In the first of a two-part series on intravenous regional anesthesia (IVRA), the author reviews the history and development of the Bier block technique. He discusses the various intravenous devices and their placement, and investigates the use of tourniquets, as well as the site and mode of action of IVRA.

In the wave of enthusiasm and experimentation which followed Koeller's introduction of cocaine as a local anesthetic agent in 1884, a number of regional nerve block techniques were advanced. Corning reported experiments with subcutaneous cocaine while Conway advocated the injection of 4% cocaine directly into fracture sites. Perhaps the first record of cutaneous analgesia as a result of chemicals injected intravascularly is that of Alms, who in 1886 demonstrated the loss of sensation along the course of an artery into which a cocaine solution had been instilled. Interestingly, no mention was made of whether intravenous injection was attempted.

The duration of action of cocaine was brief and numerous reports appeared describing “poisoning” or shock following the injudicious use of the drug. In 1892, Schleich, hoping to decrease the incidence of toxic reactions, introduced the massive infiltration of dilute cocaine solutions for literally all types of surgical procedures. Similarly, the use of the Esmarch bandage as a type of vascular tourniquet became widely used to prolong the duration of cocaine and to lessen its systemic toxic effects. It was not until 1901 however, that Braun suggested the addition of dilute epinephrine to infiltration solutions in order to slow circulatory uptake of the drug.

By the late 1890s, Halstead and Crile had reported their techniques of regional anesthesia for the upper extremity. Their approach apparently was not popular as it required the surgical exposure of the brachial plexus and direct injection of cocaine into the nerve roots.

The Bier block

By the time August Bier introduced his now famous venous anesthesia in 1908, Einhorn had synthesized and Braun had popularized a new, less toxic chemical local anesthetic agent—procaine. It comes as no surprise to learn that Bier's work was a direct outgrowth of his interest in "cocainization" of nerves and use of the tourniquet to decrease blood loss during extremity surgery. He was so excited by the success of his new technique that he published his work in no less than five separate journals and was able to report on over 100 cases without a single misadventure.

A number of anecdotal reports followed Bier's papers but added little new information other
than expanding the list of surgical operations for which intravenous regional anesthesia (IVRA) had been shown to be successful. In 1911, Hirschel and Kulenkampff introduced their percutaneous auxiliary and supraclavicular brachial plexus blocks, respectively. The apparent popularity of these techniques and the development of safer general anesthetic agents overshadowed Bier's intravenous block. With only a few exceptions, it did not receive further attention in the professional literature for more than half a century.

As the popularity of regional conduction anesthesia increased, the complexity, and hence the duration of surgical procedures, required the development of new local anesthetic agents of longer action and lower systemic toxicity. From this demand came Lofgren's development and introduction of lidocaine hydrochloride in 1946, the first of a series of long-acting amide local anesthetic agents.

In 1963, Holmes reintroduced IVRA and included several modifications based on the newer technology of intravenous therapy and pneumatic tourniquets. In addition, he suggested the use of lidocaine HCl, an idea which is still very popular today.

Following Holmes' paper, a plethora of research articles and additional anecdotal accounts glutted the surgical and anesthesia literature. Most have praised the value of IVRA while others have warned of its potential shortcomings or considered it frankly dangerous. In 1965, an editorial in the Journal of the American Medical Association openly condemned the technique.

At least two major symposia have explored the state of the art in IVRA. Interestingly, the findings of the first symposium in 1969, which were to have been published as a text, were clouded by the U.S. Federal Drug Administration's denial to approve lidocaine HCl as an intravenous anesthetic. These important papers were subsequently published in Acta Anesthesiologica Scandinavica—Supplementum XXXVI (1969). Reports of the second conference held in 1978, sponsored by the American Society of Regional Anesthesia, appear in their official publication Regional Anesthesia. (Volume #4 Number 1).

An interesting historical aside, it was not until 1970, that Colbern suggested the now popular eponymous name Bier Block for the technique of IVRA.

Since its inception, and more particularly, its reintroduction, considerable controversy has surrounded several aspects of the IVRA technique. These include conflicting opinions about anatomic placement of injection sites, exsanguination of the extremity, and use of various tourniquet devices. Each of these will be discussed in this article, as well as the role of premedication. A review of the literature regarding the pharmacokinetics of local anesthetics in IVRA will be included in Part II (to be featured in the October AANA Journal).

Premedication for the IVRA technique

The choice of preanesthetic medication for patients who will receive IVRA does not differ significantly from that chosen for any patient receiving other forms of regional anesthesia. Although personal preferences may vary widely, the goal of any premedication regimen should consider the following.

**Analgesia for the patient in pain preoperatively:** Narcotics are presently the agents of choice, however, the recently introduced agonist-antagonist analgesic combinations may find an increasing role in the near future. A number of these drugs are available, each with its distinctive advantages as well as disadvantages. One should not consider the technique of IVRA (placement of an intravenous cannula and tourniquet) as indication alone for preanesthetic analgesics.

**Protection from harmful reflexes:** Vagus nerve-induced bradycardia, the so-called vaso-vagal response, is clearly not desirable. The clinical incidence of this event would seem too infrequent to warrant the routine use of vagolytic doses of the parasympatholytic drugs such as atropine sulfate or glycopyrrolate to patients receiving IVRA.

