

Human skin battery potentials and their possible role in wound healing

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Accepted for publication 10 March 1983

SUMMARY

Measurements of transcutaneous voltage have been made on seventeen normal volunteers. The results show the presence of 'skin battery' voltages comparable in size to those previously reported for amphibian and mammalian skin. No correlation was found between battery voltage and age or sex in the group studied, but consistent anatomical variations were observed. The possible role of these voltages in the natural wound healing process is discussed.

The ability of several species, for example some amphibians, to regenerate lost body parts is well documented. Recent work has shown the presence of natural direct currents in the vicinity of regenerating amphibian limbs driven by so-called skin batteries (Borgens, Vanable & Jaffe, 1977a; Jaffe & Nuccitelli, 1977). These currents have been measured with the aid of a vibrating probe, a device which enables the measurement of current densities entering or leaving a biological source immersed in an aqueous conducting medium and overcomes the problems of d.c. electrode offset potentials (Jaffe & Nuccitelli, 1974). It has been shown that these currents are essential for normal regeneration and that their reversal will induce degeneration. The source of the currents appears not to be related to motor or sensory nerves as they are also present in denervated limbs. The currents have been shown to come from the epidermis and can be altered by changing the sodium concentration of the medium or by blocking the sodium uptake by the skin with amiloride or methyl ester of lysine (Borgens *et al.*, 1977a). It has also been shown that if currents are artificially introduced into species such as the frog, which are not natural regenerators, then partial regeneration of an amputated limb will be initiated (Borgens *et al.*, 1977b). These regenerated frog limbs contain a cartilage core, nerve fibres and mature thorn-shaped epidermal papillae as would be found in a normal adult frog limb.

It has been reported that children's fingertips will regenerate with excellent cosmetic and functional results if treated conservatively after accidental amputation distal to the distal

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inter-phalangeal joint (i.e. no suturing, skin grafting or other surgical procedures performed) (Illingworth, 1974; Rosenthal, Reiner & Bleicher, 1979). With the aid of a hand-held vibrating probe (Barker, 1981) it has been shown that amputated fingertips in children produce current densities of up to $35 \mu\text{A}/\text{cm}^2$ flowing for several days during the regeneration process, similar to those demonstrated in amphibians (Illingworth & Barker, 1980).

Further investigation of the source of these currents in mammalian skin has been performed on the foot pad of the guinea-pig (Barker, Jaffe & Venable, 1982). This area was chosen because of the absence of sweat glands and hair follicles, both of which are known to affect the electrical properties of the skin (Fowles & Venables, 1970). Measurements showed that as in amphibian skin, a voltage of approximately 40 mV exists across the epidermis with the stratum corneum always negative with respect to the dermis. These batteries have been shown to lie within the epidermis below the stratum corneum but above the basement membrane. In addition it was found that the potential difference across the epidermis in intact skin could drive d.c. currents into epithelial wounds with an amplitude of approximately $1 \mu\text{A}$ per mm of wound perimeter. With the use of microelectrodes a voltage gradient was shown to exist in the intact skin within 1 mm of the wound edge, reaching as high as 200 mV/mm.

The object of this study was to determine whether human skin possesses similar battery potentials to those already demonstrated in other mammals and amphibians, and whether there is any variation with anatomical site, age or sex.

METHODS

Seventeen normal subjects (eight females, nine males) with an age range of 22–70 years were studied. Skin potentials were recorded between a reference electrode in electrical contact with the dermis and a mobile electrode at 121 predetermined positions on the skin. We have been able

