THE MANAGEMENT OF THE QUINIZARIN SWEAT TEST (Q.S.T.)

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The investigation of sweating represents a special and relatively new approach to clinical and physiological research on cutaneous function. The recent war has afforded great opportunities for investigating the phenomena resulting from injuries of the nervous system affecting the sweat mechanisms, and the Quinizarin method (L. Guttmann, 1937, '38, '40, '41, '46; Highet, 1942; Lewin, 1943; Seddon, 1942) has proved a reliable and the most simple method of studying these phenomena in detail. Disturbances of the central and peripheral sudomotor pathways can be accurately revealed and the purely physiologial activity of sweat glands estimated. The Quinizarin Sweat Test (Q.S.T.) is objective and, unlike sensory tests, does not depend upon statements made by the patient. In fact, in certain types of peripheral nerve lesions, such as incomplete or dissociated lesions, and for the localization of plexus lesions and the differentiation between pure cauda equina lesions and those complicated by superimposed damage to peripheral nerves or sympathetic column, the Q.S.T. has yielded information allowing accurate diagnosis, which could not be obtained by mere consideration of the disturbances of the motor and sensory functions alone. Moreover, the success of operations involving the removal of portions of the sympathetic nervous system can be determined accurately by this method.

The more widespread the use of the Q.S.T. as a supplement to other diagnostic methods and, in particular, for clinical and physiological research, the more essential it is to employ an adequate and standardized technique to guarantee optimum conditions for accurate results. The purpose of this paper is to present a full description of the author's technique in the management of the Q.S.T., as developed during the last ten years.

The Quinizarin Compound

The sodium salt of quinizarin (2-6-disulphonic acid) is the colour indicator. It is a red-brown dye and a derivative of anthroquinon similar to alizarin, purpurin and anthraruphin, all of which are used in the dye industry. For application to the human skin the quinizarin must be mixed with sodium carbonate in order that the colour change with moisture shall take place whatever the pH of the sweat secretion; rice starch is also added to economize in the amount of dye that has to be used. The following mixture is most suitable:

Quinizarin 2-6-disulphonic acid	35 g.
Sodium carbonate (powdered)	30 g.
Rice starch	60–70 g.

This compound is obtainable as a powder ready for use in containers of 250 gm. from Burroughs Wellcome and Co., London.

On occasions it has proved useful to change these proportions, and the powder has even been mixed with olive or paraffin oils for special investigations. The powder form, however, has proved satisfactory for all clinical purposes. On account of the affinity of quinizarin for water the test powder must be stored in absolutely dry and air-tight containers. When performing a test the necessary quantity of powder should be removed from the container, which should be resealed at once. It has been found that a slight change in colour from red-grey to blue-grey which occurs after a time does not interfere with the usefulness of the mixture.

Investigation Room—Sweat Cabinet

All tests are carried out in a room set out apart for the purpose, in order to provide standard conditions. This is essential if the Q.S.T. is combined with measurements of

vasomotor activity by thermocouples and plethysmographs, or if combined with cystometrography for studying the correlations of sweating and other autonomic responses to bladder activity—also for sensory tests after the thermoregulatory sweat test. Standard conditions are especially valuable for sensory tests in cases of peripheral nerve, spinal root and spinal cord lesions, in which studies of recovery of sweating in relation to sensibility are carried out at regular intervals.

The room is equipped with adequate lighting arrangements for photographic purposes.

A small bathroom adjoins the research room, where the patient can be cleaned after the Q.S.T., and the spreading of the dye to other rooms is thus avoided. The dye is easily removable with soap and water.

The two most common methods of producing thermoregulatory sweating used are immersion of limbs in hot water and exposure of parts of the body under hot air cradles. Immersion of limbs in hot water certainly provides useful information in certain instances, *e.g.*, for inducing reflex dilatation and sweating, but often finer details, especially in recovering peripheral nerve lesions, are not satisfactorily revealed. If ordinary heat cradles are used, apart from the danger of suffocating the patient and of burning anaesthetic areas of skin, it is often very difficult for the patient to adopt the most suitable position for the investigation. These difficulties have been obviated by specially designed sweating cabinets. In a previous paper (1941), description was given of a sweat box designed by the author for the work at the Peripheral Nerve Injury Unit at the Wingfield-Morris Orthopaedic Hospital, Oxford, consisting of two wooden sections, which fit into a standard hospital bed. Either section of the box can be readily removed, and the box is portable. The box is fitted with two glass windows on either side, to allow careful observation from all directions throughout the test. They can be opened for changing the patient's position or for the application of fresh powder during the test, if some of the powder has come off or it is necessary to investigate a greater area than was indicated by previous clinical signs (Fig. 1). The temperature within the box is regulated by 12 electric lamp bulbs of 25 watts each.

During the last three years, the author has designed several improved types of sweat cabinets, which are more comfortable for the patients and, in particular, more suitable for the investigation of patients with extensive paralysis due to spinal cord or brain lesions. They are also equipped with thermocouples, and these allow combined studies of sweating and vasomotor function. The latest model, which was built by the Engineering Department of the Ministry of Works (the author is especially grateful to Mr. G. Smith and his staff for their co-operation), is demonstrated in Figs. 2a, b and c.

The construction of the sweat cabinet is as follows :

Dimensions :

Length ..	6 ft. 9 in.
Width ..	3 ft. 3 in.
Height ..	3 ft. 9 in.

The patient lies on a trolley within the cabinet, 1 ft. 8 in. above the floor, and can be moved on this trolley to the bath after the test. The cabinet is timber framed and the walls and ceilings are formed of two thicknesses of plywood separated by 2 in. air space.

Ventilation. By an electrically driven centrifugal fan, mounted in a separate control desk with 1½ in. bore flexible air connection to the cabinet. The fan delivers 600 cubic ft. of air per hour, the air being delivered into the cabinet in an upward direction to avoid impinging on the patient; the volume is adjustable by a small damper. A small, 75-watt electric heater is fitted in the fan discharge to preheat the air to between 90° and 100° F. before admission to the cabinet. Air is discharged from the cabinet through a small adjustable grill.

Heating. The cabinet is heated by banks of carbon filament lamps and tubular heaters which are mounted on the ceiling of the cabinet, which is fitted with a chromium-plated reflector; 24-32 candle-power, 130-watt carbon filament lamps are provided and controlled in banks of three lamps by switches mounted on the outside of the cabinet. In addition, four tubular heaters, each 6 ft. long, loaded at 60 watts per ft., are installed. Experience has shown that the tubular heaters

are not so effective as carbon filament lamps for promoting rapid sweating of the patient. A ' Cambridge ' direct-reading, dial-type thermometer is provided to indicate air temperatures adjacent to the patient.

Cabinet humidity. A Negretti and Zambra hair-type, direct-reading hydrometer is provided for indicating relative humidity near the patient.

