VASCULAR REACTIONS OF THE SKIN TO INJURY. Part VIII. The resistance of the human skin to constant currents, in relation to injury and vascular response¹.

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In a series of recent papers Ebbecke(1) has described a number of interesting observations upon the resistance of the human skin to galvanic currents, and comes to conclusions that, if true, would be of far-reaching importance to the study of vascular responses of the skin to various stimuli.

He points out that it has long been recognised that estimates of skin resistance obtained by means of galvanic currents are very much higher in quantity than are the true resistances as measured by alternating currents of high frequency. Using small contacts, the alternating current measures the resistance in terms of a few thousand ohms; using constant currents, values of as much as 500,000 ohms are commonly obtained. The high values shown by the galvanic current Ebbecke probably rightly attributes to polarisation. He finds that these high resistances are broken down by one of two chief procedures, namely, either by the continued passage of the galvanic current, when the latter is employed in sufficient strength ultimately to produce whealing of the skin (local galvanic reaction), or by rubbing the skin. He believes that change in the epidermal cells is responsible for this lowering of resistance, and arrives at this conclusion by a process of elimination. The change is not due to altered vascularity, because it occurs equally well when the circulation to the skin is stopped or in the skin of bodies investigated some hours after death. In the last circumstance Ebbecke believes that the epidermal cells are still living and capable of reacting to stimulation. The sweat glands are excluded mainly on the ground that the local galvanic reaction can be obtained conspicuously upon the skin of the forearm, where sweat glands are scanty, but fails on the hand, where sweat glands are numerous. These two exclusions leave the epidermis for consideration. He considers the

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horny layer of the skin and describes observations, which, so he believes, show that when this is particularly dry it may offer much resistance, and that its resistance may fall if the electrode is pressed heavily upon it or if the electrode is wet. In both instances altered resistance is attributed to increased moisture of the horny layer. This change in the resistance of the horny layer introduces an error that may conceal the more significant changes in the cellular layers that lie beneath it; for this reason Ebbecke describes it and his attention then fastens upon the living epidermis. To explain the lowering of resistance to galvanic currents, he supposes that the act of rubbing the skin, or of passing a galvanic current through it, excites the epidermal cells to activity. This activity is regarded as associated with a dispersion of the polarisation charge and with an increased permeability of the cell membranes; thus stimulation of the skin is brought into line with Bernstein's hypothesis, as this is applied to muscle and nerve. Further consideration of his conclusion, that lowered resistance to galvanic currents is brought about in this way, is important from several standpoints. Upon it Ebbecke mainly bases a hypothesis that vascular changes in the skin and whealing, consequent upon the passage of galvanic currents, or in response to mechanical stimulation, results from the release of cellular metabolites, this release being a consequence of increased permeability. One of us, working in conjunction with Grant(2), came independently to a similar conclusion, in respect of the intervention of metabolites in reactions to injury, though from observations of a distinct kind.

When we became aware of Ebbecke's work upon skin resistance, we were inclined to the view that his observations might constitute important evidence in favour of the reaction of the vessels to cellular products, and that they might materially help to establish, as a conclusion, the idea we were postulating. It also seemed to us that Ebbecke's method and conclusions, if sound, might be of great value as a basis in investigating the time-relations of the skin's cellular activity; that it might be possible to find further parallelisms between the skin's capacity to conduct constant currents and the response of its vessels to cutaneous injuries; and that his work would enable us to measure accurately the period, short or long, over which cellular activity in response to various injuries lasts, and to assess more accurately the intensity of the reactions.

We have been disappointed from all these points of view, and an initial hesitation in accepting Ebbecke's attractive interpretations of his experiments has grown into a conviction that they are unsound. The following observations are selected to show our grounds for this conviction.

The visible reaction of the skin to a weak galvanic current. In the last paper of the series referred to Ebbecke uses the following method. A battery of 4 volts is connected to the body by means of two electrodes. The one, an indifferent electrode, consists of a vessel of water, and into this a hand is plunged. The other consists of a fine needle; this is laid very carefully so that its point lies on the skin of the forearm. When the current is made, and the needle point constitutes the kathode, little or no current is at first registered as passing through the skin. In less than 15 seconds the current increases abruptly and reaches a value of 70-100 microamperes, and the subject experiences burning pain at the needle point. When the needle is removed, a minute shiny or slightly brown spot is seen on the skin. This is soon associated with reddening, and before long the skin rises to form a small wheal, like that produced by the bite of an insect. The effect is obtained only if the needle point is kathodal, and Ebbecke shows that the lowering of resistance in this experiment occurs only at the kathode, and he concludes that the essential kathodal action consists of an increased permeability of the epithelial cells.