**Sedation/tranquilization:** Egbert has suggested that an informative preoperative visit by the anesthetist who will provide the anesthesia care may significantly reduce the need for preoperative sedative medications. Such visits are highly recommended, even when minor surgery is planned.

Occasionally, the anesthetist will encounter an extraordinarily apprehensive patient who is not sufficiently calmed by the preoperative visit alone. The patient's desire to be "asleep" may in itself cause him to resist conduction anesthesia techniques, thus certain considerations should be made. Sedative-hypnotics or tranquilizers may be used to decrease the emotional reactions some patients may experience when confronted with anesthesia and surgery.

In addition to their psychotropic effects, a number of these agents have been shown to protect the central nervous system from the higher blood levels of local anesthetic agents encountered.
with large volume regional conduction anesthesia techniques.

Some authors advocate parenteral barbiturates (pentobarbital) for prophylaxis against local anesthetic-induced seizures. It should be appreciated, however, that approximately 70 mg/kg of this medication must be given in this situation, a dosage certainly not without its own complications.

During the early 1970s, a number of authors demonstrated that equipotent seizure prophylaxis with diazepam produced fewer undesirable cardiovascular and respiratory side effects than barbiturates. In spite of the fact that the exact mechanism of this protection is not clearly understood, diazepam has subsequently enjoyed considerable popularity as a sedative-prophylactic premedication for patients receiving large dose regional anesthetic techniques.

Munson demonstrated that lidocaine-induced seizures could be successfully aborted by the intravenous infusion of diazepam 0.1 mg/kg with a minimum of cardiovascular and respiratory effects. In a study of primates, De Jong found that 60 minutes following an intramuscular (thigh) dose of diazepam 0.25 mg/kg, the amount of intravenous lidocaine required to cause seizure activity was increased by two-thirds (12.8 mg/kg to 21.1 mg/kg). Unfortunately, the study did not attempt a correlation between plasma diazepam levels and degree of safety provided.

**Route of diazepam administration**

Assuming that there may indeed be some correlation of plasma diazepam levels and the degree of local anesthetic-induced seizure protection, the anesthetist should make every attempt to have the patient receive diazepam at a time and in such a manner as to provide high plasma diazepam levels which will coincide with the peak plasma levels of local anesthetic agents. While it is difficult to extrapolate the exact plasma levels of diazepam necessary to provide antiseizure protection, it is known that numerous factors influence its uptake and distribution characteristics, including the route of administration.

Kortilla showed that while *intramuscular* (deltoid) diazepam produced a faster onset (20-30 min) of subjective symptoms of drowsiness than did *oral* doses, patients reported no perceivable differences at 60 minutes. Plasma levels rose more quickly with the intramuscular injection than with the oral route, but at 60 minutes, the oral dosage had produced higher plasma levels (190 mcg/cc) than did intramuscular (153 mcg/cc).

The discomfort associated with intramuscular injection and the high incidence of diazepam-related thrombophlebitis following intravenous administration, apparently caused by its solvent propylene glycol, have favorably influenced the popularity of the oral route.

When advocating the oral administration of diazepam it should be remembered that the rate of dissolution and gastric activity can markedly influence its absorption. Gamble has shown that *intramuscular* morphine, meperidine or atropine administered concurrently with oral diazepam will prolong the peak absorption time of diazepam from a control of 60 minutes to 90 minutes. It will also decrease the peak blood level attained from a control of 200 mcg/cc to 105 mcg/cc, 135 mcg/cc and 144 mcg/cc, respectively.

Gamble's work also suggests that drugs which enhance gastric emptying such as metoclopramide will decrease diazepam's peak absorption rate to less than 30 minutes and increase the peak blood levels attained to 244 mcg/cc.

The efficacious, routine use of antacids as pre-anesthetic medication is well reviewed in the literature, and is commonly used in many anesthetists' practices. Recent work has shown that, in addition to lowering the gastric pH to levels less harmful should aspiration occur, absorption dynamics of concurrently administered oral medications may be favorably altered.

Sturdee has demonstrated both a markedly increased uptake and increased plasma diazepam level (120 mcg/cc versus 70 mcg/cc at 30 minutes) when diazepam 5 mg was given orally along with an oral antacid (magnesium trisilicate). It should be noted that at 30 minutes, this surpasses levels obtained by the administration of 10 mg by either the intramuscular or oral routes without antacids. Sturdee postulates that this is due more to decreased gastric emptying time than to a direct effect of the change in stomach pH.

In contrast, Nair states that one would expect any antacid which raises stomach pH to near that of the pKa of diazepam (3.3) to enhance absorption of the drug from the stomach. He found that the concomitant administration of magnesium trisilicate slowed uptake and decreased the clinical soporific effect of diazepam. The use of sodium citrate or aluminum hydroxide hastened this effect. Patients in the aluminum hydroxide group had significantly higher degrees of absorption resulting in higher plasma levels by 60 minutes.

To further confuse the issue, Gamble found that the addition of aluminum hydroxide will indeed hasten the absorption of diazepam but that
at 60 minutes, diazepam administered alone and orally will produce higher plasma levels.\textsuperscript{85} Depending upon your interpretation of this data, it would seem that if the prophylactic effects of diazepam are desired, the drug should be administered approximately 60 minutes prior to the expected administration IVRA. Of course, keeping in mind the incidence of discomfort and vascular thrombotic activity involved, the intravenous administration of diazepam immediately prior to initiating IVRA might be considered.

