INTERSTITIAL GEL SWELLING PRESSURE IN HUMAN SUBCUTANEOUS TISSUE MEASURED WITH A COTTON WICK

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(Received 30 May 1973)

SUMMARY

1. A cotton wick probe has been used to measure the pressure in subcutaneous interstitial tissues of man.
2. The probe was inserted with minimal trauma into a plane of natural dissection at the level of the deep fascia in three sites: dorsum of the hand and foot, and the forearm.
3. The pressure was subatmospheric on every occasion (mean pressure: hand, \(-3.01\pm 0.50\) cmH\(_2\)O; foot, \(-3.54\pm 1.74\) cmH\(_2\)O; forearm, \(-2.41\pm 0.85\) cmH\(_2\)O).
4. Taking the three sites together, there was a positive correlation between wick pressure and locally measured tissue temperature (\(r = 0.55; P<0.01\)), but when each site was analysed separately the relationship was significant only in the hand.
5. Wick pressure rose when the subcutaneous tissues were warmed.
6. A negative correlation was observed between wick pressure from the forearm and the subject’s plasma colloid osmotic pressure (\(r = 0.73; P<0.01\)), but no such relationship was observed in the hand or foot.

Key words: wick pressure, interstitial gel swelling pressure, interstitial fluid pressure, plasma osmotic pressure, interstitial osmotic pressure.

The measurement of pressure in the interstitial space with a cotton wick was originally described by Scholander, Hargens & Miller (1968), who found a subatmospheric interstitial pressure (\(-3\) to \(-7\) cmH\(_2\)O) in a variety of animals. Their results have been confirmed by Strømme, Maggert & Scholander (1969), Ladegaard-Pedersen (1970) and Snashall, Lucas, Guz & Floyer (1971). Preliminary studies of wick pressure in man have been reported. Ladegaard-Pedersen (1970) found pressures in normal individuals to be higher (\(+3.8\) to \(-3.3\) cmH\(_2\)O; mean \(-0.86\)) than those from animals, and Snashall, Lucas, Guz & Floyer (1971) reported a range of

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The purpose of the present study has been to modify the catheter–wick method for use in man so that measurements can be made without bleeding. The normal range of pressures from three sites has been estimated and the relationship between wick pressure, tissue temperature and plasma protein osmotic pressure has been examined. Preliminary findings of this study have been reported (Snashall & Boother, 1972).

**METHOD**

**Wick and cannula**

The wick was composed of autoclaved long fibre (Sea Island) cotton wool. This material was described in detail by Snashall et al. (1971). Before being autoclaved, the wick was combed to remove shorter and weaker cotton fibres and held by a fine silk thread (6/0), which was then used to pull the autoclaved wick into the end of a sterile catheter and to secure it in position. The wick fitted loosely into the cannula and protruded approximately 5 mm from its end. Two types of plastic cannula were used. Initially, a polyvinylchloride cannula (A Cath., internal diameter 1.1 mm; Bard Davol Ltd) was used for a short series of experiments. Subsequently, however, a narrower cannula made of polyethylene (Plextrocan, internal diameter 0.7 mm; Portex Ltd) was employed. The cannula was connected by a length of flexible nylon tubing to a semi-conductor strain gauge (type S.E.L. 4/82; S.E. Laboratories Ltd). The whole system was filled with sterile physiological saline, care being taken to remove all air bubbles. After amplification, the pressure trace was displayed so that pressure changes of 1 mmHg could be detected. A side arm of the measuring system was attached to a saline-filled flexible plastic tube for measuring the zero reference pressure. With the transducer open to the side arm, the meniscus of the zero reference tube was held close to the wick at the estimated level of its mid-point. This was checked at 10 min intervals during the recording.

**Insertion of the wick**

The skin was anaesthetized with lignocaine (1%) containing adrenaline (0.001%). A stab incision 1–1.5 mm in length was made through the full thickness of the skin with a scalpel blade. Bleeding from this incision was minimized by the adrenaline. The probe was then inserted by blunt dissection through the subcutaneous tissue into a natural plane of dissection at the level of the deep fascia. The probe was advanced through this plane for 2–3 cm and then pulled back by a few millimetres to bring the wick in line with the cannula. The cannula was loosely taped in a position in which it appeared to be causing no distortion of the tissues. Pressure from the wick was then recorded, 20–30 min being allowed for complete equilibration. On removal, the wick was inspected for the presence of blood, and the degree of staining was allotted to one of four grades: 1, nil; 2, minimal—when the wick was yellow–orange in colour; 3, moderate—when at least part of the wick was red; 4, heavy—when the wick was uniformly reddened, usually with blood tracking up the cannula.

