Kappa Delta Award Paper

Tissue Fluid Pressures: From Basic Research Tools to Clinical Applications


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Summary: The two basic research tools developed to measure tissue fluid pressure (wick catheter) and osmotic pressure (colloid osmometer) have undergone extensive validation and refinement over the past 20 years. Using these techniques, basic science investigations were undertaken of edema in Amazon reptiles, pressure-volume relations in animals and plants, adaptive physiology of Antarctic penguins and fishes, edema in spawning salmon, tissue fluid balance in humans under normal conditions and during simulated weightlessness, and orthostatic adaptation in a mammal with high and variable blood pressures—the giraffe. Following and sometimes paralleling this basic research have been several clinical applications related to use of our colloid osmometer and wick technique. Applications of the osmometer have included insights into (a) reduced osmotic pressure of sickle-cell hemoglobin with deoxygenation and (b) reduced swelling pressure of human nucleus pulposus with hydration or certain enzymes. Clinical uses of the wick technique have included (a) improvement of diagnosis and treatment of acute and chronic compartment syndromes, (b) elucidation of tissue pressure thresholds for neuromuscular dysfunction, and (c) development of a better tourniquet design for orthopaedics. This article demonstrates that basic research tools open up areas of basic, applied, and clinical research. Key Words: Tissue fluid pressures—Clinical applications—Osmometer—Compartment syndrome—Tourniquet.

Twenty years ago, techniques were developed for basic science studies of interstitial fluid pressure and colloid osmotic pressure during the 1967 R/V ALPHA HELIX Expedition to the Amazon River (21,43). The wick catheter technique was used to examine pressure-volume relationships in animal tissues, and a simple colloid osmometer was employed to assess blood samples from Amazon animals. These techniques were refined during subsequent expeditions from Scripps Institution of Oceanography [University of California, San Diego (UCSD), CA, U.S.A.] to investigate physiological adaptations of Antarctic penguins (22), polar fishes (7), and Pacific salmon (18). Later studies using the same techniques focused upon normal transcapillary fluid balance in humans (13,36), fluid shifts related to simulated weightlessness in preparation for a Space Shuttle project (23), and orthostatic adaptations in the giraffe (15).

In 1973, a clinical wick catheter was developed for monitoring intracompartmental pressures in patients with possible acute and chronic compartment syndromes. Our initial experiments on animals, ourselves ("normal" subjects), and patients proved
successful as did subsequent research that continued our wick catheter investigations of (a) compartment syndromes, (b) pressure thresholds for nerve dysfunction, and (c) tourniquet design in orthopedics. Parallel studies using new and improved osmometers have examined (a) osmotic dehydration of sickle cells during deoxygenation (12) and (b) swelling pressures of normal and enzyme-treated nucleus pulposus. The primary theme of this review article is that simple, basic research tools, such as the wick catheter and colloid osmometer, have opened up many areas of basic, applied, and clinical research.

BASIC RESEARCH METHODS FOR MEASURING FLUID PRESSURES IN TISSUE AND BLOOD

Wick Catheter

The methods used in this paper were developed at the Scripps Institution of Oceanography, UCSD during 1966–1971. Previous needles and catheters used for measuring interstitial fluid pressure required saline infusion in order to maintain patency of the probe (9). This requirement precluded measurements of negative fluid pressure in tissue, a concept that Guyton (6) pioneered in the early 1960s. Although Guyton’s capsule provided dynamic measurements of tissue fluid pressure, it was relatively large and required implantation 6 weeks prior to any determinations (1).

The wick catheter was developed to provide immediate, equilibrium measurements of tissue fluid pressure without saline infusion (Fig. 1). Microscopical channels of free fluid between the wick fibers maintained catheter patency and offered a relatively large pickup area for sensing changes in tissue pressure. The wick technique (43) was first used during the R/V ALPHA HELIX Expedition to the Amazon River in 1967. A simple catheter system made from Teflon tubing, a cotton wick, glass tube, and custom manometer were designed especially for field-type research. The system was thoroughly tested to insure that it accurately measured hydrostatic fluid pressures only, especially under conditions of negative fluid pressures where needle techniques were found inoperative. The wick technique was also tested in model systems of dehydration (8), e.g., in monitoring development of negative pressure in starch suspensions during water evaporation. These initial studies were extended to measurement of fluid pressure in subcutaneous, peritoneal, and muscle tissues (Fig. 2).