We have repeated these experiments and agree with the results he describes in all their details; but we place a different interpretation upon them. If the current is led through the skin in the manner described, and the needle point is watched microscopically¹, we find that at or about the instant when the passage of the current becomes painful, minute bubbles of gas are seen to form around the needle point and others collect within the horny layer of the skin, lifting and disrupting it. In a large number of experiments there has been no exception to this statement, and we have never succeeded in obtaining subsequent whealing of the skin with currents of insufficient intensity to produce this visible electrolysis of the tissues. The little shiny or brownish mark on the skin that Ebbecke describes is the result of the disruption of the superficial layers of the skin by these gas bubbles. We do not go so far as to deny that the passage of a constant current may not alter the activities of the epidermal cells, with associated changes in their permeability; but it is clear that the cutaneous reaction described by Ebbecke follows a gross injury of the skin; and it will become evident later that the lowering of resistance that occurs is not due to the cause to which he ascribes it, but to an electrolysis associated with mechanical injury of the skin's horny layer.

¹ We have used Greenough's binocular microscope and 60 magnifications for the purpose.

Relation between the galvanic resistance and the visible skin reaction.

Mechanical stimulation. One hand is placed in a vessel of normal saline in which a piece of silver foil coated by electrolysis with silver chloride is immersed. The second electrode is placed on the other arm; it consists of a glass tube of 4 millimetres internal diameter, filled with gelatine, made up into a firm jelly with normal saline and having embedded in it a similar sheet of silver foil coated with silver chloride. These electrodes show no detectible polarisation phenomena. A current from a 2-, 4- or 6-volt battery is led through this circuit, and the current recorded rarely exceeds 5 microamperes¹, providing that the small electrode lies on healthy and undisturbed skin. It has been our habit always to moisten the skin so tested with a drop of normal saline a minute before applying the contact. Removal and replacement of the contact has little or no influence upon the amount of current flowing. If the current at first amounts to or exceeds 5 microamperes, it is often found that the apparent resistance tends to become lower after an interval of several minutes, but if, as is usual, the preliminary reading is decidedly less, this tendency for the resistance to fall is usually absent or trivial.

If the contact is removed and the skin vigorously rubbed or firmly stroked with a blunt point, and the contact replaced at once, the current now flowing is found to have risen abruptly, though by varying amounts. The resistance, originally of 100,000 to 1,000,000 ohms, falls to such values as 50,000 and 10,000 ohms, exceptionally even to 5000 ohms.

| Before | After stroking | | | | | | |
|----------|----------------|--------|---------|---------|---------|--------|--|
| stroking | Immediate | l min. | 2 mins. | 3 mins. | 4 mins. | 5 mins | s. Remarks |
| 0.22 | _ | 25 | 24 | 36 | 30 | 27 | Normal skin. Heavy stroke. Skin unbroken. Local red reaction only |
| 3∙0 | 600 | 625 | 635 | 600 | 600 | 600 | Normal skin. Heavy stroke; flakes of horny layer torn off. Local red reaction only |
| 0.25 | 17 | 22 | 20 | 20 | 21 | 21 | Normal skin. Heavy stroke. Very slight whealing |
| 0.25 | | 400 | 400 | 420 | 450 | 450 | Normal skin. Heavy stroke. Slight whealing |
| ·0·7 | _ | 2.0 | 2.5 | 2.5 | 2.5 | _ | Case of urticaria factitia. Moderate stroke. Full wheal in 2 mins. |

Observation 1. Skin of forearm connected to battery of 4 volts. Current readings in microamperes. Five subjects.

¹ Our object in changing the voltage is merely to obtain a definite reading of current with our meter in all cases; the meter is sensitive to $\frac{1}{4}$ microampere, and it often happens that with 2 volts no movement of the needle is recorded.

The observation agrees precisely with Ebbecke's findings and we agree with him in stating that the reaction is unchanged when the circulation to the limb is stopped. There is, however, no relation between the fall of resistance and the reaction that follows. A heavy stroke may lower the resistance to 1/200 of what it was originally and result in a local red reaction only. In the case of a susceptible skin, a stroke of moderate firmness may produce a full wheal and the fall of resistance may be inappreciable by comparison. If flakes of the horny layer are carried away by the stroke, the fall of resistance is profound; yet the reaction of this skin may be comparatively slight.