**Subjects and sites of measurement**

Observations were made on healthy volunteers of both sexes (mean age 33.3 years; range 16–75 years). The sites for insertion of the wick were the dorsum of the hand, the dorsum of the
foot and the medial forearm at the level of the elbow. In experiments on the arm or hand, the subjects were seated with the arm partially flexed at the elbow and resting comfortably on a table. The measuring site was approximately at heart level. Measurements on the foot were made with the subject lying supine on a couch. Owing to the possible influence of posture, measurements on the foot were made first thing in the morning when the subjects had been out of bed for less than 1 h.

Measurement of tissue temperature

When the pressure measurement had been completed and the wick removed, a needle thermocouple probe (type K8, copper–nickel; Ellab Ltd) was inserted through the same incision so that the tip was at the site previously occupied by the wick. The amplified signal was displayed and the system calibrated on each occasion by placing the needle in water at known temperatures. Temperature differences of 0.1°C could be discriminated.

Effect of heating on wick pressure

Three experiments were performed on the hand. Wick pressure was measured in the usual way and a steady control pressure recorded for at least 10 min. A needle thermocouple was inserted into the subcutaneous tissues several centimetres from the site of the wick. The hand was immersed in water at a steady temperature of 42.5–45°C. The skin overlying the wick was level with the surface of the water. Thermal expansion of the saline in the wick and connecting tubing would force fluid into the tissues. To prevent this the wick was exposed to the meniscus in the side arm adjusted to the level of the control wick pressure for the first 5 min after immersion in the water bath. Thereafter wick pressure was monitored continuously.

Measurement of plasma protein osmotic pressure

At the end of each measurement of wick pressure, 5 ml of venous blood was taken without occlusion and heparinized. The plasma was placed in a membrane osmometer attached to a semi-conductor strain gauge (S.E.L. 4/82). The semipermeable membrane that was used (type PM30; Amicon Ltd) was of high hydraulic conductivity and able to retain molecules of 30,000 mol. wt. and above. The development of pressure in the osmometer was prevented by increasing the air pressure above the plasma, using the transducer as a null indicator. At the point of equilibrium, the air pressure equaled protein osmotic pressure and was measured with a water manometer.

RESULTS

Insertion of the wick

In all subjects, the probe was inserted into the subcutaneous fascial plane, usually with little difficulty. Insertion was easiest in the hand and foot, particularly in elderly subjects, but it was more difficult to find the layer of dissection in the forearm. The degree of blood-staining of the wick was greatest in the forearm and least in the foot. Although slight blood-staining was attributed to pushing the wick through the skin incision, moderate or heavy staining was likely to be due to bleeding at the site of pressure measurement and the values obtained from these wicks were therefore rejected. Six out of twenty-two pressure measurements from the hand, six out of twenty-three from the forearm and one of fifteen from the foot were rejected in this
Fig. 1. Wick pressures recorded from hand, forearm and foot: •, values from unstained or slightly stained wicks; ○, values from moderately or heavily stained wicks (excluded from further analysis). Mean values from unstained and slightly stained wicks are indicated by interrupted lines.

Way. It should be noted, however, that the pressures from moderately and heavily stained wicks usually fell within the normal range observed with the less-stained wicks (Fig. 1).

Wick-pressure measurements have been performed in this laboratory over a period of 2 years. Side-effects have been limited to one case in whom the site of measurement became inflamed and presumably infected. This resolved spontaneously in a matter of days.

**Wick pressures at different sites**

Wick pressures measured in the hand, foot, antecubital fossa and forearm showed differences of mean value and scatter (Fig. 1; Table 1). The pressure was higher in the forearm than in the hand.

