THE REHABILITATION OF PATIENTS WITH DEEP BURNS CONNECTED WITH THE RECOVERY OF FUNCTION AND SENSATION OF GRAFTED SKIN AREAS

A CLINICAL, HISTOLOGICAL AND EXPERIMENTAL STUDY

BY

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I

SURGICAL INVESTIGATION *)

A. Introduction

"Les brûlures ont été de tout temps l'object des tentatives les plus bizarres de l'empyrisme." DUPUYTREN quoted this in 1839 and even now we are of the same opinion, basing this on the bad results which sometimes occur in the treatment of burns. In the course of the ages there was no illness or affection where so many methods of treatment have been suggested as the injury due to burns.

The syndrome of burns with all its unique symptoms, which have often been watched with the naked eye, has been interpreted by the different research-workers in every varying way.

With each burn we are confronted with a local and a general condition, the latter being the direct sequence of the local one.

The progress made in the field of endocrinology, namely the part of the adrenals in the so-called stress response, the greater knowledge of water and salt mechanism with their large significance for combatting shock, the still further development of the modern anti-biotics, the further research in metabolic processes, the refinement of the grafting technique and lastly the use of skin homo-grafts, all lead to that the patient with deep burns has a better chance now than in the past. The development of the abovementioned possibilities will be gratefully made use of by the medical men in charge of the treatment of seriously burnt patients in this almost atomic era. This could be called hopeful, but there still remain some troublesome aspects, because, notwithstanding the improved influence on the mortality it is particularly the recovery of function of the patient to which too little thought has been given.

In many statistics of burns, only the mortality is given as a starting point for the judgement of certain therapy. This we find unjustifiable. Many of these mortality figures are incomparable magnitudes, because as far as burns are concerned, the extent and depth differed somewhat. A favourable influence of the disability expressed in numerical value should not be absent.

We thought it would be a good idea, specially to consider further the local burn treatment whereby the recovery of sensation in the affected skin areas should be the foremost thought and secondly, the recovery of function of the skin areas extending to hands and joints. However, going further into the history of local burn treatment, would in itself give interesting data, but it is impossible to do so within the space allowed

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in this publication. Generally we can say that from the commencement of the era up to approximately the second world war, local remedies were applied in order to achieve crust formation in injured skin areas. Up to this time there was no question of an adequate treatment of the burn, whether superficial or not. Actually we can say that round about 1948, especially under the influence of the Burn Centre in Birmingham, the diagnosis of depth-expansion was brought to the fore. (BULL, LENNARD-JONES, JACKSON.) The above-named authors described the pin-prick test which led to an improved diagnosis of the depth-expansion of the burn. Especially following the Anglo-American literature one talks about burns with partial skin loss and whole skin loss. The former are the burns in which the heat agents did not destroy all epithelial elements; in the whole skin loss all epithelial elements become necrotic.

To our minds this forms the nucleus of modern burn-wound treatment. In the first case a spontaneous healing of the burnt areas of the skin can take place. On the other hand in deep burns after shedding of necrotic skin areas, defects develop which can only be treated with the aid of grafts.

B. RECOVERY OF FUNCTION

With reference to our own results and by studying the literature we are convinced that anti-biotics are not able to solve successfully the problem of wound infection in extensive burns. The relation which in fact exists between the infection of the burn and its depth-extension forces us to seek the possibilities to close these defects at a time that the infection has not yet caused a hinderance to the wound recovery. The definition which Moorhead gave in 1928, viz. "A burn is an infected wound, produced by heat", should no longer be sustained. However, in practice it appears that this definition must be maintained as an axioma.

Although continually new disinfecting remedies were applied, the wound healing was not favourably influenced. The number of operative repairs essential in conservative methods of treatment is still very extensive. Through the unavoidable appearance of infection, grafting procedures can only be performed at a very late stage; the scar formation increases, resulting in contractures. Needless to say what the result is going to be for the recovery of function of joints and hands. A great number of operative repairs will be necessary for these nearly irreversible malformations. The results of these late operative repairs are mostly unsatisfactory. One cannot think of any part of surgery where so much damage can be done to the patient by a passive attitude on our part.

Has the wound excision, according to Friedrich, not for many years appeared to be a valuable gain. This technique is also based on the desire to close the wound as soon as possible at a time when infection has not yet taken place. It is quite certain that in extensive burns it is of the utmost importance that the phase of shock has favourably passed in order to treat the local burns as soon as possible. We must consider the burns as accidental wounds, although of an exceptional character which, to our minds, must be subjected to the modern ideas of wound treatment. In 1952 KUMMER said that this wound treatment will offer the burnt patient the best chances; shock treatment is now a hopeful aspect of the treatment of burns. Three still remains a group of burnt patients who stand the shock phase favourably and still remain alive for some time and while the treatment seemed to be rational, ultimately succumbed to infection. Without any question this group of patients have been offered better chances by early excision and grafting. This early excision and grafting falls to pieces in a primary and secondary excision and grafting. Under primary excision and grafting we understand the removal of all the necrotic tissue on the day of the injury, caused by burns, in addition hereto an immediate closing of the resulted skin defect with the aid of auto-grafting eventually combined with homo-grafting. In the secondary excision, treatment of shock is carried out first. Generally on the third or fourth day after the injury excision can be proceeded with. To perform this technique, we wish to make some remarks about the diagnosis of the depth of the burn.

Dupuytren had already observed that superficial burns are more painful than deep burns. These changes of pain sensation in the affected skin areas form the basis for the diagnosis of superficial and deep burns. It was apparent that in a burned skin area a number of zones are present, which going from outwards to the centre represent different pain perceptions, an external zone of hyperaesthesia, a middle zone of hypaesthesia and a centre zone of anaesthesia is found. (Fig. 1).

It was obvious that this anaesthetic zone was completely necrotic after the penetration of the heat agent. We found this in a few hundred patients. The clinical aspects of these skin areas are verified with the aid of the pathological anatomy of removed skin sections. The pin-prick test by BULL and others appeared to us as a very valuable acquisition for the diagnosis of deep burns. We consider that the presence of a deep burn is dependant on four factors:

a. the localization of the burn;

b. the cause of burning;

c. the colour change of the skin;

d. the change of pain reception in the affected area.

Guided by these four factors the early excision and grafting of deep burns was performed. The primary as well as secondary excision we make dependant on the surface extension. If the surface extension does not exceed 20 %, a primary excision is performed. Over and above shock treatment in an adequate manner is done. A few days later the so-called secondary excision is proceeded with. We have tried to show in a diagram, the advantages of this treatment as opposed to the conservative treatment. (Fig. 2).

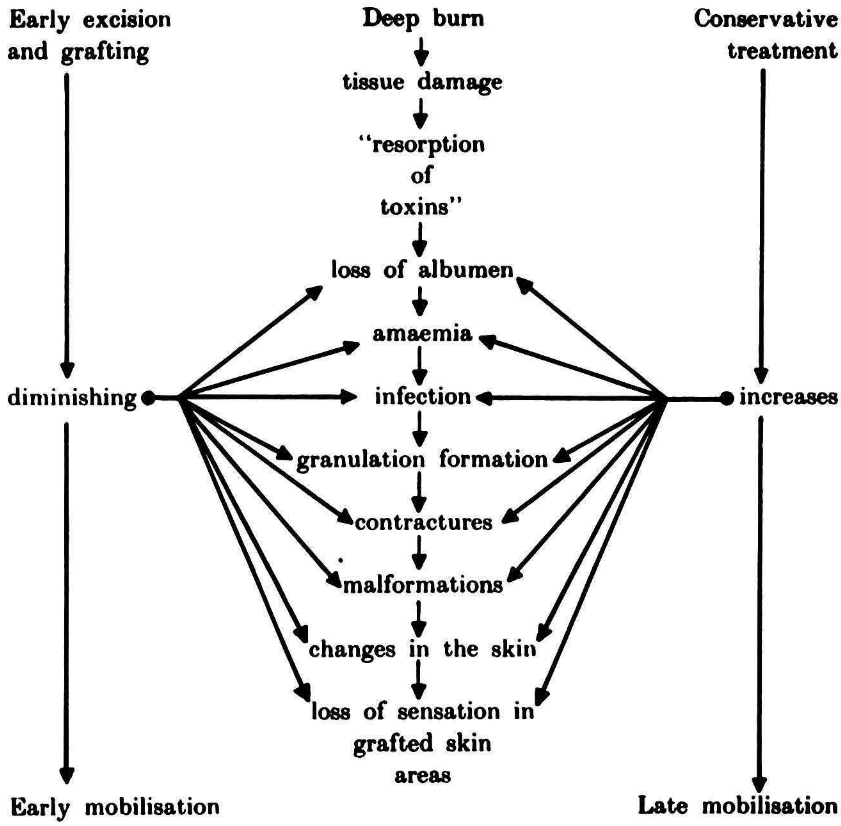

Fig. 2

With reference to the excision technique, we would like to make some remarks. The skin areas which seem to be anaesthetic with the pin-prick test are marked with a dye. If there is any doubt then the test is repeated; if the anaesthesia is not convincingly indicated by the patient, then an excision is not made. Very often we have to deal with deep second-grade burns. When the burns extend over the extremities then the excision is done in a bloodless area. With a knife and disecting forceps the necrotic skin is removed until the healthy tissue is reached. In an excision of burnt skin areas in other parts of the body, a bloodless area is naturally not possible. As the result of blood loos caused by the excision, adequate blood transfusions during the operation are necessary. The largest area undertaken by us as part of an early excision and graft amounted to a 40 % deep burn. This was the case of a workman at the Blast Furnaces at IJmuiden. It appeared that after a successfull shock treatmant, an excision was performed on the third day. A complete recovery of the function of the burnt skin areas extending over the joints and extremities, occurred in this patient in 3 months. (Fig. 4, 5.)

One of the disappointments which can be encountered in primary

Fig. 1

Fig. 3

Fig. 4

Fig. 5

Fig. 7

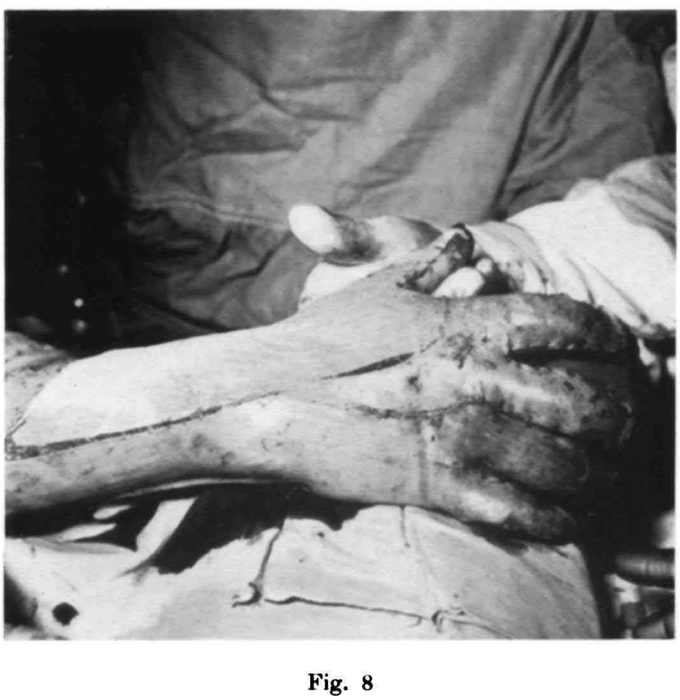

Fig. 8

Fig. 9

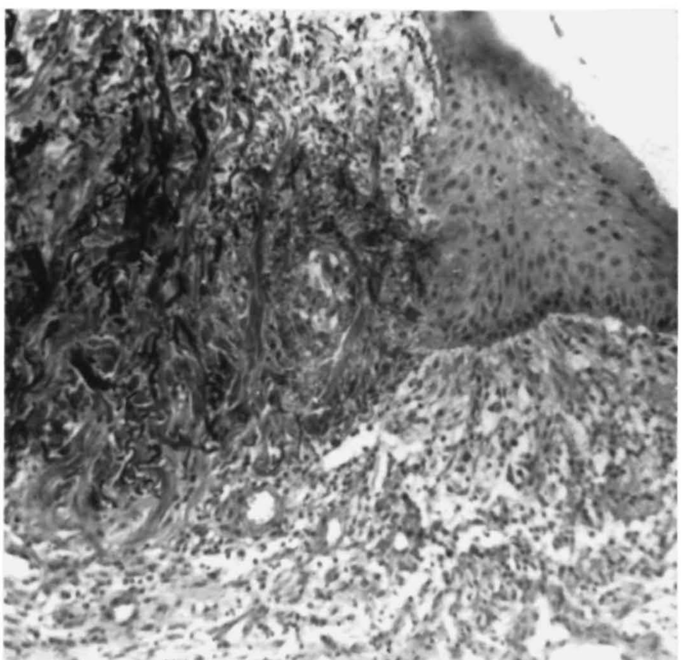

Fig. 10

excision, is an error that sometimes occurs in making too small an excision. If all the necrotic tissue is not removed, infection may take place at the edges of the graft, as a result of the partial sloughing of the graft. A wide excision is, therefore, essential; if necessary proceeding in the skin areas where only a superficial burn is present. The closing of the defects caused after the excision can be attained by means of auto-grafting, eventually combined with homo-grafting at the same time the use of embryonal graft should be considered.

C. Auto-Grafting

In extensions up to 20 % body surface, it is still possible to make use of the burnt patient's own skin. We use a Brown Dermatome for the removal of the skin. Previously, if possible, we removed the skin of certain pre-elected donor sites, preferably belonging to same enervated skin segments, but this method we do not use any more, as the result of the investigation in the re-innervation of grafts, but this we will discuss later. In actual practice it is sometimes not possible to fullfil this demand owing to the often uneven extent of the burn. In connection with the indefinite taking of the skin-homo-grafts, there are some burnt skin regions on which primary auto-grafts must be done. This generally refers to hand and joint skin areas. (Fig. 6)

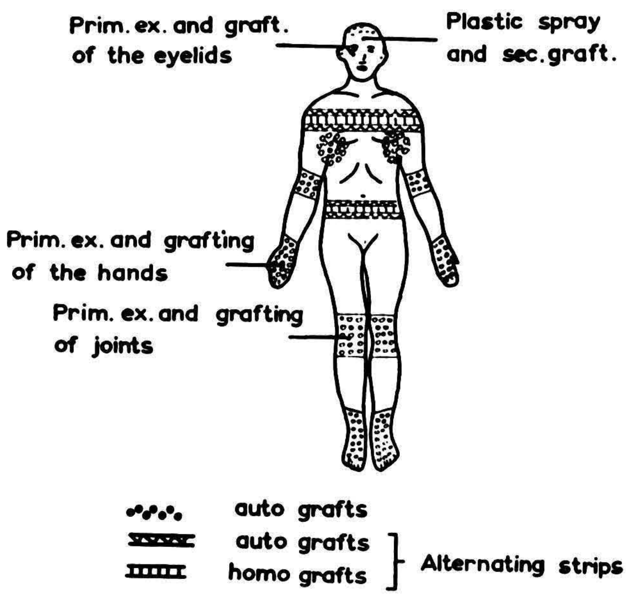

Fig. 6

We often came across hand burns at the Blast Furnaces and these always show a preference for a certain region. These burns are usually exposed to air and are caused by combatting fire. In most cases the dorsal side of the fingers and back of hand are affected. (Fig. 7)

Because the skin is thinner than on the inside of the hand, deep burns are often found here. Whatever the surface extension of the burn is, hand burns must receive major priority. The remaining burns can be left unattended, if needs be, until the patient has completely recovered from shock, but the primary excisions and grafting of the burnt hand must be done immediately. The grafts are then sutured. The hand is bandaged in a position of function. The graft is fixed with the aid of plaster of Paris. The bandage is changed five days after primary excision and grafting, and when the graft has taken, active exercises can be started.

The results of these burn wound treatments, especially of the hands, if far superior than any other type of burn wound treatment. A few photos of burnt hands will point this out. (Fig. 8 en 9)

The recovery of function is practically optimal. The so-called spark burns from red-hot metal, such as exist at the Blast Furnaces, are very easily accessible. They are often small burns of hands and feet. These red-hot pieces of metal penetrate through the shoes and cause deep burns, varying from 1 to 3 cm. More than 150 of such burns were treated in the last 3 years in a manner described above. In most of these cases the patients were able to remain working; in the majority of these cases excision and primary closing with stitching was sufficient. A simple bandage was enough. After 6 days the stitches were removed. If the defect was too large for primary closing, Thiersch's graft was sufficient. Then again practically only a week was lost from work. In this manner skin contractures over the fingers and joints were prevented. Function disorders never occurred. It is essential to do the grafting in a circular manner in the vicinity of the joints, in order to avoid contractures in a lengthwise direction. When there are deep hand burns especially of the fingers, it is desirable, after the grafts has taken, to splint the fingers for a few weeks in an extended position in order to avoid bending contractures.

Unquestionable this therapy has great advantages over the conservative therapy, whereby, already after a few days contractures develop. Characteristic of this deformity of the hands is the bent position of the interphalangeal joints and the extended position of the metacarpophalangeal joints. Repair operations of these affections, after the skin is cured, demand much time and function repair is unsatisfactory in most cases.

In extensions over 20 % body surface, or if the general condition of the patient does not permit it, we have to make use of homo-grafts or of a combination of these grafts together with auto-grafts.

It is striking to note that in this country the relation between domestic burns and industrial burns differs from other countries. For example, England, where relatively more domestic burns take place than in our country. The majority of patients where we performed homo-grafts work in factories, as the Blast Furnaces and such like. The intensity of the heat-source, the duration of penetration and the pressure under which the heat agent acts, is not surprising.

Fig. 11

Fig. 12

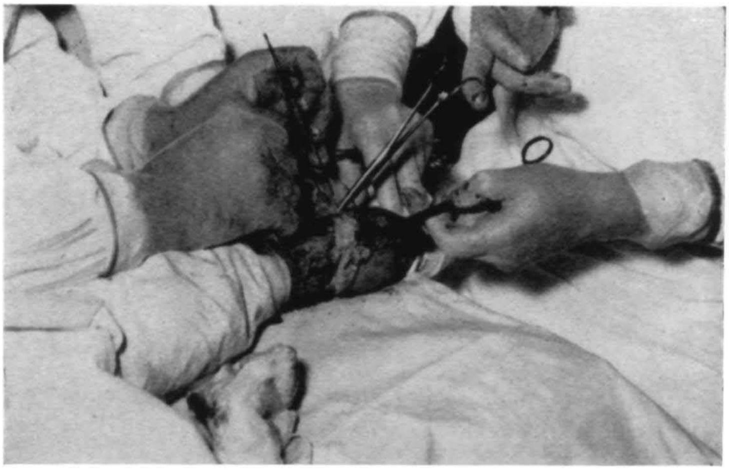

Fig. 13

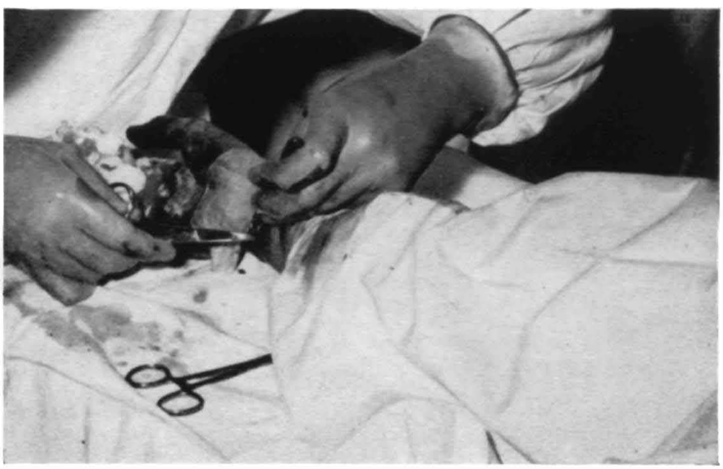

Fig. 14

Fig. 15

Fig. 16

We agree with the statements of JACKSON, VILAIN, ARTZ & REISS, BROWN and others that by performing homo-grafts the mortality is greatly diminished, conditionally however, that the homo-grafts are being used as part of an early excision and grafting. We did not observe any significant improvement when these grafts were done at a late stage. The supposition expressed in the literature by some people that this application would improve the general condition of the patient, the appetite would increase, infection would diminish and finally function recovery would benefit, cannot be confirmed by us. The mortality in extensions of more than 40 % did not show a difference in patients where no homografts were applied, or those in a late phase.

D. COMBINATION OF AUTO- AND HOMO-GRAFTS

This form of graft was introduced by MOWLEM and JACKSON. Strips of own skin are replaced by strips of homo-graft, so called alternate strips. From investigations of PENN, GILLMAN and others, it would appear that through the presence of the homo-graft the active growth of the recipient epithelium would be stimulated and that the vascular connective tissue of the recipient would persist to grow underneath the homo-graft. By means of microscopic slides we could not convince ourselves that this observation was correct. In most cases there was no obvious overgrowth of the recipient epithelium present. In our opinion it is only a suppression of the granulating tissue over which the recipient epithelium can easily overgrow. (Fig. 10).

In six patients with extensions over 30 % deep burns, we have applied as part of an early excision and grafting, combined grafts. In two patients with extensions of 40 % to 50 %, a primary excision of the hands was done on the day of burning. While after shock treatment the remainder of the burnt skin areas was excised and grafted with alternative grafts. (Fig. 11, 12, 13, 14, 15, 16.)

We considered the recovery of the function in all cases satisfactory. We kept the homo-grafts at different temperatures. An obvious lengthening in the taking of homo-grafts in very low temperatures, mentioned by some people in the literature, was not observed by us. We now keep the homo-grafts at a temperature of plus 4° C. In fact, it is possible to keep these grafts for approximately 3 weeks, but also as elsewhere, the frequency of extensive burns plays a minor part. We feel that the maintenance of an expensive skin bank is superfluous for many reasons. The need of homo-grafts in industrial burns was made possible because "skin volunteers" were supplied, amongst others, by the Blast Furnaces. If a permanent survival of homo-graft is not possible (which is now not to be expected for some time in view of the results of animal experiments) we contemplate the possibility to graft other tissue, as for example embryonal skin.

