**WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care**

**Worksheet author(s)**

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**Clinical question.**

In infants and children with cardiac arrest (P), does establishing intraosseous access (I) compared to establishing conventional (non-intraosseous) venous access (C) improve patient outcome (eg. ROSC, survival to hospital discharge (O)?

**Is this question addressing an intervention/therapy, prognosis or diagnosis?** Intervention/therapy

**State if this is a proposed new topic or revision of existing worksheet:** Revision to previous worksheet (Previous author: Allan de Caen)

**Conflict of interest specific to this question**

None.

**Search strategy (including electronic databases searched).**

- **MEDLINE (PubMed – 1966-2008)**
  - Infusions, Intraosseous (MeSH) OR Infusions, Intraosseous/instrumentation (MeSH)
  - Intraosseous AND Heart Arrest (MeSH) OR Cardiopulmonary Resuscitation (MeSH) OR cpr OR cardiac arrest OR cardiopulmonary arrest
    - Fluid Therapy (MeSH) OR fluid therapy
    - Shock (MeSH) OR Hypovolemia (MeSH) OR shock OR sepsis
    - Wounds and Injuries (MeSH) OR trauma
    - Drug Administration Routes (MeSH) OR drug administration OR drug

- **Embase (1988-2008)**
  - Intraosseous AND (shock OR injury OR trauma OR sepsis OR drug OR resuscitation OR cardiac arrest)

- **Cochrane database for systematic reviews**
  - Intraosseous (no hits)

- **AHA EndNote Master Library**
  - Intraosseous (128 hits)

References of pulled articles were also searched.

**State inclusion and exclusion criteria**

- Studies not in peer-reviewed journals (ie abstracts only) were excluded.
- Case reports reviewed in previous worksheet were not reviewed.
- Studies examining the use of marrow from intraosseous cannulation for blood sampling were excluded as they have been well reviewed in the previous worksheet.
- Given the rarity of complications, case reports discussing complications of intraosseous infusions were included for review.
- I have elected to include papers comparing different IO devices as speed of access is an important factor in the critically ill child. However, this may need to be a separate worksheet with the next ILCOR review.

**Number of articles/sources meeting criteria for further review:**

- 51 articles reviewed (including some references from previous worksheet (ILCOR 2005 W29 De Caen).
## Summary of evidence

### Evidence Supporting Clinical Question

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| | | | | | Banerjee, 1994 (E1,4)  
| | | | | | Brenner, 2008 (E1)  
| | | | | | Von Hoff, 2008 (E3)  
| | | | | | Wenzel, 1999 (E3)  
| | | | | | Fiallos, 1997 (E6)  
| | | | | | Andropoulos, 1990 (E3)  
| | | | | | Ben-Abraham, 2003 (E1)  
| | | | | | Shavit, 2009 (E2,5)  
| | | | | | | |
| Fair | | | | | Claudet, 2003 (E6)  
| | | | | | Fiorito, 2005 (E5)  
| | | | | | Horton, 2008 (E1,2)  
| | | | | | Brunette, 1988 (E1)  
| | | | | | Seigler, 1989 (E5)  
| | | | | | Ellemunter, 1999 (E5)  
| | | | | | Rosetti, 1985 (E5,6)  
| | | | | | Frascone, 2009 (E2,5)  
| | | | | | | |
| Poor | | | | | Glaeser, 1993 (E5)  
| | | | | | Gerritse, 2009 (E5)  
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**Level of evidence**

<table>
<thead>
<tr>
<th>A</th>
<th>Return of spontaneous circulation</th>
<th>C</th>
<th>Survival to hospital discharge</th>
<th>E</th>
<th>Other</th>
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<tbody>
<tr>
<td>B</td>
<td>Survival of event</td>
<td>D</td>
<td>Intact neurological survival</td>
<td>Italics = Animal</td>
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**Studies**

- E1 = Time to insertion
- E2 = Ease of use/satisfaction
- E3 = Fluid or medication delivery
- E4 = Shock correction
- E5 = Successful insertion
- E6 = Complication
### Evidence Neutral to Clinical question

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**Level of evidence**

- A = Return of spontaneous circulation
- C = Survival to hospital discharge
- E = Other
- B = Survival of event
- D = Intact neurological survival

**Studies**

- E1 = Time to insertion
- E2 = Ease of use/satisfaction
- E3 = Fluid or medication delivery
- E4 = Shock correction
- E5 = Successful insertion
- E6 = Complication

**Evidence Opposing Clinical Question**

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<td>Good</td>
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**Level of evidence**

- A = Return of spontaneous circulation
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- E = Other
- B = Survival of event
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**Studies**

- E1 = Time to insertion
- E2 = Ease of use/satisfaction
- E3 = Fluid or medication delivery
- E4 = Shock correction
- E5 = Successful insertion
- E6 = Complication

*Italics = Animal*
Introduction

Intraosseous (IO) cannulation has become an important tool for pediatric health care professionals to obtain vascular access in emergency or difficult venous access situations. In the acutely ill child, peripheral veins may become acutely collapsed and difficult to access whereas the vascular marrow space remains stable. After the release of the 2005 ILCOR guidelines and with development of new IO device technologies, IO cannulation has become an important technique in adult resuscitation as well. Unfortunately, there are no prospective randomized trials examining the use of IO cannulation versus traditional venous access techniques in children or adults with cardiac arrest. However, despite the paucity of level 1 evidence, there are a number of theoretical advantages of IO cannulation in the critically ill patient.