**Table 1. Wick pressures measured in hand, forearm and foot**

<table>
<thead>
<tr>
<th>Site</th>
<th>No. of observations</th>
<th>Wick pressure (cmH₂O)</th>
<th>Tissue temperature (°C)</th>
<th>Plasma protein osmotic pressure (cmH₂O)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Hand</td>
<td>16</td>
<td>-3.0</td>
<td>0.5</td>
<td>31.7</td>
</tr>
<tr>
<td>Forearm</td>
<td>17</td>
<td>-2.4</td>
<td>0.9</td>
<td>34.0</td>
</tr>
<tr>
<td>Foot</td>
<td>14</td>
<td>-3.5</td>
<td>1.7</td>
<td>28.8</td>
</tr>
</tbody>
</table>
Fig. 2. Wick pressures obtained by using polyethylene and polyvinylchloride (PVC) cannulae in the hand.

Fig. 3. Relationship between first wick-pressure measurement (cmH₂O) and the second made in the same or a symmetrical site in the same subject.
Fig. 4. Relationship between wick pressure and tissue temperature in three sites: $\circ$, hand; $\bullet$, foot; $\triangle$, forearm.

![Graph showing relationship between wick pressure and tissue temperature in three sites.](image)

Fig. 5. Effect on wick pressure and tissue temperature in one subject (R.C.) of immersing the hand in water at 45°C.

![Graph showing the effect of immersing the hand in water at 45°C.](image)
foot or hand ($P<0.02$ and $0.05$ respectively; Mann-Whitney U-test, two-tailed). The scatter of values in the hand (coefficient of variation $SD/\bar{x} = 0.165$) was less than in the forearm ($SD/\bar{x} = 0.338$) or foot ($SD/\bar{x} = 0.49$).

Pressures measured from the hand by using the larger polyvinylchloride catheter ($-1.68 \pm SD 0.46 \text{cmH}_2\text{O}$) were significantly higher than pressures from the same site measured with the polyethylene catheter ($P<0.01$) (Fig. 2).

**Repeat observations on the same individual**

First and second measurements from the same or a symmetrical site on the same individual correlated significantly (Fig. 3; $r = 0.74$; $0.05>P>0.01$). The interval between measurements varied from 1 day to several weeks. When this series of paired observations were compared by using the randomized test for matched pairs (Siegel, 1956) the difference between first and second measurements was not significant ($P>0.2$).

**TABLE 2. Effect of temperature on wick pressure in the hand**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Wick pressure ($\text{cmH}_2\text{O}$)</th>
<th>Tissue temperature ($^\circ\text{C}$)</th>
<th>Water temperature ($^\circ\text{C}$)</th>
<th>Wick pressure ($\text{cmH}_2\text{O}$)</th>
<th>Tissue temperature ($^\circ\text{C}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.C.</td>
<td>-2.1</td>
<td>32.2</td>
<td>45</td>
<td>-0.2</td>
<td>39.8</td>
</tr>
<tr>
<td>F.B.</td>
<td>-2.2</td>
<td>33.1</td>
<td>42.5</td>
<td>-0.5</td>
<td>38.9</td>
</tr>
<tr>
<td>G.S.</td>
<td>-3.1</td>
<td>25.0</td>
<td>43.8</td>
<td>-1.2</td>
<td>35.6</td>
</tr>
</tbody>
</table>

**Wick pressure and tissue temperature**

The subcutaneous tissue temperatures were found to be lower in the foot than in the hand or forearm (Table 1). Temperature therefore varied between these sites in the same direction as wick pressure. There was a significant positive correlation between wick pressure and local tissue temperature when values from the hand, foot and forearm were pooled ($r = 0.55$; $P<0.01$) (Fig. 4). A similarly significant relationship was seen when values from the hand are taken separately ($r = 0.57$; $0.05>P>0.01$), but not when values from the foot ($r = 0.31$; $P>0.05$) or forearm ($0.49$; $P>0.05$) were analysed separately. Variation of temperature between individuals was greatest in the foot and least in the forearm.

**Effect of heat on wick pressure**

Immersion of the hand in warm water was followed by a rise of subcutaneous tissue temperature and wick pressure (Table 2; Fig. 5). The time taken for the wick pressure to rise and equilibrate at the higher level varied from 25 to 30 min. In one subject (G.S.), water at 42.3°C had no effect on pressure over 25 min. Raising the temperature to 43.8°C was followed by a rise of 1.9 cmH$_2$O in 14 min, at which level the pressure remained steady for 22 min. In two experiments the pressure was monitored after removal of the hand from the water. A fall in pressure was seen in one case (Fig. 5). In the other, the wick pressure rose to atmospheric pressure. This wick had been in the tissues for more than 2 h and there were early signs of
inflammation, with redness and tenderness of the overlying skin. No inflammatory changes were seen in the other subjects. In each experiment the blood-staining of the wick was slight.