E. BREPHOTRANSPLANTATION (*Embryonal grafts*)

This form of grafting was firstly described in our country by KOOREMAN and GAILLARD. They succeeded in cases of post-operative tetany after strumectomy by implanting embryonal para-thyreoidal glands, after the taking of these grafts to obtain the increase of function of those implanted glands. On the same principle we tried how far embryonal skin would have lasting chances of taking. In two patients this was applied clinically and in another two patients experiments were observed how far a permanent taking was present. One of the cases was a 4 years old girl, who had a burn of 70 % extension. After excision of the granulations, pieces of embryonal skin were placed on her back on three consecutive times. These skin strips came from immature and premature children, taken within 6 hours after birth. The taking of such grafts could be explained that the antigenic properties of the embryonal skin are not so far developed that they can cause formation of anti-bodies in the recipient. (Fig. 19).

It appears to us that the younger the embryonal skin was, the taking of such a graft was better. Histological examination is difficult to perform when this skin was put on defects where auto-grafts were also used. While only now, a vast series of such grafts can lead to a definite verdict, we, however, doubt that a permanent taking is possible. Experimentally we could not follow up these skin strips for longer than 6 to 8 weeks. (Fig. 17, 18.)

We would now like to know whether, by using this graft a suppression of the granulation tissues is reached, by which faster formation of epithelium from the edges is possible. We think that the vital embryonal homograft works as a kind of scaffolding through and over which the subepidermal and epidermal tissue grows.

The clinical application of such graft, however, encounters great difficulties. The possibility to get a sufficient number of such grafts is so small that one has to depend in acute cases on homo-grafts. For extensive clinical application it appears to us that this possibility is not yet suitable. For that matter, experience of others such as BARKER, we are inclined to say that a lengthening at the most can only be present of a few weeks duration.

Summarising, we would like to state in this chapter, it is our opinion that the right treatment of deep burns will greatly depend on the influence which this treatment has on the formation of scar tissue, the appearance of contractures and as result thereof the creation of malformation. The early mobilisation made possible by timely excision and grafting justifies the precision of our point of view. Apart from the obvious diminishment of wound infection, it is also apparent that the number of repair-operations as the result of contractures is markedly decreased.

The advantages of early excision and grafting over any other form of local burn treatment are:

I. Decrease in mortality;

II. Shorter recovery and hospitalisation;

III. Substantial diminishment of invalidity;
IV. Better return of sensation in grafted skin areas.

A few remarks should be made in respect of the last mentioned advantage. In following up of patients treated according to primary excision and grafting, we noticed that there was a difference in the return of sensation in skin-grafts respectively applied as part of an early excision and grafting and secondary grafting.

Although the return of sensation was determined by us by a crude method (cotton wool plug, needle etc.) we came to the conclusion that the early applied grafts already had a pain perception after about 5–6 weeks.

The significance of the return of sensation appeared to us to be extremely important in the region of the hands. Through this our attention was drawn in how far, besides the function return of the burnt hand also the sensation recovery would be present.

It was conspicuous that in poorly taken grafts, which moreover were applied at a later date, the pain and tactile perceptions were sometimes completely absent. (Fig. 23.)

Besides the great advantages of primary excision and grafting for a deep burn we thought that a comparative investigation of the re-innervation of skin grafting in the region of the hand was essential, because this was of the utmost importance in connection with the rehabilitation of patients with deep burns.

II

NEUROLOGICAL INVESTIGATION

A. Investigation of sensation

If one wishes to form an opinion whether the return of sensation in a skin graft, it would be advisable to make a comparative investigation in respect of the contra-lateral healthy skin. Moreover, it is necessary to follow up the degree of function recovery of sensation in the grafted area.

Although observed by a number of investigators that the general return of different modalities of sensation were present, no consideration was given to the quantitative return of sensation in skin grafts.

If one wishes to explore which type of graft is the most ideal for return of receptive function, a qualitative research of sensation is inadequate and it is necessary to investigate the amount of function recovery of the grafted area.

Hutchinson, Tough and Wyburn were the only investigators who applied this quantitative method in their comparative investigation of sensation of the graft and of the donor site area. Their so-called grid-method was adopted by us in a revised form. They concluded that under optimal conditions skin grafts are inclined to assume the sensation pattern of the surrounding skin and not of the donor site region. These optimal conditions prevailed if there was an optimal taking of the graft and a healthy graft bed.

It is difficult to do a comparative investigation of sensation in two skin areas, because the classic modalities of sensation, namely tactile, pain, warmth and cold sense, are not sharply defined subjective perceptions and can merge into each other.

The patient is often not in a position to give an exact description of the endless different sensations which are observed by applying stimuli.

It is difficult to suggest that the many modalities and sub-modalities of sensation are bound to definite anatomical substrates (sensory end-organs) which was brought to the fore by Von Frey (1895) for the sensation of the skin. It is assumed in this so-called doctrine of specific energy that the stimulus of a certain end-organ causes specific re-action, independent of the nature of the stimulus.

The investigation of the sensation of the injured skin in which the neighbouring sensations are more defined than in the healthy skin and often bear an unpleasant character, give a further support to the criticism of the doctrine of specific energy of the end-organs, which has arisen of late years.

New anatomical and physiological investigations have also brought to the fore facts which make it desirable to investigate further the problem of specific irritability of the end organs.

WEDDELL and his co-workers pointed out that the skin of the ear lobe contain no specific end organs, yet touch, pain cold and heat can be observed. The red part of the lip contains, according to them, specific end-organs, but not the adjacent skin area but both areas are capable of observing different sensation modalities.

On this grounds, we can conclude that the observation of different modalities of sensation are not necessarily bound to the specific end-organs.

Next to the doctrine of specific energy of end-organs the doctrine of pattern in the latter years has developed whereby the specificity of observation is more centrally placed and the peripheral apparatus of the conduction of sensation is being made dependent on two variables, namely time and space. The variable time, is in accordance with the rate of conduction of the stimulus in a nerve fibre, that of space with the number and division of the nerve fibres which are stimulated in the skin. The nerve stimuli reach the cortex at different points and times dependent on the place where the nerve fibres in the cortex end and the rate of conduction of the nerve fibre.

In this manner an endless pattern of activity of the cortex can be roused which, during the phase of development of the individual, can be bound to definite perceptions. In this manner a more acceptable explanation is given for the many modalities and sub-modalities which are observed during the investigations of sensation.

In the literature the discussion on ideal conditions necessary for an optimal return of sensation in skin grafts is hitherto limited to the thickness and type of the graft. KREDEL and EVANS (1933), DAVIES and KITLOWSKY (1943) and LOYAL DAVIS (1934) shared their findings in a series of cases, whereby 188 old grafts were examined. These publications are in respect of pedicle-as well as so-called free-grafts. These observers agreed with each other that pain sense was the first to recover, while it was obvious that the recovery was more complete in pedicle grafts and less complete in the so-called free-grafts. The sequence of return of sensation is summarised by the abovenamed authors as follows: the velocity of return is proportional with the sequence: pedicle-grafts – full thickness grafts – split skin grafts and finally THIERSCH's grafts. From this it would seem that the velocity and degree of re-innervation would be dependent on the type and thickness of the graft used. These authors all saw a dissociation with respect to the return of pain, tactile and temperature sense. According to them pain sense would firstly return then tactile sense and finally temperature sense. Also the return of the different perceptions seem to occur from the vicinity of the graft.

In 1938 MCCARROLL also published an investigation on the re-innervation of split-skin grafts. Pain and tactile sense he already observed

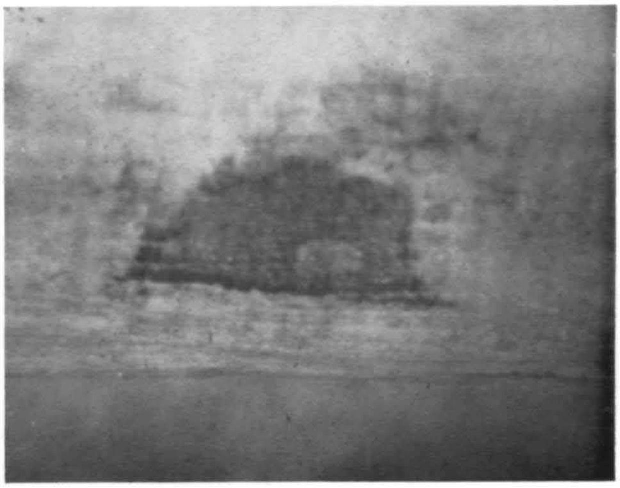

Fig. 17

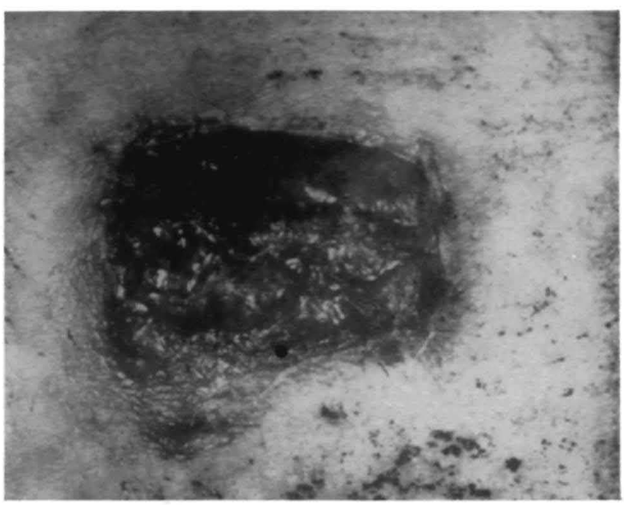

Fig. 18

Fig. 19

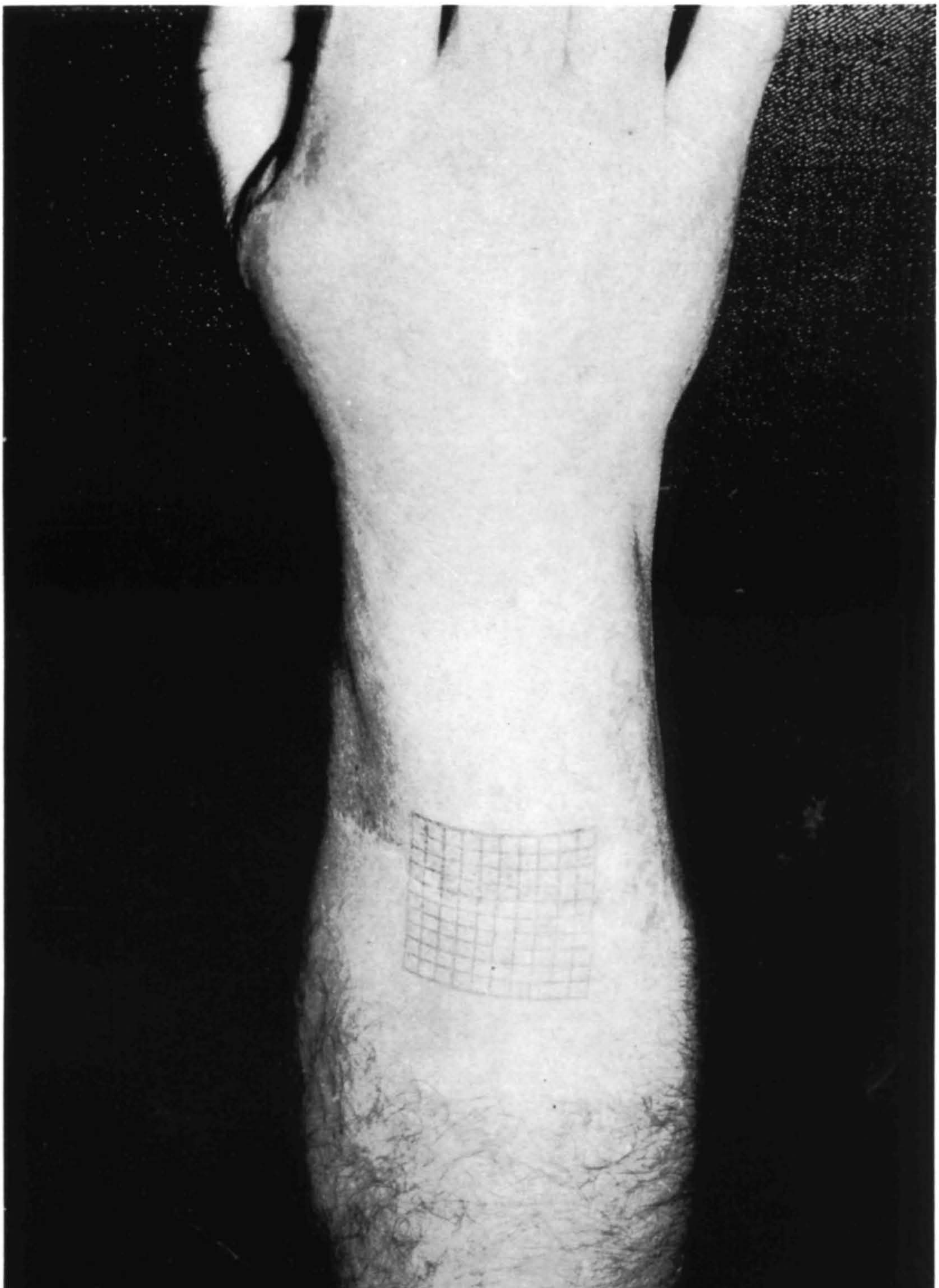

Fig. 21

Fig. 22

5 or 6 days after the application of the graft and thereafter weekly. In order to judge the pain sense he used an algesiometer with a pressure weight of 0.7 gr. The tactile sense was investigated by means of the cotton wool test. McCarroll comes to a totally different conclusion than the abovementioned authors. In free grafts he saw the simultaneous return of re-innervation in all parts of the graft. Apart from this he established that the equality and degree of return is reversely proportionate with the thickness of the graft. The dissociation of the different sensations was also observed by him, but it was more obvious as the thickness of the graft increased.

In order to obtain an optimal regeneration of nerve fibres, we consider that the moment of applying the graft is the most important criterion. As a matter of fact we found that the thickness and type of graft plays an unimportant role.

Before investigating the sensation pattern of three patients of which one was treated according to the methods of primary excision and grafting, the other two with secondary grafting, it is desirable to give a description of the method of investigation used by us.

B. Methods

The sensitivity of the grafts were compared with the sound skin of the opposite hand *at the same time* to make the results more comparable; this was done by making each prick or touch alternately from graft to sound side.

The strength of the stimulus was increased before the test until about 85–100 % of answers were correct on the sound hand. Only when the pattern in the sound hand was the same in two successive assessments was the reliability of the test on the grafted skin acceptable. As well as testing the sound hand, an assessment was made of the sensivity of the normal skin on the opposite site of the body to the donor area. In each skin site which was tested, the return of touch, warmth, cold, pain and tactile discrimination were studied. The skin temperature was also taken.

At the start of each patient's visit the test was explained to him and his co-operation invited. A grid pattern was then made on the skin with a rubber stamp (Fig. 20). The size of the grid was 4 × 4 cms, divided into 100 squares of 4 mm. each. The research work was done by two people, one making the test and the other instructing what should be done and recording the result. The instructor dictated which small square should next be stimulated by giving its co-ordinates and the tester gave the stimulus. To prevent any inductive reasoning from one stimulus to another successive stimuli were given as widely apart as possible on the grid. At the same time the graft and the sound skin were stimulated alternately. (See Fig. 20).

In testing for pain, two different stimuli, sharp and blunt, were used irregularly in succession so that the patient had to make a choice between them at each application. In both cases the weight of the stimulator on the skin was the same, and the patient was asked if the stimulus was blunt or sharp.

Assessments of cold and warm stimuli were done in the same way.

	A	B	C	D	E	F	G	H	I	J	
1	•		•		•		•		•		1
2		•		•		•		•		•	2
3	•		•		•		•		•		3
4		•		•		•		•		•	4
5	•		•		•		•		•		5
6		•		•		•		•		•	6
7	•		•		•		•		•		7
8		•		•		•		•		•	8
9	•		•		•		•		•		9
10		•		•		•		•		•	10
	A	B	C	D	E	F	G	H	I	J	

Fig. 20

As well as the instructor giving the sites for stimulation by naming co-ordinates, the tester had to know, without being told in a way the patient could understand, which of the two stimuli should be given – whether sharp of blunt, warm or cold. To do this, half the small squares in the grid were given a dot (Fig. 20) and it was agreed that the first 50 stimulations in each grid the sharp or the warm stimulus should correspond with the dotted squares and the blunt or cold with the undotted. For the second 50 stimulations on each grid the opposite connotation was used. By this method it was possible to have a silent mutual control between instructor and tester regarding the localization and type of stimulus.

Touch

Touch stimuli were applied by VON FREY nylon threads, 2–3 cms long mounted on an 8 cms handle, and having a known tension measured in gms/mm. Ten values were used, namely, 1, 2, 3, 5, 10, 16, 25, 35, 50 and 75 gms/mm.

When necessary the skin was shaved. It was then touched so as to produce a slight bowing of the thread, avoiding any rubbing movement. Every small square was touched five times in different places. When there was no response after the fifth stimulus the result was negative, and when appreciated it was positive. Most co-operative youthful patients gave 85–100 positive answers on normal hand skin when a 16 gms/mm. VON FREY thread was used.

Temperatures

The skin temperature was measured with an "Electric universal" thermomoter (type T.E.S, Ellab. Copenhagen), using a skin applicator (type HI). The applicator consisted of a thermocouple, in length the diagonal of a small square, and with this it was possible to measure the temparature in one or two seconds. In each grid the temperature was measured in nine widely distributed small squares. According to KUEMMERLE a difference of 1–1.2° C. in identical skin sites should be regarded as pathological.

Before making this assessment the room and skin temperature were recorded.

Warmth: The warm stimulus was applied with a copper applicator of 50 gms weight, with an applying surface of 4 sq. mm. This was connected through a variable resistance to the mains supply. In this the temperature could be changed rapidly. A temperature of 42–43° C. for two seconds was used as the warm stimulus, and this was done controlled with the electric thermometer. Above 44° C. evoked pain.

Cold: The cold stimulus was given with an applicator of the same shape and weight. Sixteen such applicators, with ebony handles for insulation, were cooled by standing them in a water bath filled with ice; they were changed frequently to ensure a temperature of 0° C. Tested in this way, normal youthful patients gave 85 % correct answers and in the other 15 % they gave the wrong answer or were not able to distinguish between the stimuli. Assessments in which the opposite answer was given, that is warm for cold and vice versa, were marked with a "V".

Pain: Pain stimuli were applied with VON FREY needles with increasing pressures of 2, 6, 10, 20, 30 and 40 gms. To test the continued co-operation of the patient blunt stimuli were also applied irregularly with a needle of the same weight and diameter. The sensation of pain was called sharp and of pressure blunt. A VON FREY's needle of 10 gms gave 85–100 % correct answers in young people.

Tactile discrimination: This test was done with the usual dividers, starting with a gap of 8 cms and decreasing by 0.5 cms each time. The gap which the patient was unable to discriminate after three consecutive applications was noted. The test was then repeated with the dividers set at 0.5 cm. and increasing by 0.5 cm. each time, until three correct answers were given.

C. CASE REPORTS

A total of 43 patients were examined of which further data will be given.

Out of the abovementioned group, three patients will now be discussed; the first patient treated according to the method of primary excision and graft; the other two treated by secondary graft.

In order to give a fair opinion about the re-innervation, we performed a biopsy on these patients of which the histological findings will be discussed later.

Patient M: This concerns a 39 year old man who received a contact burn in December, 1954. The right dorsum of the hand and forearm showed a burn, whereby all the layers of the skin were affected by the heat agent. The volar side of the hand showed a partial skin loss.

A full skin graft was taken from the lateral side of the left thigh. The graft took 100 % (Fig. 21.) No infection occurred, nor did a haematome form underneath the graft. The patient was dismissed from the clinic 28 days after he was admitted into the hospital.

The function and cosmetic recovery of the hand was optimal. (Fig. 22.)

There was a minimal hair formation after 5 years. The sensation examination was done in February, 1959, that is 5 years after the burn.

	Graft	Healthy dorsum of hand	(Reflected) Image Donor site
M–1: *Tactile sense* (tactile hair 16).			
	+ 96	+ 100	+ 75
	− 4		− 25
M–2: *Heat sense* (43° *C*.)			
	+ 88	+ 90	+ 95
	V 3	V 5	V 5
	− 9	− 5	
M–3: *Cold sense* (0° *C*.)			
	+ 91	+ 87	+ 92
	V 6	V 10	V 2
	− 3	− 3	− 6
M–4: *Pain sense* (10 *g*.)			
	+ 90	+ 98	+ 84
	− 10	− 2	− 16
M–5: *Tactile discrimination*			
	3 c.M.	3.5 c.M.	5
	2 c.M.	3.5 c.M.	5
M–6: *Skin temperature*		(Average value of 9 determinations. The room temperature was 22° C.)	
	32.4° C.	32.3° C.	34° C.

Conclusion: The sensory recovery is optimal and is definitely better than that of the contra-lateral donor site area. The values which were found when examining the tactile sense and the tactile discrimination showed that the sensory pattern inclined to take on the character of the surrounding skin and not that of the place of origin. Tactile sense pract ically returned to normal, notwithstanding the minimal hair formation. (See Fig. 21.)

Now follows the discussion of the two patients treated with a secondary graft.

