineffective antiseptic methods for peripheral IV catheter placement contributed to a high rate of infection and thrombophlebitis [36]. These factors led to tremendous growth in the use of IO infusion therapy during the 1940s, as the IO route was considered to be a safer (or at least no more dangerous) route of infusion than peripheral IV infusion at the time.

British physician **Joseph Bramhall Ellison** (1898–1953) of the Grove Fever Hospital (London, England) had also served in World War I, and described the intraosseous technique as "utterly simple and the discomfort momentary" [37]. By 1944, Ellison had treated 40 "collapsed and dehydrated" infants with tibial IO infusion in his own civilian practice. As he put it, "no one who has fumbled with a Bateman's cannula and a vein like a bit of chewed cotton, no one who has seen the last available venous channel firmly clotted up, no one hard pressed for time, once having tried this new method is likely to revert to the old. The only snag (barring over-enthusiasm engendered by facility) is the difficulty at the present time of getting needles sharpened" [37]. The Hamilton Bailey-type infusion needle was also one of interest at this time. It was made with a gold cannula for enhanced sterility with a beveled tip to help guide needle insertion on one end and a bulb directly attached to rubber tubing on the other [38].

While Papper and some others advocated for the use of simple "serum needles" to cannulate the sternum, many practitioners preferred Tocantins' winged catheter [37, 39]. Sternal infusion, which had already been largely replaced by tibial infusion in infants and small children, remained a risky venture due to the risk of perforation through the sternum with subsequent infusion into the mediastinum [36, 40–42]. To counter this risk, Bailey developed a winged cannula (Fig. 1.9) intended to prevent the instrument from being advanced too far into the sternum [36].

The Bailey needle itself was a derivative version of the "Witts needle," first introduced to the medical literature circa 1936 by British hematologist **Leslie John Witts** (1898–1982) and first developed for bone marrow biopsy by unnamed clinicians practicing in Egypt [43]. The Witts needle featured a stylet (a) inserted into a needle (b) with an adjustable guard (c) to prevent overpenetration (Fig. 1.10).

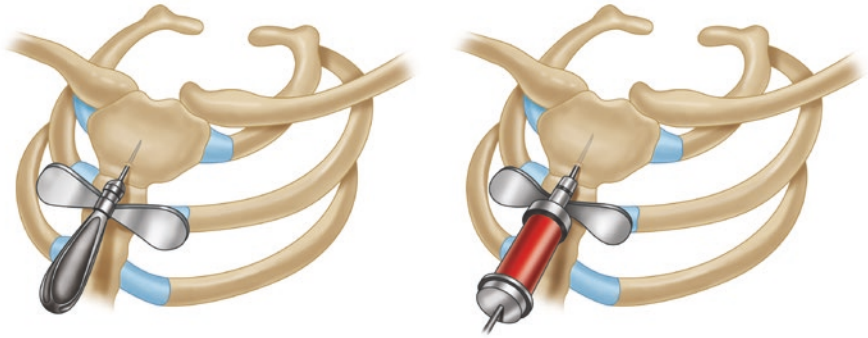

Fig. 1.9 Bailey's winged catheter design [36]

Fig. 1.10 Witts lumbar puncture needle, including internal stylet (**a**), infusion needle (**b**), and adjustable guard (**c**) [43]

The addition of wings to stabilize and guide insertion for IO catheters may have solved the problem of overinsertion with sternal placement, but some felt that these newer devices were inappropriate for use at the pediatric tibia due to their heft and size. In 1944, British pediatrician **Janet Dinah Gimson** (later Roscoe; 1914–2002) of the Hospital for Sick Children, Great Ormond Street (London, England), introduced a needle system (Fig. 1.11) specifically designed for tibial infusion among infants and small children that was lighter, smaller, and more versatile, with needle lengths of $^{1}/_{4}$, $^{3}/_{8}$, $^{1}/_{2}$, and $^{5}/_{8}$ inches. The needle was manufactured by Allen & Hanburys (London), a prominent pharmaceutical company and medical supply manufacturer, in their Bethnal Green factory. Gimson emphasized the need to insert the needle at a right-angle perpendicular to the bone's surface and to use a "strut" with a rubber strap wrapped around the infant's leg to better stabilize the device [44]. As shown in Fig. 1.11, the Gimson needle also featured a large handle to facilitate control over needle insertion.