Body Temperature Measurement

(*a*) *Skin temperatures.* Ten plug-in type thermocouples are provided for the measurement of skin temperatures. Permanent copper constantan compensating leads are connected between plugs in the cabinet and the control desk. Flexible compensating leads are taken from the ten plugs in the cabinet to within 1 ft. of the hot junctions, the remaining couples being of No. 32 S.W.G. copper constantan, terminating on a circular silver plate about $\frac{3}{8}$ in. diameter which, in turn, is mounted on a sponge rubber and bakelite finger. The sponge rubber ensures good contact between the hot junction of the thermocouple and the patient's body.

(*b*) *Rectum temperatures.* Couples are provided for taking rectum temperatures. The hot junction is inserted into and soldered to a silver tube about $2\frac{1}{2}$ in. long by $\frac{3}{8}$ in. diameter. The couple leads are suitably insulated for sterilizing.

(*c*) *Mouth temperatures.* Couples are also provided for obtaining mouth temperatures. Again the hot junction is inserted into a silver tube of oval section. The length of the tube is $3\frac{1}{2}$ in. and the cross section axes 3/32 in. by $\frac{1}{4}$ in.

(*d*) *Potentiometer and cold junction.* A Negretti and Zambra nul-point, quick-reading potentiometer calibrated to read in degrees Fahrenheit is provided on the control cabinet, together with a melting ice-cold junction and a multi-way change-over switch.

Control desk. The control desk, in addition to housing the fresh air in-put fan, potentiometer, etc., is provided with a main power control switch, switches controlling tubular heaters and banks of lamps, together with indicator lamps.

Thermocouples and main wiring connections between the control desk and the cabinet are carried via ' Plessey ' multi-pin connectors and flexible conduit.

Position of the Patient

The position of the patient is important. He must lie comfortably in such a manner that the area to be investigated may be inspected easily and the running of sweat from normal or hyperhidrotic areas into anhidrotic or hypohidrotic areas is avoided. The limbs are supported on sandbags or on slings, as required. In peripheral nerve lesions, the most suitable position of the patient varies with the nerve under investigation and with the associated contractures of the joints in the damaged area. It is beyond the scope of this paper to describe in detail the optimum position for every nerve, but a few examples may be given. In an isolated lesion of the volar branch of the ulnar nerve, the hand and forearm should be placed in full supination, in order that sweating in the areas of the median nerve and dorsal cutaneous branch of the ulnar cannot run into the denervated area. In an isolated lesion of the dorsal cutaneous branch of the ulnar, or in a lesion of all ulnar branches, the forearm should be pronated and the wrist kept in dorsiflexion to prevent the running of sweat from the median and superficial radial nerve areas and from the areas of the medial and dorsal cutaneous nerves of the forearm. In testing the external popliteal nerve, the leg should be elevated by placing a support underneath the heel, to ensure full exposure of the posterolateral distribution of the nerve in the middle and upper third of the leg. In certain instances, such as lesions of the whole sciatic nerve, sacral plexus or root lesions, the patient is placed in the abdominal position, with sufficient support underneath the knees, in order to outline the whole area involved. In brachial plexus lesions, the paralysed limb must be supported by slings and occasionally it will be necessary to perform two sweating tests to get full information about the extent of the lesion.

Method of Study

When the patient has adopted a suitable position in the box, the area of skin to be

investigated is dabbed with quinizarin compound on a swab of cotton wool and sufficient pressure is employed to ensure that the orifices of the sweat glands are filled with powder. The area must be thoroughly covered with the powder and the powder evenly distributed. Application of the powder with an atomizer was found to be unsatisfactory, owing to the lack of pressure and the unnecessary spraying of powder all over the room. It should be mentioned that the powder is quite harmless and tests can be carried out repeatedly at short intervals. This is a special advantage that the quinizarin method has over other dye tests—for instances, iodine starch methods (V. Minor, 1927), and especially the ferro-sulphate-ether-alcohol method (Rieder and Neumann, 1932). Special care should be taken in powdering the face, to avoid any dust setting up mucosal irritation during the application of the powder. Droplets from sneezes or tears may moisten the powder and spoil the test. Therefore, when the face is powdered the patient's eyes must be kept closed. In many cases, it will be necessary to powder larger areas of the body in order to study the cutaneous reflex phenomena caused by the lesion. In brachial plexus lesions one should always remember the possibility of there being an associated lesion of portions of the cervical sympathetic and therefore the face should be powdered on both sides. In cases in which insufficient powder has been applied, or in patients with a skin so smooth that the powder has not adhered, repeated powdering is necessary during the test to bring about clear contrasts.

The Thermoregulatory Sweat Test

When the powdering is completed, the doors of the sweat cabinet are closed and the temperature within the box is raised gradually. As a rule, the temperature within the box is raised from room temperature to 110° or 120° F. The duration of heating required to produce sweating is subject to individual variations (15-35 minutes) and the onset and the intensity of the sweating is influenced by various extrinsic and intrinsic factors, such as atmospheric conditions (especially humidity), age, sex, endocrine metabolic factors, the level and completeness of the nerve lesion. Onset of sweating can be facilitated, and its intensity promoted, by a hot drink and aspirin grs. 5-10 given five to ten minutes before the test. The following record correlates the changes in skin and rectal temperatures to sweating at various stages of the test (Fig. 3).

When the secretion of visible sweat commences, the hidrotic areas of skin take on a dark, blue-violet colour, whilst the anhidrotic areas remain unchanged in colour. The opening of the individual sweat ducts appear as small, dark dots. These details are shown in a close-up photograph in Fig. 4, which demonstrates complete anhidrosis in the median nerve distribution, with scattered individual sweat ducts in the border zones demonstrating the intermediate zone of the interrupted median nerve with its neighbours, the ulnar and the radial.

It is essential to observe the details of sweating throughout the various stages of the test. Unless the progress is carefully observed, the results may be quite fallacious, especially in incomplete lesions of peripheral nerves. Placing the patient under hot air cradles, powdering him and then leaving him alone until the termination of the test is a haphazard method, which is to be condemned most strongly. In the course of the test, one must note the onset, distribution and amount of sweating, not only in the area supplied by the injured peripheral nerve, sympathetic ganglia or spinal segment, but also in the areas supplied by the neighbouring normal parts of the body and even in corresponding areas on the opposite side of the body. Some reflex phenomena, such as perilesionary hyperhidrosis (Guttmann and List, 1928), or border zone reflexes (Guttmann, 1933, 1940[1]) although obvious in a great number of cases at the commencement of the test, may be obscured later on when sweating is profuse. This is shown in a case of complete lesion of the spinal cord at Th. 10/11, where at the beginning of the test the level of the lesion is well-marked by the early onset of sweating and hyperhidrosis in the border zone above the level (Fig. 5a), whilst at the end the hyperhidrotic zone is obscured by profuse sweating in all areas above the level of the lesion (Fig. 5b). Thus, it is often necessary