If, instead of rubbing the skin, we employ a fine needle, and prick the skin, similar falls of resistance occur. It occurs with regularity and is immediate, and it will happen with needle pricks of surprising lightness.

Observation 2. Skin of forearm connected to battery of 2 volts. Current readings in microamperes. Four subjects.

| Before | After pricking | | | | | |
|-------------|----------------|--------|---------|---------|---------|--|
| pricking | Immediate | l min. | 2 mins. | 3 mins. | 4 mins. | |
| 1.25 | 145 | 125 | 80 | 70 | 65 | |
| 4 ·5 | 75 | 95 | 80 | 95 | 85 | |
| 1 | 125 | 100 | 100 | 100 | 110 | |
| 1 | 65 | 50 | 50 | 50 | 45 | |

The prick necessary to break the resistance is far less than sufficient to draw blood from the skin, and often it is unaccompanied by a sensation of pricking or by visible response of the vessels; it is sufficient apparently for the needle point to pass into the horny layer of the skin. Here again the effect is obtained if the circulation to the skin has been stopped previously. If the skin has been lightly pricked in a few places, these places are easily detectible by passing the contact over the skin some while afterwards; the instant such a point is reached, the galvanometer needle moves rapidly from almost zero to a reading of 70–150 microamperes.

Exactly similar effects are to be obtained upon skin removed from the body. The skin we have used has been taken from post-mortem subjects, within a few hours of death or in some cases 24 or more hours after death; in the last cases the bodies have lain in a cold chamber. The capacity of such skin to conduct increases, so that the values for the current flow before and after pricking gradually approach each other as time elapses and as decomposition occurs in the skin. The effect of the prick on skin conduction is not dependent upon survival of the cutaneous cells, as is clearly shown in the following way. The skin is immersed in 40 p.c. formaldehyde for 30 minutes or longer; it is taken out, the surplus fluid mopped away, and the skin allowed to dry a little at room temperature until it presents no trace of surface moisture and until drops of saline placed upon it remain in place. Skin so treated behaves as does normal living skin, a prick promptly reducing its resistance very greatly.

Observation 3 a. Skin from post-mortem subject. Connected to battery of 2 volts. Current readings in microamperes.

| | | Reading |
|--|-----------------------------------|-----------|
| 12 hours after death (2 hours at room temperature). | Before pricking After pricking | 2 100 |
| | Before stroking After stroking | 2 22 |
| 36 hours after death (6 hours at room temperature, remainder on ice). | Before pricking After pricking | 50 120 |
| 60 hours after death (10 hours at room temperature, remainder on ice). Skin decomposing. | Before pricking After pricking | 75 120 |

Observation 3 b. Skin from post-mortem subject 18 hours after death (2 hours at room temperature) immersed for 30 minutes in 40 p.c. formaldehyde. Fluid mopped off surface. Connected to battery of 2 volts.

| | | Reading |
|------------------|-----------------|---------|
| 1st point tested | Before pricking | 2.5 |
| | After pricking | 100 |
| 2nd point tested | Before pricking | 20 |
| | After pricking | 125 |

Skin retained in small moist chamber for 24 hours; the skin is rigidly hardened; reexamined.

| 3rd point tested | Before pricking After pricking | $\frac{2}{85}$ | |
|------------------|-----------------------------------|----------------|--|
| 4th point tested | Before pricking After pricking | 1·5 110 | |

Freezing. If the normal living skin is hard frozen and allowed to thaw, it becomes brightly reddened and soon the skin swells to form a prominent wheal. The reaction of the skin is of the most intensive kind, but at no stage can a material fall if its resistance to constant currents be detected.

Observation 4 a. Skin of forearm. Frozen at -13.3° C. for 5 seconds. Battery of 2 volts. Readings in microamperes.

| Defens for the | Frozen area | | Control area |
|-----------------|-------------|---------------------------|--------------|
| Before freezing | $2 \cdot 5$ | | 2.0 |
| After freezing | | | |
| 3 minutes | 2.0 | Slight whealing | 1.5 |
| 7 minutes | 0.7 | Wheal distinct | 1.0 |
| 45 minutes | 0.5 | Wheal declining, skin red | 0.5 |

| frozen. | | | |
|-----------------|-------------|--|--------------------|
| | Frozen area | | Control area |
| Before freezing | 2 | | 2 |
| After freezing | | | |
| 2 minutes | 6 | | 2 |
| 4 minutes | 7 | Wheal starting | 3 |
| 38 minutes | 1 | Wheal full | 1 |
| 24 hours | 0.25 | Wheal still present and tender | 0.75 |
| l to 7 days | | ngs showed no fall of resistance, or l control areas. | difference between |
| 10 days | 1200 | Horny layer scaling off | 4 |
| 11 days | 800 | | 12 |
| 12 days | 100 | | 1 |

Observation 4 b. Skin of forearm. Frozen at - 18.8° C. for 10 minutes. Skin hard and deeply

Burning heat. If living skin is burned by placing it in repeated contact with a test-tube of scalding water until widespread redness and slight swelling of the skin is produced, the effects of this reaction of the living cells upon the resistance to galvanic currents is likewise absent or inappreciable, throughout the whole reaction.