Many other important IO researchers published their earliest results during the 1940s. Pharmacologist **David I. Macht** (1882–1961), who was working at the time for Hynson, Westcott, and Dunning pharmaceuticals (Baltimore, Maryland), reported on his work with IO epinephrine injection in 1942 [45]. Macht found that

Fig. 1.11 The Gimson needle, demonstrating variable lengths of cannulae (*left*) and large attachable handle to stabilize insertion (*right*) [44]

aqueous solutions of epinephrine administered through the tibia of various animals (e.g., cats, dogs, rabbits, rats, guinea pigs) yielded results that were virtually indistinguishable from intravenous infusions, including a sharp rise in blood pressure followed by a rapid decline [45]. Suspensions of epinephrine in oil, on the other hand, yielded only a moderate increase in blood pressure (i.e., about half of that produced with aqueous solutions), although the effect was longer lasting - up to an hour in some cases [45]. His experiments with various vegetable oil diluents demonstrated the "depot" effect of medications suspended in oil within the IO medullary cavity, suggesting that the drug was being slowly released into the general circulation. While intravenous infusion of these oil suspensions was believed to be "fraught with great danger," he found that IO infusion of oil suspensions rarely resulted in any adverse events among those animals studied [45].

Maurice Morrison (1895–1983) and **AA Samwick** of the Jewish Hospital (Brooklyn, New York) reported a successful human bone marrow transfusion at the sternum for the treatment of idiopathic pernicious anemia in 1940 [46]. Meanwhile, dermatologists **Udo J. Wile** (1882–1963) and **Ira L. Schamberg** (1909–1980) at the University of Michigan (Ann Arbor, Michigan) investigated the effects of IO injection of mapharsen (arsenious oxide), a common treatment for syphilis, on rabbits [47, 48]. They found histological evidence of fat emboli in the pulmonary arterioles of five of the seven rabbits sacrificed in this experiment, with one presumed death due to embolism, although the other four rabbits showed no immediate or

delayed clinical evidence of adverse effects [47]. The authors concluded that, "the more rapid the bone marrow infusion and the higher the pressure of the stream of fluid, the greater would be the likelihood of rupturing fat cells and forcing fat globules into the venous system" [47]. In fact, the one fatal embolism noted in this series occurred in the subject exposed to the most rapid infusion rate, approximately 10.9 mL/min (4.54 mL/kg/min). The authors did not entertain the notion that massive rapid infusion of mapharsen, an arsenic-containing substance, may have contributed to the single death in this series.

Heinrich "Henry" Turkel (1903–1992), an Austrian-born American physician and inventor, was another vocal advocate for the use of IO technology. He introduced the IO infusion of amino acids and other fluids at the sternum, ilium, femur, and tibia at the University of Michigan in 1935 and later at Wayne County General Hospital (Detroit, Michigan) in 1937. His collaborators at the University of Michigan included surgeon **Frederick A. Coller** (1887–1964) and hematologists **Frank H. Bethell** (1903–1959) and **Cyrus C. Sturgis** (1891–1966) [49]. Coller (Fig. 1.12) had earned the rank of Major in the US Armed Forces during World War I as a member of the American Ambulance Service and was a surgical consultant to the US military during World War II. As Chairman of the Department of Surgery at the University of Michigan (1930–1957) and President of the American College of Surgeons (1949), Coller was an influential figure in American medical circles

Fig. 1.12 Frederick A. Coller (1887–1964) *(Image courtesy of the Archives of the American College of Surgeons. All rights reserved.)* [50]

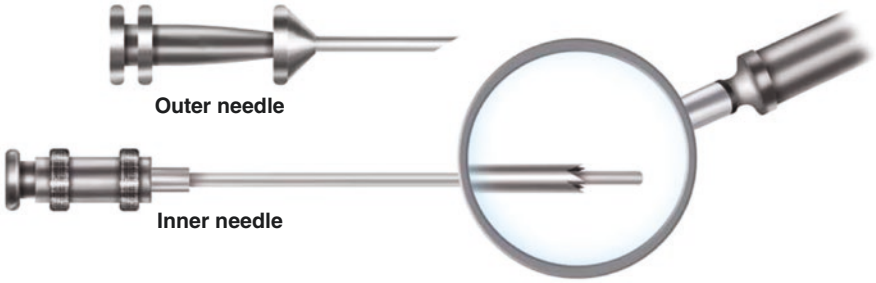

Fig. 1.13 The Turkel trephine instrument [52]

during the 1940s and 1950s. Turkel himself was a consultant to the Surgeon General's Office during the war. Consequently, these two men were instrumental in securing a place for IO catheters in every combat medic's tool kit during World War II.