Patient K: This patient was a man 50 years old, who in 1955 sustained burns. He was not given a skin graft until all necrotic tissue had sloughed. This was naturally associated with the extensive infections in affected skin areas. Patient underwent several graftings of skin in hospital elsewhere. He was finally seen by one of us two months after the injury. At that time there were large granulating defects, particularly of the dorsum of the hands and the fingers. The second finger had to be amputated. After the infection had been controlled, a skin graft was performed. The defects were covered with so-called THIERSCH's grafts obtained from the right thigh. A sensation test was done three years later. The recovery of function of both hands amounted to 50 %. Cosmetic results were highly unsatisfactory. (Fig. 23.)

Naturally no hair-growth occurred on the graft.

Sensation was tested in the centre of the graft of the dorsum of the right hand, with the following results:

	Graft	Healthy dorsum of hand	(Reflected) Image Donor site
K–1: *Tactile sense* (tactile hair 16)			
	+ 2	+ 91	+ 64
	— 98	— 9	— 36
K–2: *Heat sense* (43° *C*.)			
	+ 22	+ 98	+ 96
	V 4	V 1	V 3
	— 74	— 1	— 1
K–3: *Cold sense* (0° *C*.)			
	+ 7	+ 78	+ 68
	V 22	V 20	V 32
	— 71	— 2	
K–4: *Pain sense* (10 g.)			
	+ 11	+ 95	+ 94
	— 89	— 5	— 6
K–5: *Tactile discrimination*			
	9 c.M.	2.5 c.M.	5 c.M.
	6 c.M.	3 c.M.	4.5 c.M.
K–6: *Skin temperature*		(Average value of 9 determinations. The room temperature was 22.9° C.)	
	29.8° C.	31.6° C.	29.6° C.

Patient v.Z: This concerns a 33 year old patient who received a contact burn during the summer of 1956 on the left dorsum of the hand. Spontaneous sloughing of necrotic skin was expected and a few weeks later it was decided to do a THIERSCH's graft on the dorsum of the left hand, which was taken from the left thigh. The sensation examination was done in April 1959. The patient informed us, when being examined for sensation, that he experienced heat radiation which gave a sense of pain in the graft. He spontaneously indicated that he always had a feeling as if there was something in the graft under the skin. When examining the tactile sense, the patient had an itchy feeling on the thumb side of the graft. (Fig. 24.)

	Graft	Healthy dorsum of hand	(Reflected) Image Donor site
Z–1: *Tactile sense* (tactile hair 16)			
	+ 84	+ 92	+ 73
	– 16	– 8	– 27
Z–2: *Heat sense* (43° *C.*)			
	+ 92	+ 98	+ 90
	– 8	V 2	V 8
			– 2
Z–3: *Cold sense* (0° *C.*)			
	+ 75	+ 90	+ 79
	V 20	V 9	V 21
	– 5	– 1	
Z–4: *Pain sense* (10 *g.*)			
	+ 81	+ 100	+ 100
	– 19		
Z–5: *Tactile discrimination*			
	3 c.M.	3.5 c.M.	5 c.M.
	2 c.M.	3.5 c.M.	5 c.M.
Z–6: *Skin temperature*		(Average value of 9 determinations. The room temperature was 21° C.)	
	33.2° C.	33.1° C.	33.4° C.

Patient v.Z. showed the sensation pattern far better than that of patient K. This is to be expected as – seeing the course of the illness in both patients – it can be accepted that the ingrowth of nerve fibres in patient K. has encountered a stronger barrier than in patient v.Z. In both patients the sensation pattern was not as good as that of patient M. in whom a primary excision and graft was done.

In the primary grafts we always found a normal skin temperature; sometimes in the secondary grafts a normal, then again a lower skin temperature than the one of contra-lateral healthy skin was present. A difference of 1.2° C. must, according to KUEMMERLE, be considered pathological. If we found a difference in temperature greater than 1.2° C., as in patient K. this was then always associated with a powerful disturbance in the tactile sense. In how far a relation exists between the skin temperature and the tactile sense, is not as yet clear to us. In this respect the conception of MASSON is of importance, who points out that the tissue tension influences the strength of the tactile sense. The tissue tension is in close relation to the blood vessels of the skin which in their turn are again dependent on the vegetative nervous system.

The phenomenon (shown in the tables by the letter V.) whereby cold as warmth and warm as cold is indicated, demands a further explanation.

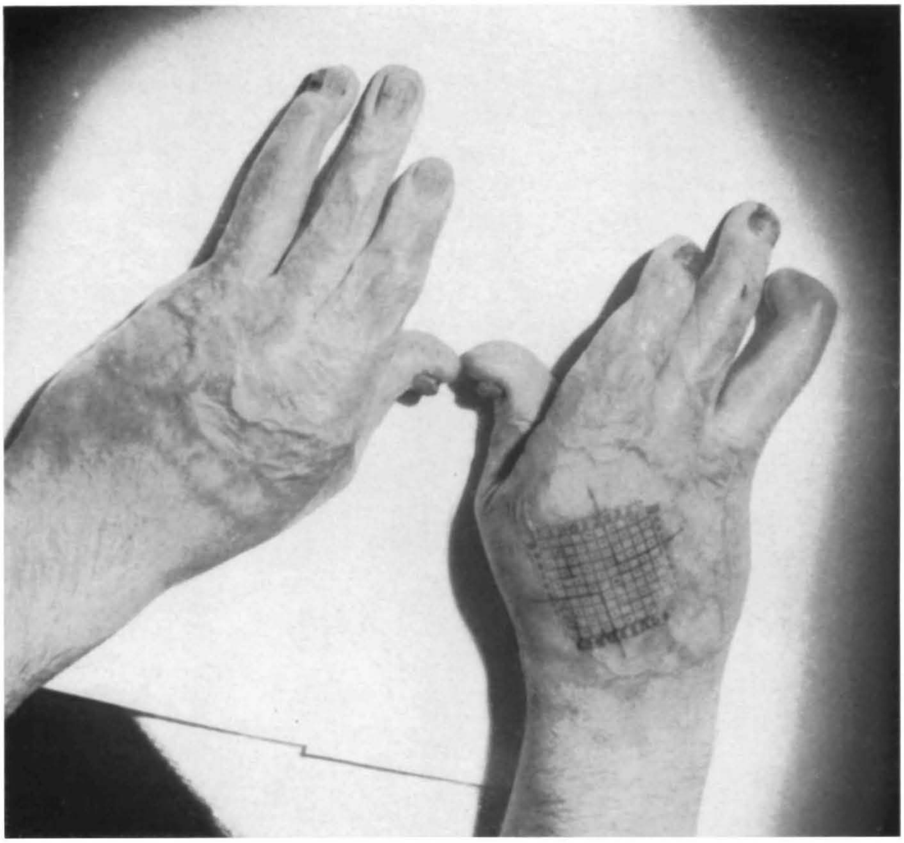

Fig. 23

Fig. 24

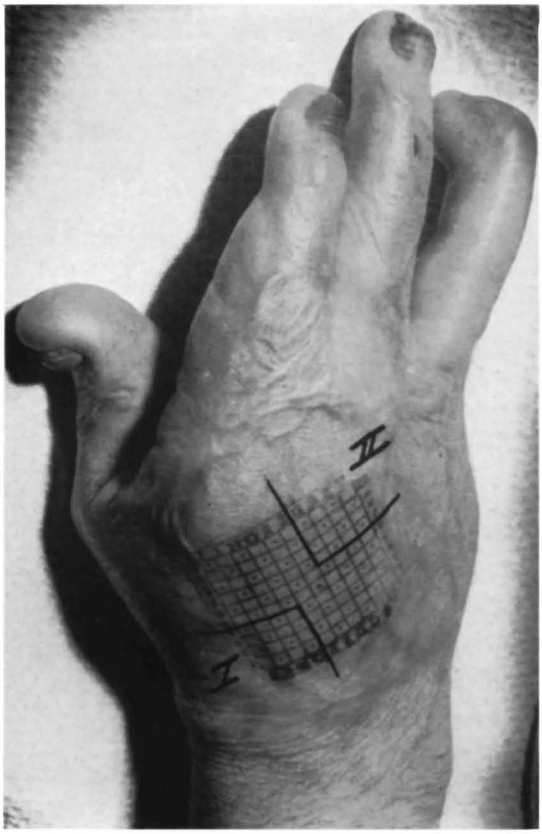

Fig. 25

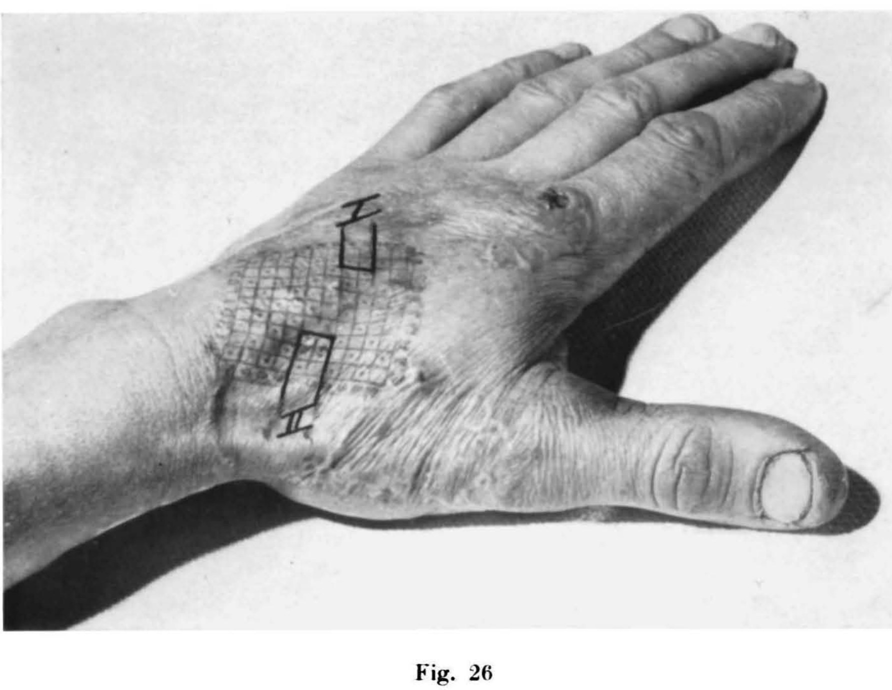

Fig. 26

When a heat stimulus is observed as cold, then in the literature one speaks of a paroxysmal cold reaction. In this respect the researches of ZOTTERMAN and his collaborators are of importance who, by applying warmth and cold stimuli led away potentials of the nerve fibres of the cats tongue. It was obvious to them that potentials which were led away from the fibres which conduct the heat stimulus had a lower frequency than those which were led away from the fibres which conducted the cold stimulus. The first named fibres responded somewhat arhythmic, the latter fibres rhythmic.

The cold fibres continually discharged, when the tongue had a temperature between 10 and 38° C., with a maximum of 10/sec. in a temperature from 30 to 32° C. A second peak was found between 10° and 15° C. where the frequency was 6/sec. Between 38 and 45° C. no potentials appeared, while between 45 and 50° C again a discharge appeared of 8/sec. In this manner we could give an acceptable explanation of the phenomenon of the paroxysmal cold reaction as we specially observed this in our patients with secondary grafts and whereby the stimulus with a warm object was experienced by the patient as cold.

More difficult to understand is the phenomenon whereby the cold stimulus is observed as warm. We had the impression that specially in secondary grafts, where many changes for cold and warm appeared, both stimuli evoked side-reactions. In this manner it was difficult for the patient to differentiate the two qualities. When the patient at last became confident with these side-reactions then the sensation pattern improved as well for cold as for warm.

The return of pain sense which we observed in patient K. and patient v.Z. is an apparent recovery which showed itself in these patients, amongst others, by the side-reactions which appeared with the applied pain stimulus. The pain sensations were indicated by these patients as stinging, itching, glowing. These pathological reactions were less clearly observed in patient treated with primary grafts.

Clinically we find differences in the discrimination sense in affection of the parietal lobe. A condition for this investigation is, however, that the tactile sense must be completely intact. The divergent values which we found in patient K. in whom we can assume that the cortical functions occur normally, must be considered to be related to a disturbed sensation pattern due to the lack of ingrowth of the nerve fibres. If, however, sensation recovery has occurred as in patient v.Z. then we find values which correspond with those of the contra-lateral healthy skin. This can be expected as the nerve fibres which grow into the graft maintain their original cortical representation.

Biopsy of the skin was performed in these three patients. In Patient M. a complete recovery of sensation appeared. Biopsy was done in the centre of the graft as distal as possible. In the patients K. and v.Z. a piece of skin was taken out in two places from the graft for histological examination.

(I and II). The sensation pattern in patient K. was in I as well as II strongly disturbed for all qualities. (Fig. 25.)

In patient v.Z. the tactile sense in I as in II was completely abolished, the cold stimulus was experienced as warm and the warm stimulus observed as normal. An analgesia existed in area I, in area II a hyperalgesia. The temperature of the skin in area I is 1° lower than in area II. (Fig. 26.)

It was not possible with regard to the findings in the sensation patterns to form an opinion on the question whether the nerve fibres grow from the healthy skin horizontally in the graft or penetrate from the depth.

In the litarature opinions are divided in this respect.

This can be expected as up till now the sensation pattern was only determined in secondary grafts. In the literature the controversial conclusions of this problem originate, in our opinion, that in secondary grafts a barrier more or less prevente the ingrowth of the nerve fibres. From the examination of our patients with secondary grafts we found, therefore, changing sensation patterns. Our investigation of primary grafts could throw no further light on this question as the investigation was done some years after the application of the graft and the graft had taken a practically normal sensation pattern.

In examining patients treated according to the method of primary excision and graft in whom the recovery process was undisturbed, and in whom the sensation investigation is performed in the primary stage, a further enlightenment can possible be thrown on this question.

III

HISTOLOGICAL INVESTIGATION

A. Methods

The following techniques were used for the study of the grafts, the skin of the donor site and the normal skin at the site of the graft.

1. Hemalum-eosin staining. To study the general structure of the skin-specimen, especially the shape of the dermal papillae.
2. Method for cholinesterase (Koelle modified by Gerebtzoff 1953). To differentiate between specific and non-specific cholinesterase D.F.P. (diisopropylfluorophosphate) was used. Eserine was used to inhibit both cholinesterases, and so to demonstrate aliesterases only. For specific cholinesterases acetylthiocholine was used as substrate and for non-specific cholinesterases bytyrylthiocholine.
3. The Champy-Coujard technique (a solution of osmic acid and sodium iodide); this method stains almost selectively the autonomic interstitial cells as Champy–Coujard (1945), Droz (1954 and 1955) have shown.
4. The silver impregnation technique after Bielschowsky-Gros.

B. Introduction

On studying a few grafts for orientation, we got the impression that the graft, concerning both its structure and its innervation, adapted itself to the skin of the area where the graft was applied. In order to study this phenomenon of transformation in more detail, we decided to do experimental grafting in animals. This has two advantages. In the first place cross grafts can be placed on two skin areas which differ greatly in structure and innervation. The snout of the pig was chosen and the skin of the medial aspect of the thigh. The snout of the pig is a typical sense organ, provided with sinus hairs (vibrissae) which are characterized by blood sinus in the connective tissue sheath and a rich innervation, totally different from the ordinary hairs in other places of the skin. Moreover, the skin of the snout shows Merkel's tactile cells, not to be found in the skin of the thigh.

The animal experiment, moreover, offers a possibility to follow the process of transformation, as commencing at the moment when a graft takes, and at certain intervals thereafter a biopsy can again be taken for examination.

Before a description is given of the obtained results, it seems desirable to make a few remarks about the innervation of the skin, especially as to the vegetative innervation. There are still several different conceptions of the structure and significance of the peripheral extension of the vegetative nervous system and as a result a different interpretation of the nervous structures in the skin.

In the first place there are followers of the original conception of CAJAL (1911) and RETZIUS (1892) who proclaimed that the vegetative fibres retain their individuality at the periphery thus forming separate endings which connect directly with the tissue elements, such as the cerebrospinal, sensory and motor nerve fibres do (NONIDEZ, 1944; KUNTZ, 1956; WEDDELL, 1941, 1948, 1954 and 1955).

In the second place there are many authors who hold that the ultimate peripheral extension of the vegetative nervous system in the tissues consists of a nervous network (APATHY, 1897; BETHE, 1903; BOEKE, 1933, 1938, 1944; STÖHR, 1928, 1935; STEFANELLI, 1938; LANDAU, 1944; SCHABADASCH, 1930, 1934; JABONERO, 1953, 1954; MEYLING, 1938, 1953, 1955; AKKERINGA, 1949; JOHN, 1951, 1958; CHAMPY, COUJARD and CHAMPY–COUJARD, 1945; DROZ, 1954, 1955).

About the nature of this vegetative nervous network opinions, however, differ. STÖHR (1928, 1935) and BOEKE (1937, 1938, 1944) agree that this nervous network consists of a Schwann-cell syncytium in which the neurofibrils form a network.

LAWRENTJEW (1944), HILLARP (1946), NAGEOTTE (1938, 1939), SCHIMERT (1937, 1938) agree that a terminal Schwann plasmodium is present, but the nerve threads in the plasmodium are, according to these authors, not neurofibrils, but axons, which run independently from each other in this syncytium of Schwann cells.

A third group of authors (LEEUWE, 1937; OKAMURA, 1934; MEYLING, 1953, 1955; CHAMPY and COUJARD, 1945; DROZ, 1955 and others) consider the peripheral nervous network as being built up by anastomosing autonomic interstitial cells, which, according to CAJAL, BETHE, OKAMURA, LEEUWE, MEYLING and others, are small primitive nerve cells.

It is still doubtful whether the peripheral nervous network forms the direct continuation of the vegetative nerve fibres (postganglionic- and afferent fibres). MEYLING thinks he has found indications that the latter fibres end synaptically on this nervous network. In any case, several authors have observed that this network persists intact for a long time after experimental degeneration of the postganglionic-and afferent fibres. Because the autonomic nerve fibres degenerate peripherally of the cutting within 3 days, this is an argument in favour of the discontinuity between the vegetative nerve fibres and the peripheral vegetative nervous network.

It is important to note that the anastomosing autonomic interstitial cells can, apart from silver impregnation, be shown by vitally staining with methylene blue and by the technique of CHAMPY–COUJARD.

As to the innervation of the skin, a distinction must be made between vegetative- and cerebro-spinal nerve elements. LEONTOWITCH (1901) already has given beautiful pictures of a nerve net in the skin, stained vitally with methylene blue. The presence of a vegetative peripheral nervous network in the dermis and in the epidermis is not opposed anymore, according to RICHTER (1958). He stated this in his introduction to the Symposium held in Vienna: "Das neurovegetative System der gesunden und kranken Haut des Menschen".

In connection with the vegetative innervation of the skin, attention must be paid to the so-called LANGERHANS' cells in the epidermis as we could stain them by the Champy-Coujard method, in the same manner as DROZ (1954, 1955). They lie mainly in the stratum granulosum and have in gold chloride stained slides as well as in methylene blue and Champy-Coujard slides a branched form, the cells anastomosing together by means of their processes.

LANGERHANS (1868) considered them as nerve cells, but later, however, different opinions arose in respect to their nature. BILLINGHAM and MEDAWAR (1948, 1953) considered them to be melanoblasts which, during their migration to the surface of the epidermis together with other epidermis cells, should gradually give off their melanin to these cells and finally be discarded as dead cells together with the cornified epidermis cells. A completely different interpretation of their nature was given by FERREIRA–MARQUES (1951). This author considered the Langerhans' cells as nerve elements which should grow out from the peripheral nerve network in the dermis, but with which they retained their connection. He attributes to these cells a nervous function; they form a network in the epidermis which should act as an intra-epithelial sense organ; it should be the receptor of the superficial primary sharp pain sense. For this reason he proposed the name of "Systema sensitivum intraepidermicum".

WIEDMANN (1953–1955) also accepts that the Langerhans' cells receive impulses from the surroundings and transmit these to the vegetative nerve network in the dermis. But contrary to FERREIRA–MARQUES he attributes to these cells a neuro-hormonal function. NÖDLE (1953) agrees with the conception of FERREIRA–MARQUES because they are found in a large number when painful leiomyoma are present in the dermis. Other authors, however, attribute to them a trophic function. RICHTER (1958) also holds the opinion that the Langerhans' cells are a system of sensory cells, which is connected with the vegetative network in the dermis. He doubts, however, whether they have anything to do with pain sense. According to him they are the most peripherally situated elements of the vegetative nerve system of the skin. He saw that in lepramatous leprosy they degenerate, and from this he concluded that they serve a trophic function, as WIEDMANN did. NIEBAUER (1956) is of the same opinion. We have gone more fully into the problem of the Langerhans' cells, because in our slides, treated by the Champy-Coujard technique, they appear distinctly black in colour, their processes anastomosing reciprocally, and also connect with the vegetative nerve network in the dermis. In comparison with the neurologic study of the grafts, up till now we have not been able to give indications about their probable function.

In contradistinction to the vegetative fibres, the cerebro-spinal sensory fibres do not merge into a nerve network, they retain their individuality and form separate endings in the outer root sheath of the hairs or they form encapsulated endings, (MEISSNER's corpuscles) or disc-like endings on the tactile MERKEL's cells.

WEDDELL and his school (1955, 1956), however, do not differentiate between vegetative and cerebro-spinal innervation of the skin. He discriminates two types of endings. Everywhere in the skin he sees so-called free nerve endings. The second type of endings is to be found in the non-hairy volar aspect of the hand and the plantar aspect of the foot, in the form of encapsulated endings; in the hairy skin in the form of nerve endings on the hair follicles, which he considers as a form of encapsulated nerve endings. As to the free nerve endings, he describes in earlier publications (1941) that under the epidermis nerve nets are formed by repeated branching of fine nerve fibres. These separate nerve nets are situated in circular confined skin areas; WEDDELL states that they overlap each other but there should be no continuity between the fibres of these separate nerve nets. From these nerve endnets, the free nerve endings are supposed to issue, which penetrate as fine beaded fibres in the deeper layers of the epidermis. The same endnets should be formed around the blood vessels, from which again fine beaded fibres issue, to run in the wall of the blood-vessel and along the capillaries. From this it may be concluded that the so-called free nerve endings of WEDDELL are identical with the vegetative endnets in the skin, which has been described by many other authors. WEDDELL (1955, 1956) in his latest publications does not mention these nerve nets anymore, but states that all nerve fibres end in the same way, namely in "fine naked axoplasmic filaments, which spring from ensheated parent or stem nerve fibres; the axoplasmic filaments all end freely and although they may overlap and interdigitate with filaments derived from neighbouring ensheated stem axons, they never come into actual contact or fuse with them."