**Wick pressure and plasma protein osmotic pressure**

Plasma protein osmotic pressure correlated negatively with wick pressure measured from the forearm \((r = -0.73; P<0.01)\) (Fig. 6). No correlation was seen between osmotic pressure and wick pressure from the hand \((r = 0.12)\) or the foot \((r = 0.16)\). When values from the three sites were pooled there was no significant correlation \((r = 0.18)\).

![](image)

**Fig. 6.** Relationship between wick pressure measured in the forearm and plasma colloid osmotic pressure.

**DISCUSSION**

The nature of the pressure measured by the wick remains controversial. Most workers have assumed that the wick measures the hydrostatic pressure of interstitial fluid (Scholander *et al.*, 1968; Strømme *et al.*, 1969; Ladegaard-Pedersen, 1970; Guyton, Granger & Taylor, 1971), but have ignored the fact that the interstitium has a gelatinous consistency in which fluid, as such, cannot be demonstrated (Clark & Clark, 1933; McMaster & Parsons, 1939; Friederici, 1968). The wick pressure must therefore be related to interstitial gel, rather than fluid.

The gel structure results from the entrapment of mucopolysaccharide macromolecules in a network of collagen fibrils (Fessler, 1960; Laurent, 1972). In loose connective tissue the most important mucopolysaccharide is hyaluronic acid. The osmotic pressure of the mucopolysaccharides holds water in the interstitium; the mucopolysaccharide is, in turn, immobilized in the interstitium by entanglement with adjacent molecules and with the collagen fibrillar network of the interstitial space. Snashall *et al.* (1971) presented evidence that the wick measures the 'swelling pressure' of the interstitial gel—a pressure due largely to the osmotic pressure of trapped mucopolysaccharide macromolecules. Saline is drawn out of the wick by this osmotic force until the negative hydrostatic wick pressure balances the swelling pressure of the inter-
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Interstitial gel. This ‘swelling’ pressure may be less than the colloid osmotic pressure of the macromolecules in the gel owing to the gel’s elastic resistance to stretching. The osmotic pressure of plasma proteins in the gel contributes little to the wick pressure as these molecules can diffuse from the interstitium into the wick with little restriction (Snashall et al., 1971).

Wiederhielm (1971) made direct measurements of the swelling pressure of excised rabbit skin in an osmometer fitted with a membrane permeable to plasma proteins. The pressures produced in the osmometer (−2.6±1.6 cmH₂O) were quantitatively similar to the subatmospheric pressure reported with the wick method. It was thought that this pressure was due to the osmotic activity of tissue mucopolysaccharides.

Snashall (1973) showed that in Wharton’s jelly of the human umbilical cord, wick pressure correlates significantly with both hyaluronic acid content and the degree to which the material swells in saline.

The catheter–wick method is well suited to the measurement of interstitial pressure in man. In the sites studied the pressure was consistently subatmospheric to the extent of −1.0 to −5.0 cmH₂O, in agreement with the preliminary findings of Snashall et al. (1971). This pressure range is also close to that described in the dog (Ladegaard-Pedersen, 1970), the rabbit (Prather, Bowes, Warrell & Zweifach, 1971) and the rat (Snashall et al., 1971), but it is higher than the pressures reported by Stromme et al. (1969) in rats, mice and guinea-pigs, which averaged −6 to −7 cmH₂O.

Satisfactory measurement of wick pressure can be made only in non-traumatized tissue. With the catheter–wick technique this can be achieved if the probe is inserted into a natural plane of dissection. Such a plane is found at the deep fascia which in most animals is found immediately beneath the skin, but in man is separated from the skin by a layer of subcutaneous tissue, which is mainly fat. Cannulation of the deep fascia is therefore much more difficult in man than in animals. If the wick is inserted beneath the skin of an animal by using the Seldinger technique, it will automatically slip into the deep fascial plane and a successful recording can be made. In man, however, this technique will deliver the wick into subcutaneous fat with inevitable haemorrhage, tissue damage and distortion. This can be avoided if sites are chosen where the deep fascia is fairly superficial. In the dorsum of the hand or foot, and also around the elbow, the plane can be cannulated with little difficulty by blunt dissection from a small skin incision, the wick being positioned several centimetres from the traumatized skin. Advancing the probe beneath the skin in this way is almost painless.