Finally, some would advocate no prophylactic coverage, favoring instead to use this important agent only when CNS symptoms are observed. Moore feels that ventilation with oxygen alone is sufficient should systemic symptoms be noted.\textsuperscript{38} He believes that hypoxia and hypercarbia play a significant role in the manifestation of seizure activity and since such activity is short lived, the post-ictal state is worsened by administration of sedative drugs.

Regardless of the clinical data presented, preblock therapy with these medications cannot be considered a guarantee against drug induced seizures, nor should their administration be considered a substitute for proper technique.

Intravenous devices and their placement

As mentioned earlier, Bier’s original technique remained essentially dormant for more than 50 years following its introduction in 1908. In defense of this, it must be remembered that his technique must have been considered cumbersome as it required two separate tourniquets and an operative procedure (venous cutdown) for placement of the intravenous cannula (Figure 1).\textsuperscript{10} It was not until 1931 that percutaneous venipuncture was advocated, thus making the technique more practical.\textsuperscript{89}

The site of cannula placement is another matter altogether. Bier suggested the injection be made into vessels located in the antecubital fossa, possibly because it was more accessible for surgical exposure, and that the cannula be directed distally in order to force the liquid toward the hand (presumably the surgical site). Such direction of injection is interesting as the presence of valves in the extremity’s superficial venous system would seem to create an obstruction to distal flow. Indeed research by Fleming more than half a century later, using radiopaque solutions to study the site of action of intravenous local anesthetics, demonstrated that venous valvular competency could cause retrograde flow, even to the point of leakage beneath a pneumatic tourniquet. From this, there appears to be no advantage in directing an intravenous device distally when performing IVRA.

Present concepts of anatomical preference for percutaneous intravenous devices are closely related to the proposed site of action of IVRA. Those who subscribe to the theory that IVRA works by simple diffusion of liquid agents from the intravenous space into the soft tissues, thereby anesthetizing the nerve endings at the tissue level, advocate the placement of the injection site as close to the site of injury or proposed surgery as practical, usually a vein on the dorsum of the hand.\textsuperscript{40-44}

![Figure 1](attachment:Figure_1.png)

August Bier’s original technique of Intravenous Regional Anesthesia. Placement of a metal cannula required a surgical procedure which no doubt deterred from its ready acceptance. Of interest is the use of both a distal and proximal tourniquet to isolate the surgical site and to lessen the total volume of injectate.


SKIN MARKING OF NOW ISCHEMIC VEIN
Advocates of the opposing view, which is that IVRA works at the major nerve trunks in a manner similar to traditional peripheral nerve block techniques, have promulgated the practice of placing the injection site in close proximity to these structures, such as in superficial veins in the antecubital fossa. Caution should be taken, however, when injecting at the antecubital fossa as competent valves in the veins may prevent retrograde flow. This would cause injection pressure to surpass that created by the tourniquet, thus allowing liquid anesthetic agent to flow into the general circulation (Figure 2).

Sorbie mentions this argument in favor of placing the intravenous cannula in the hand or forearm in spite of his belief that the drug works primarily at the nerve trunk. A slow injection will lessen the risk of this problem as well as preventing possible rupture of the vein. Van Niekerk has reported a similar complication when a long cannula device was placed at the antecubital fossa and threaded to a point proximal to the tourniquet, with resultant systemic injection.

Raj has shown that within five minutes of injection, regardless of the site, the majority of liquid injectate concentrates in the large superficial veins of the antecubital fossa (Figure 3).

Regardless of the site preferred, the selection of the percutaneous indwelling intravenous device should be made with due care. The technical development of numerous highly flexible cannula devices would seem to antiquate the further use of inflexible metallic needles. Such cannulae are available in virtually all sizes (25-12 gauge) and a myriad of adaptations. It is recommended that a small bore (22-25 gauge) be used as this will reduce the size of rent remaining in the vein when the device is removed and will lessen extravasation of local anesthetic agent into the subcutaneous tissue or out through the skin.

By attaching a sterile intravenous extension tubing and syringe of local anesthetic agent, a sterile closed system can be achieved which allows considerable flexibility during exsanguination of the extremity (Figure 4) without fear of dislodgement or infiltration into the subcutaneous tissue. Brown suggests leaving such a system intact during a case in order to conduct a continuous technique.

One may wish to employ an indwelling cannula which accommodates a tight fitting obturator stylet or a Heparin-Lok® device (Figure 5) as these will remain in the vein during exsanguination and are less cumbersome to use than the syringe-tubing arrangement.

Exsanguination

In the years following Holmes' popularization of IVRA, a number of papers appeared which anecdotaly described modifications of Bier's original work. Among these were reports exploring the efficacy of exsanguination prior to inflation of the tourniquet. In modern practice this issue is only academic as most surgeons desire a "bloodless field" in which to work, thus requiring careful exsanguination prior to tourniquet inflation. Additionally, the present concept of the site of action of IVRA, which is detailed later, mandates conscientious and complete vascular exsanguination.