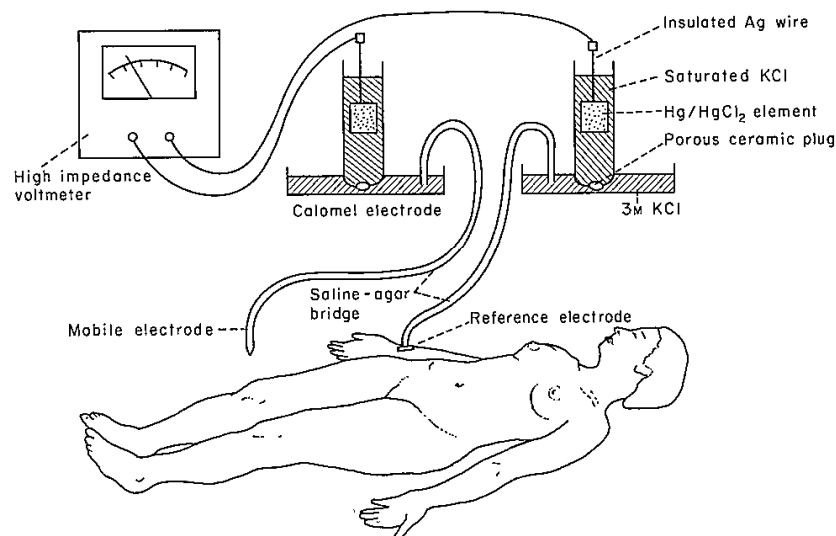


FIGURE 1. Schematic diagram of the recording apparatus.