Observation 5. Skin of forearm. Burnt with test-tube of scalding water repeatedly applied until a vivid local red reaction, with surrounding arteriolar flare, was obtained. Battery of 4 volts. Readings in microamperes.

| | Burnt areas | | Control areas | |
|---------------------------------|-------------|-------------|---------------|-------------|
| | ĩ | 2 | 1 | 2 |
| Before burning After burning | 1·0 2·0 | 0·75 0·5 | 3.5 4.75 | 1.0 0.75 |

Ultraviolet light. If the skin is burnt with ultraviolet light so that it reddens within 1 or 2 hours and is red and swollen on the subsequent day, no appreciable change of skin resistance is to be detected throughout this period of time. If the resistance of the skin is followed for a period of many days, then on the day when the superficial layers of the skin, which has become discoloured and wrinkled, begins to scale away, a conspicuous fall of resistance is frequently found to have occurred.

Observation 6. Skin of forearm. Ultraviolet light burn, mercury vapour lamp at 18 inches for 6 minutes. Battery of 6 volts. Readings in microamperes.

| Time after | Irradiat | ed areas | | Control | l areas |
|------------|----------|----------|--|---------|---------|
| exposure | | <u> </u> | | <u></u> | |
| 6 minutes | 2.5 | | | 1.75 | |
| 35 minutes | _ | 0.25 | | · · · | 1.5 |
| 81 minutes | 5.0 | 7.0 | Redness starting | 2.0 | 5.0 |
| 24 hours | 0.2 | 0.75 | Bright red and swollen skin | 0.25 | 3.5 |
| 96 hours | 3.0 | 2.0 | Redness fading, no swelling | 2.5 | 3.5 |
| 144 hours | 150 | 8 | Horny layer wrinkled | 12.5 | 5.5 |
| 216 hours | 1350 | 1800 | Horny layer scaling, removed several hours previously by gentle friction | 5.5 | 5.5 |

Blistering. We applied a strong cantharadin plaster to the skin of the arm. On the next day the resistance was taken from the skin covering the blister and from control areas; these blisters were filled with clear fluid and usually stood well above the level of the surrounding skin. In none of these tests was a decreased resistance detected. If, however, the layer of dead skin covering the blister was pricked lightly with a needle point, an immediate and profound fall of resistance invariably resulted.

Observation 7. Skin of forearm. Blistered 24 hours previously. Battery of 2 or 4 volts. Readings in microamperes. Two subjects.

| Blistered skin | | Control skin |
|-------------------|--|-----------------|
| 9 | | 8 |
| 1000 | Horny cover of blister removed | 11 |
| 4 210 | Horny cover of blister lightly pricked | 4 4 |

DISCUSSION.

These observations seem clearly to establish that the profound changes in the skin resistance (to galvanic currents) described by Ebbecke are not due to stimulation of the living cells, nor to consequent change in the permeability of their walls. The high resistance found in the uninjured skin resides in the superficial and horny layers of the skin and not in the living cells; and the profound changes of resistance occurring in response to the passage of the galvanic current itself, to vigorous friction, and to superficial needle pricks, are due to breaks in the continuity of this horny layer. It follows that his observations upon skin resistance may not justifiably be used as evidence that various stimuli, mechanical and galvanic, when applied to the skin, produce a reaction increasing the permeability of the epidermal cells with an associated release of metabolites, which proceed to act upon the blood vessels, dilating them and increasing their permeability. However suggestive Ebbecke's observations upon skin resistance may be, they can no longer be regarded as providing support to the view that tissue metabolites regulate the blood flow through, or the permeability of, the minute cutaneous blood vessels; and the method in its present form does not seem to offer any prospect of substantially increasing our knowledge of such regulation.

CONCLUSIONS.

The high resistance displayed by skin to galvanic currents resides in its superficial and horny layer and not in the living cells. Conspicuous changes in this resistance are not due to stimulation of the living cells but to breaches in the horny layer.

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