Rapid vascular access is an important component in the management of the critically ill or arresting patient. Animal studies suggest that a delay in resuscitative medications can decrease the likelihood of ROSC (Rittenberger et al. 2007 pgs 154-160; Angelos et al. 2008 pgs 101-110). A retrospective review of children in cardiac arrest less than 2 years of age presenting to a single center ED demonstrated that the average time for vascular access was 7.9 minutes. Percutaneous peripheral vein cannulation was only successful in 3/17 patients (18%) while 10/12 (83%) had an IO successfully placed with a mean time of 4.7 minutes (Brunette and Fischer 1988 pgs 577-579). Central line and surgical cutdowns had similar success rates as IO cannulation but required much longer times for successful vascular access (8.4 and 12.7 minutes respectively).

IO Insertion Success Rates

Pediatric residents were able to place an IO successfully in a task trainer 84% of the time, with no relation to year of training or when they had last completed a PALS course (White et al. 1998 pgs 1232-1235). Pfister and colleagues studied a national IO structured training program that was instituted in Switzerland for physicians, nurses and pre-hospital providers (Pfister et al. 2008 pgs 223-229). Participants in the course were able to achieve a 100% success rate in IO access vs. 74% in non-participants. Interestingly, success rate did not correlate with previous IO experience. Intraosseous infusions have been used successfully in pediatric trauma patients (Smith et al. 2005 pgs 1034-1038; discussion 1039), in pediatric transport (Fiorito et al. 2005 pgs 50-53), in the operating room (Joseph and Tobias 2008 pgs 469-473) and in term and preterm neonates in which umbilical catheterization has been unsuccessful (Ellemunter et al. 1999 pgs F74-75). In adults, Iserson and colleagues have demonstrated that cannulation in the distal tibia with a Jamshidi cannula was 100% successful in 22 adults in cardiac arrest (Iserson 1989 pgs 587-591).

Pre-hospital

Prehospital, paramedics were successful in establishing an IO in 16/17 acutely arresting pediatric patients, 13 on their first attempt (Seigler et al. 1989 pgs 173-177). Interestingly, successful bone marrow aspiration, a commonly used test to ensure correct placement, was only possible in 2 instances, despite successful fluid and medication administration. In a 5 year observational study of EMT-P providers, Glaeser reported an overall 76% success rate in 152 patients (the majority were < 10 years old) in arrest or in whom IV access was unsuccessful (Glaeser et al. 1993 pgs 1119-1124).

In one of the few prospective randomized studies on IO cannulation, the speed and reliability of IO cannulation was demonstrated. Banerjee (Banerjee et al. 1994 pgs 1511-1520) randomized 60 severely dehydrated children to a 2 hour-rehydration protocol utilizing a peripheral IV or an IO. There was no difference in effectiveness in improving clinical and laboratory signs of shock. However, in 10/30 (67%) of the IV group, vascular access was not obtained within 5 minutes and they were crossed over to receive an IO. 100% (40/40) of IO insertions were successful within 5 minutes. Vascular access was significantly faster in the IO group (67 seconds vs. 129 seconds) likely related to numerous peripheral IV attempts in the IV group. IO
cannulation can be performed successfully in a variety of clinical scenarios by both pre-hospital and hospital health care providers.

**Potential Sites for IO Access**

A number of different sites have been proposed for IO insertion. The proximal tibia, medial to the tibial tuberosity remains the most common. Care must be undertaken to place the needle slightly distal to the tuberosity to avoid entering the epiphysis (Boon et al. 2003 pgs 15-18). In this adult cadaver study, IO attempts >2cm distally from the tibial tuberosity were more difficult due to the density of the cortex. Historically, it was believed that only sites that had active marrow would be useful for fluid and medication administration. In addition to the proximal tibia, this included the distal tibia (medial malleolus), distal femur, and proximal humerus. However, active marrow may not be required, as demonstrated by adult cadaver studies using dye infused into the calcaneus and radial styloid, two bony sites with no active marrow (McCarthy et al. 2003 pgs 183-186; Clem and Tierney 2004 pgs 107-112). This suggests that any easily accessible bone could be used for IO infusion. In adults, the sternum has been used successfully for IO placement, especially with the development of the FAST system for sternal IO access (discussed below). Whatever site is used, bedside ultrasound may be an effective technique to confirm placement when it is in doubt (Stone et al. 2007 pgs 515-519).