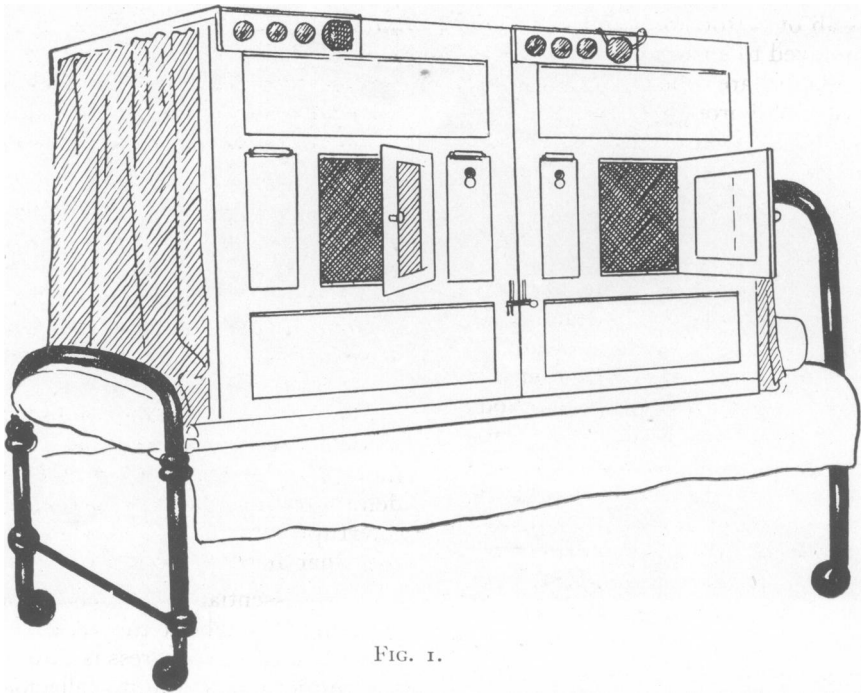


FIG. 1.

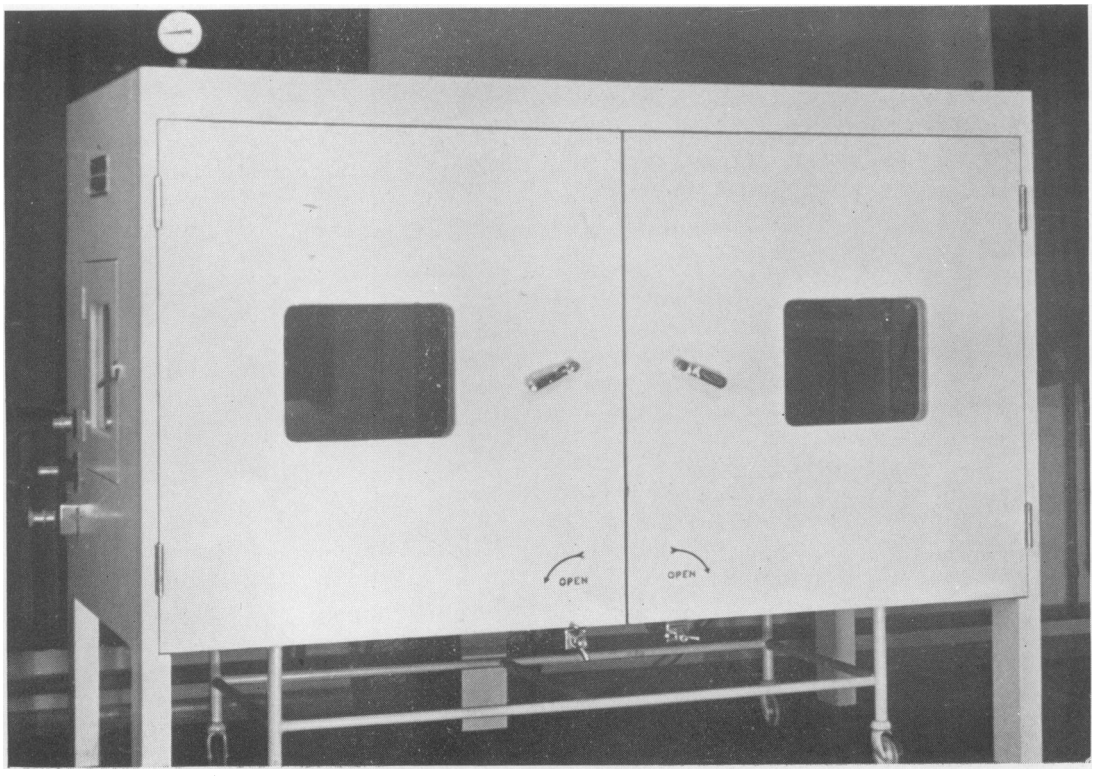


FIG. 2a.

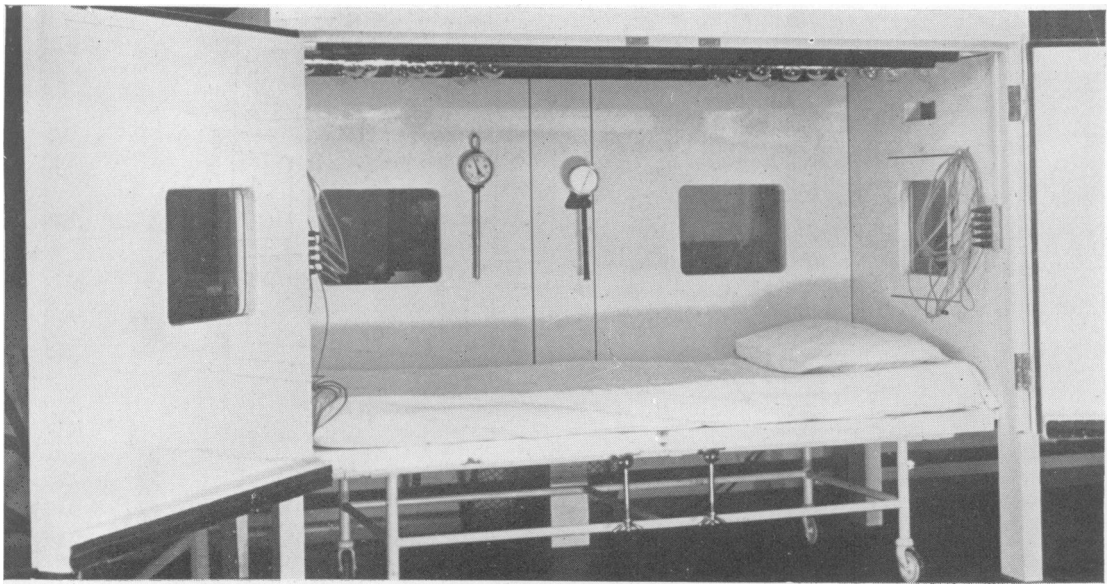


FIG. 2b.