This conception of WEDDELL concerning the innervation of the skin is discussed here because it has many adherers, especially in England and the United States.

As already stated we agree with most of the authors that in the skin a diffuse and continuous nerve network exists in the same way as in all other tissues and organs of the body, and which is of a vegetative nature.

Apart from this vegetative innervation, the skin is provided with cerebro-spinal nerve endings of different shape (MEISSNER's corpuscles, KRAUSE's end-bulbs, MERKEL's discs). These endings are practically only present in the hairless, glabrous skin. In the hairy skin we only observed cerebro-spinal nerve endings in the external root sheath of the hairs.

In the skin of certain tactile organs in animals, for instance the snout of the pig, where no ordinary hairs occur, so-called tactile or sinus hairs (vibrissae) are to be found, provided with a rich cerebro-spinal innervation;

MERKEL's tactile cells occur in a great number in the basal layer of the epidermis, on which also cerebro-spinal nerve fibres end in the shape of a disc.

We agree with the conclusions of WEDDELL and his co-workers that there are only two kinds of nerve endings in the skin, but we do not think it is correct to classify them as free and encapsulated endings; they should be classified according to their nature as a peripheral vegetative nerve network on the one hand and as cerebro-spinal nerve endings (in the shape of terminal corpuscles and endings in the hair follicles) on the other hand.

The vegetative peripheral nerve network also closely winds around the cerebro-spinal nerve endings, as has already been described by several authors; in this way the function of both the systems may be correlated.

C. RESULTS OF HISTOLOGICAL EXAMINATION OF THE GRAFTS

Based on this view the structure and the innervation of skin grafts, which had been examined on the different sensory modalities (tactile-, pain-, cold- and heat sense) will be described. Endeavours were made to compare the neurological findings with the histological structure and innervation of the graft. Because the grafts studied were similar as to the region i.e. dorsum of the hand and the donor site dorso-lateral aspect of the thigh, the structure and innervation of the normal skin of these areas are firstly described; the structure of the grafts shall be compared with these findings.

Donor Skin, dorso-lateral surface thigh

In hemalum-eosine stained slides it is seen that the dermal papillae are poorly developed, i.e. the epidermal cristae do not protrude deeply into the dermis and lie, in a cross-section of the skin, at irregular distances of each other (Fig. 27). In cholinesterase slides a positive layer (a band in the cross-section) is to be seen at the place of the stratum lucidum (Fig. 28). This is not typical for this skin area, because this positive layer in the epidermis is practically present in all skin areas, as MONTAGNA (1955) has already described. It is, according to this author, a non-specific esterase, which is absent in the glabrous skin, in the palm of the hand. We can agree with this, as the positive reaction remains with eserine and when butyrylthiocholine is used as substrate. In the basal layer of the epidermis some cells show positive grains. This, too, is mainly non-specific esterase. Specific cholinesterase (acetylcholinesterase) is to be found on the surface of the external root sheath of the hairs and around the sweat glands (Fig. 30); this is seen in all areas of the skin (see Fig. 36 and 47). In Champy-Coujard slides the autonomic interstitial cells of the vegetative nerve network are clearly seen in the dermis, some processes penetrating into the epidermis. This network is also present in all areas of the skin (see Fig. 31 and 40). In some cells of the basic layer of the epidermis, black grains appear, the significance of which is obscure.

Langerhans' cells are seen in the epidermis, mainly in the granular layer, the quantity of which differ a little in the different areas of the skin (see Fig. 32 and 39). In the blood vessels this network of autonomic interstitial cells is well developed. Fibre bundles are to be seen, mainly in the deep layers of the dermis, but smaller bundles are also present in the more superficial layers, mostly accompanying small arteries. It cannot be determined whether these are vegetative or cerebro-spinal nerve fibres or miscellaneous.

Skin normal dorsum of the hand

In cholinesterase slides it is seen that the dermal papillae are higher than in the skin of the dorso-lateral aspect of thigh (Fig. 29). The positive band at the level of the stratum lucidum, (non-specific cholinesterases or aliesterases) is also present in this skin area. This band runs contrary to the one in the skin of the thigh, more undulating, probably in accordance with the fact that here, on the surface of the skin, grooves occur. There is a strong reaction around the sweat glands (Fig. 30) which remains after D.F.P. treatment and therefore it is probably a specific cholinesterase.

In Champy-Coujard slides, the vegetative nerve network (anastomosing autonomic interstitial cells) is well marked (Fig. 31). The anastomosing processes of these cells are typically beaded. The anastomosing of the processes is not so clear in this photomicrograph, because by this method the network is stained often partially and because the meshes of the network lie mainly level, parallel to the surface. The beaded processes of the autonomic interstitial cells penetrate into the epidermis, running between the cells of the basic layers. Fig. 32 shows some Langerhans' cells with anastomosing processes. On studying many slides the impression is gained that these cells appear in a larger number than in the skin of the donor site.

The nerve network in the dermis is particularly strongly developed in the papillae. This can be seen in Fig. 33, where two transversally cut papillae are observed. The autonomic interstitial cells specially lie here along the capillaries. In this picture it is also seen that in the basal layer of the epidermis, blackly stained ramified cells lie, the so-called dendritic cells. Also in the dermis many more or less blackly stained nerve fibre bundles are seen, mostly accompanying blood vessels (Fig. 34).

These bundles consist of probably myelinated thick fibres (more blackly stained) and smaller non-myelinated fibres (stained more grayish); I would like to stress that they can be seen in practically all sections. This is of importance in regard to the statement whether nerve fibres have grown into a graft or not.

The grafts of three patients were studied histologically; patients K. and v.Z. with a secondary- and patient M. with a primary graft.

Patient K.; (secondary graft four years old). Two small fragments of the skin were taken within the grid applied (see Fig. 23). Compared with the donor skin, the dermal papillae are stronger developed (Fig. 35); they are more numerous and penetrate more deeply into the epidermis, or it can be said that high epidermal cristae are developed. As the papillae in the normal dorsum of the hand (Fig. 29) are higher than in the donor site (Fig. 27), it must be concluded that the epidermis – dermis margin has, according to shape, adapted itself to the place where the graft was attached and has lost its original shape. The cholinesterase positive layer at the place of the stratum lucidum, is present; the basal layer of epidermis cells shows a very strong cholinesterase activity, as compared to the normal skin of the dorsum of the hand and the skin of the donor site. After D.F.P. treatment this activity remains, but the reaction is also positive after preliminary treatment with eserine and using butyrylthiocholine as substrate. If the reactions are dependable, then this would show the presence of, not only specific, but also non-specific cholinesterases and aliesterases. Perhaps this strong enzyme reaction is a reflection of the activity of the stratum germinativum in the graft.

In fragment II, hairs were found (Fig. 36 and 37), with a positive cholinesterase reaction on the outer root sheath. No hairs were found in sections of fragment I; this may be due to the fact that hairs were thinly sown and could barely be seen at the surface.

In Champy-Coujard slides (Fig. 38 and 40) it is seen that the vegetative network (the autonomic interstitial cells with their beaded processes) is completely intact. Some processes penetrate into the epidermis and seem to anastomose with the beaded processes of dentritic cells in the basal layer.

Langerhans' cells are present in the graft. By studying a great number of slides, we got the impression that their number is not less than in the normal skin of the dorsum of the hand, in any case much more than in the skin of the donor site.

In connection with the well-developed peripheral vegetative network, it is curious that no nerve fibre bundles could be observed in the graft. It is difficult to state whether they are entirely absent, but because they are found in each slide of the normal skin, it must be assumed that perhaps only a few nerve fibres had penetrated into the graft. It is possible that in a secondary graft the nerve fibres grow in less easily, showing that in such a graft a kind of barrier is formed on the edge of the graft and the underlying connective tissue, whereby the ingrowth of nerve fibres is retarded or perhaps, made impossible. Notwithstanding this, the peripheral vegetative network is equally developed as in the skin of the normal dorsum of the hand. This may indicate that the peripheral vegetative network in the donor skin remains intact and does not degenerate as the nerve fibres do. The latter must grow again into the graft from the tissue lying under the graft, eventually sideways, to connect with this network which persists in the graft. As the peripheral vegetative network is probably not the direct continuation of the vegetative nerve fibres, but a relatively independent network of small primitive nerve cells, (see introduction) this supposition is not impossible. Abovementioned facts could even support our conception of the structure and significance of the peripheral vegetative nerve system. To be certain of this early grafts must be studied, where certainly the ingrowth of nerve fibres could not, as yet, have taken place.

The fact that practically no nerve fibres had grown into this graft can possibly be the cause of the significant decrease of the different sensory modalities.

Patient v.Z.: (secundary graft three years old). In this patient two fragments from the applied grid were also studied (see Fig. 24). This graft was particularly interesting for histological investigation, because in fragment II a hyperalgesia was present but not in fragment I.

It was possible for us to obtain a biopsy of the donor skin (lateral aspect thigh) and of the contra-lateral normal skin of the dorsum of the hand, for histological examination. As to the normal dorsum of the skin we can refer to Figs. 29, 30, 31, 33 and 34. The donor skin shows, in slides treated with the cholinesterase method, poorly developed dermal papillae, a positive band at the place of the stratum lucidum and more or less positive grains in the cells of the basal layer of the epidermis (Fig. 41).

Graft, fragment I

High dermal papillae in the dorsum of the hand are developed in the same way as in other grafts (Fig. 42). The cholinesterase activity is also similar to other grafts in the dorsum of the hand. The positive layer on the spot of the stratum lucidum and the positive grains in the cells of the basal layer of the epidermis again in this graft represent probably mostly aspecific- or aliesterases. Because the Champy-Coujard slides were not successful, silverimpregnations, according to the method of Bielschowsky-Gros were made, which show the interstitial cells of the peripheral vegetative network and the nerve fibre bundles in approximately the same manner as the method Champy-Coujard does. The interstitial cells, forming the peripheral nerve network, could be demonstrated, showing a normal aspect (Fig. 43). On examining a large series of slides, no ingrown nerve fibre bundles were found in this fragment of the graft, while, as previously mentioned, in the normal skin of the dorsum of the hand, nerve fibre bundles are found in the dermis in practically every slide. Reference can be made to the remarks given to the same findings in the graft of Patient K.

Fragment II

The findings in this piece of the graft were remarkable. In hemalum-eosine slides (Fig. 44) it showed very irregular dermal papillae, high and low ones, not all running exactly perpendicular to the surface.

In the dermis abnormal structures are to be seen, looking like epithelial strands. They, too, resemble the leiomyoma described by NÖDL (1953) in a painful skin. The fact that epithelial strands could be seen issuing from the dermis (Fig. 46) speaks for the first conception.

The cholinesterase reaction showed mainly the same picture as in the other grafts (Fig. 45 and 46). The stratum germinativum of the epidermis shows many positive grains in the cells, far more copious than in the normal skin. For the greatest part they probably are non-specific cholinesterases or aliesterases; it may be that this strongly positive reaction is the reflection of a great activity of the stratum germinativum.

As to the epithelial strands, at several places an ingrowth of epithelium into the dermis could be observed (Fig. 46). It may be that this is the origin of the irregular epithelial strands in the dermis. The outer layer of cells of these epithelial strands (the continuation of the stratum germinativum of the epidermis) shows a strong positive cholinesterase activity. This reaction is also positive after D.F.P. treatment, and therefore probably is at least partially specific cholinesterase.

The parts, deeply penetrated into the dermis, also show on the surface, a positive cholinesterase reaction, similar to that on the external root sheath of hairs (Fig. 47).

It may be supposed, from these facts, that we have to deal with an attempt to form hairs, but which has led to the formation of abnormal structures.

Of special importance is that ingrowing nerve fibres could be observed in silver preparations, which could not be seen in segment I, nor in the graft of Patient K. (Fig. 48 and 49).

Probably, therefore, the presence of ingrown nerve fibres in this part of the applied pattern is related to the hyperalgesia. Although many authors are of the opinion that the peripheral nerve network acts as receptor for the deep pain sense and that afferent vegetative nerve fibres carry the impulses centrally, it is difficult to confirm this opinion on the basis of our findings. It is not possible to determine histologically whether one deals with vegetative fibres, with cerebro-spinal or both kinds of fibres in one bundle. As seen in Fig. 49, the bundle is composed of thick and small nerve fibres and because small bundles often follow the course of the small arteries, this would indicate that at least some fibres are of vegetative nature. It can, however, also be presumed, that the cholinergic nerve elements on the surface of the abnormal epithelial strands act as pain receptor.

Because NÖDL saw that the Langerhans' cells were present in an abnormal great number in skin with hyperalgesia, he attributes to these cells the function of pain receptor. Therefore, in continuing our research, we still hope to get a biopsy of this hyperalgenic area in order to study in Champy-Coujard preparations the number of Langerhans' cells present in the epidermis and to compare this with those in fragment I and the normal skin.

Patient M.: (primary graft five years old, see Fig. 22 p. 00). In this graft too, the papillae had developed in a manner more similar to the normal dorsum of the hand than to the donor site (Fig. 50).

The number of Langerhans' cells in the epidermis of the graft did not show a clear difference to that in the donor skin. In the graft definite hairs had developed with sebaceous glands. Between the cells of the outer root sheath branched cells were found in Champy-Coujard slides, similar to the Langerhans' cells in the epidermis (Fig. 51). The vegetative nerve network in the cutis, as shown in the slides, did not differ from that found in the normal skin of the dorsum of the hand.

In histological method for cholinesterases the outer root sheaths of the hairs showed a positive reaction. These are certainly not exclusively specific cholinesterase because the reaction remains positive when butyryl-thiocholine was used as substrate, also after treatment with eserine. The most typical feature of this graft was that nerve fibre bundles were seen in Champy-Coujard preparations, both in the deeper (Fig. 52) as in the more superficial layers (Fig. 53). Their number did not differ significantly from that in the normal skin of the dorsum of the hand. This primary graft showed in this way a structure and an innervation, not noticeably different from that in the normal skin of the dorsum of the hand. In a primary graft the nerve fibres had less resistance to grow in than they have in secondary grafts; a finding which coincided with the clinical observations.

D. Experimental research

For our experiments pigs were used, because the snout of this animal is a specific tactile organ, the skin of which differs from the remaining skin, due to its typical innervation and the presence of tactile hairs (sinus hairs).

Cross-grafting was performed by one of us (Sneep) between the skin of the snout and that of the medial aspect of the thigh. The snout's skin was removed in total thickness to the rostral bone. From the medial aspect of the thigh an intermediate split-skin graft was taken. The difference between the two skin areas manifested itself in the first place in the shape of the cutis papillae, while in the skin of the snout narrow, rounded papillae are present which penetrate deeply into the epidermis to approximately the stratum lucidum (Fig. 54), the skin of the medial aspect of the thigh shows poorly developed papillae, by which the cutis epidermis edge has a slightly wavy aspect (Fig. 55). It can be presumed that the height of the papillae may be related to a more or less sensibility of the skin, (perhaps with one or more modalities). This may be because, apart from the skin of the snout of the pig, also in other areas of the skin with well developed sensibility (volar aspect of the finger tips in human beings and on the snout and the digital pad of dogs and cats etc.), also high and narrow cutis papillae are to be found. The sinus hairs in the snout (Fig. 56) of the pig show rich cerebro-spinal innervation of the outer root sheath. (Fig. 57).

The skin of the medial aspect of the thigh has no sinus hairs.

MERKEL's tactile cells are present in the skin of the snout of the pig, situated at the top of the epidermal crests. These cells have a cerebro-spinal innervation in the shape of a disclike swelling at the end of the fibre which embraces the cell at the basal side (Fig. 58). In the thigh skin no MERKEL's tactile cells occur.

In cholinesterase slides the innervation of the MERKEL's tactile cells show a positive reaction (Figl 59). It is certainly not only exclusively specific cholinesterase, because after preliminary treatment with D.F.P. the reaction is significantly less intensive, whereas when bytyrylthiocholine is used as substrate and after preliminary treatment with eserine, the reaction is still positive. THIERS and GALENTE (1957) found the same in cholinesterase reaction of the MEISNER's corpuscles in the human being. Because the endings in the outer root sheaths of the hairs also show a positive reaction, we agree with these authors that probably the whole cerebro-spinal sensory innervation is cholinergic. The cholinesterase positive layer which is to be found in the hairy skin of the human being, above the granular layer does not occur in the skin of the snout. Regarding this, the skin of the snout shows the same as the glabrous skin of the palmar side of the hand in the human being, where, after MONTAGNA (1955), this cholinesterase band is also absent.

In Champy-Coujard slides the vegetative nerve network is clearly seen as well in the skin of the snout as in the skin of the medial aspect of the thigh. In the skin of the snout this network is specially well developed in the high cutis papillae where the anastomosing interstitial cells lay mainly along the capillaries (Fig. 60).

It is remarkable that with this method black stained nerve fibres were seen situated against the top of the epidermal crest where the MERKEL's tactile cells are situated (Fig. 61).

In how far they are related to the innervation of these MERKEL cells, is difficult to say. Many authors found that, apart from the cerebro-spinal innervation of sensory end-corpuscles, a vegetative innervation often occurs, described by BOEKE as an accessory nerve fibre. In this connection I may point out that after KOELLE (1955) the theory of the chemical transmission of the impulse by cholinergic and adrenergic innervation, does not mean that the transmitting substance is in the first instance exclusively acetylcholine, or secondly exclusively adrenaline (noradrenaline). Probably they are both present at the nerve endings. Only in cholinergic innervation the acetylcholine (and in connection therewith the specific cholinesterase) should be present in greater quantities, while in adrenergic nerve endformation, the adrenaline- like substance should be preponderant.

It is, however, possible that this only holds good for vegetative end-formations, while in this case we have to deal with a cerebro-spinal innervation. There were a few Langerhans' cells found in the epidermis of the snout's skin.

In the skin of the medial aspect of the thigh, the network of the autonomic interstitial cells is rich in that part of the cutis, situated immediately under the epidermis (Fig. 62). In the epidermis a slightly larger quantity of Langerhans' cells were found than in the snout 's skin.

The material for studying the normal structure and innervation of the skin of the snout and the medial aspect of the thigh was obtained during the cross-grafting on the 26.11.'58.

The first biopsies of the grafts were taken on the 23.12.'58. A biopsy was also taken of the graft of the snout on 4.2.'59. The former two biopsies were therefore 27 days old and the latter 67 days old.

Graft snout (Donor site, medial aspect thigh).

The dermal papillae have already developed in a direction of the kind which is typical for the normal snout's skin (Fig. 63). Hairs are also to be seen which resemble the sinus hairs, because blood sinuses are observed in the connective tissue sheath of the hairs (Fig. 64). In Champy-Coujard slides the network of interstitial cells is completely intact in the cutis as well as in the papillae. In a biopsy 67-days old, the cutis papillae are still higher than in the 27-days old biopsy and contain the rich network of autonomic interstitial cells, typical for the snout's skin (Fig. 65). In both the biopsies nerve fibre bundles lie in the cutis, mostly in the vicinity of small arteries; the nerve fibres are stained black or more grayish (Fig. 66). In 27-days old grafts with Bielschowsky-Gros technique nerve fibre bundles are to be seen mainly in the basal layer of the cutis (Fig. 67), but they were also already found in the more superficial layers (Fig. 68). Along the fibres large numbers of Schwann cells are present. Apart from cerebro-spinal fibres vegetative post ganglionic and afferent fibres are probably present, especially in the deeper situated nerve fibre bundles. The small bundles, which are found in the superficial layers probably contain mainly fibres which form endings on the Merkel's tactile cells which are, therefore, probably cerebro-spinal sensory fibres, because on the top of the epidermal crests an innervation of Merkel's tactile cells are in the process of development (Fig. 69). On this place, swellings at the end of nerve fibres are already observed near large clear cells which already show the aspect of tactile discs, (compare with Fig. 58). The typical cerebro-spinal sensory innervation of the snout's skin is in the process of development in this graft.

Graft: Medical aspect thigh. (Donor-site snout)

Biopsies of this graft were 27-days old when studied. In Champy-Coujard slides in the first place is seen that the sinus hairs are lost and that ordinary hairs are already developed (Fig. 70). The dermal papillae are lower than in the snout's skin and are similar to thos found in the normal thigh's skin. Here also the network of autonomic interstitial cells is well developed under the epidermis and beaded processes of these cells penetrate into the epidermis (Fig. 71). The epidermis contain more Langerhans' cells than in the snout's skin; the pattern of the graft also has, in this respect, taken on the aspect of the surrounding thigh's skin.

From the results of these experiments it appears that where the graft is placed it adapts itself in both structure and innervation to the surroundings and therefore does not retain the usual type of the original skin.

The opinions hereon differ vastly; some investigations done on experimental grafts may be mentioned here. KADANOFF (1926) grafted in guinea pigs and rabbits the skin of the foot-pad on to the snout and vice versa. The latter took badly. He stated that in grafts on the snout the newly developed nerve endings showed a great similarity to those which normally occur in the skin of the snout. That is why this author assumes that the ingrowing nerve fibres have the pretention to form in this grafted skin (from foot-pad skin) the endings which are formed under normal circumstances in the snout's skin. But according to this author Merkel's tactile cells, typical of the snout, are absent in the graft. That is why KADANOFF has not come to a definite conclusion. DIJKSTRA (1933) undertook cross-grafts in ducks, in which the beak-skin (with typical Grandry's corpuscles) was placed on the foot-pad and vice versa. He concluded that the graft showed no changeable signs in structure and so maintained its original type. The sensory end-corpuscles completely degenerated in the grafts and entirely new end-corpuscles were formed of the type of the donor skin and not of that of the surrounding skin.