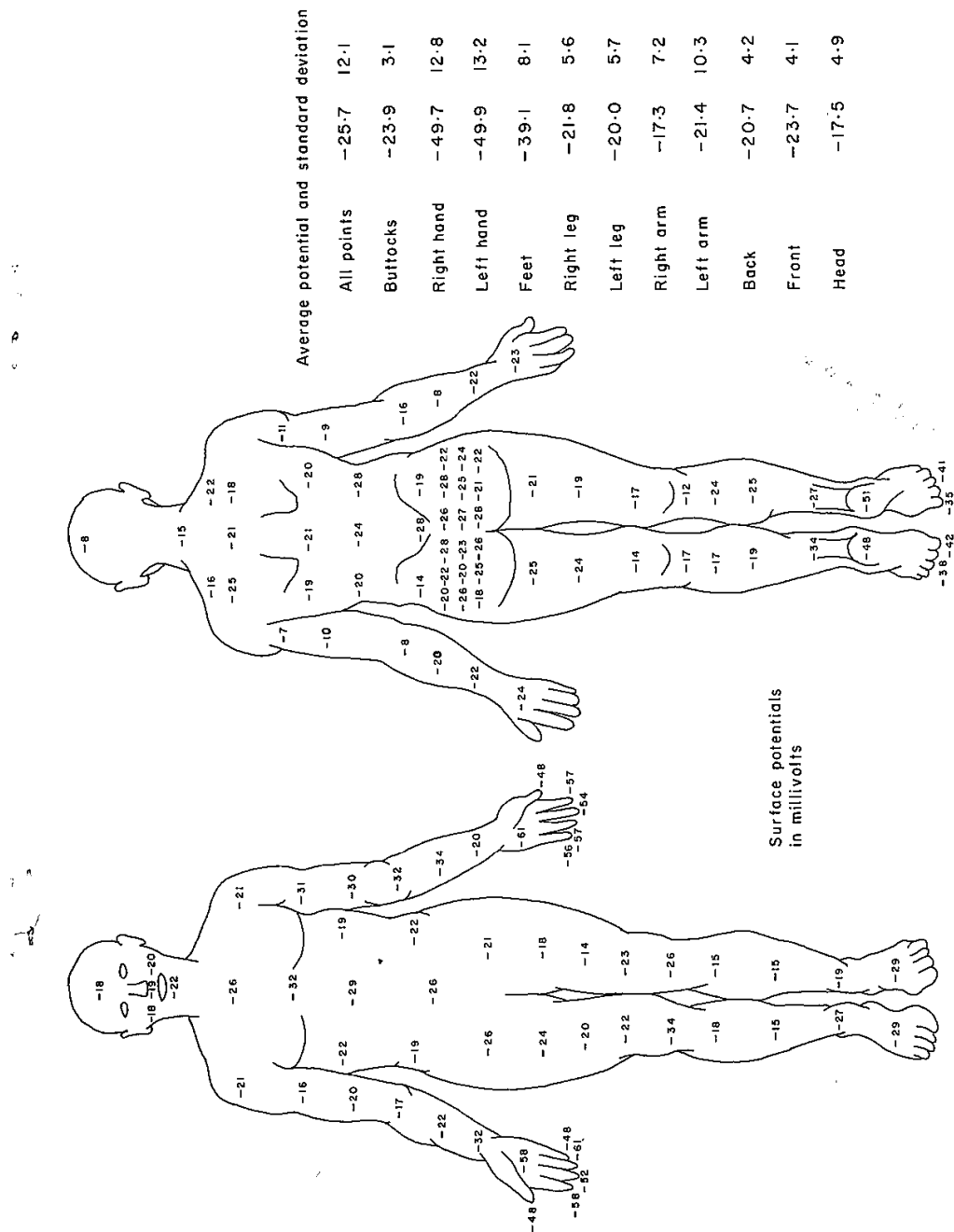


FIGURE 2. Potentials recorded from a typical subject, a man aged 29.

to show, by experiments on ourselves, that there is less than a 1 mV potential difference between any two dermal sites making contact with the human body by means of measurements made at multiple sites making contact with the dermis. Therefore only one dermal reference connection is required, which allows a mobile surface electrode to measure the transcutaneous potential beneath it without the need for multiple skin punctures. We found that an effective dermal contact could be simply obtained by the use of a Heaf gun on the volar aspect of the forearm, with the reference electrode placed over the puncture site. The integrity of this dermal contact could be checked during the experiment by placing the mobile electrode on another Heaf gun site wound which then recorded a zero potential difference.

The electrodes consisted of cotton wool soaked in physiological 0.9% saline, connected by means of a saline–agar bridge to calomel electrodes immersed in 3 M KCl. These bridges were made by filling plastic tubes, 120 cm long and 3 mm internal diameter with a solution of 1.5 g of agar dissolved in 100 ml of 0.9% saline.

Silver/silver chloride electrodes were not chosen because of the problems of electrode offset potential and because they are sensitive to the concentration of chloride ions. Calomel electrodes have the advantage of a stable electrode offset potential of less than 1 mV, and the saline–agar bridge allows chemical isolation of the electrodes from the patient. A high impedance voltmeter ($10^{12}\Omega$) was chosen to avoid measurement errors due to skin impedance which can be as high as $10\text{ M}\Omega/\text{cm}^2$ in areas of ichthyotic epidermis.

The measurements were made with the subject supine in an air-conditioned room. The predetermined electrode sites were chosen to cover most of the skin surface and were consistent in all subjects. The mobile electrode was held with minimum pressure to maintain contact with the stratum corneum via a drop of saline covering an area of approximately 10 mm^2 . Fig. 1 shows a schematic diagram of the recording apparatus.

RESULTS

Negative potentials from the stratum corneum with respect to the dermis were recorded consistently at all sites examined and in all individuals. The average potential over all sites and subjects was -23 mV with a standard deviation of 9 mV .



FIGURE 4. Average potentials recorded for all sites related to age and sex of subjects.

Fig. 2 shows a map of the recordings made from a typical subject and Fig. 3 shows the average potentials at each site for all subjects examined. The results showed a consistent anatomical variation, with the battery voltages recorded from the hands and feet significantly higher than elsewhere. Fig. 4 shows the average potentials recorded for all sites related to age and sex of the subjects. For the age range examined there appeared to be no significant correlation between skin battery voltages and age or sex. However, a consistent variation of battery potential with anatomical site was found to exist. Areas such as the hands and feet have relatively high battery potentials whereas the back and upper arms have relatively low potentials. All subjects demonstrated this general variation.