**Medication Infusion through an IO**

For the patient in cardiac arrest, once IO access has been established, all resuscitative medications can be infused. Andropoulos compared central vs. IO infusion of a 10 mcg/kg epinephrine bolus in healthy lambs and in a hypoxic cardiac arrest model (Andropoulos et al. 1990 pgs 312-315). There was no difference in hemodynamic effect or epinephrine levels in either group. There was a delay in peak epinephrine levels after IO bolus (15 s vs. 1 min) though similar peak levels were eventually achieved. Spivey (Spivey et al. 1992 pgs 127-131) noted similar plasma epinephrine levels after IV vs. IO bolus in a swine VF model. Epinephrine infusions (at high doses – 0.5 to 5.0 mcg/kg/min) through an IO in a lamb model had similar hemodynamical and pharmacological effects as IV infusions (Sapien et al. 1992 pgs 179-183). Other resuscitation medications such as sodium bicarbonate, atropine, calcium chloride, 50% dextrose, vasopressin and lidocaine have been studied in various animal models demonstrating comparable peak effect of medications administered through an IO as through central venous access (Prete et al. 1987 pgs 101-104; Orlowski et al. 1990 pgs 112-117; Wenzel et al. 1999 pgs 1565-1569). These medications have all been given successfully to both children (Brunette and Fischer 1988 pgs 577-579; Seigler et al. 1989 pgs 173-177; Fiorito et al. 2005 pgs 50-53) and adults (Davidoff et al. 2005 pgs suppl 20-23; Gillum and Kovar 2005 pgs suppl 24-25; Cooper et al. 2007 pgs 314-316) with clinical effect in observational studies. There are numerous case reports describing the IO administration of various medications which have been recently reviewed by Buck (Buck et al. 2007 pgs 1679-1686). This includes various antibiotics, benzodiazepines, opioids (Von Hoff et al. 2008 pgs 31-38), and muscle relaxants. There are case reports of using IO insulin infusions for treatment of DKA (Alawi et al. 2008 pgs 110-112). IO infusions have also been used in an animal study to treat organophosphate poisonings (Eisenkraft et al. 2007 pgs 145-150) and hemorrhagic shock with rFVIIa (Wright et al. 2009 pgs 119-123). IO administration in this situation may be ideal as insertion is still possible with a high success rate even by providers wearing full protective gear (Ben-Abraham et al. 2003 pgs 1407-1410).

In addition to medications, resuscitation fluids can also be successfully administered through an IO. In animal models, using radionuclide tracers, IO fluids reached central circulation as rapidly as IV fluids (Cameron et al. 1989 pgs 123-127). In a pig model, Warren et al compared rates of fluid infusion in various IO sites versus IV (Warren et al. 1993 pgs 183-186). On average, flow through an 18g tibial IO was 30% slower than through a peripheral IV while flow through a humeral IO was comparable.

**IO Devices**
Different devices are being developed to improve time and success rate for IO access. Several manual devices are available and all have high success rates in bench testing and in observational trials (Brunette and Fischer 1988 pgs 577-579; Iserson 1989 pgs 587-591; Glaeser et al. 1993 pgs 1119-1124; Calkins et al. 2000 pgs 1068-1074; Boyd et al. 2003 pgs 330-333).

Three mechanical IO devices are now available. The bone injection gun (BIG) is a spring-loaded device to “shoot” the IO cannula into the bone. Pre-hospital providers in a task trainer study were slightly faster in placement than with a traditional manual IO device (Spriggs et al. 2000 pgs 1168) with a success rate of 71% in children (Gerritse et al. 2009 pgs 1739-1741). The FAST system is an adult device designed for IO access in the sternum. EMT-B students were able to deploy the device with a 93.1% success rate within 4 attempts (Miller et al. 2005 pgs 73-78). The EZ-IO utilizes a small battery-powered IO driver with a needle set and allows the operator to “drill” the needle into the bone. In observational clinical trials in adults and children, it has an 87 to 100% success rate (Davidoff et al. 2005 pgs suppl 20-23; Gillum and Kovar 2005 pgs suppl 24-25; Cooper et al. 2007 pgs 314-316; Frascone et al. 2007 pgs 164-171; Horton and Beamer 2008 pgs 347-350; Frascone et al. 2009 pgs 329-332; Ong et al. 2009 pgs 8-15). When compared to a manual IO device in a randomized trial, a mixed group of health care professionals were able to successfully insert a EZ-IO 97.8% of the time on first attempt vs. 79.5% with a manual device into a human cadaver model (Brenner et al. 2008 pgs 314-319). All participants were successful by the second attempt with the EZ-IO though 12.8% of participants in the manual group were unable to obtain an IO at all. In a randomized crossover trial, paramedic trainees had a higher one-attempt success rate with the EZ-IO (96.6%) then with the BIG (65.5%) (Shavit et al. 2009 pgs 1029-1033). In an adult study, the EZ-IO (placed in the humerus) had a significantly faster insertion time when compared to peripheral intravenous cannulation in a historical control (Paxton et al. 2009 pgs 606-611).

**Complications of IO insertion**

Complications of IO infusions classically reported have included osteomyelitis and compartment syndrome from needle displacement. In a review of 4,270 IO insertions from historical studies, Rosetti found 27 cases of osteomyelitis, an incidence of 0.6% (Rosetti et al. 1985 pgs 885-888). These cases were most common in patients with bacteremia or in which the IO was in place for a prolonged period of time. These concerns can be minimized by promptly replacing the IO with an IV once the patient is more stable. Concerns had been raised about fat embolism with IO infusions. Fiallos and colleagues, using an animal cardiac arrest model, demonstrated that there was no increased incidence of fat embolism in animals with an IO vs. those who received CPR alone (Fiallos et al. 1997 pgs 73-79). Recent case reports have reported gas embolism (Hillewig et al. 2007 pgs 149-153; Van Rijn et al. 2008 pgs 259-262), gangrene (Al-Ayed 2008 pgs 456-457), leg amputation secondary to compartment syndrome (Launay et al. 2003 pgs 788-790), tibial fracture (Bowley et al. 2003 pgs 786-787) and fracture mimic which could be misinterpreted as non-accidental injury (Harty and Kao 2002 pgs 188-190). As with any vascular device, care must be taken to prevent dislodgement or disconnection. No long term effects on tibial growth following an IO insertion have been reported (Claudet et al. 2003 pgs 397-401). IO insertion should not be attempted in a child with osteogenesis imperfecta. It is contraindicated in a limb with a fracture, osteomyelitis, or an overlying infection.