This author points out that the tissue of the graft determines the development of the sensory end-corpuscles.

The result of our investigation coincides more with those of KADANOFF than with those of DIJKSTRA. Both investigators, however, do not yet differentiate between cerebro-spinal innervation and vegetative innervation. The snout of the pig offers, as we think, an advantage over the smaller animals used by these authors, because, when the skin of the snout is taken away totally, a much larger graft is obtained. If one also takes biopsies out of the middle of the attached graft, then one does not run the risk of taking skin which has grown from the edge of the surrounding skin over the wound. In addition thereto, the skin of the snout lends itself better for grafting than the stubborn hard skin of the beak and the foot-pads of the duck.

Also, the new techniques of investigation, such as the histochemical reaction for cholinesterases and especially the technique of Champy-Coujard, are more suitable for studying the re-innervation than the silver-impregnation technique exclusively used up till now.

We intend to study further the transformation of the structure and the re-innervation of older grafts and we also wish to study with the aid of new similar experiments, still earlier grafts on the snout.

Preliminary observations have already given the impression that the latter may throw more light on the process of changing the shape of the dermal papillae and can give more assurance that the vegetative nerve net persists in the graft and is not newly formed by ingrowth from the surrounding tissue.

DISCUSSION

In order to judge the correct local treatment of burns, the second degree burns are of no consideration. If we treat such burns strictly aseptically (in the first instance nursing is of importance) these burns can be cured without any loss of function. In this case the cosmetic effect will always be optimal. The formation of keloid should not occur.

To judge the correct treatment of third degree burns will depend greatly on the influence which the treatment has on the formation of scar tissue, the appearence of contractures and as a result thereof, malformations. The quick mobilisation made possible by means of early excision and grafting, in our opinion, justifies the precision of the view we have now taken.

Due to the obvious diminishment of the infection it has also shown that the number of repair operations as the result of malformations, has decreased. Not only by studying the literature but also from our own experience it has clearly shown that by primary excision and grafting three important advantages have come to light for the patient:

1. decreased mortality;
2. shorter duration of recovery and subsequent brief stay in hospital;
3. the chance of disability is greatly diminished.
4. Better return of sensation.

The diagnosis of third degree burns is now possible at an early stage by means of the pin-prick test. Slides taken from the excised skin segments always produced a full skin-loss where this test was positive.

Apart from the abovementioned advantages, the prevention of infection should be mentioned and serious consideration should be given whether early excision and grafting in extensive third degree should be applied. Where, however, in cases of extensive burns the mortality appears to be more or less 100 % as the result of serious infection a quick excision may not be taken as a contra-indication.

The results of the treatment of deep injuries to the hand by means of primary excision and grafting are greater than those of other methods of treatment. This is specially noticed in burns of the hands whereby the duration of rehabilitation is shorter than in other methods of treatment. The recovery of function is proportional to the duration of rehabilitation; the shorter the rehabilitation the better the recovery of function will be, in this case the formation of connective tissue does not occur nor shrinking of tissue which is due to the formation of connective tissue. The results of late mobilisation and rehabilitation have appeared to be no better. Repair operations of contractures and scar formation cause a great deal of difficulty. From our investigation it has also clearly shown that, apart from the greatly diminished chance of disability the return of sensation in the skin graft is practically complete. This last point is particularly important for the workman doing precision work. For this group of patients it will be of the greatest importance that, apart from recovery of function, re-adjustment will be possible to their previously chosen occupation.

As the results of our investigations on the sensation we have come to the conclusion that sensation in primary grafts almost completely recovers and takes on the sensory pattern of the surrounding skin. Our histological investigation proved this point as it clearly showed that the structure and innervation of the grafts adjust themselves to the surrounding skin. This again was clearly confirmed by animal experiments on pigs, where the skin of the snout was replaced by skin of the medial surface of the thigh and vice versa. (the crossed experiment). This experiment is therefore so convincing because in the skin of the snout sinus hairs and Merkel's discs are present which are not found on the skin of the medial part of the thigh. It showed that in a 27-day old graft from the thigh and applied to the snout sinus hairs and Merkel's tactile cells with typical innervation had developed. In the graft from the snout and applied to the medial surface of the thigh, ordinary hairs developed and sinus hairs and Merkel's cells with their innervation disappeared. In relation thereto it is also important that the corpus papillare had completely adjusted itself to the surrounding skin, which could clearly be stated because in the skin of the snout the cutis papillae are extremely high, contrary to those which are present in the skin of the medial aspect of the thigh. We could perceive this in our patients, of whom the skin of the lateral aspect of the thigh was placed on to the dorsum of the hand. In the skin of the thigh the corpus papillare is slightly developed but in the skin of the dorsum of the hand the dermal papillae are higher. Here also the corpus papillare of the graft adjusted itself to the surrounding skin.

In the animal experiment both grafts had adjusted themselves completely in structure and innervation to the surrounding skin within a time limit of 27 days. If one wishes to give an opinion about the degree of recovery in patients of sensory qualities in the graft then next to a quantitative investigation of the sensation, a comparative investigation with the contra-lateral side is necessary. The respective areas must be examined alternately in one session and the sensory pattern found in the healthy skin gives us an impression of the degree of the co-operation of the patient.

The many modalities and sub-modalities of the sensation, which the patients on examination indicated in the normal skin and the strong side-reactions which were observed in secondary grafts, do not make it acceptable that for this definite anatomical substratae must be made responsible. In agreement herewith, by histological examination of the dorsum of the hand, to which area our investigation limited itself, we found no specific end-organs, a fact which had already previously been observed in other hairy skin areas, amongst others by WEDDELL. The so-called doctrine of pattern therefore, gives a more acceptable explanation for our observations in the sensation investigation than the doctrine of specific energy (VON FREY).

In secondary grafts in which the tactile sense was disturbed, we always found sub-normal skin temperatures, from which we must conclude that between the tactile sense and the skin temperature certain relationship could exist. In histological examination the ingrowth of nerve fibres in secondary grafts is notably much less than in the normal skin and the primary grafts. They were not found but this does not necessarily mean that there was no sign of an ingrowth. The diminished tactile sense can therefore be vested on a too little ingrowth of the cerebro-spinal fibres which generally conduct the tactile sense, but also, however, on a too small an ingrowth of postganglionic and afferent vegetative fibres. In this respect the opinion of MASSON is important, who points out that the tonus of the skin influences the tactile perception; the tonus of the skin is connected with the blood circulation, which in turn is influenced by the vegetative nerve system.

Based on our histological investigation we are of opinion that the nerve supply in the skin is partially brought about by the vegetative nerve system on the one hand and by the cerebro-spinal nervous system on the other hand. The cerebro-spinal fibres are connected in the glabrous skin (palm of the hand) with specific end organs, in the hairy skin (dorsum of the hand) with the hair follicles. We agree with WEDDELL that two kinds of nerve endings exist, however, not in the sense of free and encapsulated, but of vegetative origin on the one hand and cerebro-spinal on the other hand. The free nerve endings described by WEDDELL are caused, in our opinion, by an incomplete staining of the vegetative end-net. In this respect we may refer to the „Introduction of the Histological Investigation" in which our opinions of the peripheral vegetative network are outlined. The principle brought to the fore by one of us (Sneep) some years ago that the nerve endings in the graft remain intact during the grafting process in situ, now finds support in our histological investigation, from which it appeared that the peripheral vegetative nerve network in the skin remains intact in the graft, independent of the fact whether ingrowth of nerve fibres takes place. This is in agreement with the experimental investigation of different authors, who point out that the peripheral vegetative nerve net of a definite area can remain intact for a very long time, notwithstanding the fact that all nerve fibres entering this area are cut. These experiments could possibly still be contested because not all vegetative nerve fibres were cut, as for example the vegetative nerve fibres which run in the walls of blood vessels.

Our investigation can, therefore, be a new confirmation of the opinion of one of us (MEYLING) that the peripheral vegetative nerve net is relatively independent and not the direct continuation of postganglionic- and afferent vegetative nerve fibres.

Between the nerve fibres on the one hand and the peripheral vegetative nerve network on the other hand, possibly a synaptic connection exists. In continued experimental investigations which will be carried out further, it occurred to us that after 14 days the peripheral vegetative nerve net is still intact in the graft without the ingrowth of nerve fibres being observed.

Up till now it is generally accepted that the peripheral vegetative nerve net is the perceptor of pain. In our opinion it is still questionable whether the perception of the tactile sense is only brought about by way of the cerebro-spinal nerve endings, seeing the fact that in clinical glabrous grafts a practical normal return of the tactile sense takes place, when these grafts were applied as part of an early excision and grafting.

Notwithstanding the fact that clinically no hairs could be observed, histologically it was found that completely developed hairs were present in the cutis, which evidently had not reached the surface. This contrary to the histological appearences in secondary grafts, where hair formation appeared less clearly and possibly showed an abnormal picture.

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SUMMARY

A description is given of a new method of investigating the return of sensation in connection with the question as to whether grafts may assume the sensation pattern of the adjacent skin or retain the properties of the site of origin. Histological examinations of the normal skin and the grafts were made by using mainly neuro-histological methods and histochemical methods for differentiating between cholinergic- and adrenergic innervation These showed that the grafts are transformed in the way to obtain the structure and innervation pattern of the surrounding skin.

Based on the investigations of sensation, performed on 43 patients, with deep burns of the hands, either treated by primary or secondary grafting, it was concluded that the sensation in primary grafts almost completely returned to normal and assumed the sensory pattern of the surrounding skin.

The recovery of sensation in secondary grafts is less favourable. Concurring with this, we find by histological investigation that in secondary grafts, the ingrowth of nerve fibres is notably less than in primary grafts. The nerve supply in the skin is brought about partially by the vegetative nervous system and on the other hand by the cerebro-spinal nervous system. Our investigation gives a further confirmation of the view of one of our collaborators (MEYLING) that the peripheral vegetative nerve net is relatively independent and not a direct continuation of postganglionic- and afferent vegetative nerve fibres. The impression is gained that the vegetative nervous net persists intact in the grafts. Our findings are further confirmed by experiments. (pigs).

To obtain optimal regeneration of the nervous elements, the time of application of the graft is the chief criterion. Our clinical investigations have shown that the thickness and the type of grafts used, in this respect are of minor importance.

Primary excision and grafting, therefore, are the ideal requirements which must be fulfilled if the problems involved in the re-innervation of grafts are to be studied in detail.

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PLATES

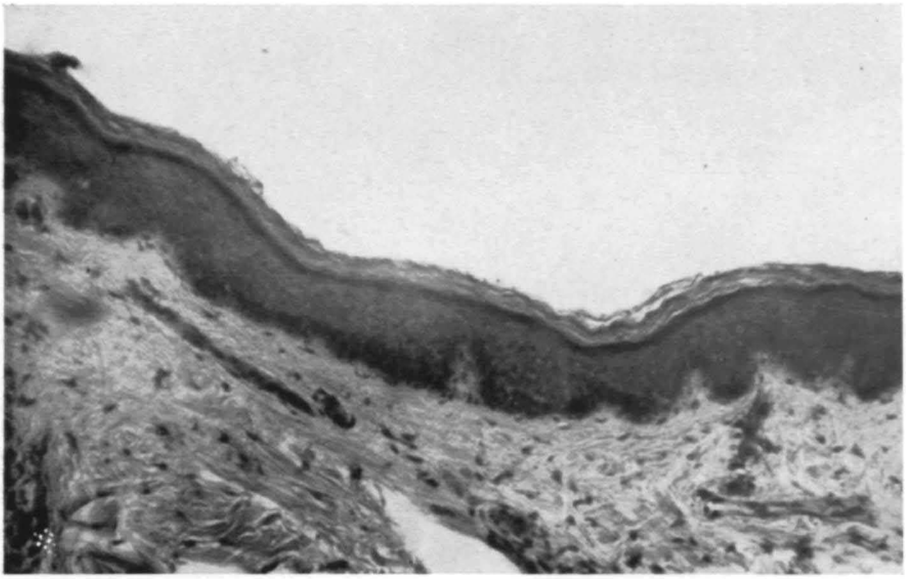

Fig. 27. Donor skin dorso-lateral aspect thigh. Hemalum-eosine staining. Poorly developed dermal papillae.

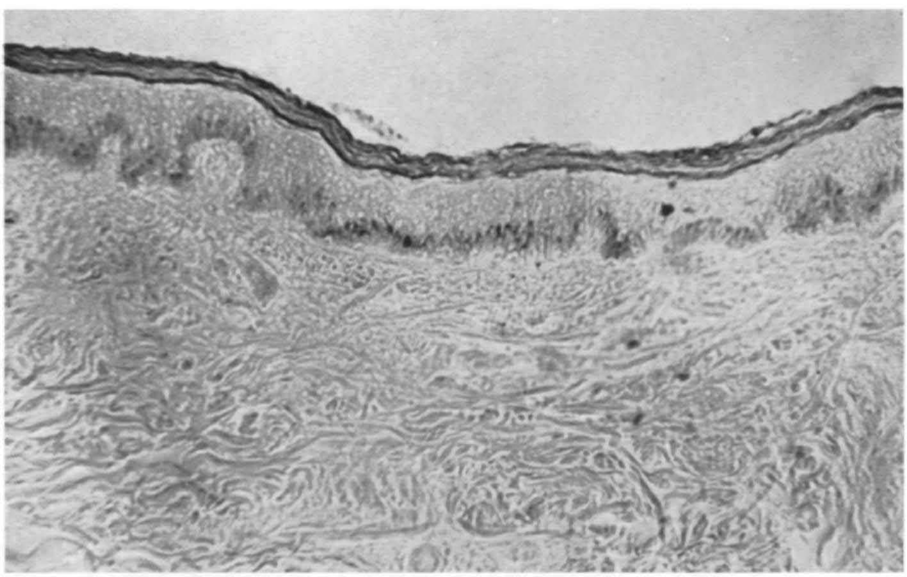

Fig. 28. Donor skin dorso-lateral aspect thigh. Histochemical method for cholinesterase. Positive layer at the place where the stratum lucidum is situated. Positive grains in the cells of the stratum germinativum.

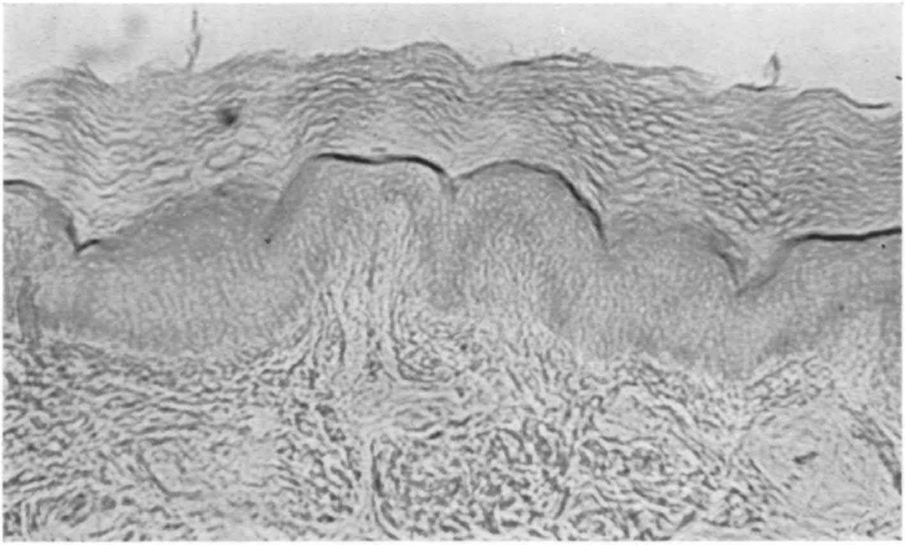

Fig. 29. Normal dorsum of the hand. Cholinesterase reaction. Positive reaction where the stratum lucidum is situated.

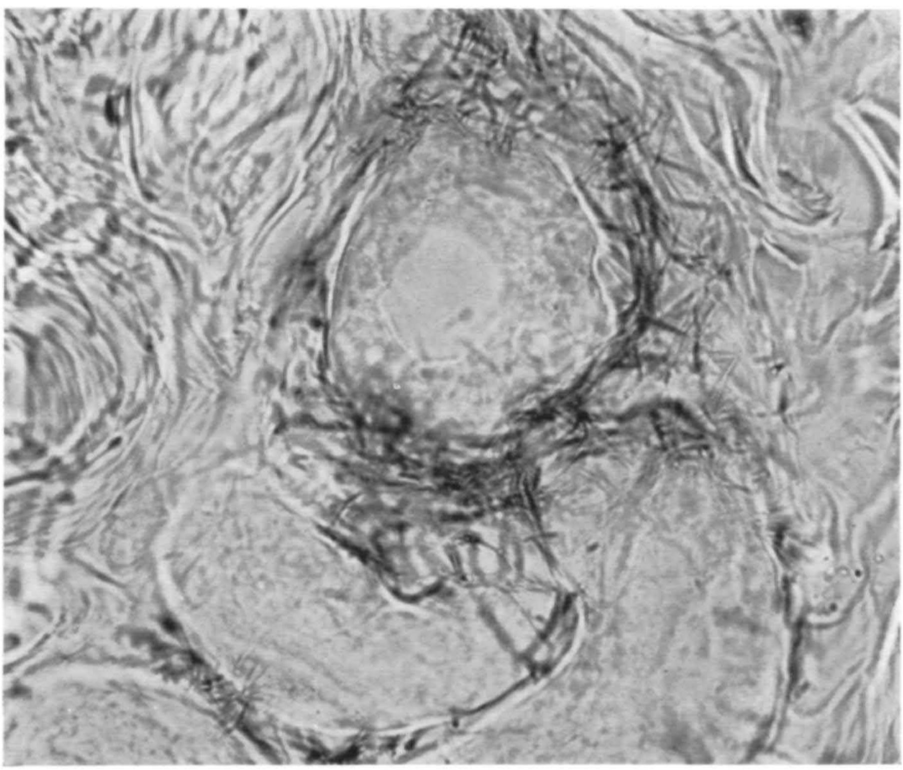

Fig. 30. Normal dorsum of the hand. Positive cholinesterase reaction on the sweat glands.

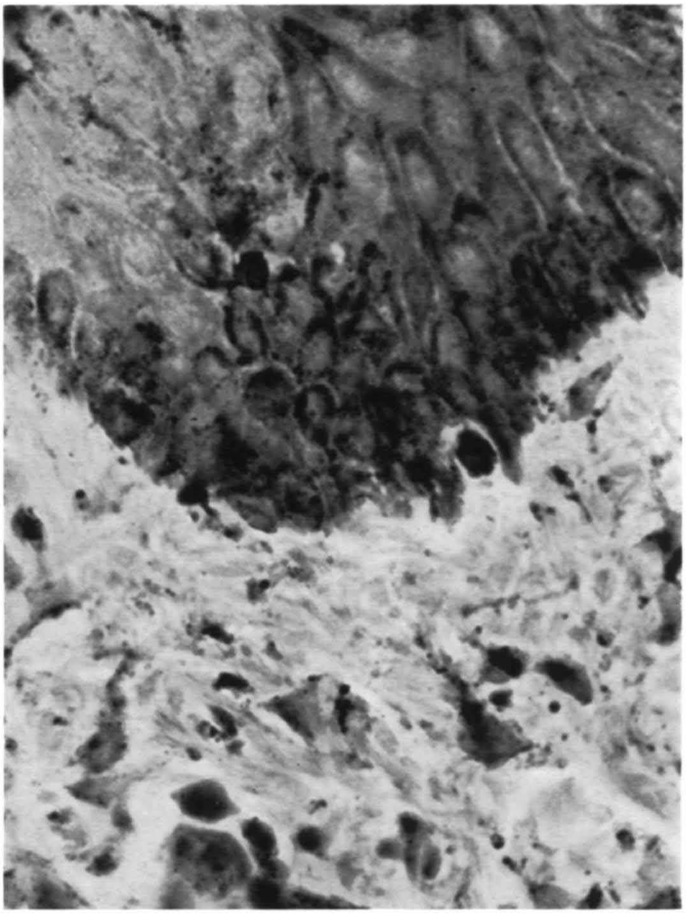

Fig. 31. Normal dorsum of the hand. Champy-Coujard technique. Nerve cell network in the dermis and in the basal layers of the epidermis.

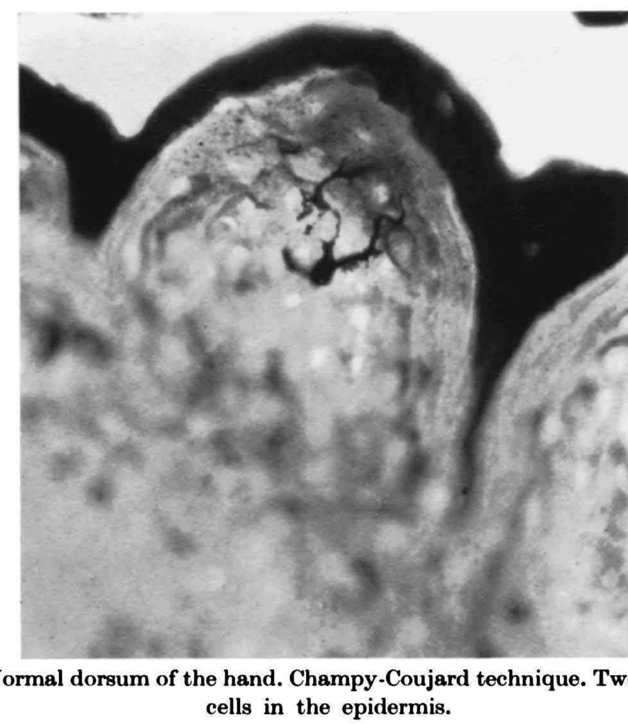

Fig. 32. Normal dorsum of the hand. Champy-Coujard technique. Two Langerhans' cells in the epidermis.