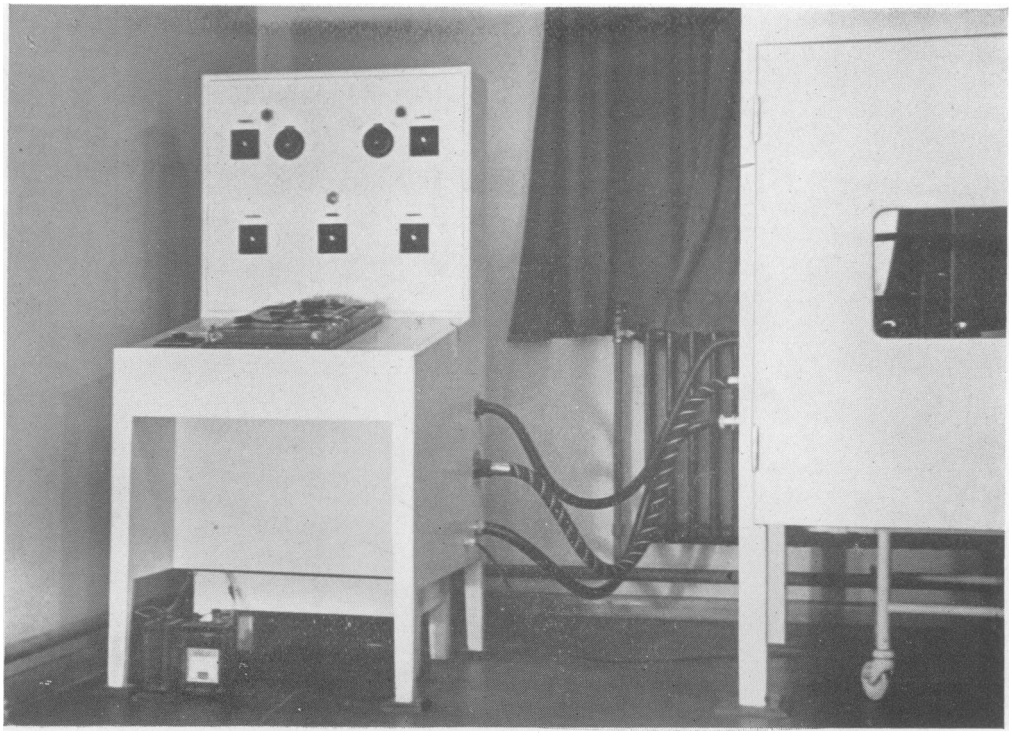


FIG. 2c.

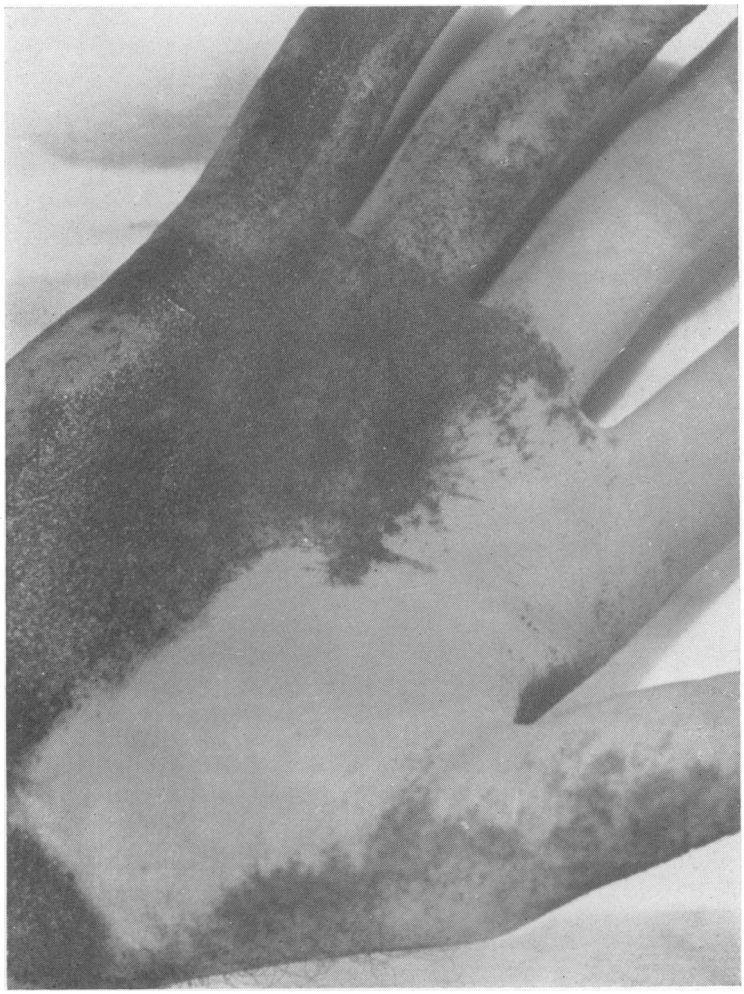


FIG. 4.

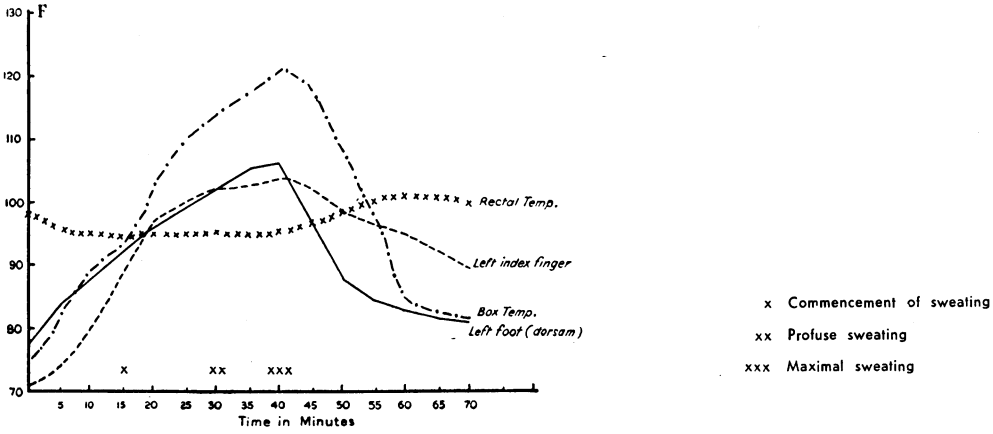

130 F
120
110
100
90
80
70
Rectal Temp.
Left index finger
Box Temp.
Left foot (dorsam)
x
xx
xxx
5 10 15 20 25 30 35 40 45 50 55 60 65 70
Time in Minutes
x Commencement of sweating
xx Profuse sweating
xxx Maximal sweating

FIG. 3.