Henry Turkel developed a novel trephination and IO infusion device that would come to be marketed by Turkel Trephine Instruments (Detroit, Michigan) and was ultimately adopted by the US National Research Council for use by the American military during and after World War II [49, 51]. Turkel claimed that his proprietary trephine (i.e., hole saw) catheter tip needle (Fig. 1.13), with the use of an internal stylet, had been proven safe for infusions up to 24 h in duration [49].

The Turkel Trephine Instruments for Biopsies and Marrow Infusions, Adult Sternal Infusion Set, was manufactured by Trephine Instruments (1302 Industrial Bank Building, Detroit, Michigan) and included a 14–17 gauge catheter with 20 mm length. This kit included right-angle connectors, which served to connect the IO cannula to the infusion tubing (Fig. 1.14).

The use of intraosseous vascular access among adults declined sharply after the end of World War II, but pediatric use would continue in many countries. Danish pediatrician **Svend Heinild** (1907–1994) at the Refsnaes Kysthospital (Refsnaes, Denmark) reported the largest case series to that time, with nearly 1000 pediatric infusions, in 1946. Most of his infusions were of crystalloid fluids for the treatment of acute gastroenteritis, with patients often receiving more than one infusion [53]. Heinild highlighted the safety of the approach in children, but did mention the risk of osteomyelitis as a potential complication [53].

Following the end of World War II, civilian reports of therapeutic intraosseous infusion within the English-speaking literature became more rare, although they continued to filter in from Dutch-, Russian-, German-, and Bulgarian-language journals [54–58]. The reasons for this declining interest in IO infusion remain unclear, although several factors likely contributed to the trend. While combat medics were uniformly taught IO insertion techniques (usually at the sternum), most of these medics resumed their nonmedical civilian jobs at the end of the war. Thus, most of the training and familiarity with IO infusion that these medics developed was ultimately lost to the medical community. The introduction of penicillin and other antibiotics may have also mitigated concerns about potential infectious risks associated with direct peripheral venous infusion, which seemed to be more prominent at the time when compared to the rare reports of osteomyelitis attributed to IO infusion.

Fig. 1.14 Turkel Trephine Instruments for Biopsies and Marrow Infusions, Adult Sternal Infusion Set. (*Image provided by the authors*)

Newer materials and methods for intravenous infusion also became available during this time, likely drawing attention away from the use of IO devices. During the first half of the twentieth century, intravenous access was generally achieved with steel needles that were sterilized between uses by boiling them in water [59]. The sterilization process caused the needles to become dull or barbed after multiple uses, increasing the risk of venous injury and complicating their insertion. Once dulled, the needles had to be hand-sharpened with flint stones [59]. But the introduction of disposable intravenous needles dramatically improved the provider experience with IV insertion. The first disposable peripheral IV cannulae (made of polyethylene) were introduced by Becton-Dickinson in 1945, followed by the Rochester needle in 1950, and the first over-the-needle plastic winged catheter in 1963 [59]. Disposable needles proved to be much cheaper and easier to insert than multiuse steel cannulae, signaling the end of the steel needle era for intravenous access. As steel IO catheters featured many of the same disadvantages as steel IV catheters, these trends likely contributed to decreased interest in reusable IO devices as well.

Central venous catheters, designed to be inserted into the major veins of the thorax, also became more commonly used in the 1960s, often made of "modern" disposable materials (e.g., silicone rubber and polyurethane) that allowed for greater flexibility with insertion [59]. The Seldinger technique, named for the Swedish radiologist **Sven Ivar Seldinger** (1921–1998), was introduced in 1953 and was rapidly applied to central line placement, making central venous access an increasingly

feasible alternative to IO or peripheral IV access in the unstable patient [60]. Each of these advances in direct venous access likely moved indirect (e.g., IO) venous access further and further down the vascular access algorithm for medical providers [61].