**Summary**

In summary, although there is no Level 1 evidence for the use of intraosseous cannulation as a resuscitation technique in children with cardiac arrest, there is ample evidence that they can be used safely in patients from the newly born (in which UVC access has failed) to adults. In addition to the traditional proximal tibial approach, there are a number of different sites that are effective. A large variety of medications and fluids have been successfully infused through these devices with minimal complications.
Acknowledgements:
None.

Citation List


A case report of amputation following IO insertion and infiltration without compartment syndrome.

Evidence: Opposing
Level of Evidence: 4
Quality of Evidence: Poor
Outcome: Complication
Pediatric study


A case report discussing IO use of an insulin infusion for DKA.

Evidence: Supporting
Level of Evidence: 5
Quality of Evidence: Fair
Outcome: Medication efficacy
Children


15 lambs received 10 mcg/kg epinephrine centrally, through an IO or 10 cc/kg of saline only. BP and epinephrine levels were measured. This was repeated after the animals suffered a hypoxic cardiac arrest with CPR. There was no difference in hemodynamic effect or epinephrine levels after IO vs. CVL. In the arrest model, the IO injection took longer to achieve peak levels (15s vs. 1 min) but the eventual peak level was similar.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Good
Outcome: Medication delivery
Animal study


An animal study (rats) in which a KCl-mediated cardiac arrest model was used. Animals were randomized to 3 groups (1) CPR and epi/placebo after 2 minutes of arrest, (2) CPR and epi/placebo after 4 minutes of arrest, or (3) CPR after 6 minutes of arrest with epi given only if ROSC not obtained by 15 minutes. All animals in group 1 had ROSC. In group 2, 14/29 of placebo and 14/16 of epi animals had ROSC (significant). In group 3, the no-epi group had ROSC in 10/31 of animals compared to 17/21 in animals that received epi (significant). In group 3, there was a higher amount of post-ROSC myocardial depression in the epinephrine group. Early epi appears to have a benefit in obtaining ROSC in this animal model compared to just CPR alone.

Not included in worksheet evidence summary as for reference only.


This is a prospective pediatric trial in which patients with severe dehydration were placed alternatively into a IV or IO group. Both groups received resuscitation fluids for 2 hours and then switched to oral rehydration when tolerated. 60 patients were enrolled (30 in each group). An IV was possible in 66% of the IV patient group within the first 5 minutes, 100% of IO cannulations were successful (30 in the IO group and 10 in the IV group that IV access was unsuccessful). Time for IV was 129 seconds vs. 67 seconds for IO. Patients in which IV access was not possible tended to have more severe shock on clinical exam.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Good
Outcome: Time to insertion, correction of shock


This is an observational study of ED physicians with crossover randomized to placing BIGs with and without protective gear on. Success rates were lower with the gear on, however, IO access was achieved 100% of the time within two attempts.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Good
Outcome: Time to insertion
Adult task trainer study


A cadaver study demonstrating anatomical positions of IO catheters inserted using different surface landmarks in newborns. Catheters placed at the inferior limit of the tibial tuberosity entered the epiphyseal growth plate 19 out of 28 times (68%). If placed 1cm below the inferior limit of the tibial tuberosity, no catheter entered the growth plate. If insertion was attempted 2cm below the inferior border to the tibial tuberosity, placement became difficult due to the thickness of the bone. It is recommended that insertion be performed 1cm distal to the tibial tuberosity and direct the needle in a posterior and inferior direction.

Evidence: Supporting
Level of Evidence: 5
Quality of Evidence: Fair
Outcome: Successful insertion
Cadaver study


A case report detailing a tibial fracture thought to have occurred during IO insertion in a 2 year old child that had fallen from a 3rd story balcony. A bone injection gun was used during initial resuscitation without success and two further manual attempts were performed in the same site. No clinical signs of fracture were apparent prior to the IO attempt and all other injuries were to the torso, upper extremities and head, suggesting a head-first impact. Tibial fracture was detected on skeletal survey.

Evidence: Opposing
Level of Evidence: 5
Quality of Evidence: Poor
Outcome: Complication
Pediatric human study


This is an observational study on a animal task-trainer model in which paramedic trainees were randomized (cross-over) to place IOs with two Cook manual IO devices. The Cook Osteo-site needle had a 16/16 success rate (100%). Time to insertion was 48.9 seconds vs 96.6 for the other device.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Fair
Outcome: Ease of insertion, time to insertion
Animal study (task-trainer)


This is a prospective randomized study in which 84 participants attended a 45 minute lecture and 15 minute demonstration on IO insertion. They were then randomized to a manual IO system or the EZ-IO for IO insertion in a cadaver lab. Approximately 85% of participants had not put an IO in previously. 97.8% of participants were successful on first attempt in inserting an EZ-IO vs. 79.5% of manual users. The devices were inserted and 10cc of saline flushed within 33 seconds. All EZ-IO users were eventually successful, 12.8% of the manual group were unsuccessful after 3 attempts. The EZ-IO appears to be a simple to use and a reliable device for IO placement.

Evidence: Supporting
Level of Evidence: 5
Quality of Evidence: Good
Outcome: Time to insertion
Cadaver study


A retrospective examination of charts of patients presenting to a single center ED with cardiac arrest. There were 33 cases, mean time to establishing IV access was 7.9 (+/- 4.2) minutes. 10/12 IOs were successful (83%) with a mean time of 4.7 minutes (vs. 3.0 min for PIV with 3/17 successful (18%)). CVL and surgical cutdown had lower success rates and much longer times (8.36 and 12.7 minutes).