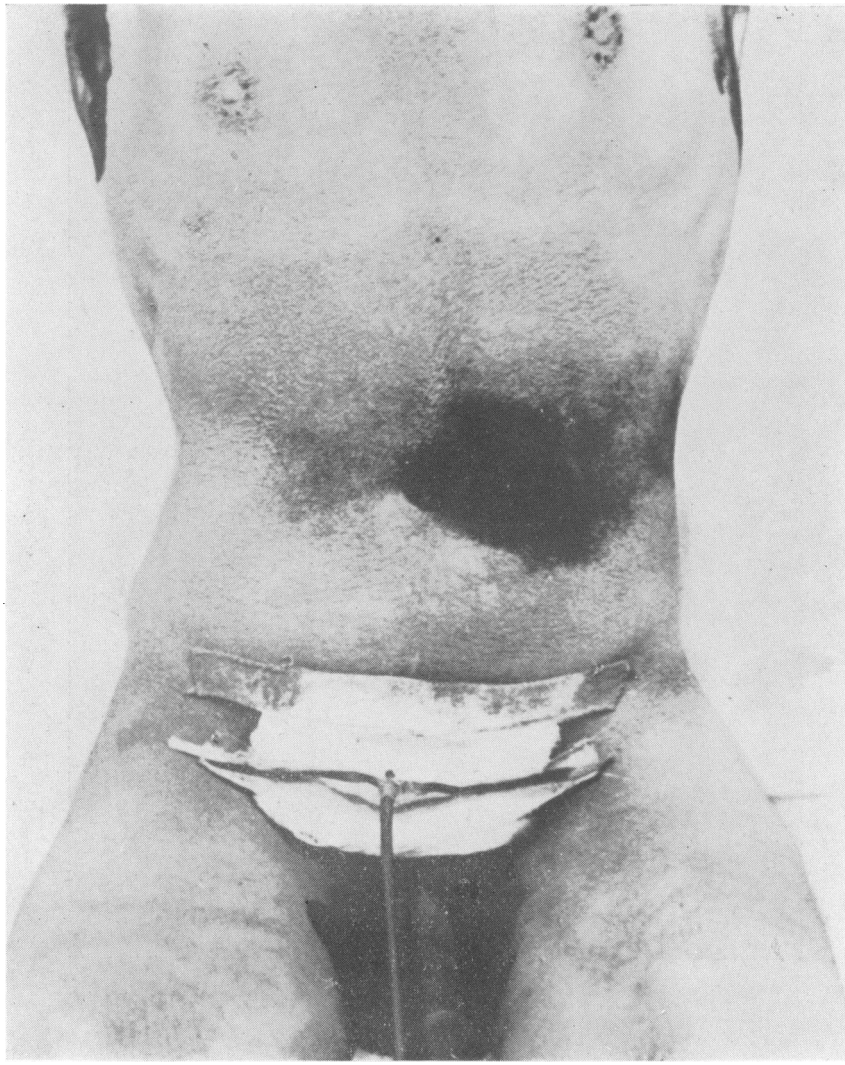


FIG. 5a.

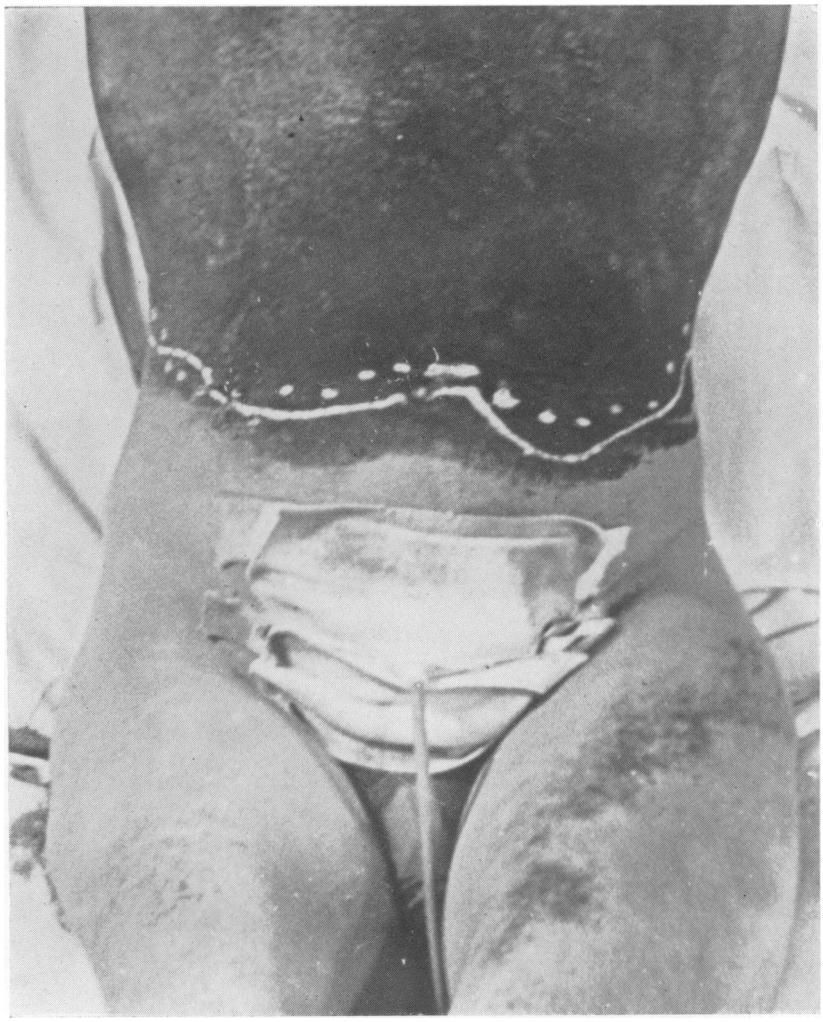


FIG. 5b.

——— area of anaesthesia

. . . . . : area of analgesia

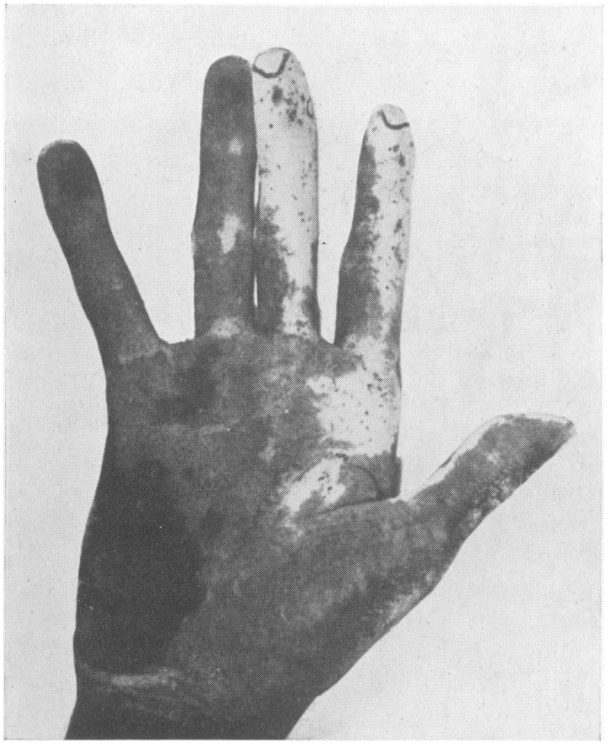


FIG. 6.