Occasional voices from outside of the United States were heard promoting the use of IO access during the late 1970s. One of the first clinicians to promote IO use in the English-language literature during the 1970s was **Manuel M. Valdes** at the Institute of Tropical Diseases (Mexico City, Mexico). Valdes routinely used intraosseous venography for phlebographic studies and noted that IO infusions of fluids and medications other than contrast agents appeared to be both safe and effective. In 1977, he reported a case series of 15 adult patients who received 2–42 L of fluid over a period of up to 30 days via either medial malleolar (12 cases) or lateral malleolar (3 cases) IO infusion using a standard 14-gauge Becton-Dickinson needle [62]. This publication by Valdes appears to have stimulated additional interest in the IO route during the late 1970s and early 1980s, including bovine studies of epinephrine injection at the distal tibia [63] and early studies on IO infusion for regional anesthesia during orthopedic surgery [64].

A resurgence of interest in IO cannulation came during the early 1980s, following a series of editorials published in the United States. The first of these editorials was from Henry Turkel, now retired and living near Detroit, Michigan. In his 1983 editorial published in *Southern Medical Journal*, Turkel commented on a local news story involving a 3-year-old child who was allegedly blinded and brain-damaged when her anesthesiologist was unable to establish an intravenous line for the infusion of general anesthesia in a timely manner [65]. Turkel lamented that the IO route was being "ignored in medical schools" and suggested that the use of an IO catheter to obtain earlier vascular access could have prevented these complications [65]. Turkel's claim that IO cannulation was not being widely taught in American medical schools was fairly accurate. In fact, the first American Heart Association (AHA) Advanced Cardiac Life Support (ACLS) guidelines (published in 1974) did not mention IO access at all, although these early guidelines did suggest the use of cutdowns or intracardiac injections of medication when peripheral veins were not immediately accessible [66, 67]. The first appearance of IO infusion in the ACLS guidelines would come in 1986, but only for use in pediatric emergencies [68, 69]. The first reference to IO access in the adult ACLS guidelines emerged in 1992, couched in the claim that, "intraosseous infusion of drugs is an excellent alternative when IV access is not readily available, particularly in pediatric patients" [70].

Robert A. Berg (b. 1950), a pediatric intensivist at Maricopa County General Hospital (Phoenix, Arizona), was the first to report in the English-language literature on the continuous IO infusion of dobutamine and dopamine following cardiac arrest (Fig. 1.15) [71]. The subject of this report was a 6-month-old infant who had already failed multiple intravenous catheterization attempts, including a femoral vein cutdown, but was able to receive bilateral proximal tibial IO cannulation using a standard 18-gauge hypodermic needle [71].

Fig. 1.15 Robert A. Berg. *(Image courtesy of Dr. Robert A. Berg. © 2023 Robert A. Berg. All rights reserved)*

As Berg recalled,

I actually learned how to place a needle in the proximal tibia IO space from Hem-Onc physicians to obtain specimens for diagnostic purposes, such as cancers and for karyotyping newborns (e.g., to diagnose Trisomies 21, 13 and 18 in newborns). Thus, I had learned that IO access could be used for resuscitation and I had developed the clinical skills of IO access for bone marrow diagnostic purposes. The case report was the first time that I [had] used this combination of historical knowledge and clinical skill experience to provide IO access for resuscitation. I had never seen anyone use it for resuscitation before I used it, and I was not aware of others using over the last couple decades (but that says more about what I knew than whether others were using it elsewhere).

I wrote the case report for *AJDC* (now renamed *JAMA-Pediatrics*) because the editor Vince Fulginiti (Chair of Pediatrics at U of Arizona in Tucson at the time) specifically wrote an editorial that year asking for case reports of experiences using clinically important interventions that had been part of medical care in the past but were not as well known in the early 1980s.

Apparently, that simple case report and accompanying editorial by Jim [Orlowski] led to increased interest over the next several years with both animal studies and clinical studies supporting its value. Perhaps most importantly, the first [American Heart Association Pediatric Advanced Life Support] course in 1987 and the associated first PALS textbook published in 1988 highlighted the importance of prompt vascular access for fluid resuscitation and drug administration during resuscitation. Under Priorities in Venous Access, the PALS textbook stated, 'In children under 3 years of age, an intraosseous cannula should be placed immediately and used for volume expansion and additional medications.' (*Communication between RA Berg and the authors, 2022, unreferenced*).