The basic principles for measuring tissue fluid pressure in animals were applied and refined for intracompartmental studies in humans (11,33). For example, intramuscular fluid pressures in the forearm could be measured instantaneously using the glass capillary technique or continuously using a pressure transducer (17). Revisions of the original technique included use of braided suture for wick material, smaller catheter tubing and improved techniques to minimize trauma during insertion, heparinized saline to prevent coagulation, and sterilization of all system components to minimize risks of infection. Over time, a “wick kit” was developed that included a pressure transducer, minirecorder, wick catheters, and all other items necessary for sterile measurements of intracompartmental pressure. Later, a “slit catheter” was developed and

FIG. 1. Close-up view of wick catheter tip showing microscopic wick fibers that provide contact with tissue fluids and maintain catheter patency without saline infusion. (From Adair et al., ref. 1, with permission.)

FIG. 2. Principles of measuring tissue fluid pressure in muscle using the wick technique. Wick (w) is held within tubing by thread (t). Glass capillary (g.c.) is adjusted vertically until read-out meniscus (m) is stationary, indicating equilibrium is reached. In this case, intramuscular fluid pressure equals hydrostatic height (−5.5 cm H₂O) plus capillarity (−4.5 cm H₂O) to give −10 cm H₂O. (Modified from Hargens et al., ref. 11, with permission.)

tested. This catheter was based upon the wick principle and offered higher frequency of response for exercise studies (32,40). During 1975–1984, patients were evaluated for suspected acute compartment syndromes within the San Diego and Orange County areas using these methods (over 150 cases in these patients were positive). More than 2,000 studies of intramuscular pressure were undertaken in patients and volunteers at UCSD over the past 10 years, and only one infection occurred using our technique.

Colloid Osmometer

Colloid osmometers have been available for over 100 years, but recent improvements in membrane and pressure-sensing technology make their use more general and reliable. Colloid osmometry is important for studying (a) the capacity of blood to absorb tissue fluid, specifically edema fluid, (b) the colloid osmotic pressure of interstitial fluid that counteracts the colloid osmotic pressure of blood, and (c) the ability of a tissue matrix (e.g., nucleus pulposus of the intervertebral disc) to swell. The importance of these phenomena in tissue fluid homeostasis and other orthopaedic considerations will become evident below.

Our first colloid osmometer was developed for field physiology research where electric power was not always available (Fig. 3). Principles for measuring osmotic pressures were similar to those outlined previously for the wick catheter technique. Basically, our new technique employed a stretch mounting of the membrane in order to measure weak osmotic pressures accurately to within 1% (21).

All techniques for measuring negative tissue fluid or osmotic pressures use the "push" or "pull" technique to release trapped fluid. Scholander and colleagues (42) employed the push technique to verify experimentally Dixon's transpiration model (3) for the ascent of fresh water sap in all vascular plants. Briefly, Scholander and co-workers (42) placed a cut branch in a pressure bomb and compressed the plant tissue until the water meniscus returned to its initial position at the cut surface. Recently, we employed a similar technique to measure the enormous swelling pressure of tissues with high glycosaminoglycan content (e.g., nucleus pulposus). Previous osmometric techniques were unreliable because of cavitation (gas bubble formation) on the side of the membrane opposite the swelling tissue.

Our new compression-type osmometer (Fig. 4) consists of a sample chamber over a rigid Millipore filter (0.5-μm pore diameter). Samples of nucleus pulposus are compressed over the membrane by nitrogen gas to prevent swelling of the tissue. Equilibrium swelling pressure is reached within 10–30 min and measured by a Heise precision gauge. Pressure gradients across the membrane are detected using a low volume displacement, pressure transducer, and nullified by the pressurized gas.

To examine the accuracy of our new osmometer, five 20-mg samples of pooled dog or pooled pig nucleus pulposus from lumbar intervertebral discs were placed in the osmometer and the maximum swelling pressures were measured (5). Samples of dog and pig nucleus pulposus were also evaluated with the equilibrium dialysis technique (26) using 2,000 M.W. cutoff dialysis tubing and 8,000 M.W. polyethylene glycol (PEG) solutions ranging in concentration from 0.05 to 0.80 mg of PEG/ml of H₂O.