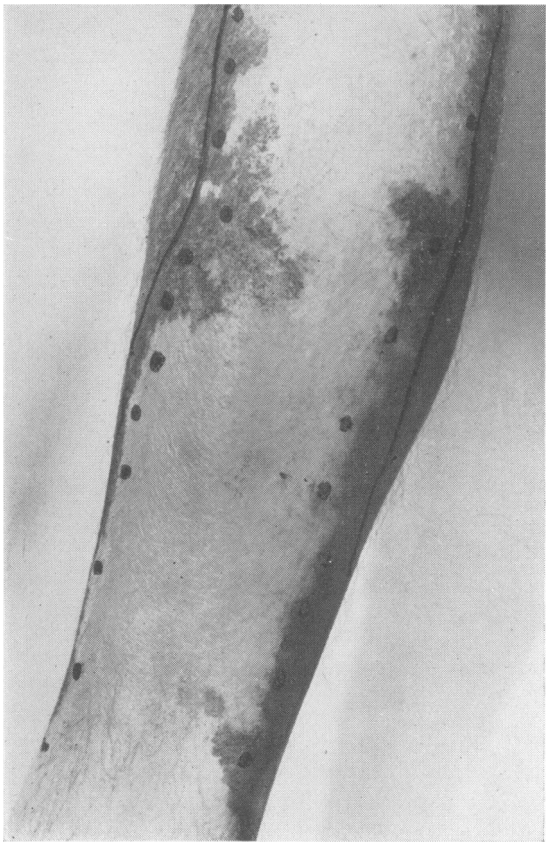


FIG. 7.

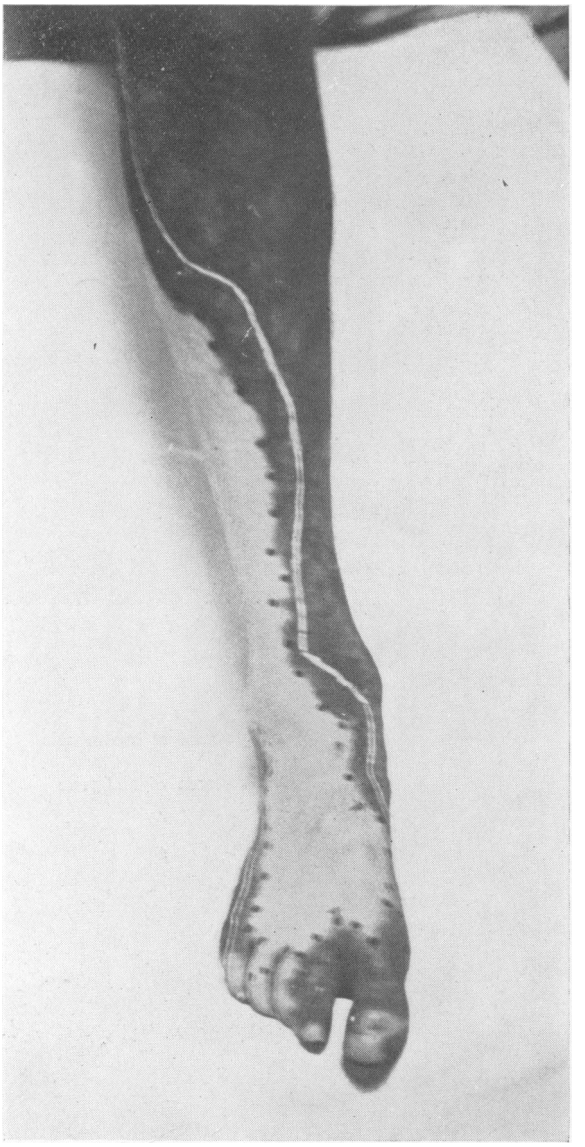


FIG. 8.

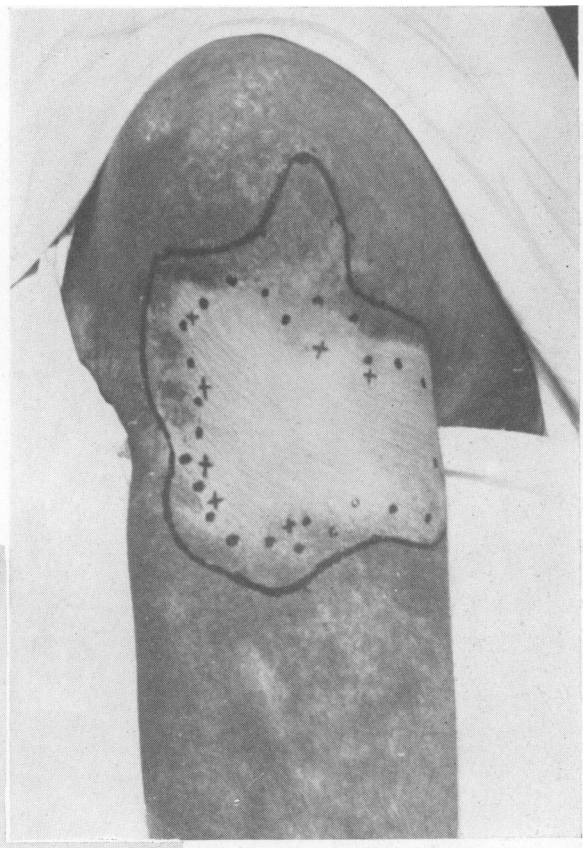


FIG. 9.