In current practice a latex Esmarch bandage, an elastic wrap such as an Ace® bandage or a Crepe bandage is wrapped snugly around the extremity from the fingers toward the shoulder. Occasionally this practice is impractical due to pain or an open wound. In such cases a pneumatic
orthopedic splint or 3-5 minutes of gravity drainage may be used.

Care must be taken when utilizing the Esmarch or elastic bandage as excessive shearing forces (up to 1000 mmHg) may be produced particularly on previously traumatized areas, or exquisitely sensitive skin as found in elderly or cachectic patients. Pulmonary embolism has been reported following this type of exsanguination when used for delayed internal fixation of long bone fractures.

A number of authors have presented convincing arguments favoring exsanguination with IVRA. Adams has determined the venous volume of the upper extremity below a mid-humerus tourniquet to be approximately 170 cc. If this volume were not exsanguinated, the injection of a small volume (40 cc) of a local anesthetic agent into this vascular pool would considerably dilute the agent, making it weak and ineffective. Atkinson believes this dilution may prevent or severely retard the spread of agent from the vascular bed into surrounding tissue thus re-
resulting in a large reservoir of agent available to enter the systemic circulation when the tourniquet is released.\textsuperscript{57}

Furthermore, Adams also feels that the exsanguinated vascular tree plays a significant role in transport of local anesthetic agents to the nerve substance. Thus, he strongly favors complete exsanguination prior to injection.\textsuperscript{58}

Bradford has reported that exsanguination of a single upper extremity can increase central venous pressure up to 6 cm H\textsubscript{2}O and advises that caution be used when exsanguination is considered in a patient with a history of congestive cardiac failure.\textsuperscript{59}

When injecting local anesthetics into the exsanguinated extremity, one will often notice a blotchy appearance of the skin (cutis marmorata) caused by residual blood being forced from deep vessels into small subcutaneous capillaries.\textsuperscript{19} This apparently has no clinical significance and is mentioned only so that the anesthetist is aware of its possible occurrence.

The anesthetist is reminded that even with complete exsanguination and tight fitting tourniquets, some vascular leakage may occur via the intramedullary vessels of the humerus and may appear as “oozing” at the operative site.\textsuperscript{60} Again, other than being an annoyance for the surgeon, this is apparently of little clinical significance.

**The use of tourniquets**

It is perhaps obvious that without the use of a tourniquet, there would not be a technique such as IVRA. However, the physiologic and pharmacologic effects of this device are perhaps the least discussed aspects of the technique.

The development of resistive/restrictive tourniquets invariably is linked with the surgical amputation of extremities. As early as the 16th century, Pare advocated such a technique to decrease blood loss and thereby ease the surgical exposure.\textsuperscript{61} In 1718, Petit introduced a screw-type device and coined the term *tourniquet* from the French *tourner*, to turn.\textsuperscript{62}

In the 1860s, Lister became the first to use a tourniquet for a surgical procedure other than amputation.\textsuperscript{63} Shortly thereafter, Esmarch introduced his eponymous rubber bandage for the dual

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**Figure 5**

(A) Alternative system of injection for Intravenous Regional Anesthesia. Once placed, a sterile obturator is inserted into the intravenous cannulae and secured. Following exsanguination the obturator is removed and a drug-filled syringe is connected to the cannula for injection.

(B) Placement of a “Heparin Lock” device onto the indwelling cannula allows additional mobility during exsanguination of the extremity. Following this, a syringe/needle is placed in the device and injection made.
purpose of exsanguination and producing ischemia of the extremities. This was later modified by von Langenbeck to its present wide band-like form. In 1904, Harvey Cushing revolutionized surgical tourniquets by his development of a pneumatic device to which a manometer and tank of compressed air could be attached, thus creating a controllable constant pressure in the tourniquet.

Cushing's idea apparently went unnoticed, at least relative to IVRA, as Bier's original works utilized only the Esmarch bandage. Indeed, even Holmes' work in 1963 mentioned only the application of a single Riva-Rocca type blood pressure cuff as a tourniquet for performing IVRA. In 1964, apparently unaware of Herreros' earlier work, Hoyle introduced a specially designed two-compartment pneumatic tourniquet for IVRA. His suggestion was that the proximal compartment be inflated first and IVRA be carried out as usual. After 15-20 minutes, the distal compartment was to be inflated over what was now anesthetized tissues, and the proximal compartment deflated. This concept and device found many ardent advocates and is widely practiced today.

Despite the widespread clinical use of pneumatic tourniquets, there is a paucity of experimental and clinical data establishing the duration of ischemia which may be considered safe and the optimum pressure at which a tourniquet should be maintained.

In common practice, two hours is often stated as the maximum time a tourniquet can be safely left inflated. This empirical limit apparently dates from Bruner's work in 1951, and has survived essentially unchanged to date.

Prolonged ischemia of an extremity is obviously contrary to physiologic well-being. Following two hours of tourniquet induced ischemia, the venous pH falls in a linear fashion from a normal of 7.4 to 6.9. Venous pO₂ falls from a normal of 45 mmHg to a low of 4 mmHg while venous pCO₂ rises from a normal of 35 mmHg to 104 mmHg. Miller has shown that after 60 minutes of tourniquet induced ischemia, tissue pO₂ levels are significantly lower than venous oxygen tensions taken at the same interval. Additionally, following release of the tourniquet, tissue gas tensions and pH return to normal levels much more slowly than do venous values.

