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A NEW METHOD OF SKIN AND BONE DIGITAL RECONSTRUCTION

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Digital reconstruction by means of skin and bone plastics was performed, for the first time, by Nicoladoni in 1903. According to literary data Nicoladoni's method was used by numerous authors during the last decades. On the accumulation of clinical data and experience some insufficiencies of this method have become obvious, such as: —

1. inadequate trophism of the reconstructed digit,
2. impossibility to restore deep sensitivity,
3. difficulty in grasping tiny objects by the reconstructed digit owing to increased motility of the skin of its tactile surface.

In connection with these drawbacks some authors have abandoned the use of this method altogether, while others use it only in a very limited number of cases.

In cases where the thumb has been lost, Gillies suggests the prolongation of the stump by means of local and free skin plastics. A similar operation was performed by Hilgenfeldt. By these methods, however, the thumb cannot be prolonged more than 1½ to 2 cm. The application of a free skin graft, in addition to a bone graft, involves a certain danger because of the possible infection of the bone graft. All these facts justify the search for new methods of skin and bone digital reconstruction. We treated two patients by a new method. A Filatov flap is formed on the abdominal wall of the patient from a strip of skin twice as long as the digit to be reconstructed. Simultaneously with the formation of the abdominal flap, another flap with an insertion 3 to 4 cm. wide and 6 to 8 cm. long is formed on the dorsal part of the hand along the base of the amputated finger. The flap is formed in such a way that its insertion is based in the healthy part of the skin beyond the scar after the amputation of the finger. This flap is subjected to biological training in three phases: in the first phase the flap is sectioned on two sides only, after 10 to 15 days the preparation of the third side is performed and, finally, in the third phase, the whole flap is elevated in situ and then sutured back again. Fifteen days after the last phase of the biological training the shaping of the new finger is initiated. For

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. Sectioning of the skin flap. — Fig. 2. Turning of the skin flap by 180^0. — Fig. 3. Shaping of the posterior surface of the digit by the tissues of the Filatov flap.

this purpose the flap on the dorsal part of the hand is first rotated 180 degrees, so as to obtain the integumentary part of the volar surface of the finger under reconstruction. After that, one of the pedicles of the Filatov flap is cut through, an incision is made at the site of the old scar and the flap is applied to the wound on the surface of the hand; thus forming the dorsal surface of the new finger (Fig. 1, 2, 3). After 18 to 20 days the other pedicle of the flap is cut through and the distal part of the finger is definitively shaped. After waiting

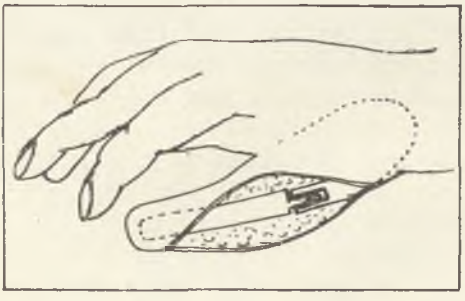

Fig. 4. Osteosynthesis after the "Russian lock".

two to three months, the patient is readmitted for a bone plastic of the reconstructed finger. For this purpose a bone autotransplant of corresponding length from the rib is used. A graft of slightly curved profile is introduced through an opening formed for this purpose in one of the lateral scars of the finger. During this operation a part of the subcutaneous connective tissue and the superfluous part of the skin of the Filatov flap are removed so as to improve the shape of the finger. The proximal part of the graft is wedged into the bone of the

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 5. Left hand of the patient J. E. K. before treatment. — Fig. 6, 7. The same hand after treatment.

Fig. 9.

Fig. 11.

Fig. 12.

Fig. 9. Left hand of patient V. K. K. before operation. — Fig. 11, 12. Left hand of patient V. K. K. after operation.

stump (by the method of "Russian lock") and in this way good osteosynthesis is attained by wide contact of the bone surfaces (Fig. 4). Immobilization with plaster is used until the bone transplant has completely taken. The following are the case reports:

1. Patient J. E. K., 12 years old, Reg. No. 1255/25. 3. 1958, home injury. Condition on admission: 3 digits of the left hand lost, deformity of the fourth digit with ankylosis of the phalangeal joints, limited motility of the fifth digit (Fig. 5). Thumb of the left hand was reconstructed by the method described. Fig. 6, 7, 8 show the result of treatment.

2. Woman, patient V. K. K., aged 20, Reg. No. 5984/1958. Diagnosis on admission: Amputation digitorum II—V manus sin. Industrial injury. Four fingers were amputated together with the respective metatarsal joints. Only the thumb was preserved on the left hand (Fig. 9—10). A finger in opposition to the thumb was reconstructed by the described method. Figs. 11, 12, 13 show the result of bone and skin reconstruction of the digit. The advantages of the described method are as follows:

1. Good trophism of the digit is secured.
2. The skin of the volar surface of the digit is not very different from normal skin.
3. Sensitivity of the digit is restored more rapidly.
4. There are better conditions for the restoration of deep sensitivity. Further observations should be carried out in this direction.