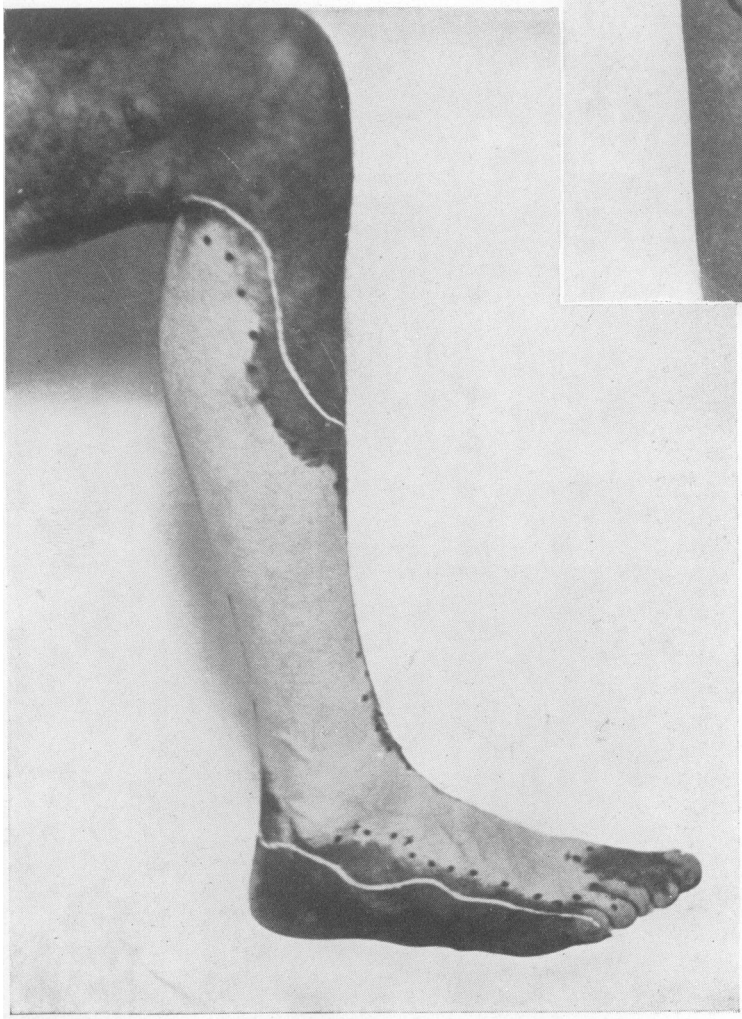


FIG. 8b.

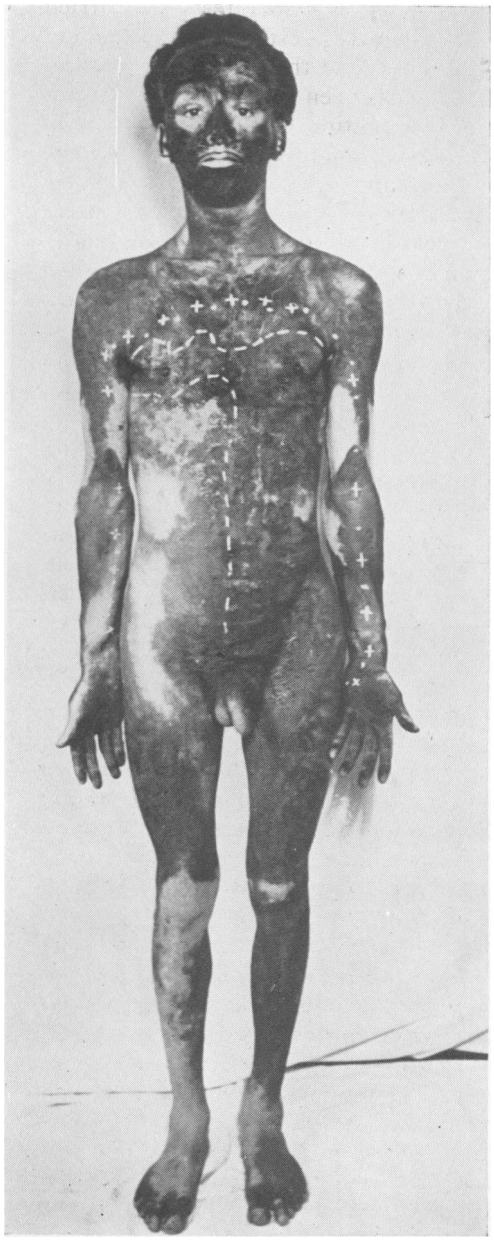


FIG. 10.

FIG. 11.

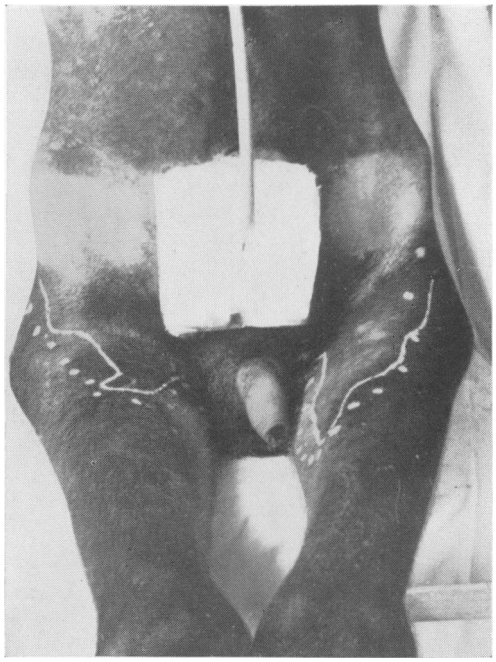
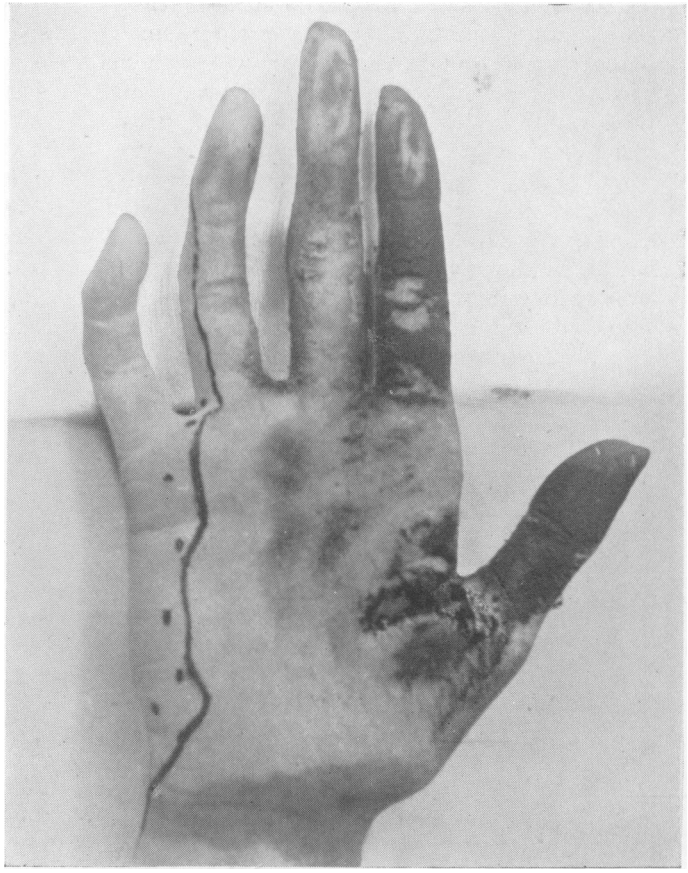


FIG. 12.



to make photographic records of the early stages of the test. The test must be continued until maximal sweating has occurred in all parts of the body. Only in this way can one compare findings in successive tests. This is of particular importance in testing peripheral nerve lesions in the various stages of regeneration. It must be remembered that the activity of recently reinervated sweat glands is characterized by a delayed onset, and diminished degree, of secretion and, therefore, a stronger and prolonged heat stimulus is necessary to bring these glands into action.