Evidence: Supporting
Level of Evidence: 4
Quality of Evidence: Fair
Outcome: Time to insertion
Pediatric study


A concise review of IO use in CPR. A list of medications that have been given successfully in an intraosseous, either clinically or in a lab setting is provided. No new clinical data is presented.

This is an observational study in which Special Operations medical care providers demonstrated 4 different IO devices on human cadavers. There were no differences in time to insertion or ease of operation of any of the devices. No clinical outcomes are discussed.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Poor
Outcome: Ease of insertion, time to insertion
Adult cadaver study


This is an animal study (adult dogs) in which nuclear medicine flow studies were performed after a crystalloid bolus. One group received a bolus through a IO in the proximal tibia, the other through an IV. This was repeated after a 35% volume loss. There was no difference in time to central circulation between the groups.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Fair
Outcome: Fluid delivery
Animal study


This is a prospective cohort study analyzing X-rays of children who have had an IO placed in the anterior tibia. X-rays were reviewed by a blinded radiologist and compared to either same-side controls (if only one puncture was done) or to standardized measurement charts. Follow-up occurred after 29.2 months (mean).

78 children received an IO, 64 in one tibia, 14 in two. There were 20 subcutaneous diffusions, 1 osteomyelitis and 1 articular puncture. 23 children were followed up (42 children died, 10 lost to follow-up, 1 refused). Duration of perfusion was 5 hours in the study population (2.5h in the initial population) with a mean infused volume of 225ml (150-1100mls). 18 received artificial colloids, 3 received hypertonic NaHCO₃ and 2 received blood.
No differences were noted on x-rays after IO placement (including the child with an accidental articular puncture). IO infusion did not seem to effect tibial growth after 2.5 years of follow-up.

Evidence: Supporting  
Level of Evidence: 4  
Quality of Evidence: Fair  
Outcome: Complication/tibial growth  
Pediatric human study


A cadaver study in which IO needles were placed in the calcaneus and dye infused. The calcaneus may represent another potential IO site.

Evidence: Supportive  
Level of Evidence: 5  
Quality of Evidence: Fair  
Outcome: Successful insertion  
Cadaver study


This is an observational study examining the use of the EZ-IO device during forward operations in Afghanistan by the UK Joint Forces Medical Group. The device was inserted in 26 patients with 32 IO needles, 10 of which were children (defined as 2-10 years). 31/32 (97%) of needle insertions were effective and a variety of medications were infused (including cardiac arrest medications in 1 child and 2 adults). No complications other than pain were noted.

Evidence: Supporting  
Level of Evidence: 5  
Quality of Evidence: Fair  
Outcome: Successful insertion, medication/fluid delivery  
Adult and children


This is a prospective observational study on the use of a mechanical IO device (EZ-IO) in the pre-hospital environment. Information on the patients is incomplete; their ages are
not reported. At least 22 patients were in cardiac arrest and had ROSC. The device was successfully placed in 242 of 250 (97%) of patients. All were placed within 20 seconds, 94% had one placed within 10 seconds. A visual analog scale was used to measure pain, insertion was rated at 3.8 and infusion of fluid at 5.0. The most common “complication” was a low flow rate, there were no cases of osteomyelitis, embolism, fracture or extravasation. The manufacturer aided in collection of the data and provided devices.

**Evidence:** Supporting  
**Level of Evidence:** 5  
**Quality of Evidence:** Poor  
**Outcome:** Time to insertion  
Adult study


This is an animal study examining the pharmacokinetics of midazolam and anti-epileptic effect when given IV vs IO vs IM. IO midazolam had a similar pharmacokinetic profile (including time to $C_{\text{MAX}}$) as IV midazolam and was as effective in ceasing organophosphate-induced seizures.

**Evidence:** Supporting  
**Level of Evidence:** 5  
**Quality of Evidence:** Fair  
**Outcome:** Medication delivery  
Animal study


A series of neonates in which 30 IOs (Cook) were placed in 27 newborns (20 preterm) within 5 hours of birth in which “routine means of access had been exhausted”. Various resuscitation drugs and fluids were infused. 3 patients had dislocation requiring a second needle. There were 2 cases of extravasation, no other complications and success was 100% and took less than 2 minutes. No adverse effects on limb growth were noted in the survivors (15) in long-term followup.

**Evidence:** Supportive  
**Level of Evidence:** 4  
**Quality of Evidence:** Fair  
**Outcome:** Successful insertion

An animal study (piglets) using a hypoxic cardiac arrest model who then received no IO, IO with no infusion, IO with resuscitation drugs or no treatment at all. Only the sham group did not demonstrate fat embolism on autopsy and there were no differences between the groups. IO use does not increase risk of fat embolism vs. CPR alone.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Good
Outcome: Complications
Animal study


This is a retrospective review of a pediatric critical care transport team (resident-led) and their IO use. In 27 months and 1792 transports, 47 children had an IO placed (58 total catheters placed). 26% of these patients were in cardiopulmonary arrest. Ages ranged from 3 weeks to 14 years. 78% of IOs were placed on IO attempts, only one child could not have an IO placed. 5% were placed in the femur, the rest in the tibia. 7 patients had self-limited local swelling and infiltration. One patient not in the study period did develop severe inotrope extravasation (the patient subsequently died). The IO was used for fluids, inotropes, sedative medications, bicarb, anticonvulsants, insulin and antibiotics.