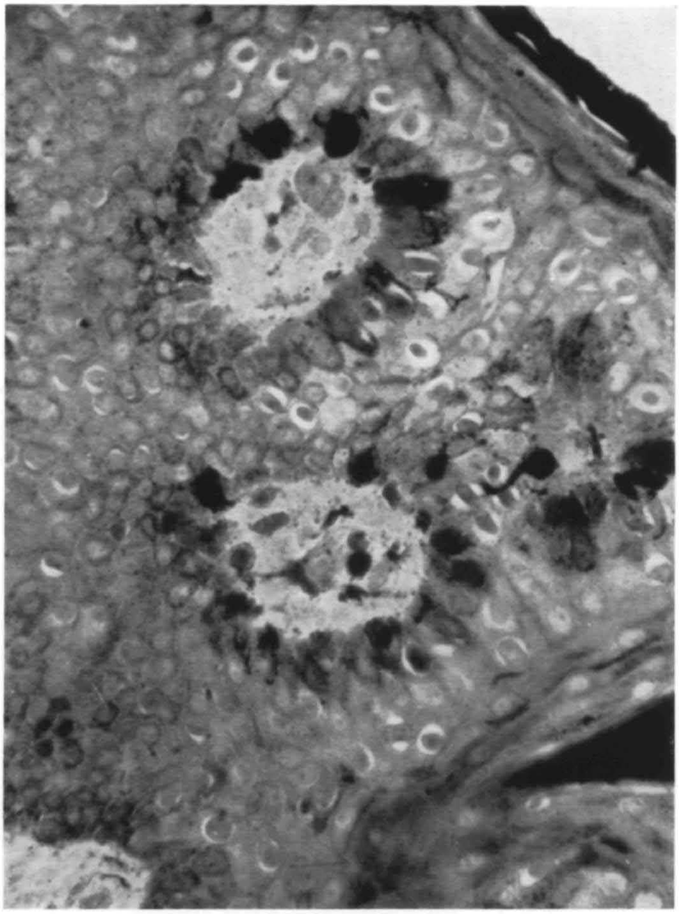

Fig. 33. Normal dorsum of the hand. Champy-Coujard technique. Two crossly-cut dermal papillae with blackly stained autonomic interstitial cells.

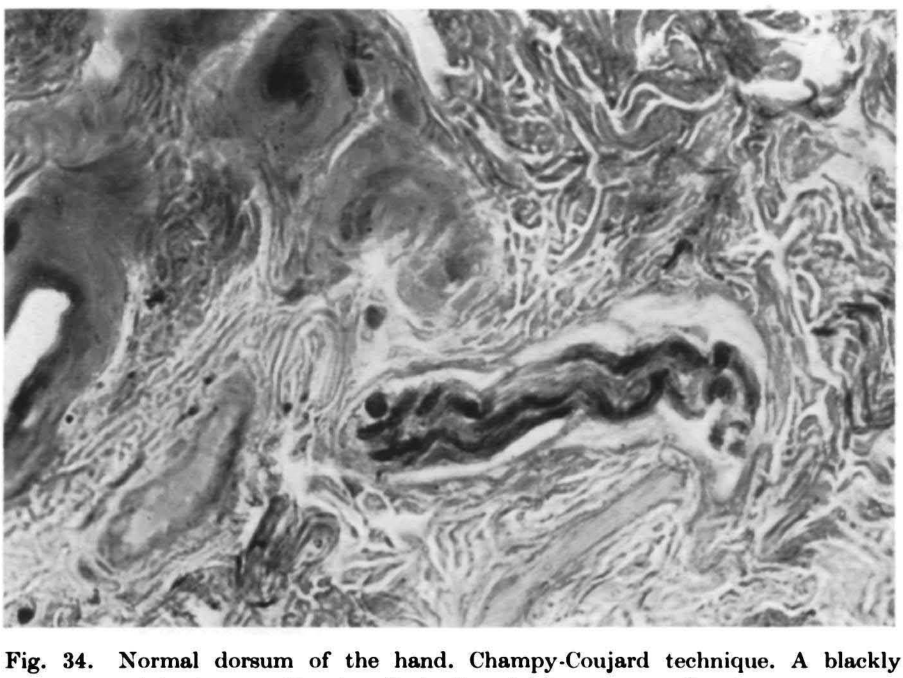

Fig. 34. Normal dorsum of the hand. Champy-Coujard technique. A blackly stained nerve fibre bundle in the vicinity of a small artery.

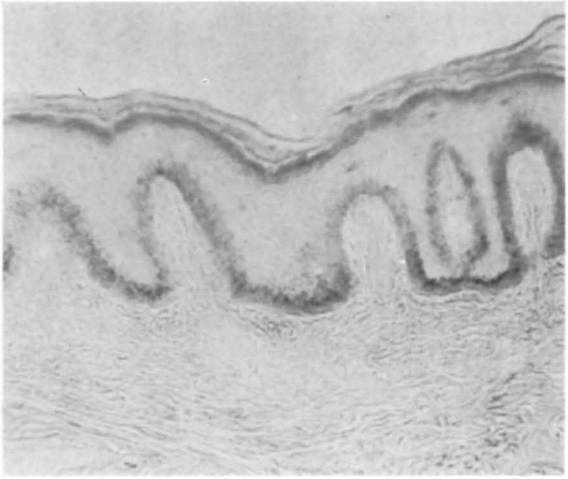

Fig. 35. Graft of the dorsum of the hand. Patient K. Fragment II (see Fig. 23). Cholinesterase reaction. Compared with donor skin (lateral surface thigh), high papillae have developed. Positive reaction in the layer where the stratum lucidum is situated The cells of the stratum germinativum show a strong cholinesterase activity.

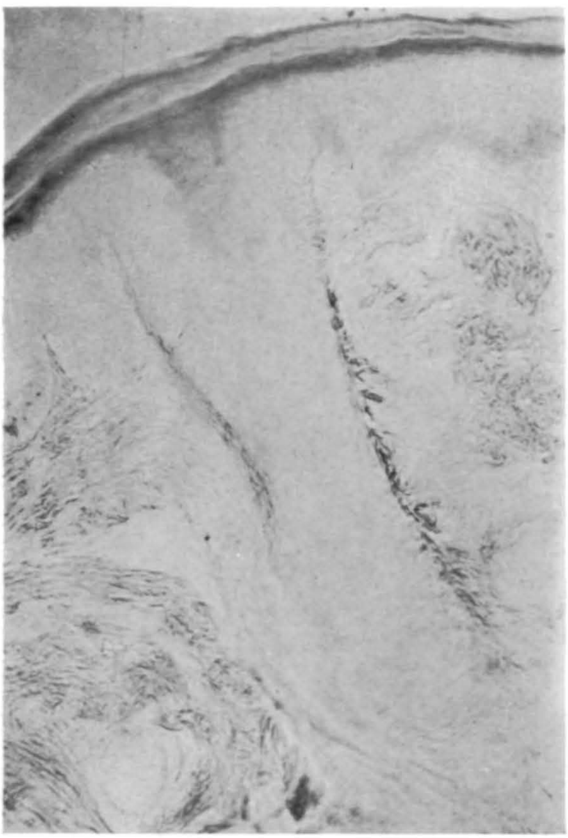

Fig. 36. Graft dorsum of the hand, Patient K. Segment II. Cholinesterase reaction. Hair follicle with positive reaction, on the external root sheath.

Fig. 37. Same slide as Fig. 36. A hair follicle in the deep layers of the dermis with positive reaction at the external root sheath.

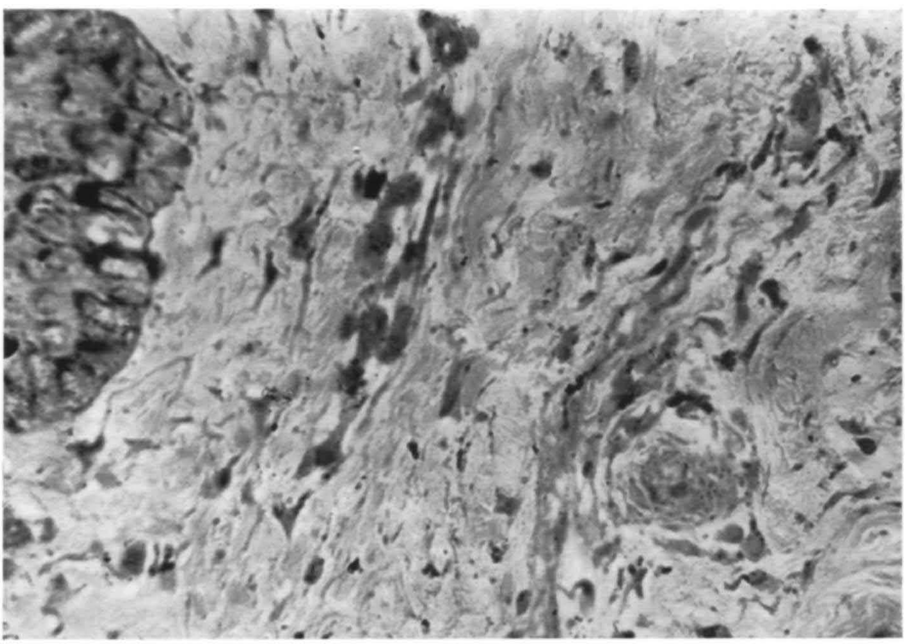

Fig. 38. Graft dorsum of the hand, Patient K. Fragment II. Champy-Coujard technique. Adrenergic nerve elements (parts of the peripheral nerve network in the dermis). On the right side of the photograph a small artery with varicose fibres of the peripheral nerve network around and in the wall.

Fig. 39. Graft dorsum of the hand, Patient K. Fragment I. Langerhans' cell. Dendritic cells in the basal layer of the epidermis.

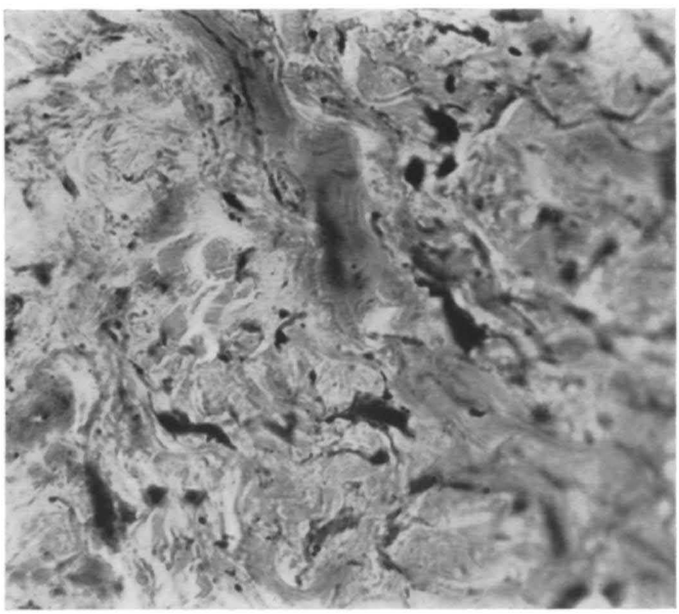

Fig. 40. Graft dorsum of the hand, Patient K. Fragment II. Champy-Coujard technique. Interstitial cells in the deeper layer of the cutis with higher magnification.

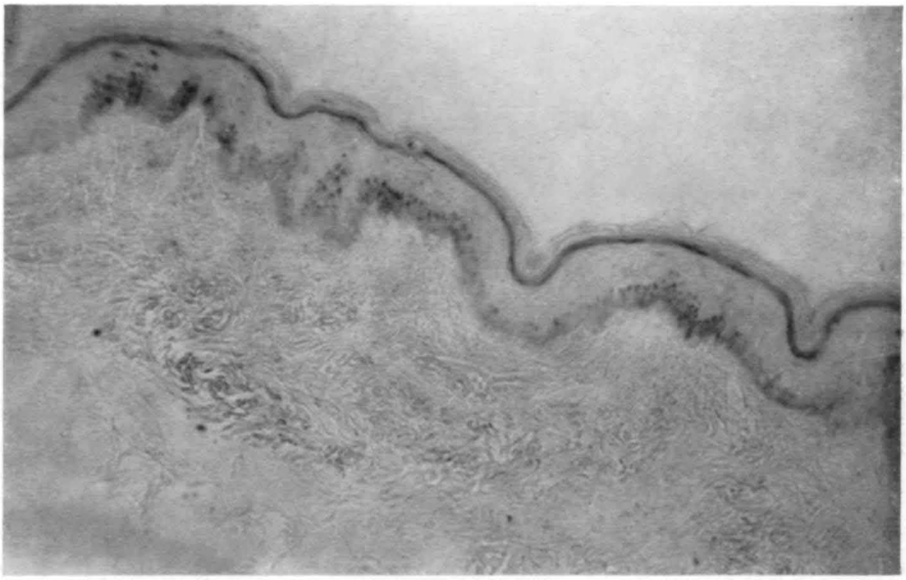

Fig. 41. Patient v.Z. Donor skin lateral aspect thigh. Cholinesterase reaction. Poorly developed papillae, positive band where the stratum lucidum is situated and positive grains in the cells of the stratum germinativum.

Fig. 42. Graft dorsum of the hand. Patient v.Z. Higher papillae than in the donor skin. Positive grains in the cells of the stratum germinativum.

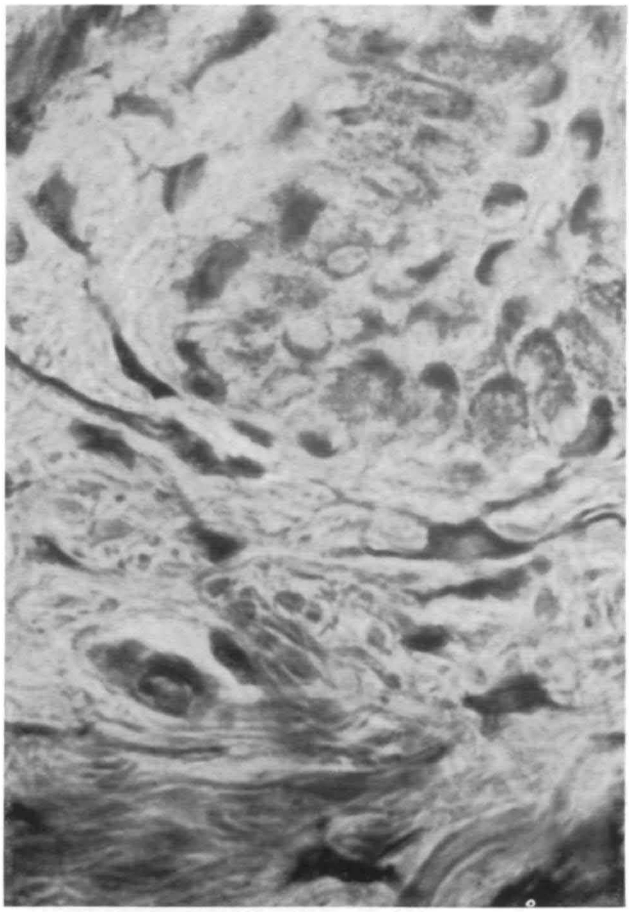

Fig. 43. Graft dorsum of the hand. Patient v. Z. Fragment I. Bielschowsky-Gros method. Interstitial cells in the dermis under the epidermis.

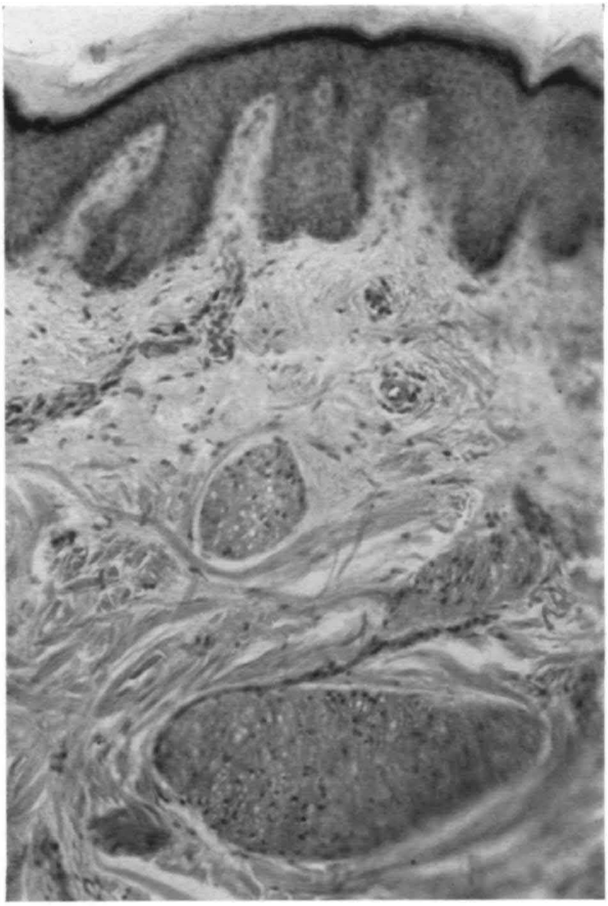

Fig. 44. Graft dorsum of the hand. Patient v. Z. Fragment II. Hemalum-eosine staining. Irregular papillae. Epithelial strands in the dermis.

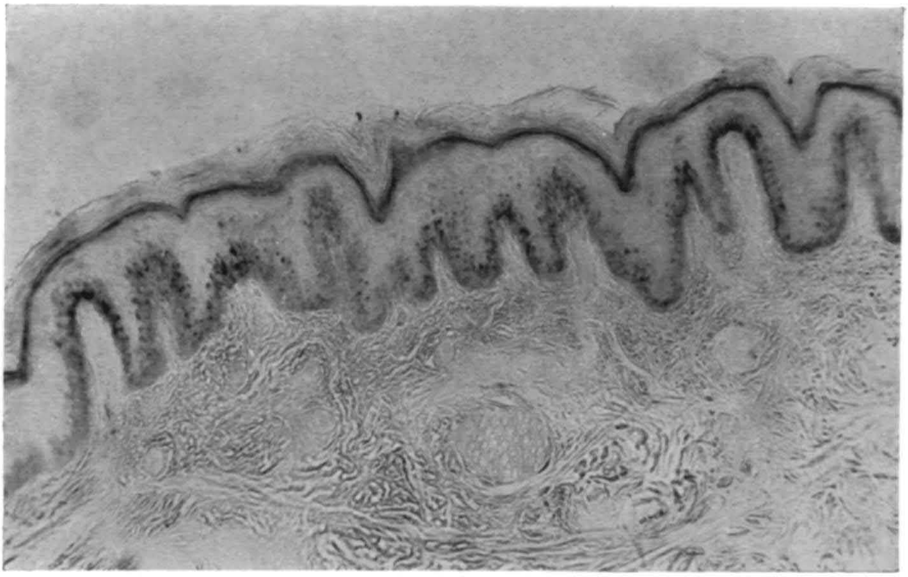

Fig. 45. Graft dorsum of the hand. Patient v.Z. Fragment II. Cholinesterase reaction. Positive band where the stratum lucidum is situated. Positive grains in the stratum germinativum. In the centre of the photo-micrograph an epithelial strand, crossly-cut.

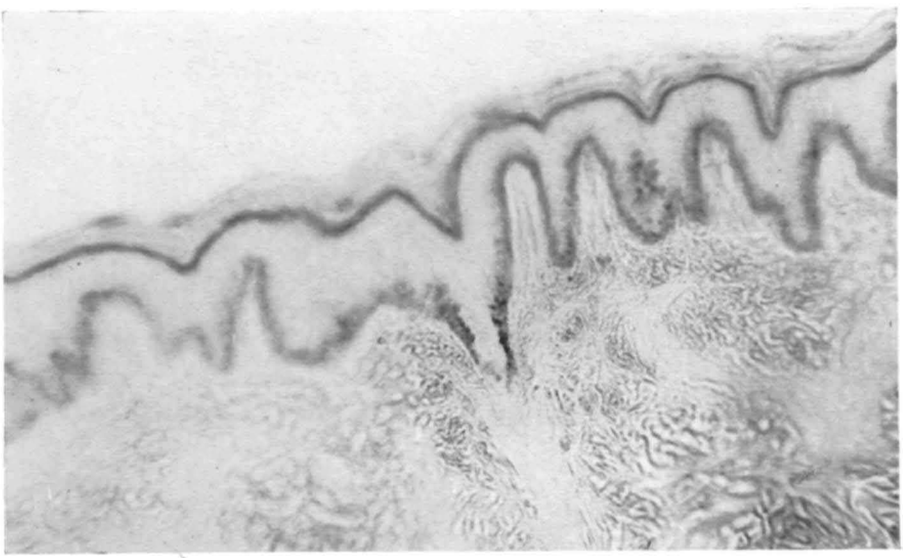

Fig. 46. Graft dorsum of the hand. Patient v.Z. Fragment II. Cholinesterase reaction. Epithelial strand growing from the epidermis, with positive reaction in the outer layer of the epithelial strand.