At the termination of the test, the temperature within the sweat cabinet is gradually reduced. The powder, which has been moistened and discoloured by sweat secretion, adheres to the skin. Superfluous dry quinizarin powder is removed by careful dusting with a small piece of cotton wool. Areas of normal or excessive sweating are clearly outlined by a uniform deep purple staining. In areas of hypohidrosis, such as in incomplete lesions, or in the intermediate zone of complete lesions of peripheral nerves or areas of early regeneration, sweating is characterized by small patches or isolated pin-points of sweat, which show various degrees of colour intensity, thus demonstrating the various degrees of sweat gland activity. The anhidrotic areas are not discoloured. Fig. 6 demonstrates a state of recovery of sweat glands in the distribution of the median nerve about 20 months after nerve suture in the middle of the forearm. There was recovery of pain and touch sensibility also, with the exception of the tips of index and middle fingers, which were still anaesthetic (marked by uninterrupted line).

The results of the sweat test and also of the sensory examination are recorded photographically. The fine pin-points of sweating in hypohidrotic areas can be shown up satisfactorily only by close-up photography (Fig. 4). In many cases, particularly of regenerating nerve lesions, the fine pin-points of sweating require accentuation by fine ink spots, to achieve accurate photographic records of the most distal distribution of sweat glands activity.

Correlation of Q.S.T. and Sensory Test

The Q.S.T. can be usefully employed as a guide for sensory tests in peripheral nerve and plexus lesions. Sensory tests are carried out after the sweating test, when the patient has adapted himself to the room temperature. This technique has been adopted by the author since 1939 as a routine in many hundreds of peripheral nerve and spinal cord lesions. Generally speaking, in complete lesions of peripheral nerves, the area of anhidrosis corresponds closely to the area of analgesia in the autonomous zone, *i.e.*, that zone supplied solely by the interrupted nerve. In the intermediate zone, which is also supplied by the neighbouring nerves and where loss of sensibility is partial, there is usually obvious reduced sweating. However, experience frequently has shown that there is dissociation between the areas of analgesia and anhidrosis. If pain sensibility is carefully tested and both superficial and deep needle pricks are employed, it will be found that anhidrosis corresponds more closely to the area of analgesia to superficial or moderate needle pricks, and within the border of this superficial analgesia there is an irregular zone in which deep needle pricks are appreciated. Moreover, sweating may also occur well within the border of superficial analgesia. This extension of sweating occurs usually in the form of irregular encroachments or indentations. Sometimes, in these encroachments of sweating, even a deep needle prick is not appreciated as pain. This is shown in Fig. 7, demonstrating a part of the area of sensory loss and of anhidrosis in a case of complete division of the external popliteal nerve. It shows the encroachments of sweating from either side into the denervated area and the dissociation between anaesthesia (uninterrupted line), analgesia (dotted line) and anhidrosis. Figs. 8a and b demonstrate a case of dissociated lesion of the external popliteal nerve, in which the branches of the lateral cutaneous nerve of the leg and the musculocutaneous nerve were completely interrupted, whereas the anterior tibial branch showed an incomplete lesion only, *i.e.*, marked weakness of the tibialis anticus and extensor hallucis longus, whereas sensibility and sweating were not appreciably disturbed, as shown by the good sweating of the dorsum of the first and second toes and of their interspaces. In this case, there was a close correlation between analgesia (dotted line) and anhidrosis.

The white line demonstrates the area of anaesthesia. Fig. 9 demonstrates the anhidrosis and sensory loss in a full thickness skin graft a few weeks after operation, in which the close correlation between analgesia and anhidrosis is obvious also (the crosses demonstrate the area of analgesia to deep pin prick, the uninterrupted line the area of anaesthesia). Certain types of plexus lesions and, in particular, lesions of the spinal cord show pronounced dissociation between the disturbance of sweating and the various modalities of sensibility. In incomplete lesions of the cervical cord, for instance, the lesion may select sudomotor fibres only in certain segments of the distal parts of the body. This is shown in Fig. 10 by the marked impairment of sweating on the right side of the trunk and leg in a case of an incomplete lesion of the cervical cord due to fracture—dislocation of the sixth cervical vertebra. The analgesia (interrupted line) involves the whole left side of the body below Th. 4 and on the right side the fourth and fifth thoracic dermatomes. The thermoanaesthesia (dotted and crossed lines) involves both sides of the body below the first thoracic dermatomes. On the motor side, there was spasticity in both lower limbs, particularly in the right leg.

Local Factors in Influencing Sweat Secretion

The Q.S.T. often reveals disturbances of sweating which are produced by factors other than lesions of the nervous system. It is necessary to refer here to at least the more important of these factors, as they can be superimposed on a nerve lesion and thus produce an area of disturbance of sweating larger than one would expect from the nerve lesion alone. It must first be remembered that sweating is already diminished under normal conditions in areas of skin which are exposed to permanent pressure and friction by underlying bony prominences, such as tip of the shoulder and elbow, the lower end of the ulnar, the knuckles of the fingers and toes, the trochanteric area, the patella, the medial and lateral malleoli and the fifth metatarsal. Classical examples of the pathologically increased impairment of sweating (often combined with sensory disturbance) due to pressure by prominent bone, are seen in cases of hallux valgus.

Sweating may be affected also by extrinsic factors due to pressure, such as splints, plaster of paris, adhesive plaster and other dressings (Fig. 11 shows a complete lesion of the cauda equina at the level of L.1/L2.). As one would expect in such a case, there is good sweating over both lower limbs. There is, however, a sharply defined quadrangular area of almost complete anhidrosis over the lower abdominal region on either side, obviously produced by elastoplast strapping, which was used to fasten the dressing over the suprapubic cystotomy wound.

In numerous cases of peripheral nerve lesion, an atypical large area of sweat disturbance is found, provided by superimposed local damage to the skin due to pressure by splints, plaster and other factors. For instance, in an ulnar nerve lesion it may involve the whole palmar aspect of the hand. In patients with certain occupations, such as labourers or butchers, this local damage is due to permanent pressure caused by their tools, and the disturbance of sweating corresponds to the hyperkeratosis of the palm in these cases. Fig. 12 demonstrates a case of complete lesion of ulnar nerve without evidence of injury to the median nerve. There was, however, poor sweating in the median area in the palm of the hand, due to local hyperkeratinization, whereas sweating over the palmar aspect of the fingers in the median area was unimpaired and profuse.

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