Evidence: Supporting
Level of Evidence: 4
Quality of Evidence: Fair
Outcome: Successful insertion
Children


An observational trial of the EZ-IO for EMS providers. 19 patients had an EZ-IO placed with 18/19 having successful insertion. There were 5 complications, 2 infiltration, 2 "slow flow rate" and 1 needle dislodgement during transport. There is scant detail presented on the patient's clinical characteristics though 4 were pronounced dead on arrival and presumably were in arrest during transport.

Evidence: Supporting
Level of Evidence: 4
Quality of Evidence: Fair
Outcome: Successful insertion
Pediatric study

This was a prospective observational study with two IO devices, the EZ-IO and the FAST1 in a prehospital environment (adults only). The FAST had 64/89 (72%) vs. 78/89 (87%) successful insertions as compared to the EZ-IO. Previous use of the device had no effect on insertion success. Time to insertion was self-reported after estimates by prehospital personnel. The trials were consecutive and there may have been a learning effect with the EZ-IO. There were 9 pediatric patients that received an IO during the EZ-IO field trial, they were not included in the study but success rate was 9/9.

**Evidence:** Supporting  
**Level of Evidence:** 5  
**Quality of Evidence:** Poor  
**Outcome:** Successful insertion  
**Adult study**


An observational study in which 40 pre-hospital patients had an IO attempt with a BIG including 14 children. A success rate/patient of 73% was obtained.

**Evidence:** Supportive  
**Level of Evidence:** 4  
**Quality of Evidence:** Poor  
**Outcome:** Successful insertion  
**Pediatrics**


This is a prospective observational trial of a EMS system in Texas that received a 4 hour training session on the use of the EZ-IO. IO use was limited to critically ill adults in which a peripheral IV could not be obtained in 2 attempts or 90 seconds or immediately in patients with cardiopulmonary arrest or hypotensive hypovolemic shock. Over 9 months, 125 patients had an IO placed of which 82% were in cardiac arrest. Placement was successful 94% of the time (118/125) within 5 minutes of arrival of the team. There was one catheter dislodgement, no other complications and a variety of cardiac medications were infused.

**Evidence:** Supportive  
**Level of Evidence:** 5  
**Quality of Evidence:** Poor
Outcome: Successful insertion
Adult study


This is a prospective pre-hospital study in which EMT-P providers placed proximal tibial IOs (Jamshidi) in arrest patients and other patients after medical order. 1 PIV was allowed (<1min) in patients under 3, 2 attempts in those over 3. 152 patients (165 attempts) were enrolled over the 5 year study period (138 were <10 years and 109 were < 1 year). 76% had successful placement (70% per attempt) which was higher in younger children (85% in 1-2 yr old). Placement occurred in < 1min, at least for the first year of the study when it was noted. 12% developed infiltration with no sequela, one patient had an IO in the patella. All resuscitation medications were used.

Evidence: Supportive
Level of Evidence: 4
Quality of Evidence: Poor
Outcome: Successful insertion


This is a case report detailing two infants who had skeletal surveys done due to suspicion of non-accidental injury. Cortical irregularities were noted which initially were thought to be fractures but were likely secondary to recent IO placements during resuscitation.

Evidence: Neutral
Level of Evidence: 4
Quality of Evidence: Fair
Outcome: Potential complication/confounder
Pediatric human study


This is a case report of a 4 month old who died from SIDS. On autopsy and post-mortem CT, small amounts of venous intravascular gas was noted. This was thought to have occurred through the IO needle during the resuscitation, possibly during a disconnect of the needle. It is unclear if similar results could have occurred with an intravenous catheter. The gas was not felt to be significant enough to lead to death of the child.

Evidence: Opposing
Level of Evidence: 4
Quality of Evidence: Poor
**Outcome: Complication**

**Pediatric study (post-mortem)**


This is a prospective observational study of the EZ-IO device in pediatric patients. All participants (pre-hospital, ED, ICU) received a training session after entering the study. 95 patients were eligible (5 days to 17 years; median 2y). Successful insertion occurred in 89/95 (93.7%), this was within 10 seconds (estimated time) in 80.2%. There were 6 failures of insertion and 4 complications (extravasation, dislodgement, mechanical failure x2). 35.8% of patients received “cardiac agents”.

Evidence: Supporting
Level of Evidence: 4
Quality of Evidence: Fair
Outcome: Ease of insertion, time to insertion
Children


A single center, single author largely prospective study in which a Jamshidi IO was placed in adult cardiac arrest patients in whom peripheral IV access was unavailable or not functioning. 22 patients were entered in the study, 100% success was reported in distal tibial IOs.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Poor
Outcome: Successful insertion
Adult study


A case report reporting the use of an IO for the delivery of anesthetic drugs in a cyanotic congenital heart patient with difficult venous access. Fluids, ampicillin, atropine and propofol were given successfully with no complications noted.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Poor
Outcome: Ease of insertion

This is a case report of a 7-month old infant presenting in hypovolemic shock who was initially fluid resuscitated through an IO at a referring hospital and transferred to a pediatric hospital. He subsequently developed a compartment syndrome and popliteal artery thrombosis which, despite fasciotomies, thrombectomies and numerous debridements, resulted in a below knee amputation. It was thought to be secondary to needle displacement during transport.

Evidence: Opposing
Level of Evidence: 5
Quality of Evidence: Poor
Outcome: Complication
Pediatric human study


This is a adult cadaver study using IO infusions of methyl green dye that suggests the calcaneus and the radial styloid, bones without a medullary cavity, could be used as potential IO sites. This suggests that any accessible bone may be useable for an IO site.