An editorial accompanying Berg's report in the September 1984 issue of the *American Journal of Diseases of Children* (AJDC) written by pediatric intensivist **James P. Orlowski** (b. 1947) of the Cleveland Clinic (Cleveland, Ohio) further advocated for increased use of the IO route [72]. Orlowski had learned about the use of IO catheters on a medical missionary trip to India as a senior-year medical student at Case Western Reserve University (Cleveland, Ohio) in 1973. While there, he witnessed profoundly dehydrated patients being treated with IO infusions of fluids during a cholera epidemic. Returning to Cleveland, he began using IO infusion in his own practice. As Orlowski wrote:

> There is no more exasperating situation than the inability to establish intravenous (IV) access in a critically ill child. Yet this predicament confronts physicians. It is not uncommon for a child to come to an emergency room in severe shock, with no visible or palpable veins, or for the only venous access to a child to be lost in an emergency [72].

In a 2002 interview with Larry Miller, Orlowski reported that many of his colleagues considered the use of IO catheters to be "barbaric, or overly aggressive. The IO route had become a lost skill." Despite this resistance, Orlowski continued to teach manual IO catheter placement and infusion to his residents and colleagues. Over the next two decades, Orlowski would contribute significantly to the IO literature. In 1989, he reported a study of 21 canine subjects demonstrating that all of the dogs had "fat and bone marrow emboli" in their lungs following femoral IO infusion of ACLS drugs, regardless of which drugs were used [73]. However, none of the animals developed any clinical symptoms of fat embolism syndrome, suggesting that the emboli remained clinically insignificant [73]. That same year, he reported on the similarity of common laboratory studies (e.g., electrolytes, hemoglobin, lactate, liver function tests) from IO marrow samples when compared to arterial or venous samples [74]. In 1990, he reported that the pharmacokinetics of six common ACLS drugs (epinephrine, sodium bicarbonate, calcium chloride, hydroxyethyl starch, 50% dextrose, and lidocaine) in a canine cardiac arrest model did not appear to differ significantly whether the drugs were administered through a 14-gauge distal femoral IO, 16-gauge forepaw peripheral IV, or 16-gauge femoral central venous catheter [75]. In this series of experiments, Orlowski compared each drug's magnitude of peak effect, drug level, and duration of action among both normovolemic and hypovolemic subjects [75]. Although IO infusion of sodium bicarbonate or hydroxyethyl starch was associated with increased time to peak level and increased duration of effect when compared to the other routes, the differences that he found were not statistically significant with any drug [75].

Meanwhile, other authors were studying the potential role of IO access for cardiac arrest resuscitation. In 1992, **William H. Spivey** (1954–1993) and colleagues at the Medical College of Pennsylvania (Philadelphia, Pennsylvania) reported that 0.1 mg/kg rapid IO infusions of epinephrine (but not 0.01 mg/kg aliquots) were able to increase blood pressure in a swine model of cardiac arrest [76]. Other studies by Spivey and colleagues included IO infusion of anti-epileptic medications [77], sodium bicarbonate for cardiopulmonary arrest [78], and crystalloids and blood

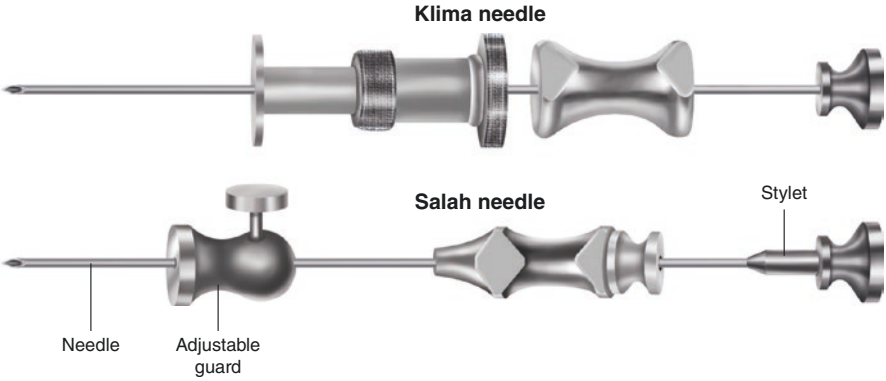

Fig. 1.16 Klima and Salah needles [83]

products using standard 13-gauge hypodermic needles [79]. Spivey would go on to serve as a scientific advisor to LifeQuest Medical (San Antonio, Texas) on the development of that company's Osteoport® device, before his sudden death on 20 February 1993.