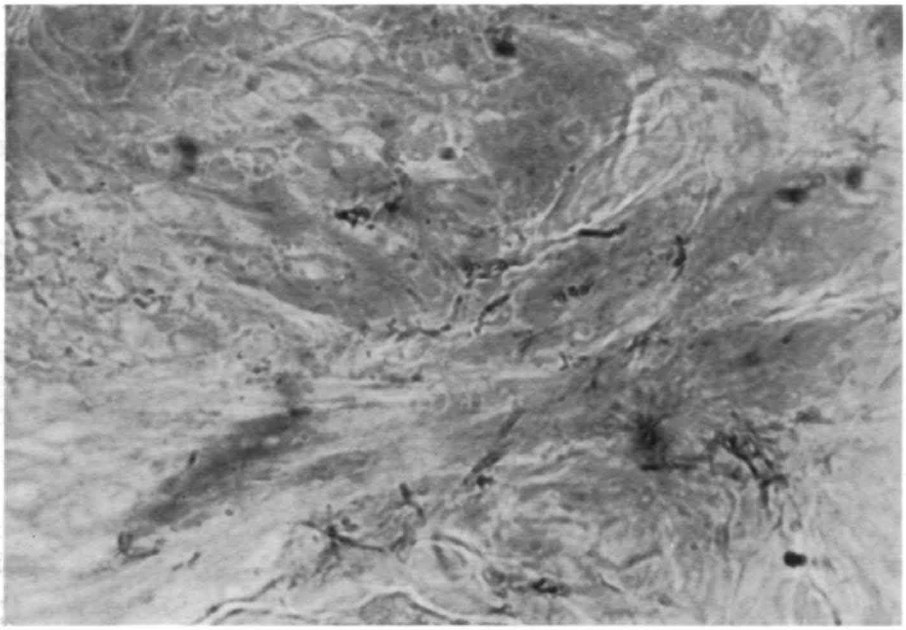

Fig. 47. Graft dorsum of the hand. Patient v.Z. Cholinesterase reaction. Positive cholinesterase reaction on the surface of the epithelial strands.

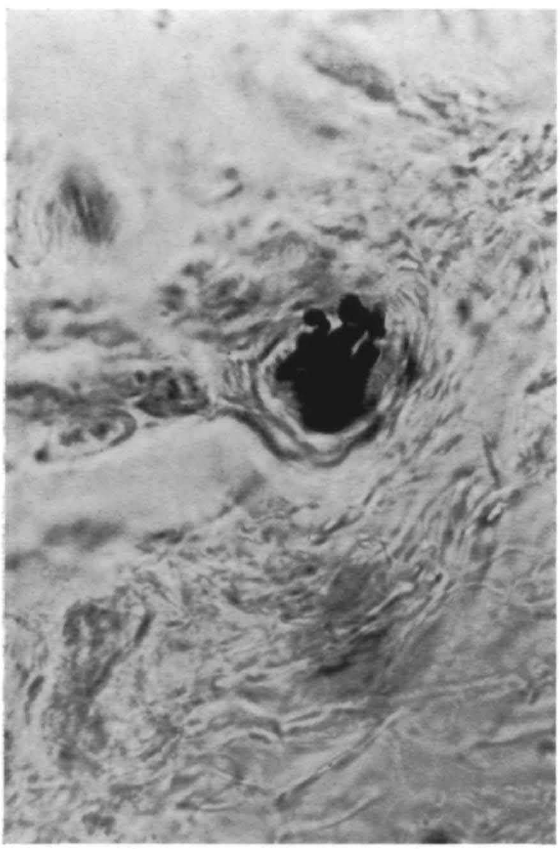

Fig. 48. Graft dorsum of the hand. Patient v.Z. Bielschowsky-Gros method. Nerve fibre bundles in the dermis.

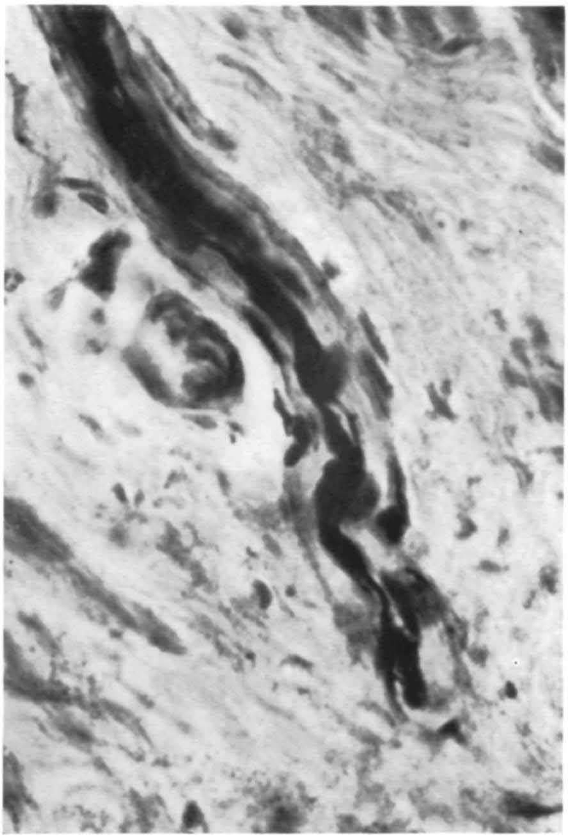

Fig. 49. Graft dorsum of the hand. Patient v.Z. Bielschowsky-Gros method Nerve fibre bundle in the dermis.

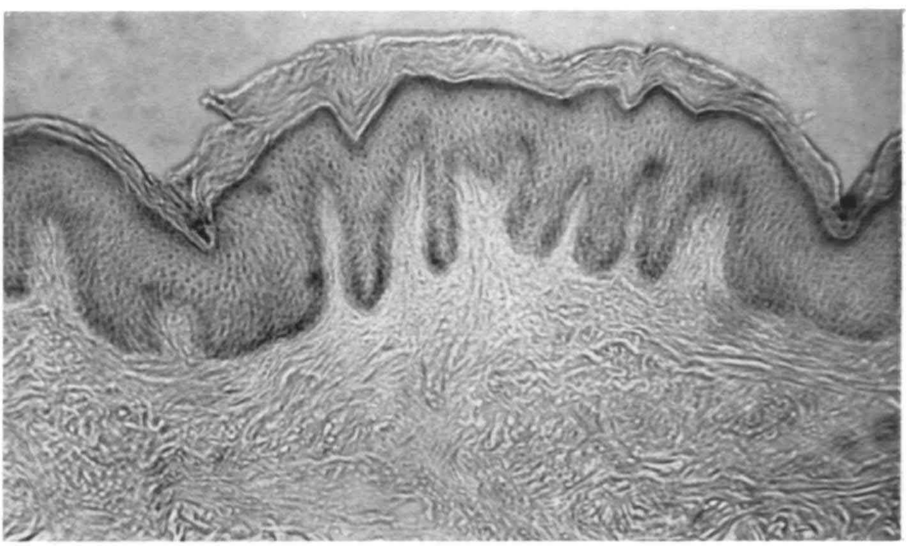

Fig. 50. Graft dorsum of the hand. Patient M. Cholinesterase reaction (substratum acetylthiocholine iodide). Positive band where the stratum lucidum is situated. Positive grains in basal layer of epidermis cells.

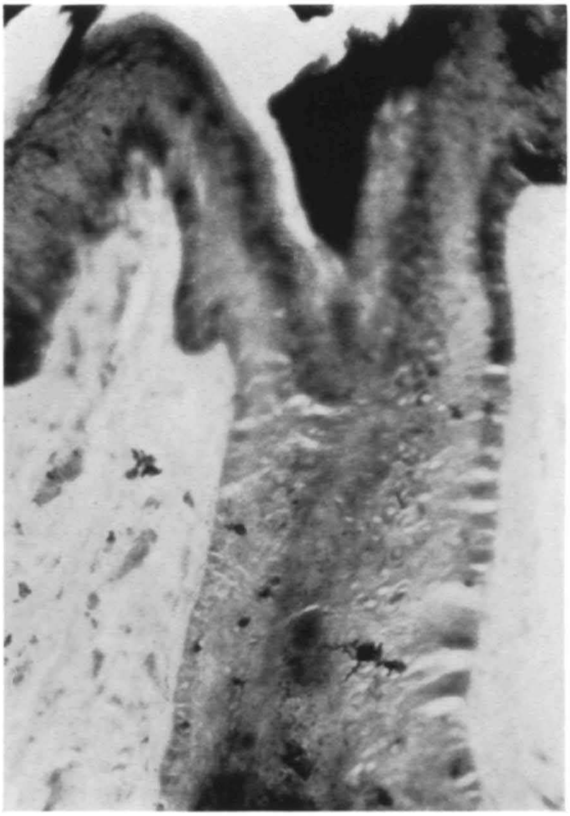

Fig. 51. Graft dorsum of the hand. Patient M. Champy-Coujard method Hair with Langerhans' cell situated in external root sheath.

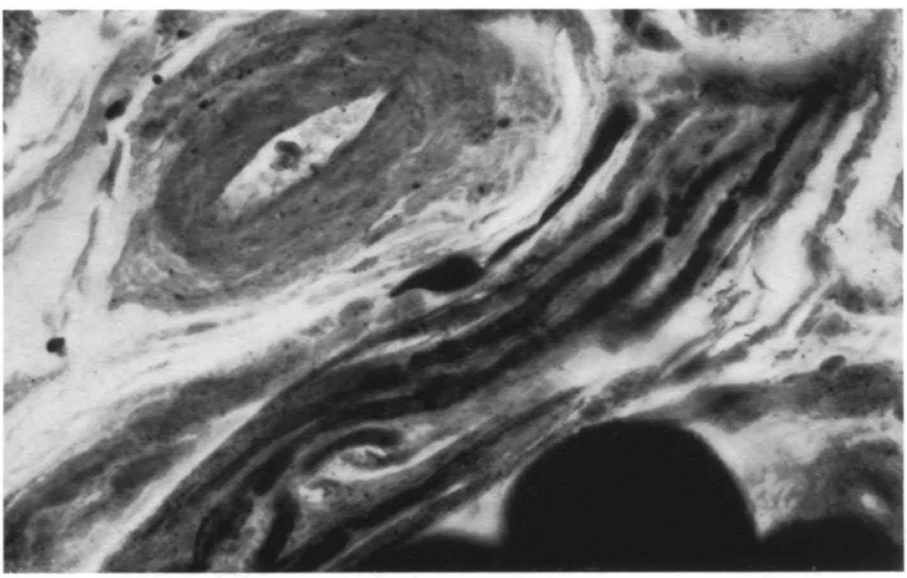

Fig. 52. Graft dorsum of the hand. Patient M. Champy-Coujard method. Nerve fibre bundle in the deep layer of the cutis.

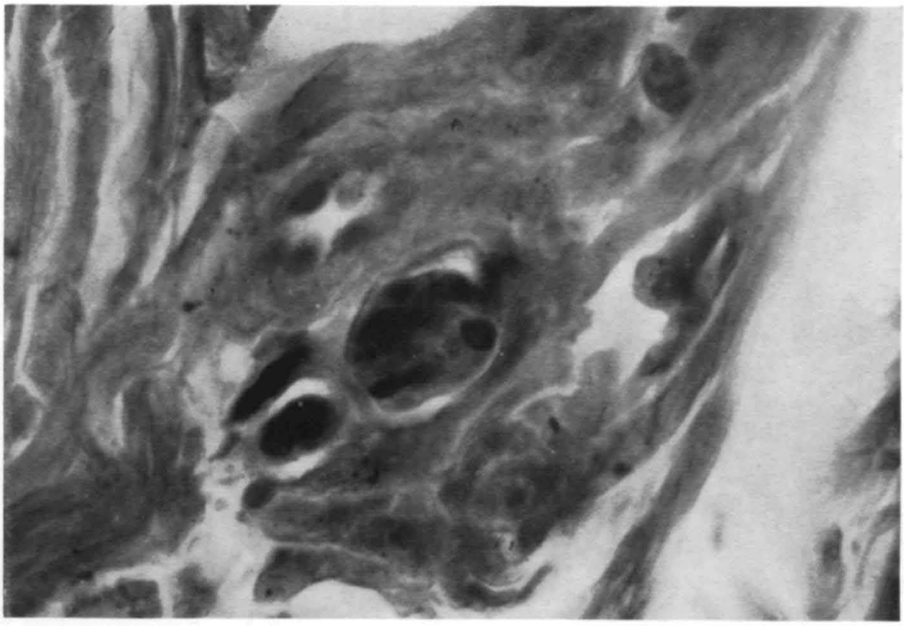

Fig. 53. Graft dorsum of the hand. Patient M. Champy-Coujard method. Small nerve fibre bundle in a more superficial layer of the cutis in the course of a small artery.

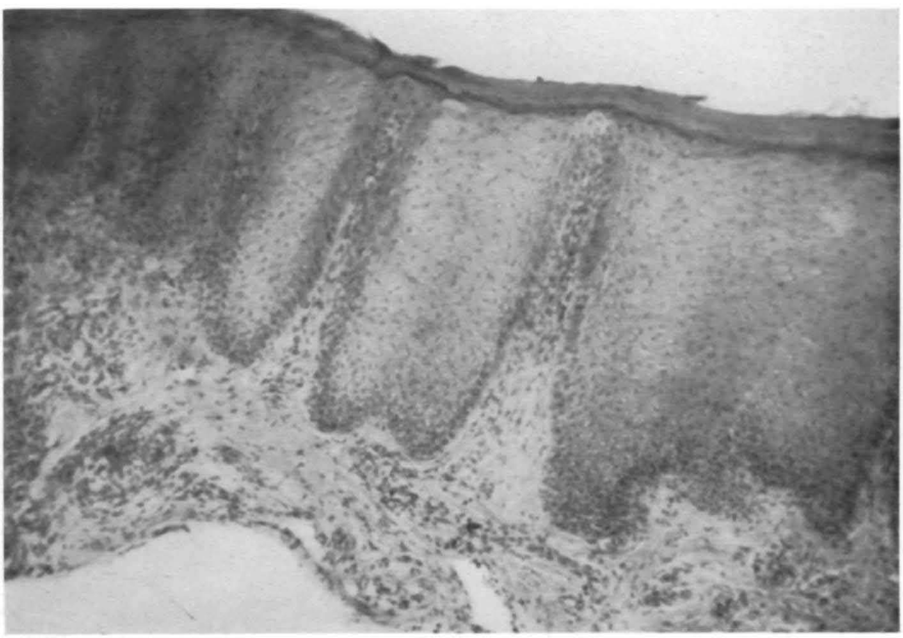

Fig. 54. Normal skin snout pig. Hemalum-eosine staining. High dermal papillae, which penetrate up to the stratum lucidum.

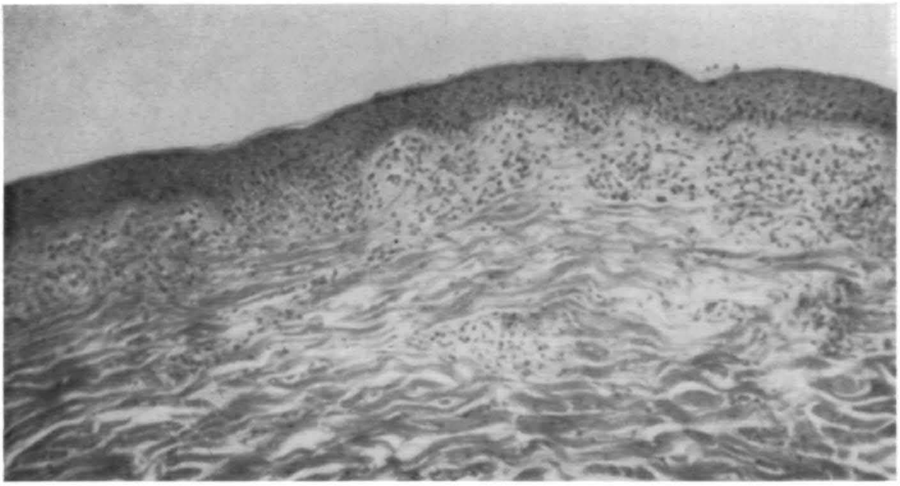

Fig. 55. Normal skin medial aspect thigh pig. Hemalum-eosine staining. Poorly developed papillae.

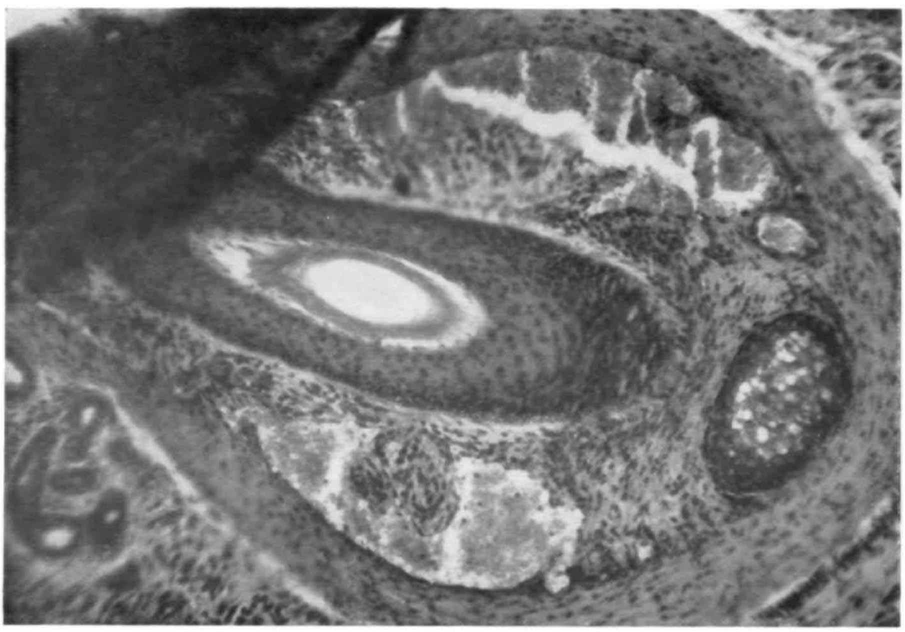

Fig. 56. Normal skin snout pig. Hemalum-eosine staining. Sinus hair. Blood sinus in the connective tissue sheath, filled with blood cells.

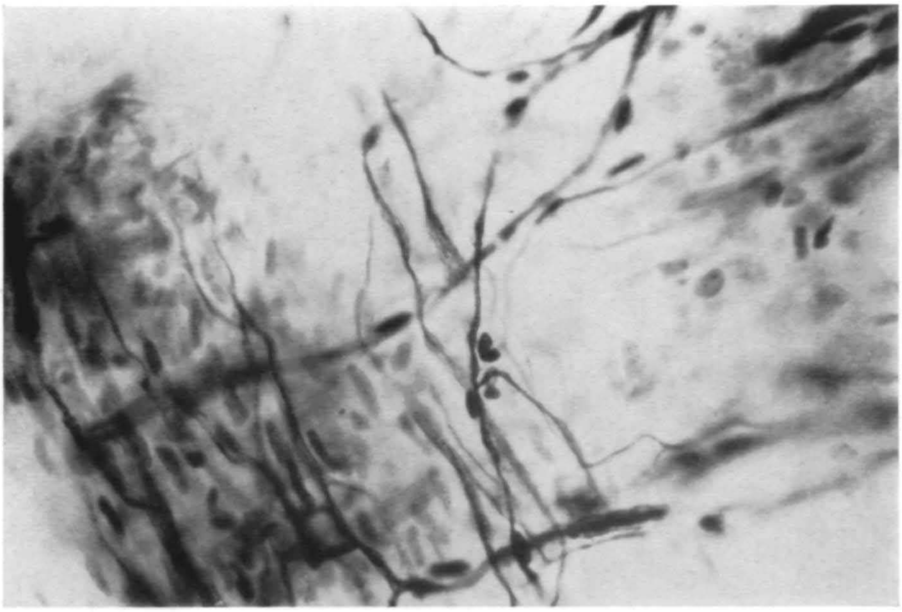

Fig. 57. Normal skin snout pig. Bielschowsky-Gros silver-impregnation technique. The outer root sheath of a sinus hair is cut tangentially. Nerve fibres with enlargements run length-wise and circular.

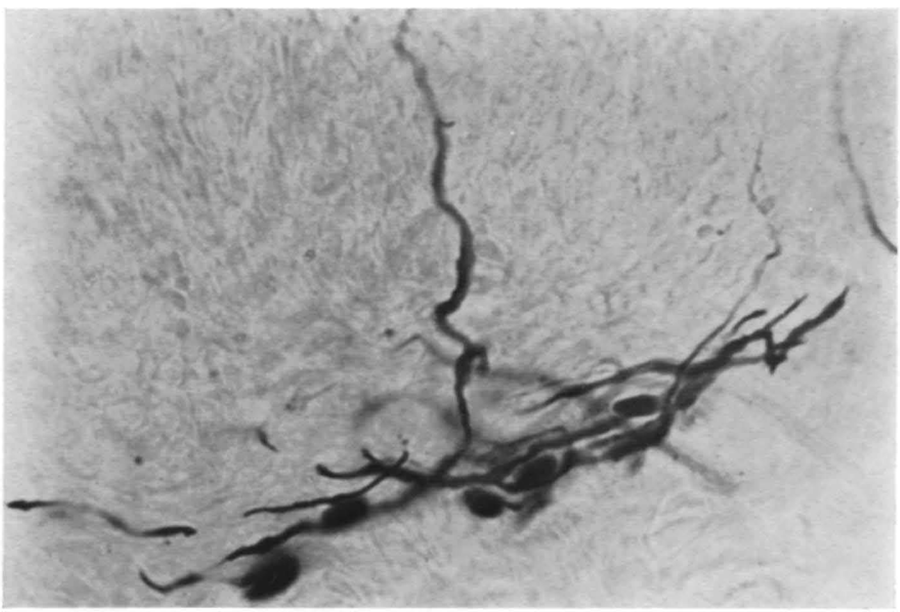

Fig. 58. Normal skin snout pig. Bielschowsky-Gros technique. Nerve fibres form disc-like endings on the Merkel's tactile cells. A nerve fibre runs in the direction of the surface of the skin, probably along the surface of an epidermal crest.

Fig. 59. Normal skin snout pig. Histochemical method for cholinesterase (substrate acetylthiocholine). Merkel's tactile cells show a strong positive reaction.