Evidence: Supporting
Level of Evidence: 5
Quality of Evidence: Poor
Outcome: Successful insertion
Cadaver study


This is a prospective educational trial studying the use of the FAST-1 sternal IO device by EMT-B students. The students were successful at inserting the device on first pass 55% of the time and overall were successful 93.1% of the time within 4 attempts. All students were able to deploy it successfully on first attempt in a task trainer supplied by the manufacturer. Median time to placement was 50 seconds.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Poor
Outcome: Time to insertion
Adult task trainer study

*A non-randomized observational study in which critically ill adult patients in a single-center ED received a tibial +/- humeral IO if PIV access could not be obtained in <90 seconds. Rates of successful placement, flow rates, adverse events and operator satisfaction were recorded. 24 patients were recruited with 24 tibial and 11 humeral injections. 34/35 were successful on first attempt, 100% by second attempt. There were no complications. All insertions were within 20 seconds. Flow rates were similar between sites, though faster with a pressure bag.*

**Evidence:** Supporting  
**Level of Evidence:** 5  
**Quality of Evidence:** Fair  
**Outcome:** Site selection  
**Adult study**


*This is an animal study (dogs) comparing PIV, central IV and IO administration of medications and either drug level or clinical effect (BP, ETCO₂, etc.) The IO route was comparable for BP effect of epinephrine, calcium levels with calcium chloride and blood glucose with D50. IO sodium bicarbonate was slower to reach peak effect but had a longer duration. Infusion of IO 6% hydroxyethyl starch also took longer to reach peak but had a larger magnitude of change. Lidocaine IO took longer to reach peak but had similar magnitude of peak drug level and duration of measured drug level as centrally infused lidocaine. PIV infusion of both D50 and lidocaine had a lower peak effect than IO infusion. IO infusions of key resuscitation medications were similar to intravenous infusions.*

**Evidence:** Supportive  
**Level of Evidence:** 5  
**Quality of Evidence:** Fair  
**Outcome:** Medication delivery  
**Animal study**


*A prospective cohort study in adult patients comparing proximal humerus cannulation with PIV or CVL placement. In phase 1, speed and complications "standard therapy" (PIV or CVL insertion) were measured. Mean time to good flow was 3.6 minutes with*
PIV (57 pts) and 15.6 minutes in 5 patients who had a CVL placed (4/5 done after failure to obtain PIV, one was primary venous access attempt). 1.5 attempts were required for PIV placement. In phase 2, consecutive patients had an EZ-IO placed if all first vascular access attempts (in patients without a CVL or 2 good PIVs). 29 patients had 30 IOs placed (one patient had 2 separate resuscitations needing one each time), mean time to flow was 1.5 minutes (significantly faster than PIV). No major complications noted. There were 2 failed attempts. 11 catheters dislodged (median time of dislodgement was 6.9h). Most dislodgements (10/11) occurred with the shorter EZ-IO needle.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Fair
Outcome: Time to insertion, successful insertion
Adult study


This is a Swiss study examining the effect of a national IO insertion training program on successful insertion rates. The educational program consisted of a 45 minute workshop including time to practice with a task trainer. Over 600 people took the course. There were 49 IO cannulas placed in the 3 year study period, 29 were in children < 6 years old. 24/35 (68%) of cannulations were for resuscitation purposes. Attendees were successful 100% of the time (within 3 punctures) vs. 77% of non-attendees (NS). Previous IO experience did not correlate with success. This simple program appeared successful though the study was under-powered to see a statistical difference.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Fair
Outcome: Successful insertion
Educational study


An animal study (adult pigtail macaques) in which anaesthetized animals received atropine by IV, IO (left proximal tibia) or ETT. Atropine levels and HR were analyzed. Time to peak concentration was significantly shorter with IV than with IO (1.37 min vs. 3.87 min) and ETT (9.62 min). Mean plasma concentration was higher in the IV route vs. IO only at 1.25 minutes but then higher in the IO route for up to 30 minutes (NS). There was no correlation b/w atropine concentration and HR though a computer model
suggests that the lower IO/ETT levels of atropine may be enough for adequate tissue levels for clinical effect.

Evidence: Supportive  
Level of Evidence: 5  
Quality of Evidence: Fair  
Outcome: Medication delivery  
Animal study


This is a retrospective analysis of a number of different animal (swine) models of VF cardiac arrest. Time to CPR, first shock and first drug were analyzed using logistic curves to determine relationship with ROSC. Time to first medication was predictive of ROSC.

Not included in worksheet evidence summary as for reference only.


This is a review of historical papers on IO insertion (reporting on over 4000 reported cases). Osteomyelitis was reported in only 0.6% of insertions.

Evidence: Supportive  
Level of Evidence: 4  
Quality of Evidence: Fair  
Outcome: Successful insertion, complications


An animal study (using a healthy newborn lamb model) which measured effect of IV and IO epinephrine infusions. Epinephrine was infused at high doses (0.5-5.0 mcg/kg/min) and pharmacodynamic and pharmacokinetic studies were performed. The threshold for effect on BP was slightly lower in the IV route vs. IO but all other responses were similar. In this model, IO epinephrine has a similar pharmacological effect as IV.