Although many researchers and clinicians in the 1980s were still using standard hypodermic needles to access the intramedullary space, various specialized manually placed IO devices had been developed. The earliest IO devices were modeled on bone marrow biopsy needles and were generally developed by hematologists for use in bone marrow aspiration. Some of the earliest models included the Vim-Silverman needle with pronged bifid needle insert [80], the Favorite needle with a screwlike obturator [81], the Turkel needle [49, 52], and the grooved Reddy needle [82]. Despite a wide range of needles developed during the mid-twentieth century, the most popular for sternal IO biopsy appears to have been the Klima-Rosegger needle developed by **Rudolph Klima** (1896–1983) and **Hellfried Rosegger** (d. 1940) of the University of Vienna circa 1935 [83] and the Salah needle, both of which featured an adjustable guard to prevent overpenetration (Fig. 1.16).

In 1971, Iranian hematologist **Khosrow Jamshidi** (b. 1929) reported the development of a new bone marrow biopsy needle with a T-bar handle, tapered edge, and a cutting interior [84]. The Jamshidi™ needle (Fig. 1.17) was designed for iliac crest biopsies, featuring a much longer cannula than most previous devices used for sternal and tibial access. The Jamshidi needle design would inspire a new generation of iliac crest biopsy devices, including the Islam biopsy needle [86].

But needles developed for bone marrow biopsy are not necessarily well suited for IO infusion. The original reusable Jamshidi™ iliac crest biopsy needle (Fig. 1.18), for example, was quite long (e.g., 76–150 mm) with a tapered end designed to reduce crush artifact with marrow retrieval. These features also lengthened and narrowed the chamber through which fluids were infused, increasing resistance to flow. The modern Jamshidi™ needle typically used for IO infusion is disposable and much shorter than the reusable stainless steel model originally developed for iliac crest biopsy. The Illinois lancet tip modification, introduced in 1988 with the Monoject®

Fig. 1.17 Jamshidi™ needle for iliac crest biopsy. *(Image Courtesy of Becton, Dickson and Company. © 2023 Becton, Dickson and Company. All rights reserved.)* [85]

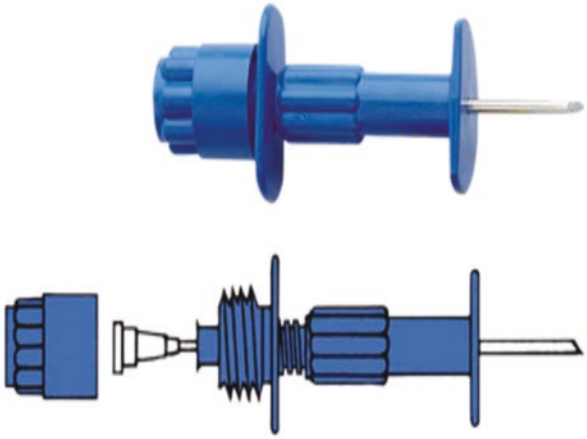

Fig. 1.18 Jamshidi™ modified Illinois disposable needle *(Image Courtesy of Becton, Dickson and Company. © 2023 Becton, Dickson and Company. All rights reserved.)* [87]

Illinois Needle (Sherwood Medical, St. Louis, Missouri), was later incorporated into the Jamshidi™ Illinois needle (Becton, Dickinson, and Company, Franklin Lakes, NJ).

With the resurgence of interest in manual IO devices, many new manual IO devices would become available for emergency care providers in the late 1980s and early 1990s. Cook Medical (Bloomington, Indiana) released the Cook intraosseous

needle in 1986, available with various features including a 45° trocar, 35° lancet, or pencil point tip. The Cook needle with Dieckmann™ modification (Cook Medical) included two opposed side ports positioned near the needle cannula's distal tip to ensure proper flow when the tip is obstructed by bony cortex. The Cook needle with Dieckmann™ modification is shown in Fig. 1.19.