Mean equilibrium swelling pressures of dog and pig nucleus pulposus measured by direct osmometry were 2.3 ± 0.3 and 0.5 ± 0.002 atm, respectively, agreeing well with the calculated values obtained by the dialysis technique (1.9 and 0.4 atm, respectively). Therefore, this osmometer provides a simple, rapid, and direct measurement of swelling pressure. It can be used to investigate enzymatic and hydration effects on the nucleus pulposus swelling pressure in relatively small samples. The
FIG. 4. New compression-type osmometer for measuring swelling pressure of nucleus pulposus. Left: Plexiglas osmometer mounted on stand with nitrogen gas inlet at top. The osmometer is connected to a nitrogen gas source, precision pressure gauge, and pressure transducer. Transmembrane pressure gradients are continuously measured by a strip-chart recorder. Right: Cross-section of osmometer with sealing of membrane by the crimp rings (CR) on the screw-down Plexiglas plate. The nucleus pulposus is placed in the sample well (SW) on top of the membrane (M). Pressure gradients across the membrane are transmitted by the fluid column (S) and monitored by the pressure transducer (PT) fitted tightly to the bottom of the osmometer by an O ring (OR). (From Glover et al., ref. 5.)

high swelling pressures of disc samples cannot be measured using standard osmometers because of cavitation problems beneath the membrane. This osmometer provides equilibrium measurements within 10–30 min as compared to 24–48 h for the indirect, equilibrium-dialysis technique.

ACUTE CHRONIC COMPARTMENT SYNDROMES

Definitions

A compartment syndrome is a condition characterized by high muscle pressure, myoneural pain, paresthesia, paresis, pink skin color, and presence of distal pulse (the six p’s of a compartment syndrome) (Fig. 5). The syndrome is induced by high tissue pressure within a confined region of skeletal muscle, causing sufficient ischemia to compromise myoneural structures (27). Elevated pressure is produced by internal swelling or external compression of muscle and may occur in almost any region of the body. Muscle compartments of the leg are involved most frequently, but compartment syndromes are reported in thigh, buttock, shoulder, arm, and hand muscles as well (31,37). Typically, muscles involved in this ischemic process are enclosed within relatively impermeable, noncompliant osseofascial boundaries that preclude spontaneous dissipation of tamponade within the involved compartment. Therefore, surgical decompression by fasciotomy is required to renew adequate blood flow through ischemic tissues. If intracompartmental pressure remains elevated for a sufficiently long period of time without fasciotomy, necrosis of intracompartmental tissues will occur. The well-known clinical entity of Volkmann’s contracture may thus result if prompt diagnosis and treatment of the jeopardized limb are not undertaken (31).

FIG. 5. Comparison of normal leg (left) and leg with compartment syndrome (right). When tissue fluid pressure within one or more muscle compartments rises above the capillary blood pressure (30–40 mm Hg), ischemia occurs and blood flow is confined solely to large vessels and collateral circulations. (From Mubarak and Hargens, ref. 31, with permission.)

Acute Compartment Syndrome

Compartment syndromes are commonly divided into two forms, acute and chronic, based on etiology and reversibility. An acute compartment syndrome develops when intramuscular pressure exceeds capillary blood pressure for a prolonged period of time. In this setting, immediate decompression is necessary to prevent myoneural necrosis and Volkmann’s contracture. Acute compartment syndromes are produced by trauma, arterial injury, arterial reconstruction, extreme exertion, or prolonged limb compression.

Chronic Compartment Syndrome

A second form of syndrome is defined as a chronic (exertional) compartment syndrome, also termed recurrent compartment syndrome by some authors. This condition occurs when exercise increases intramuscular pressure sufficiently to cause ischemia, pain, and, on some occasions, decreased sensibility or dysfunction (39). Commonly, these symptoms disappear when the activity is stopped and reappear during the next exercise activity. However, if muscular activity is maintained despite pain, neurologic deficit, and persistent tamponade, a chronic compartment syndrome can precipitate an acute compartment syndrome, which then requires immediate fasciotomy.

Measurement of Intracompartamental Pressure

Because high intracompartamental pressure is the underlying pathogenic factor common to all acute compartment syndromes, its measurement is often required, especially in patients who are uncooperative (children), unresponsive, or comatose. Several clinical techniques for monitoring intracompartamental pressure are available today. However, some techniques are preferred over others in terms of accuracy, safety, and cost.

Advantages of the wick technique include a relatively large area for sensing tissue fluid pressure, avoidance of saline infusion (equilibrium measurements are thus obtained), and continuous monitoring of pressure. Disadvantages include possible coagulation around the catheter tip, especially if the wick fibers are packed too tightly in the catheter tip, and relatively slow response to pressure changes during exercise studies. Overall, the wick technique is simple, accurate to ±1 mm Hg, and reliable for diagnosis of compartmental tamponade.