While the clinical application of such data is inconclusive, Adams has shown that irreversible muscle fatigue develops at two hours of ischemia. Webb has demonstrated evidence of cell damage in striated muscle which results in marked increases in capillary permeability to fluid and protein. That this fluid loss may be clinically significant is supported by Fine's report of acute renal failure and circulatory shock following release of an extremity tourniquet. Although modern practice of aggressive perioperative systemic fluid therapy generally precludes such disasters, the large shift of protein and fluids following tourniquet ischemia cannot be discounted. The importance of this phenomenon at the microscopic level has only recently been suggested as a course of post-tourniquet sequelae.

Miller's work suggests increased interstitial pressure resulting from such edema may be hazardous, particularly when it occurs in muscles which are highly compartmentalized by fascial sheaths, preventing adequate perfusion of these tissues. His finding that a six-fold increase in interstitial pressure may persist as long as 24 hours following only one hour of tourniquet ischemia should be noted. Fowler demonstrated nerve conduction delays which he attributed to intramyelin and periaxonal edema which resulted in swelling of the myelin sheath. The somatic and nervous complications resulting from such insults such as the post ischemic hand syndrome have long been recognized by surgeons and should be considered by anesthetists any time a tourniquet has been employed.

In contrast to the concept of ischemia related sequelae, another popular opinion is that direct compression of tissues beneath a tourniquet may play a significant role in such complications. In 1954, Moldaver inferred that the decrease in the number of reports of tourniquet-related nerve damage was due to the increased use of the pneumatic tourniquet, the popular rubber tube style of that period. He noted that even with the pneumatic tourniquet, some residual damage did occasionally occur. He described a tourniquet paralysis syndrome which was manifest as functional disturbances in the neural distribution distal to the site of compression which could not be explained on the basis of ischemia alone.

Ochoa supports this concept with his demonstration of localized edema in the myelin layer of the compressed segment. Lundborg also demonstrated marked changes in the epithelium of infraradicular capillaries located beneath the cuff site, more so than nerves in the ischemic limb distal to the compression.

From the data reviewed, it is difficult to identify a singular causative situation. Quite probably, neural sequelae are a result of a combination of compression and ischemia; changes from com-
pression begin immediately with inflation of the device while ischemic changes develop later. It would be evident that the majority of tourniquet related complications can be avoided by careful attention to technical details. Certainly, misapplied pneumatic tourniquets can produce undue pressure on a concentrated site. When a tourniquet is initially applied too loosely, the fabric cuff may restrict lateral expansion of the rubber bladder, thus narrowing the pressure band as much as 75%. There is no simple direct relationship between the pressure applied at the skin surface and that realized in the interior of the limb. Lundberg has shown that the sciatic nerve may realize a pressure of only 110 mmHg when 700 mmHg is applied over the thigh. Stewart suggests that a tourniquet be applied at the point of maximum circumference, thereby compressing nerves and vessels within the bulk of periosteous muscle rather than direct compression of these vital structures over bony prominences. In this regard, it is generally advised that a tourniquet not be utilized distal to the elbow or knee.

Prior to application of the tourniquet, it is recommended that orthopedic wool (Webrill®) be wrapped circumferentially around the extremity so as to completely cover the area beneath and approximately one inch to either side of the device (Figure 6). The imprint wrinkle which is usually present following deflation and removal of the tourniquet apparently is of little clinical significance. Ecchymosis or blistering of the skin is the most common complication observed following the use of an unpadded tourniquet. Additionally, care should be taken to prevent prepping solutions from pooling under the tourniquet or its padding, as serious chemical burns may result.

The recommended inflation pressure of a pneumatic tourniquet remains an illusive subject. Such pressures will depend in part on the site of application, size of the limb involved and the patient’s systemic blood pressure. Cuff pressures in the range of 250-300 mmHg for the upper extremity and 450-500 mmHg for the lower extremity are widely published and practiced. The derivation of these figures is, however, unclear. Nobel has demonstrated that in the arm, a cuff pressure of 250 mmHg will totally occlude intraneural as well as superficial vasculature in the compressed segment. Sanders suggests that arbitrary inflation pressures should not be used. He favors instead a min-

**Figure 6**

Prior to application of the tourniquet a layer of cotton wool (Webrill®) should be placed circumferentially beneath the tourniquet to extend approximately one inch beyond the tourniquet’s margins. Care should be taken during the preparation of the extremity not to saturate the padding with antiseptic solutions.
imum effective pressure (MEP), achieved by adjusting the tourniquet pressure, regardless of the indicated gauge pressure, until distal pulses are no longer felt in the extremity.\textsuperscript{86} It must be remembered, however, that systemic arterial pressures may change, often as much as 70-100 torr, particularly if any discomfort is felt. Therefore, some advocates that the MEP be identified and an additional 100 mmHg be added to the tourniquet gauge pressure.\textsuperscript{87} This technique has been found clinically satisfactory by the author with no known complications after several hundred procedures.

A properly functioning tourniquet is a necessity. This should consist of a double compartment cuff and switching device which is inflation-tested prior to each application (Figure 7). Additionally, the rubber bladders should be removed from the fabric binder and inspected periodically for deterioration. If there is any question as to their condition, new bladders should be obtained.