The Sussmane-Raszynski needle (Cook Medical) included a brass hub and base plate, a stylet with a trocar bevel (45° angle), and a cannula shaft with a fine needle-screw design to prevent dislodgement of the needle cannula (Fig. 1.20). This catheter was developed by pediatric intensivists **Jeffrey B. Sussmane** (b. 1955) and **Andre Raszynski** (b. 1948) at the Miami Children's Hospital (Miami, Florida).

The Sur-Fast™ needle (Cook Critical Care) was patented in 1996, featuring an angled trocar tip and screw threading along the length of the cannula to facilitate advancement of the needle (Fig. 1.21) [90].

Fig. 1.19 Cook manual IO needle with Dieckmann™ modification *(Image courtesy of Cook Medical. © 2023 Cook Medical. All rights reserved.)* [88]

Fig. 1.20 Sussmane-Raszynski™ needle. *(Image courtesy of Cook Medical. © 2023 Cook Medical. All rights reserved.)* [89]

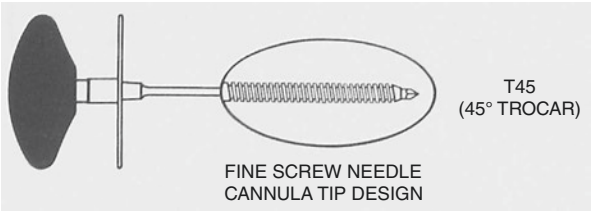

Fig. 1.21 Sur-Fast™ needle *(Image courtesy of Cook Medical. © 2023 Cook Medical. All rights reserved.)* [90]

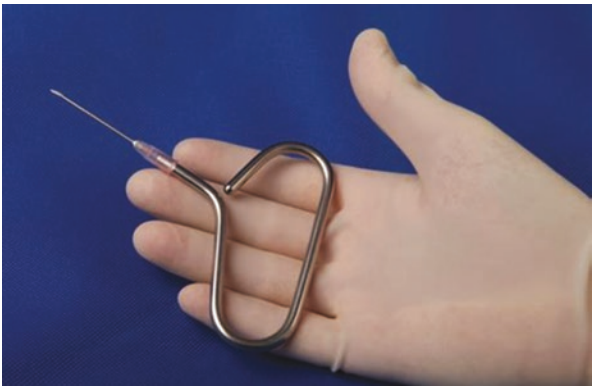

Fig. 1.22 The Near Needle Holder™ device. *(Image courtesy of Richard Near. © 2023 Near Manufacturing, Ltd. All rights reserved.)* [91]

The entire Cook Medical portfolio of manual IO catheters, with the exception of the Dieckmann™ catheter, was discontinued by late 2022.

Novel devices to assist with manual IO catheter insertion have also been developed, including the Near Needle Holder™ (Near Manufacturing, Camrose, Alberta, Canada) (Fig. 1.22), a reusable handle allowing a standard hollow steel infusion needle to be inserted in the intraosseous space [92]. It was developed as a safe, inexpensive option to facilitate IO infusion in developing countries and other limited-resource areas. It should be noted that the Near Needle Holder™ is not FDA approved in the United States.

Pediatric IO infusion at the proximal tibia experienced a renaissance in the late 1980s, but it would be many years before the denser tibia of adult subjects was commonly targeted for IO cannulation. Meanwhile, manufacturers and investigator-clinicians began to revisit the sternal IO insertion site during the 1990s. The FAST-1® (First Access for Shock and Trauma) intraosseous infusion system, originally introduced by Pyng Medical (Vancouver, Canada) in 1998, was the first new sternal IO catheter to appear on the market in decades (Fig. 1.23). Pyng Medical was founded in 1986 by **Michael W. Jacobs** and colleagues, and this company led the early development of adult IO catheters during the 1990s. In its earliest days, Pyng had considered licensing the Sternal Access Vascular Entry (SAVE) manual IO infusion device from the US Army and University of California, which featured a self-tapping screw and stabilization features to prevent over-advancement. Ultimately, they found that a novel approach was needed, leading to the development of the FAST-1® system.