Differences in method of insertion probably explain the discrepancies between pressures measured in this study and those of Ladegaard-Pedersen (1970), who reported wick pressures in man over the range +3.8 to −3.3 cmH₂O. He used a Seldinger technique for inserting the probe. We are not told the site of insertion but bleeding may well have been a problem since he found it necessary to soak the wick in adrenaline (0.001%) before insertion.

The pressures recorded in preliminary experiments using a polyvinylchloride cannula were significantly higher than those recorded with a smaller and more rigid polyethylene cannula. The change to the polyethylene cannula was made because the polyvinylchloride cannula could only be advanced through the tissues with difficulty, so that many recordings had to be made with the wick less than 1 cm from the traumatized and injected tissue at the site of insertion. This is the most likely explanation of the higher pressures obtained with this cannula. Clearly one must be very cautious in comparing the values obtained with the wick method by different workers unless their techniques and equipment are the same.
The findings that the wick pressure was lowest in the foot and highest in the forearm is the reverse of what one might expect considering the influence of gravity. Clearly, other factors must play a part, and the present work suggests that tissue temperature may be important. The correlation between tissue temperature and pressure was found to be significant in the hand and also significant when the data from the three sites were pooled. The correlation in the forearm did not attain statistical significance but this may be due to the limited range of temperatures found in the forearm (range = 3.4°C) in contrast to the hand (range = 9°C). The temperature range in the foot was 10.7°C, but despite this no significant correlation was seen. Warming the subcutaneous tissues of the hand caused a rise of wick pressure. Heat causes arteriolar dilatation, raising capillary pressure and favours filtration into the tissues; relaxation of precapillary sphincters increases the area of the capillary bed available for filtration. Landis & Gibbon (1933) demonstrated that heating a limb to a skin temperature of 44–45°C doubled the rate of capillary filtration at any given venous pressure. As a tentative hypothesis we suggest that capillary pressure tends to be higher in warmer tissues, leading to higher interstitial pressure.

Difference of pressure between different measuring sites may also be due to differences of tissue tension. Several wick-pressure measurements have been made in the antecubital fossa, where pressures were much lower than elsewhere (mean -6.1 cmH₂O ± SD 1.98) and were dependent upon the degree of flexion at the elbow. The skin tends to recoil from the natural hollow of the antecubital fossa and the tension within the tissues in this area holds the skin in the fossa. This tension in the subcutaneous tissues will be transmitted to the wick and is the probable explanation for the very low values found in this site. In positioning the probe in the tissues at any site it is essential to ensure that there is as little tissue distortion as possible.

The osmotic pressure of the plasma proteins, acting across the semipermeable membrane of the capillary endothelium, is an essential factor in the maintenance of the fluid-free state of the interstitial space. In conditions of hypoproteinaemia there is a tendency for fluid to leave the vascular compartment and move into the interstitial space causing oedema. In fact, while a good correlation between wick pressure and osmotic pressure was seen in the forearm, no correlation was apparent in the hand or foot. The wide temperature ranges of the hand and foot might tend to obscure a relationship with osmotic pressure, but when a correction for temperature was made, the degree of correlation was not improved.

Clinical applications of this technique have yet to be defined. Observations to date show that wick pressure rises to atmospheric and above in oedema. In dehydration, the pressure is low to a degree dependent upon the degree of extracellular fluid depletion. It has not been determined if the method is sufficiently sensitive to be of value in the assessment of dehydration and overhydration or in monitoring the treatment of these conditions. In addition, the method may be of value in the assessment of a variety of peripheral and central circulatory disorders. These possibilities are at present under investigation.

ACKNOWLEDGMENTS
We thank Professor J. B. L. Howell and Dr G. M. Sterling for their help and encouragement throughout this study. P.D.S. is the recipient of a grant from the British Heart Foundation.

REFERENCES
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