Before purchasing an inflation device, one must be sure that it will totally satisfy its intended purpose. While numerous styles are available, the author prefers a compressed air or oxygen powered model which includes a constant read pressure gauge and minute timer to remind the user of elapsed time. Portable models are available which will allow patients to be transferred (for example, to the radiology department) with the IVRA intact.

Pressure gauges should be tested against a liquid mercury manometer prior to each application and the inflated tourniquet squeezed while observing for a deflection or “bounce” on the pressure gauge. This latter maneuver is done to observe patency of the delivery line and to insure that a “flap valve” effect is not present in the lumen of the delivery tube. Mullick has reported a case in which a pressure gauge displayed 350 mmHg while the tourniquet was pressurized to over 1200 mmHg.\textsuperscript{88}

Prior to initiating IVRA, the anesthetist is advised to consult the surgeon as to projected operative time. If this time plus preparation exceeds two hours, an alternative form of anesthesia is suggested such as brachial plexus block. When employing IVRA, the judicious utilization of time is imperative. The anesthetist should request the surgeon to make any necessary skin marks with an indelible marker prior to the block technique and that he time his scrub and gowning to coincide with the termination of the patient’s skin prep. Accordingly, the anesthetist should make sure that a technician is available to commence the skin prep immediately following the injection of local anesthesia. Conservation of this precious time will make a significant contribution toward successful IVRA.

The technique of tourniquet deflation plays a significant role in the uptake and distribution

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**Figure 7**

(A) Double-cuff tourniquet recommended for Intravenous Regional Anesthesia. Note that two compartments are combined within one strap, each compartment having a separate inflation nipple. Luer-Lock\textsuperscript{®} fittings are highly recommended to prevent disconnects. Single valving system from which either tourniquet compartment can be individually regulated. With this device a single pressure source (O\textsubscript{2}, compressed air, nitrogen, etc.) can be utilized.

(B) Pressure regulator and gauge. Gauges on such devices must be checked against a mercury manometer prior to each use. Inaccurate gauges may result in patient injury.

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of local anesthetic agents following IVRA and will be discussed in Part II of this article.

Tourniquet pain

Of all complications associated with the use of pneumatic tourniquets for IVRA, the most common and least clearly understood is the occurrence of tourniquet pain.

The application of tourniquet compression of approximately 250 mmHg over the upper aspect of an extremity will invariably result in some degree of discomfort after 30-45 minutes. This pain has been attributed to the direct compression of tissues, including nerves and muscle. Subjectively, this pain may vary among patients but is most often intolerable after one hour. While systemic analgesics and hypnotics may attenuate the intensity temporarily, some degree of basal narcosis is often required to make completion of surgery possible. This pain may even be noted during inhalation or intravenous general anesthesia as a narrowing of pulse pressure and a gradual rise in mean blood pressure and pulse rate.

In order to better understand this phenomenon, the somatic distribution of the upper arm is illustrated in Figure 8. The lower lateral and posterior cutaneous nerves arise from within the brachial plexus and innervate the anterior, lateral and posterior aspects of the upper arm whereas the intercostobrachialis, which innervates the medial aspect, is formed by branches of the second thoracic nerve (T2).

Sorbie postulates that the terminal branches of these nerves possess a minimum of vasculature at this point, therefore, their axons are exposed to a minimum of local anesthetic agent when utilizing conventional techniques of IVRA. Expanding this concept, Haas has suggested a second wrap modification wherein the extremity is exsanguinated as usual, the proximal cuff of a double tourniquet is inflated and the Esmarch bandage or elastic wrap is removed. A local anesthetic agent of choice is injected intravenously and the extremity is then rewrapped in the same manner as the initial exsanguination. The premise of this maneuver is that it will force the liquid injectate into the smaller vasculature, thus exposing the terminal branches of the proximal nerves to the agent, particularly those innervating the skin beneath the distal tourniquet.

As these nerves become subcutaneous proximal to the site of an upper arm tourniquet, an effective and technically simple method is a subcutaneous wheal of local anesthetic agent placed around the circumference of the arm just proximal to the tourniquet.

Exploring further the physiology or origin of tourniquet pain, Kuntz had demonstrated that some afferent (somatic) spinal nerve fibers traverse the white communicating rami and are associated with the sympathetic trunk as it enters the dorsal roots of the spinal cord. These afferent fibers are not normally considered in the same functional category as the somatic fibers of the integument and are not found distributed in the skin or muscle.

Threadgill has shown that direct noxious stimulation of blood vessels distal to the site of mechanical or chemical somatic disruption will result in afferent conduction of pain. From this he hypothesized that small somatic afferent fibers travel in concert with the sympathetic nerves from the vasculature of the extremities. Further, it is known that sympathetic vasomotor nerves play a significant role in pain associated with ischemic extremities. Such pain stimulates an increase in vasomotor tone which in turn results in still further painful ischemia. Chemical or surgical sym-

Figure 8
In Intravenous Regional Anesthesia terminal fibers of the intercostobrachial, posterior and lateral cutaneous nerves arise proximal to the tourniquet and are not exposed to the intravenous spread of local anesthetic agents. Failure to satisfactorily block these nerves will, in time, give rise to tourniquet pain.
pathectomy has been recognized as therapeutic in resolving this unfortunate situation.