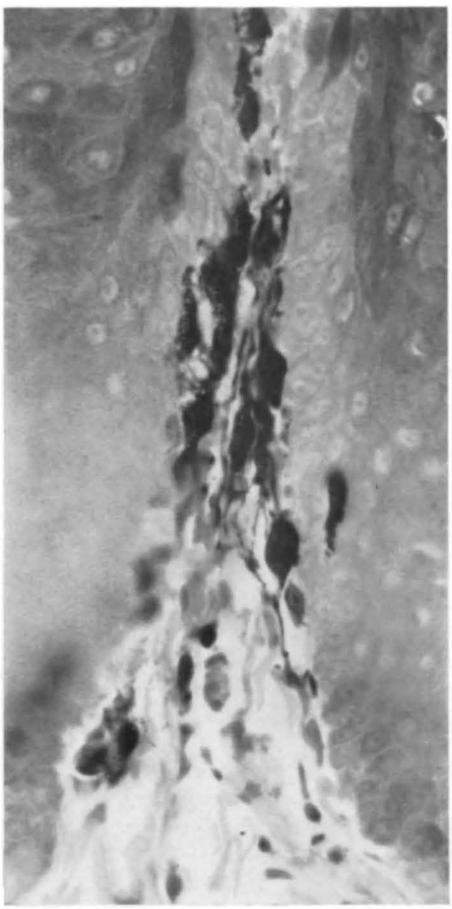

Fig. 60. Normal skin snout pig. Champy-Coujard technique. A rich network of autonomic interstitial cells, with beaded processes, lies in the high dermal papillae.

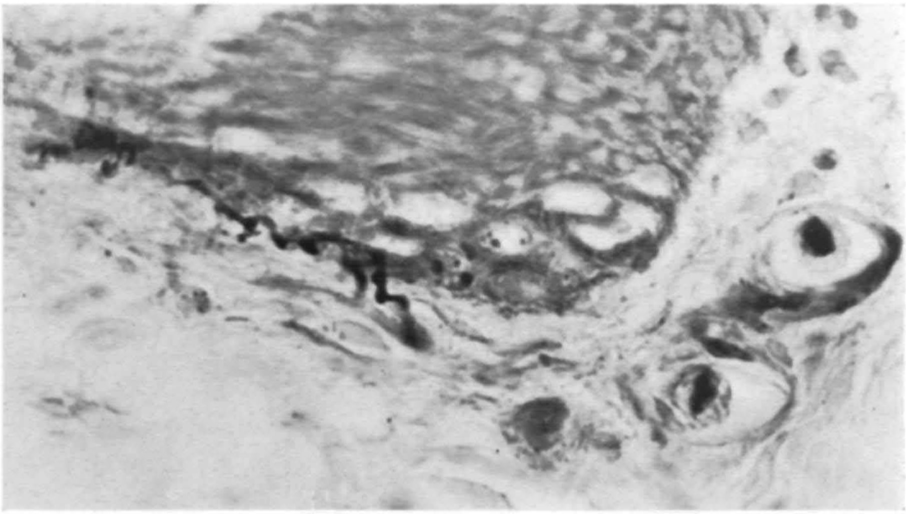

Fig. 61. Normal skin snout pig. Champy-Coujard technique. An adrenergic nerve fibre is seen, running underneath Merkel's tactile cells, which are unstained by this method.

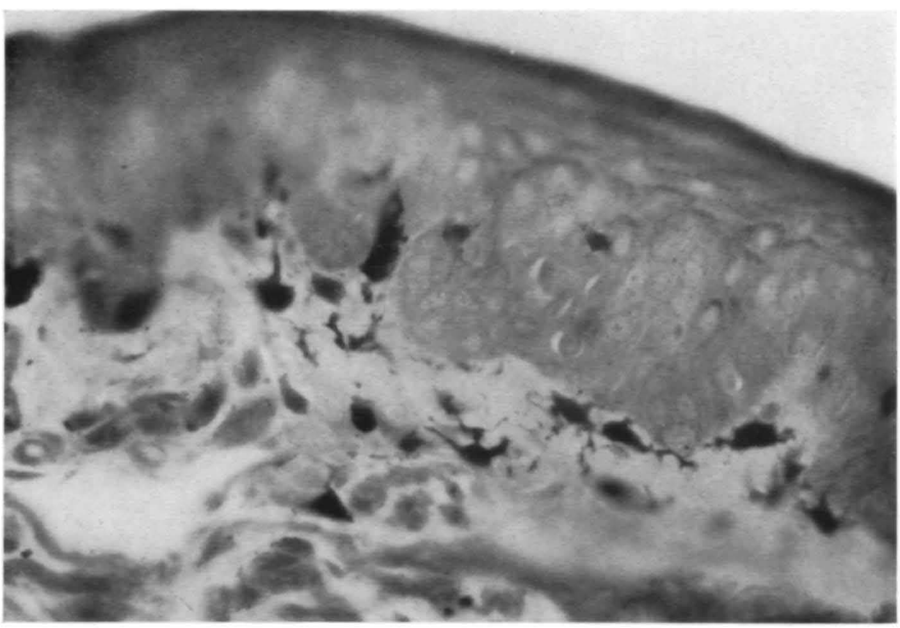

Fig. 62. Normal skin medial aspect thigh pig. Champy-Coujard technique. Typical autonomic interstitial cells of the dermal nerve net are seen beneath the epidermis.

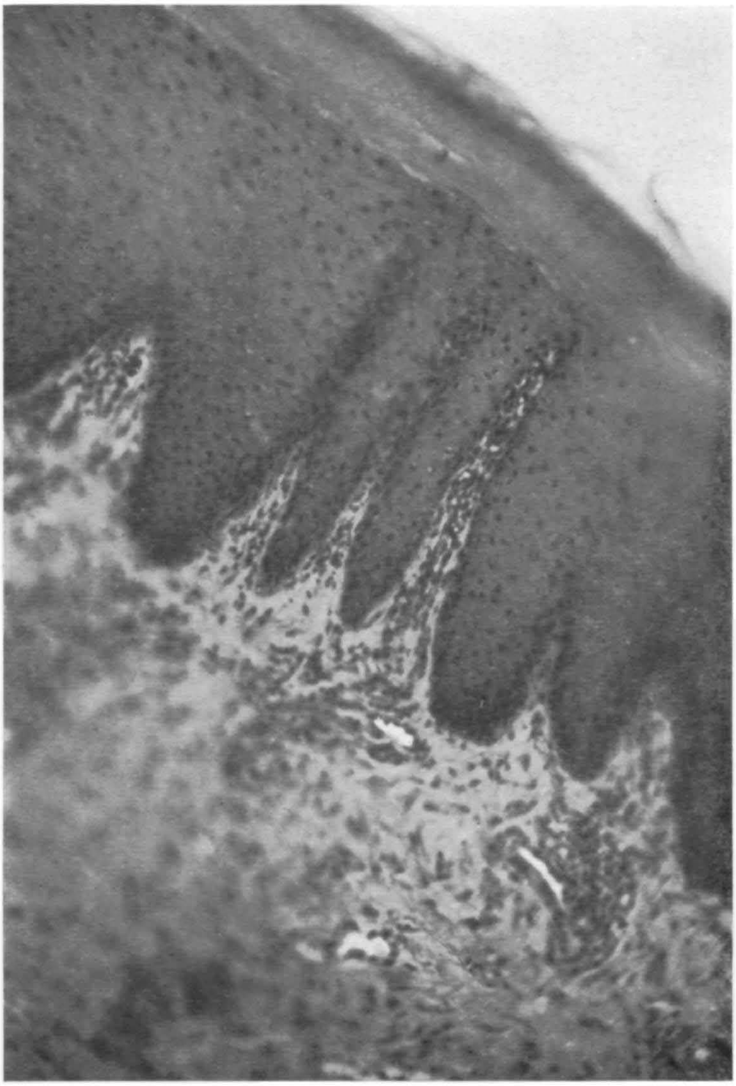

Fig. 63. Graft snout pig, 27 days old, (donor site thigh). Hemalum-eosine staining. High dermal papillae have developed.

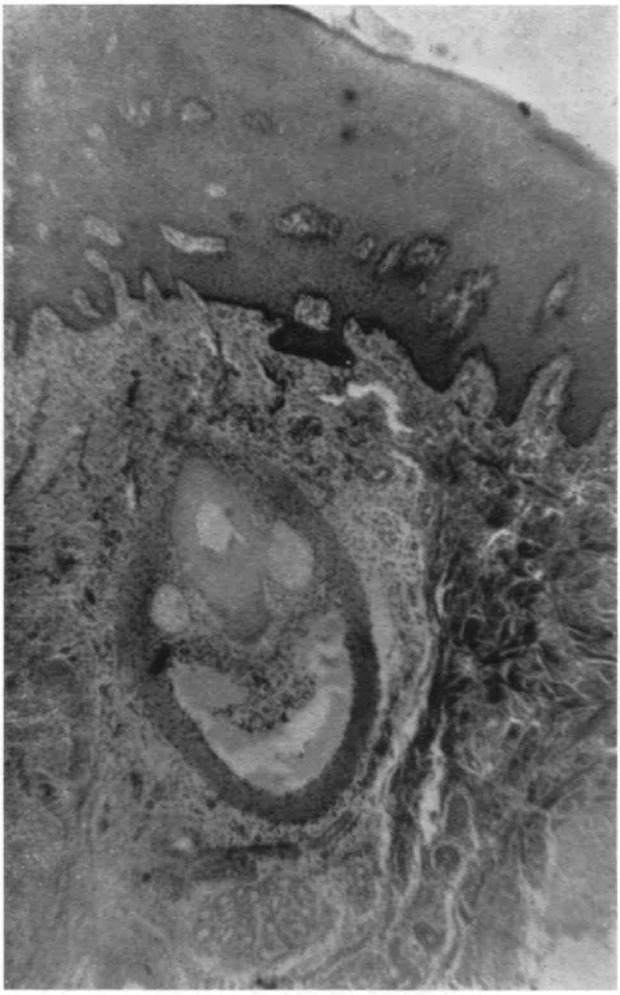

Fig. 64. Same grafts as Fig. 63. Bielschowsky-Gros technique. A sinus hair with large blood sinus, filled with blood cells, is seen.

Fig. 65. Graft snout pig 67 days old. (donor site medial aspect thigh). Champy-Coujard technique. High dermal papillae with autonomic interstitial cells and some adrenergic fibres in the epidermis.

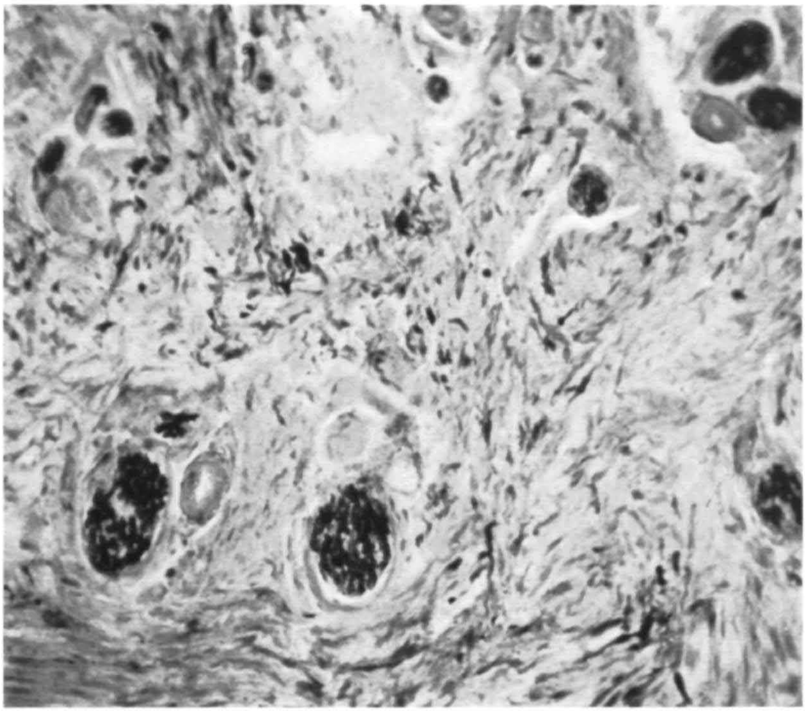

Fig. 66. Graft snout pig 27 days old. Champy-Coujard technique. Transversally cut nerve fibre bundles, in the vicinity of small arteries and interstitial cells in the dermis.

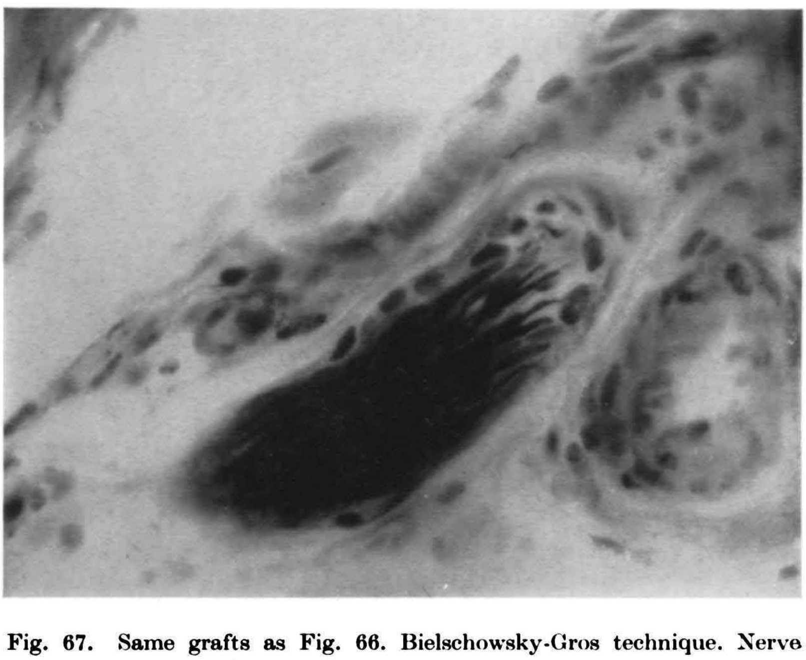

Fig. 67. Same grafts as Fig. 66. Bielschowsky-Gros technique. Nerve fibre bundle which has grown into the graft.

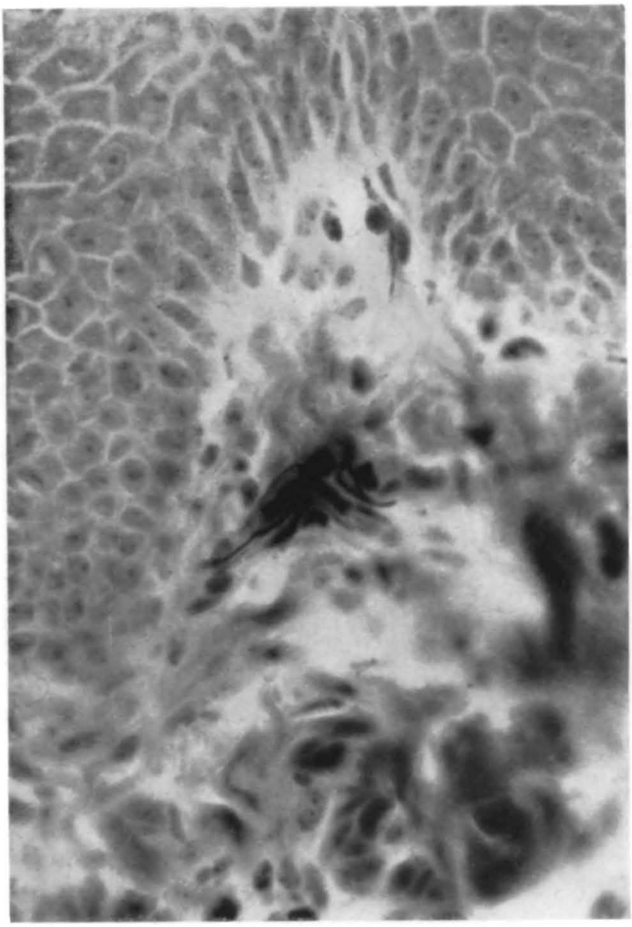

Fig. 68. Same graft as Fig. 66 and 67. Bielschowsky-Gros technique. Nerve fibre bundle accompanied by a great number of Schwann cells, lying at the base of a dermal pailla.

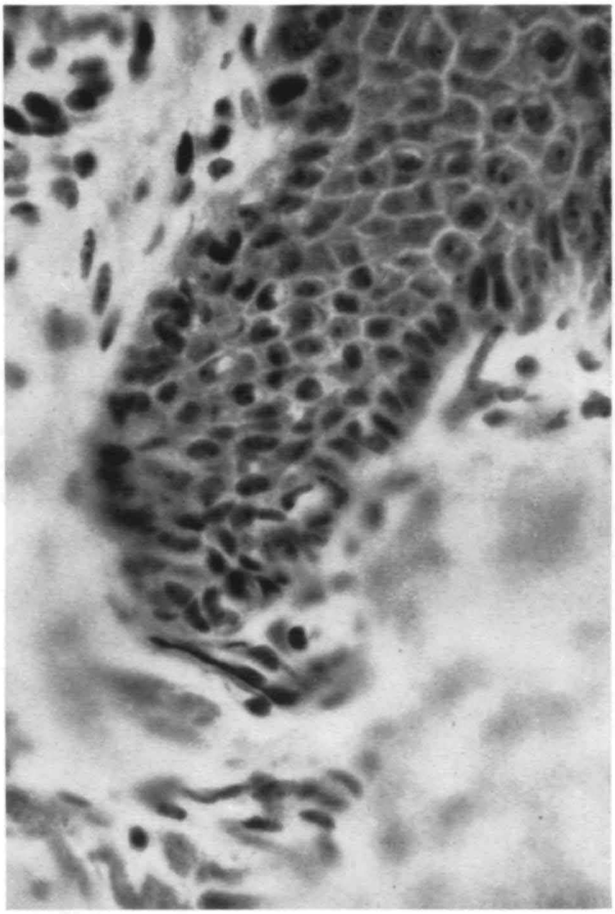

Fig. 69. Same graft as Fig. 68. Bielschowsky-Gros technique. Developing Merkel's tactile cell innervation at the top of a epidermal crest. A fibre shows a disc-like swelling at its end.

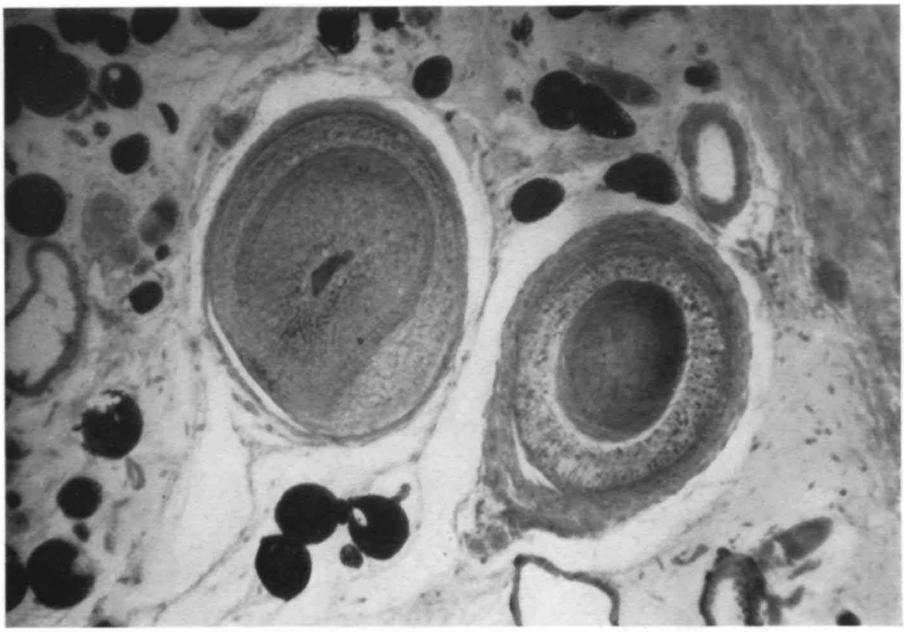

Fig. 70. Graft, 27 days old, medial aspect thigh pig (donor skin snout). Two ordinary hairs have developed.

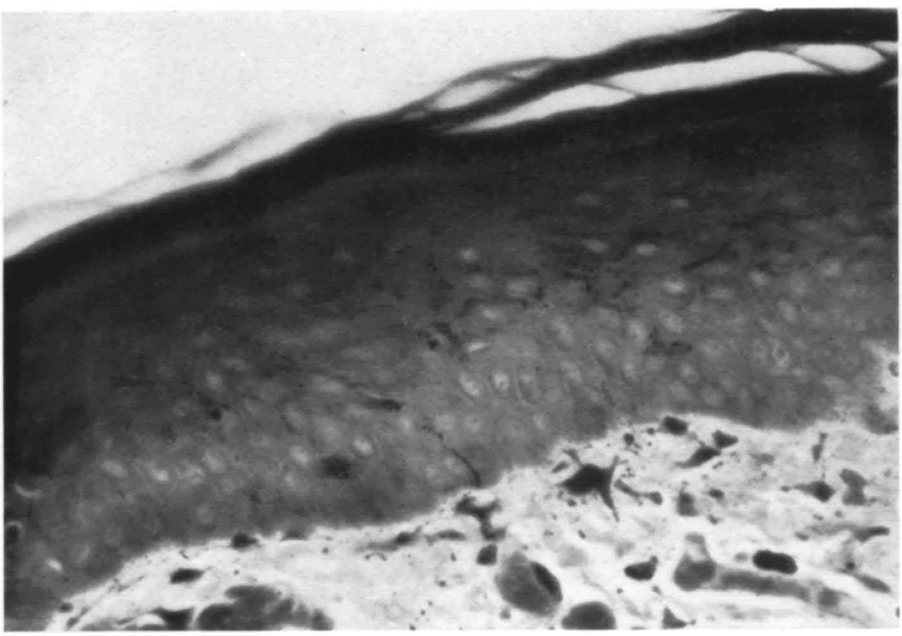

Fig. 71. Same graft as Fig. 70. Champy-Coujard technique. Autonomic interstitial cells are seen under the epidermis similar to those in the normal skin of the thigh (see Fig. 62). Fine beaded processes of these cells penetrate into the epidermis.