DISCUSSION

The measurements have been made across the skin, that is to say between an electrode in contact with the stratum corneum and an electrode in contact with the dermis. Electrical properties of the skin have been used for many years in psychological studies to assess emotional state. The two main measurements used have been the electrical resistance of the skin, as an indicator of sweat gland behaviour, and surface potential measurements, either between two intact sites or between an intact site and an abraded area (see for example, Christie, 1981). By using a transcutaneous recording system we have obtained results which will combine potentials due to structural characteristics of the epidermis and due to electrical activity originating from eccrine sweat glands (Wilcott, 1966). Hence a correlation between skin battery voltage and sweat gland distribution might be expected to exist. The higher voltages measured over the palms of the hands and soles of the feet are compatible with this, but the relatively low voltages recorded on the forehead suggest there may also be substantial variation in sweat gland independent 'basal' skin potential levels. A possible explanation for this regional variation may be epithelial thickness. Additionally, it has been shown that there is sharp depression of transcutaneous potentials in hairy regions of mammalian skin probably due to current leakage along hair follicles (Barker *et al.*, 1982). Hence, the anatomical variation of skin battery potentials is a complex combination of several factors and does not appear to be related to dermatone distribution. The apparent lack of correlation between battery potentials and age up to 70 years is surprising in view of the known ageing process of the skin, with diminishing epidermal thickness and decreased sweat production.

The potentials we have measured are of a similar magnitude to those already demonstrated in other mammals and amphibians, and which have been shown to generate large voltage gradients

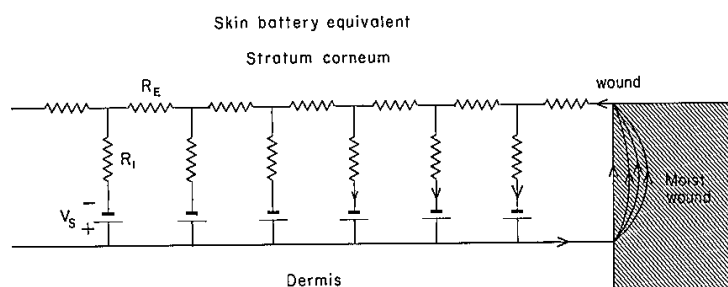


FIGURE 5. Schematic representation of current flow at a wound edge.

at the edges of epithelial wounds (Barker *et al.*, 1982). For practical reasons, it has not been possible to measure voltage gradients in the vicinity of experimental wounds in humans. However, the fingertip current measurements made in children showed that human skin batteries are capable of driving substantial currents into wounds and voltage gradients similar to those measured in the guinea-pig can be expected to exist. These voltage gradients may have a significant effect on cellular function at wound margins. Fig. 5 shows a schematic representation of current flow at a wound edge.

One of the important mechanisms of wound healing is the process of re-epithelialization. Studies using pigs have shown that the cells migrating across a wound come from a strip of intact skin approximately 0.5 mm wide around the wound (Winter, 1964) and it is in this area that substantial voltage gradients occur. The mechanisms by which cells migrate are not understood but one possibility is that they may move under the influence of voltage gradients either passively, for example by electrophoresis, or by active polarization of charged molecules in the cell membranes. Some cells are known to become orientated in voltage gradients as low as 7 mV/mm (Hinkle, McCaig & Robinson, 1981) which is considerably lower than the expected voltage gradients at a wound margin.

The existence of epidermal batteries and the resultant voltage gradients at the edges of intact skin may also explain the phenomenon of epiboly in organ culture whereby epidermal cells migrate around the edge of the culture and subsequently grow back into the dermis (Reaven & Cox, 1965). This cell movement would appear to be along the expected path of current flow.

It is tempting to speculate as to whether skin batteries are connected with acupuncture sites. Whilst there is no evidence of this it can be expected that a needle which penetrates the epidermis will cause local currents to flow and these may have a similar effect to those deliberately applied in electro-acupuncture.

There has been some clinical evidence that electrical stimulation of wounds may encourage wound healing (Wheeler *et al.*, 1971) and indeed this may act by enhancement of the skin batteries. If wound healing is mediated by electrical signals, at least in part, the possibility exists of electrically stimulating wounds to enhance the healing process.

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