From this information the combination of ischemia and chronic compression of vascular innervation is thought to contribute to the afferent transmission of the discomfort known as tourniquet pain.

**Site and mode of action of local agents**

The site of action of intravenously injected local anesthetic agents is perhaps the most thoroughly studied but least clearly understood aspect of IVRA. A number of explanations have been advanced in recent years, however, the subject is very abstract and highly vulnerable to statistical manipulation of data for the sake of emphasizing a particular point of view.

The proposed sites of action generally emphasize one anatomical location or a combination of locations: (1) peripheral sensory nerve endings; (2) neuromuscular junctions; and (3) major nerve trunks. In addition, a dual mechanism is considered.

**Peripheral nerve endings: tissue level**

Bier, using procaine stained with methylene blue, demonstrated that injectate dispersed rapidly throughout the extremity, including the substance of major nerves. He felt that this dispersion was facilitated by the rich vasculature and absence of valves in small vessels (less than 2 mm in diameter) which emerge along the course of the major nerves. From this he concluded that local anesthetics injected intravenously worked at the "end apparatus of the nerves."

Using radioisotope labeled lidocaine, Knapp demonstrated that the drug rapidly enters the extracellular fluid and reaches a state of equilibrium within the muscle mass.

Atkinson suggests that the rapid injection-to-onset and tourniquet deflation-to-resolution times and the anatomical pattern of analgesia distribution favor the vascular perfusion of peripheral tissue and sensory nerve endings as the site of action. He suggests that one would not expect to effectively block nerve trunks with the dilute solutions of lidocaine (0.5%) which are clinically employed. He further postulates that the superimposition of acidosis resulting from ischemia may potentiate this effect, thus mimicking a true nerve block. Mazzeo suggests that this acidosis increases capillary and venule permeability to the small lidocaine molecule, allowing it to easily escape into the surrounding extracellular fluid and tissue.

Atkinson supports this concept with a case report in which IVRA was incomplete in a finger on which the skin and muscle had been avulsed. He felt this indicated that the interruption in vascular flow precluded exposure of these tissues to the local anesthetic agent.

Using electrophysiologic nerve conduction studies, Miles showed that while a 66% increase in latency of action potential in sensory nerves can be attributed to ischemia alone, there was a 180% increase with the addition of lidocaine. Interestingly, the rate of conduction in motor nerves was not affected by ischemia or the combination of ischemia and lidocaine. From this he concluded that intravenously injected local anesthetic agents acted at the sensory nerve ending and not major nerve trunks. Though unclear to what degree, ischemia certainly plays some contributing role in the establishment and maintenance of IVRA.

Referring to perfusion studies using radiopaque anesthetic solutions, Fleming implied a strong correlation between the onset and pattern of sensory loss and distribution of opacity in the soft tissues of the arm. She thus proposed the site of action to be at the tissue level. In similar studies, Sorbie and Raj came to quite the opposite conclusion.

Allen found a localization of agent 6-8 times greater in traumatized tissue than in normal tissue. He felt this was due to easier diffusion of agent via broken capillaries.

**The neuromuscular junction**

The neurophysiological studies by Miles yielded interesting muscle response data similar to that found when patients received a non-depolarizing muscle relaxant. It was demonstrated that with lidocaine, a point could be reached at which nerve stimulation failed to generate a muscle response while direct muscle stimulation could still elicit muscle contraction. Unlike the non-depolarizing block, administration of neostigmine to patients blocked with lidocaine did not alter the muscle responses. Considering this and similar results reported earlier by Harvey and Jaco, Miles concluded that lidocaine inhibited production of acetylcholine and opposed its action at the neuromuscular junction.

To demonstrate the anatomical distribution of intravenously injected drugs, Atkinson used a dilute solution (0.1 mg/cc) of d-Tubocurarine and found profound relaxation of the muscles below the tourniquet.

Using elaborate electrophysiologic experi-
ments, Fujita demonstrated post-tetanic facilitation during IVRA, especially with procaine and suggests that local anesthetic agents vary in their anticholinesterase activity. He feels that agents are carried via the vessels to the myoneural junction where there is "direct competition between acetylcholine and the local anesthetic agent to occupy the receptor site on the postjunctional membrane."

While these demonstrations do not adequately explain the profound analgesia obtained with dilute local anesthetic solutions, the clinical observation of undesirable volitional motor movement during hand surgery has prompted the author to adopt the addition of dilute solutions of a non-depolarizing muscle relaxant (d-Tubocurarine 0.1 mg/cc). This mixture has proven adequate to block all motor activity below the tourniquet and is of little clinical significance when released into systemic circulation following completion of the technique.

**Nerve Trunks**

A number of authors have suggested the site of action to be the major nerve trunks as they traverse the tissue distal to the tourniquet. In his original description of IVRA, Bier noted the delayed onset of analgesia in tissue distal to the injection site and isolated by a second tourniquet. He concluded this delay in onset represented block of nerve trunks.