The slit catheter technique (40) represents an attempt to improve the wick catheter by a more open catheter tip. This design allows a higher frequency response to intracompartamental pressure changes and thus is preferred for studies of chronic compartment syndrome as discussed below. The slit catheter is less prone to coagulation, but air bubbles form more easily around the tip, which may reduce response time and invalidate a measurement. Overall, however, the wick and slit catheters are equally accurate and reliable for diagnosis of acute compartment syndromes.

Thresholds of Pressure and Time for Fasciotomy

Based on several clinical studies (31,33,35) and animal experiments (10,19,20), decompressive fasciotomy is recommended for normotensive patients with positive clinical findings and intracompartamental pressures >30 mm Hg when duration of increased pressure is unknown or thought to be ≥8 h after the initial trauma event. Undoubtedly, there exists a broad spectrum of tolerance to compartmental tamponade and ischemia among patients. However, considering the disastrous results of an unrelied acute compartment syndrome, we recommend that any compartment with stable or rising pressures >30 mm Hg be decompressed if clinical indications are positive. When clinical signs of a compartment syndrome are difficult to obtain (e.g., uncooperative or unconscious patient), fasciotomy should be performed on any compartment with pressure >30 mm Hg. Recent animal and clinical experiments indicate that, in some instances, the previously indicated thresholds for fasciotomy should be revised. Under conditions of low blood pressure, the fasciotomy pressure and time thresholds fall to 20 mm Hg and 6 h, respectively (47).

Using a reliable technique for assessing long-term muscle function in dogs (16), a significant decrease in contractile properties occurs 2 days after maintaining intracompartamental pressure at 40 mm Hg for 8 h. In the subsequent period of 7–28 days, isometric twitch torque and isometric tetanic torque return to their normal, precompartment syndrome values (30). Muscle fiber types in dogs, however, may be more resistant to ischemia than human muscle. Our studies of pressure thresholds for nerve dysfunction in normal human subjects provide im-
important insights into pressure and time thresholds for fasciotomy and emphasize the important role of systemic blood pressure. Finally, recent studies using hyperbaric oxygen (HBO) to treat impending compartment syndromes in dogs indicate that muscle necrosis and edema formation are significantly reduced following immediate (45) and 2-h delayed (46) treatments with HBO \( (p < 0.05) \). Clinically, however, HBO treatments are still experimental and their availability does not alter our recommended fasciotomy thresholds.

**Treatment**

The principles of treating compartment syndromes and specific surgical procedures for the arm, hand, and leg are presented in detail elsewhere (31). We recommend the curvilinear volar incision (4) for arm compartments and a double-incision fasciotomy technique (34) to decompress the anterior, lateral, posterior, and deep posterior compartments of the leg. Besides its usefulness in diagnosing acute and chronic compartment syndromes, intracompartmental pressure measurement is valuable in following the adequacy of treatment of compartment syndromes. During fasciotomy, the decrease in intracompartmental pressure is measured at the proximal and distal limits of the compartment to monitor the effectiveness of surgery. Moreover, intraoperative recording of pressure enables us to close skin incisions without again inducing tamponade. Dermotomy (skin incision) decreases pressure in a minor way, whereas fasciotomy lowers intracompartmental pressure to a level within normal range. Epimysiotomy also has little effect on pressure. With early fasciotomy, muscle color usually goes from gray to pink. In summary, intraoperative measurements of muscle pressures have allowed us to optimize fasciotomy procedures, avoid fibulectomy, and minimize the extent of skin incisions.

**DEVELOPMENT OF BETTER TOURNIQUET DESIGN**

**More Effective Compression of Deep Tissues Using Wider Tourniquet Cuffs**

Occlusion of blood flow by a pneumatic tourniquet is used routinely for orthopaedic surgery on the upper and lower limbs to provide a bloodless operating field. The common acceptance of the tourniquet as a surgical tool, however, should not suggest that its use is without risk. Complications are more common than may be appreciated, and some of the morbidity of tourniquet use is often unrecognized (25). Reported complications are muscle damage observed histologically, functionally, and biochemically and vascular problems such as deep vein thrombosis, arterial thrombosis, false aneurysm, fractured vessel walls, and postischemic edema (for review, see ref. 14).