It must be mentioned that, in the described method of digital reconstruction, the total duration of treatment is prolonged as compared with Nicoladoni's method. Our method of treatment is indicated, in the first place, in cases of total loss of the thumb or of 4 fingers, if the thumb is at least partially preserved. The length of the reconstructed digit does not usually exceed 6 cm. The main purpose of the operation is improvement of the grasp and, to a limited extent only, cosmetic effect.

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REPAIR OF A LARGE DEFECT OF THE HARD AND SOFT PALATE BY MEANS OF A FILATOV FLAP

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In a number of patients with congenital clefts of hard and soft palate uranoplasty proves absolutely unsuccessful, irrespective of the method and time of its performance. Repeated attempts to correct the existing defect by the use of local tissues do not meet with success either, in some cases. The patient not only continues to suffer from the cleft but this cleft becomes wider in the course of time. Under these conditions it is possible to perform reconstruction of the soft palate and closing of the defect of the hard palate by means of a Filatov flap, using various methods.

In a patient with an extensive defect of the hard and soft palate the authors achieved not only a good anatomical result, but also, if it may be expressed so, a quite promising result as to the functional capacity in the reconstructed soft palate.

Patient S., aged 22, was born with a congenital cleft of the upper lip, the alveolar process, the hard and soft palate on the left side. In early childhood cheiloplasty was performed with subsequent attempts at uranoplasty, which were never successful. Up to the age of 12 the patient was repeatedly operated on for this reason. Later, he was advised to use an obturator because of lack of local tissue. He was admitted to our Institute for a last attempt at operative treatment for the defect of the palate.

On admission (January 1957): a large defect to the alveolar process of the maxilla, the hard and soft palate was present (Fig. 1). The palatal and alveolar processes of the maxilla were covered with scar tissue. The soft palate was absent altogether.

In view of the size of the defect a Filatov flap was used for repair. The flap was formed on the right abdominal wall, sized 16×8 cm.

After the formation and preparation of the flap its medial pedicle was transplanted to the dorsal surface of the left hand. At the same time a small protective rectangular prosthesis was constructed to enable one end of the flap to be transplanted into the oral cavity (Fig. 2). The end of the flap was sutured into the posterior wall of the pharynx in the region above Passavant's bar. The

Fig. 1. Fig. 2.

Fig. 1. Defect of alveolar process, hard and soft palate in patient S. — Fig. 2. Plastic prosthesis by means of which the bite is kept open and the flap protected when transplanted into the oral cavity.

Fig. 3. Fig. 4.

Fig. 3. Patient S. after transplantation of pedicle of flap into posterior wall of pharynx. — Fig. 4. Suturing of flap to anterior margin of defect in hard palate.

bed into which the pedicle of the flap was sutured was prepared by elevating a flap from the posterior wall of the pharynx, with a caudal pedicle.

It must be mentioned that, in spite of the large size of the flap and the narrow operative field, this operation ended successfully in complete taking of the pedicle of the flap (Fig. 3).

Fig. 5. Patient S. before operation for closing gap between the tissue of the flap and right margin of defect in hard palate.

The next operation was performed following the preparation of the flap and consisted in sectioning the distal pedicle of the flap so that it had the required length and suturing it to the anterior margin of the defect in the hard

Fig. 6. Patient S. with his mouth open.

Fig. 7. Patient S. with open mouth while swallowing.

palate in the region of the alveolar process of the maxilla (Fig. 4). The lateral surfaces of the pedicle flap were then sutured to the margins of the defect on the right and left side, where the alveolar process of the mailla ends; this operation was performed in two stages. During these operations the fatty tissue of the flap was eliminated, as necessary. Fig. 5 shows the patient before the closure of the gap between the tissue of the flap and the left margin of the defect of the hard palate.

After this local plastic by means of a pedicle flap the entire defect between the tissues of the flap and the nasal cavity, in the region of the front teeth of the maxilla, was covered.

As a result of treatment the defect of the alveolar process of the maxilla and of the hard and soft palate was completely repaired. In addition to the improvement in nutrition and respiration an evident amelioration of speech was observed which became especially obvious after some logopedic training.

At the present time, nasal breathing is effected by means of the fissures at both ends of the posterior part of the tissues of the flap (Fig. 6). During swallowing these apertures are completely closed by the activity of the trained muscles of the posterior and lateral walls of the pharynx as can be seen in Fig. 7.

With regard to the good anatomical and functional results it is justified to consider the use of a Filatov flap suggested in principle by Gillies, as practicable and quite suitable for the repair of extensive palatal defects following unsuccessful attempts at uranoplasty, when the local tissues of the soft and hard palate are reduced to scarred remnants the use of which, for the reconstruction of the soft palate by the method of one-stage radical uranoplasty, becomes very doubtful or even impossible.