Atkinson noted a paresthesia when utilizing IVRA and attributed this to forceful perfusion of intraneural vessels. Using nerve conduction studies to identify the role of ischemia and radiographic studies to determine the vascular distribution of injectates, Sorbie felt that the effects of lidocaine were due to direct contact of the drug with the large nerve trunks. He too implicated the intraneural vasculature as a possible site of this important interface. Using radioisotope-tagged lidocaine to study tissue distribution of IVRA, Cotev found that shortly following injection the concentration in nerve tissue was four times that of muscle or skin.

In nerve conduction studies performed by Shanks, motor and sensory conduction velocity delays were attributed to effects of local anesthetics at the nerve trunks. This is in opposition to the conclusion drawn by Miles who felt similar findings were primarily the result of tourniquet ischemia.

**Combined site of action**

Bier was the first to suggest a dual mechanism of action for IVRA, stating, "The direct anesthesia in the area between the two tourniquets occurs immediately if one uses Novocain® in sufficient amounts. The indirect anesthesia distal to the peripheral tourniquet needs some time to develop." His implication was that the direct anesthesia is due to block of peripheral nerve endings in the tissues saturated by local anesthetics agents while the indirect anesthesia distal to the distal tourniquet results from block of the large nerve trunks as they traverse the proximal tissue.

Using a combination of clinical investigation techniques, Raj derived convincing documentation for the bi-phasic theory. Following the injection of only 5 cc of radiopaque stained lidocaine (0.5%) solution into a dorsal hand vein, contrast material can be noted in the large superficial veins of the forearm: radial, ulnar and median antebrachial (Figure 3). Of particular note, even with this small volume, is the presence of contrast in the basilic, cephalic and median cubital veins at the elbow. Additionally, no contrast material is noted distal to the injection site, presumably blocked by venous valves. Only following injection of 30 cc could contrast be noted distally and then only as far as the second set of venous valves at the first proximal phalanx (Figure 9).
The onset of sensory loss was immediate, beginning first in the digits and traveling proximally toward the anterior and medial aspects of the forearm in a "glovelike" fashion, finally reaching the posterior aspect of the elbow. A total of 10-15 minutes elapsed before any contrast was noted to have extravasated into muscle tissue (Figure 10).

When this experiment was repeated with a rubber band-tourniquet occluding the midforearm, the 5 cc volume again passed proximally, presumably via the perforating and interosseous veins, to the level of the elbow (Figure 11). With 15 cc, the majority of contrast was again found at the elbow with only a small amount having extravasated into the hand and wrist.

In a similar experiment, injection was made into the medial cubital vein at the elbow. A similar filling pattern and onset of anesthesia was noted as before (Figure 2), with good filling of vessels around the elbow. Virtually no contrast was seen in the distal one-third of the forearm. The presence of contrast intravascularly above the mid-humerus was of particular interest. It is postulated that injection pressure exceeded the tourniquet pressure, allowing proximal flow of local anesthetic into systemic circulation. Transient CNS symptoms were noted in this patient. Similar leakage of solution during forceful injection was radiographically documented by Fleming.

In experiments using radioisotope-tagged local anesthetic agents, Adams estimated the intravascular volume of the upper extremity to be 170 cc. Instillation of 40 cc of local anesthetic will not produce any significant hydrostatic pressure, thus, it will seek the path of least resistance, the large superficial veins. Along with radiographic documentation indicating that contrast does not significantly leave the vascular system for approximately 15 minutes following injection, this must be taken as strong evidence against the concept of localization at the peripheral nerve endings, at least in the early stages of the technique. This does not preclude such a site of action later in the technique.

It is interesting to note that regardless of the injection site used, the pattern of onset was the same. This gives rise to further questions concerning the peripheral nerve ending as the site of action.

By investigating the microvascularity of peripheral nerves, the proposed site of action can be clarified. DeJong has shown that the fibers which
serve the distal extremity are located primarily in the middle or core of major nerve trunks while those which serve the proximal tissues are around the mantle or periphery of the trunk (Figure 12).\textsuperscript{10} Figures 13 and 14 demonstrate the microvascularity of such a peripheral nerve trunk. The majority of the larger intraneural vessels are located near the “core”. Raj postulates that immediately following injection of local anesthetic agent into the exsanguinated and isolated vessels of the extremity, these vascular channels carry the agent to the nerve trunks in the vicinity of the elbow. From there, the fluid flows into the intraneural vessels near the core of the trunk and diffuses into the nerve fibrils due to a concentration gradient. Ten to 15 minutes later, diffusion of the local anesthetic agent into the extracellular fluid of muscle tissue ensues and continues until an equilibrium with the intravascular drug is approached.

Sensory perception returns in a similar pattern, proximal to distal, and is similarly explained. When circulation is restored, the drug is first washed from the nerve core, thus restoring the proximal distal sensory distribution. This is followed immediately following injection of local anesthetic agent to the nerve trunks of muscle tissue ensues and continues until an equilibrium with the intravascular drug is approached.

Regardless of the site of action, the onset of analgesia is immediate and generally complete within 5-10 minutes, thus coinciding with completion of the presurgical skin preparation and draping.

Part II will focus on local anesthetic agents and principles of pharmacokinetics. It will also investigate complications and contraindications of IVRA as well as special considerations for its use.

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The author wishes to state that the opinions or assertions contained in his article are his private views and are not to be construed as official and/or reflecting the views of the Department of Anesthesia, USS Nimitz, the Navy Nurse Corps, the Department of the Navy, or the Department of Defense.