Evidence: Supporting  
Level of Evidence: 5  
Quality of Evidence: Poor  
Outcome: Medication effect  
Animal study

*An observational study examining a pilot project in which pre-hospital providers were instructed in the use of Jamishidi IO needles when IV attempts were prolonged. Paramedics were successful in 16/17 patients after 22 attempts (13 successful first-attempts). Bone marrow aspiration was only possible in 2 patients.*

**Evidence:** Supportive  
**Level of Evidence:** 4  
**Quality of Evidence:** Fair  
**Outcome:** Successful insertion


*This is a randomized crossover study in which 29 EMTs undergoing initial paramedic training were randomized to place a BIG or EZ-IO in a turkey leg model (meat stripped off). Each participant watched videos on each device and a demonstration on their use. After placing the device, infusion of coloured fluid was videotaped and rated by blinded observers. 28/29 had a successful first time attempt with the EZ-IO vs. 19/29 with the BIG (p=0.016) and it was rated as easier to use and the device of choice.*

**Evidence:** Supportive  
**Level of Evidence:** 5  
**Quality of Evidence:** Good  
**Outcome:** Successful insertion, ease of use


*This is a retrospective study analyzing the use of IOs in pediatric trauma patients throughout England and Wales. A total of 23,489 trauma cases were pulled from their database (between 1988 and 2003). 129 patients (0.55%) had an IO placed. These patients tended to be younger (media 3 years vs. 9 years) and were more severely injured (based on increased trauma scores and mortality (4% vs. 64%). There were relatively fewer IOs placed in pediatric vs. non-pediatric hospitals (14% vs. 8%). The authors comment that is likely due to better intravenous skills at pediatric centers. Success rates and complications are not discussed.*

**Evidence:** Neutral
Level of Evidence: 5
Quality of Evidence: Poor
Outcome: Successful insertion
Pediatric human study


This is an animal study (pigs) using a VF-model. Animals received 10 mcg/kg or 100 mcg/kg of epi through an IO at 10 and 20 minutes post-arrest. Both doses were rapidly absorbed and gave similar values to IV epinephrine done using a similar model in a previous study (Schoffstall, et al 1990). The authors comment that there was no change in BP with the lower dose of epi, but the clinical efficacy of the higher dose has been already studied and rejected.

Evidence: Supporting
Level of Evidence: 5
Quality of Evidence: Fair
Outcome: Medication delivery
Animal study


An educational cross over study in which pre-hospital providers placed IOs with either a Jamshidi or BIG. Placement time was slightly faster in the BIG group with similar ease of use measurements.

Evidence: Supportive
Level of Evidence: 5
Quality of Evidence: Fair
Outcome: Ease of insertion, time to insertion
Adult task trainer study


Ultrasound was performed on 16 IO (Jamshidi) catheters placed either in correct position (as judged by adequate saline flow) or incorrect position and then examined by a blinded radiologist. Doppler flow was 100% accurate in determining correct position. Interestingly, 75% of incorrectly placed catheters had free flow of saline into the drip chamber. Bedside ultrasound may have a role determining position of an IO catheter if it is in doubt. It is unclear if this is extractable to live pediatric patients.
Evidence: Neutral  
Level of Evidence: 5  
Quality of Evidence: Fair  
Outcome: Successful insertion  
Adult (post-mortem)


This is a case report documenting a cerebral arterial air embolism in a 7-month old baby (ex-prem, omphalocele) who presented to ED apneic and pulseless after an apparent aspiration event. No other intravenous access was obtained and air was documented on post-mortem CT. The child had a PFO on autopsy though no other clear cause of death could be appreciated.

Evidence: Opposing  
Level of Evidence: 4  
Quality of Evidence: Poor  
Outcome: Complication


This is a prospective randomized crossover study in which adults with cancer received implantable IO catheters in the iliac crest and received morphine boluses by IO and IV. Morphine levels were drawn and pharmacokinetic studies were performed. No differences were noted in morphine levels between IO vs. IV.

Evidence: Supporting  
Level of Evidence: 5  
Quality of Evidence: Good  
Outcome: Medication delivery  
Adult study


This is a randomized animal (pigs) study examining flow rates of crystalloid through peripheral IV vs. various IO sites. IV allowed faster flow rates followed by humerus, femur, malleolus and tibial. Tibial flow was (on average) 35% that of PIV flow. Similar changes were noted in hypovolemic animals though flows were reduced by roughly 30% at all sites. With a pressure bag at 300 mm Hg, humeral IO and peripheral IV flow were similar.
**Evidence: Supportive**
**Level of Evidence: 5**
**Quality of Evidence: Fair**
**Outcome: Fluid delivery**
**Animal study**


*This is an animal study (piglets) comparing the effects of IV vs. IO vasopressin on a VF model. All piglets were successfully resuscitated, there were no differences in levels of vasopressin between the 2 groups. The IO piglets had a significantly higher MAP, MPAP which may represent a depot effect of VP in bone marrow. In this animal model, IO VP resulted in similar doses and clinical efficacy in treating VF.*

**Evidence: Supporting**
**Level of Evidence: 5**
**Quality of Evidence: Good**
**Outcome: Medication effect**
**Animal study**


*This is a cohort study of pediatric residents demonstrating various resuscitation skills on task trainers. 84% (38/45) were able to successfully place an IO line. The median time to being able to use the IO was 60 seconds (slower than in other studies).*

**Evidence: Supporting**
**Level of Evidence: 5**
**Quality of Evidence: Fair**
**Outcome: Time to insertion**


*A case report detailing the use of FVIIa use in an animal model through an IO. Blood levels of FVIIa infusion were similar with IO and CVL infusions.*

**Evidence: Supportive**
**Level of Evidence: 5**
**Quality of Evidence: Fair**
**Outcome: Medication delivery**
**Animal study**