The time period during which it is safe to apply a tourniquet on a limb is important in surgical practice (24,41). Similarly, the orthopaedist should know the minimum pressure necessary to occlude blood flow in a limb so as not to cause complications due to excessive compression. However, these minimum pressures for adequate hemostasis are not well defined. For a standard 8-cm wide tourniquet, recommended cuff pressures for the arm and leg range between 250–300 and 300–400 mm Hg, respectively. Most previous studies of tourniquet injury have focused upon the effects of ischemia in tissues \textit{distal} to the applied cuff. Importantly, however, recent studies of the effects of tissue pressures on muscles, nerves, and blood vessels directly beneath the tourniquet cuff suggest that these underlying tissues are more seriously jeopardized (14,28,38,44).

Distributions of tissue fluid pressure were examined beneath a standard pneumatic tourniquet in six upper extremities and six lower extremities of fresh human cadavera, disarticulated at the shoulder and hip, respectively, leaving muscle compartments intact. An 8-cm wide tourniquet cuff was applied at midhumerus or midfemur position. Tissue fluid pressure was always maximal in subcutaneous tissue at midcuff. Transmission of cuff pressures to deeper tissues was significantly less in the 40–52-cm girth thighs than in the 22–33-cm girth arms. At the four tissue depths studied, tissue fluid pressures fell steeply in a longitudinal direction near the cuff edge to levels near 0 at a point 1–2 cm outside each cuff edge (14). In another study (2), longitudinal and radial tissue fluid pressure distributions were determined beneath and adjacent to wide (12 and 19 cm) pneumatic tourniquet cuffs placed on intact human cadaveric arms and legs. Tissue fluid pressures exhibited relatively broad maxima at midcuff and in most cases showed no difference at the various depths studied. Therefore, wide cuffs transmit a greater percentage of the applied tourniquet pressure to deeper tissues than 8-cm cuffs, which are conventionally used for extremity surgery. Our results suggest that wider cuffs are required on thighs than on arms to provide a bloodless field during
surgery. Also, because they allow lower inflation pressures, wider cuffs may avoid underlying tissue injury associated with high cuff pressures.

**Relationship Between Pneumatic Tourniquet Width and the Inflation Pressure Required to Eliminate Blood Flow**

In another series of tourniquet experiments (29), we investigated the pressure required to eliminate blood flow (measured by a Doppler flowmeter) to the upper extremity using three different tourniquet widths in 10 normal volunteers. The clinical utility of a wide cuff (15.5 cm) was then assessed in a variety of unselected upper and lower extremity procedures, employing a reduced tourniquet inflation pressure.

A significant negative correlation was found between cuff width and the pressure required to eliminate arterial flow. The widest cuff eliminated blood flow at the lowest inflation pressure in all subjects. Specifically, the mean pressure that eliminated flow was significantly lower for the 15.5-cm wide cuff (104 mm Hg) than for the standard 8.0-cm wide cuff (123 mm Hg) and the narrow 4.5-cm wide cuff (150 mm Hg). Arterial occlusion pressure was also significantly correlated with arm circumference.

A wide (15.5 cm) cuff was used in 23 unselected upper and lower extremity surgeries while the patients’ blood pressures were recorded every 15 min. In most cases, initial inflation pressures were 150 and 200 mm Hg for upper and lower extremity surgeries, respectively. The surgeon then judged whether or not the bloodless field was adequate, and cuff pressure was increased if necessary. Clinical evaluation of the wide (15.5 cm) tourniquet was performed in 16 upper extremity and seven lower extremity cases. For upper extremity cases, adequate hemostasis was obtained in 69% of cases with maximum inflation pressures of 180 mm Hg using the wide cuff. For lower extremity procedures, 100% of patients had adequate operative hemostasis with inflation pressures of 200 mm Hg. Two patients requiring bilateral lower extremity tendon transfers had a wide tourniquet on one leg and a standard 8.0-cm tourniquet on the contralateral leg. Initial inflation pressure for both cuffs was 200 mm Hg, but inadequate hemostasis with the narrow cuff required inflation to 300 mm Hg. The wide cuff required no adjustments in inflation pressure.

Current recommendations for pressurization of pneumatic tourniquets used in surgery range from 250–300 mm Hg for the upper extremity and 300–400 mm Hg for the lower extremity. Our data suggest that significantly lower pressures produce a bloodless field for orthopaedic surgery if wider tourniquets are used. Lower inflation pressures may reduce the incidence neuropraxiae and postoperative muscle injury.

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