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ONE-STAGE FLAP

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In the history of plastic surgery the deep loss of skin was primarily replaced simply by shifting skin from the immediate vicinity. Gradually, with bolder incisions of the skin and undercutting from its bed and surroundings, the mobilized skin which was to be transferred was left connected to the donor bed by only a thin pedicle serving for nourishment. It was then possible to rotate the mobilized skin around the pedicle and advance it into the defect in various ways. Thus, the skin flap originated, and its transfer is called pedicle flap technique. Skin transfer was used particularly on the face, and the most famous and one of the oldest methods is the Indian flap from the forehead with a nourishing pedicle over the glabella. It was used to close defects of the nose. This type of flap, which may be designated as a single-pedicle, one-stage Indian flap, could, in a similar manner, be excised and transferred to any place on the body to cover the defect in the immediate neighbourhood.

Lack of material in the region around the defect and the subsequent deforming scar on the secondary defect logically led to attempts to obtain a flap from a distant place. The donor areas had to be approximated to the defect which was to be covered and held in this position until healing took place. The Italian flap technique, the oldest example of this type dating to the 15th century, was used to replace the lost skin on the nose with an arm flap, thus circumventing the formation of ugly scars on the forehead. This flap technique represents the first example of the one-stage, single-pedicle flap from a distant site and, by right, all flap procedures from a distant site should bear the name Italian technique.

Primitive operative technique, operations without asepsis and anaesthesia, led to frequent failures, to sclerosis of the pedicle, and contracture of the transplanted skin, all of which hampered the development of the old flap procedures. However, even in the Middle Ages, the plastic surgeon of the famous Branca family, which was interested in the plastic surgery of the nose, attempted to insure the success of his operations by delaying the immediate transfer of the excised skin from the arm. He left the skin for a time simply raised from the bed but connected with it by one or two pedicles. This resulted in the

principle of delayed transfer which was to insure better nourishment of the skin flap by accustoming it first to nourishment from the pedicles only.

The greatest success in modern plastic surgery, which utilized the advances of aseptic surgery in skin transplantation, was the development of the tubed flap which eliminated all of the disadvantages of the one-stage, single-pedicle flap from a distant site. It represented a conscious two-stage procedure for transfer of a flap of skin folded into a tube on a distant site, making it possible, after healing, to select a suitable pedicle for the nourishment of the flap. The two-stage tubed flap of Gillies-Filatov entered, after the first world war, a victorious stage in the treatment of extensive, practically unlimited loss of skin in any part of the body and serves today principally for complex reconstruction procedures.

The success of the two-stage tubed flap which made plastic operations safe cannot be doubted or minimized. It has extended the domain of plastic reconstruction and permitted the achievement of excellent results. Nevertheless, the quicker one-stage flap from a distant site has not lost its value, especially when it makes use of progress in grafting technique. The surgeon is often confronted with a number of situations where he must decide whether to use the one or multiple-stage flap.

The main factors which are of decisive importance in this connection are the extent of the skin defect, the time during which suitable skin must be transplanted, and finally the accessibility of skin which can be transferred into the defect by the flap method. There are many defects, which in their size and localization, are of such an ideal nature that they can be closed by using the skin flap without danger of the pedicle being unable to provide nourishment temporarily. Forming a separate chapter, one-stage flaps on the face have been developed up to the type of arterial flaps, in which the pedicle is reduced to a narrow pedicle containing the regional blood vessels or the subcutaneous pedicle. All of the flap procedures in the face are characterized by their relatively limited use and the troublesome scar in the donor site. For these reasons, the one-stage flap cannot compete with the tubed flap in extensive defects and deformities and, therefore, has its definite indications and uses. Neither has the one-stage Josef flap from the arm to the total defect of the nose proven to be effective.

The one-stage flap competes with the tubed flap in those cases where the availability of appropriate donor site permits the transfer of more sizeable flaps in a shorter period. The best site for the transfer of one-stage flaps in large defects is the abdominal wall. The most common deformities which can be covered in this way are traumatic defects and small deep skin defects in reconstruction procedures in the hand or upper limb.

In few areas of the body surface the vascular supply for the skin is insured by a definite group of vessels which nourish the excised skin. However, with proper operative technique it is possible to increase the safety of the transfer by careful excision and preparation by the delayed method. The delayed raising and the suture of the flap back into the bed, of course, prolongs the time of treatment and, in reality, makes the procedure two-staged. But in contrast to the

Fig. 1 a.

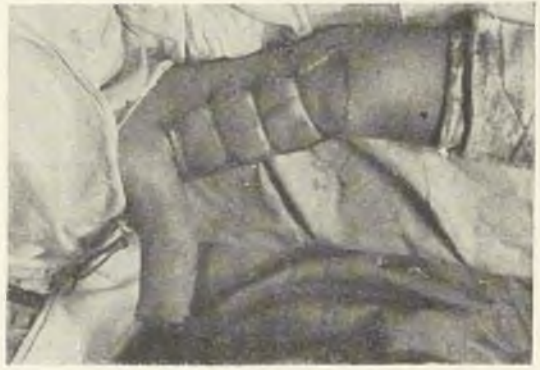

Fig. 1 b.

Fig. 1 c.

Fig. 1 d.

Fig. 2a.

Fig. 2b.

Fig. 2c.

Fig. 2d.

Fig. 3a.

Fig. 3b.

Fig. 3c.

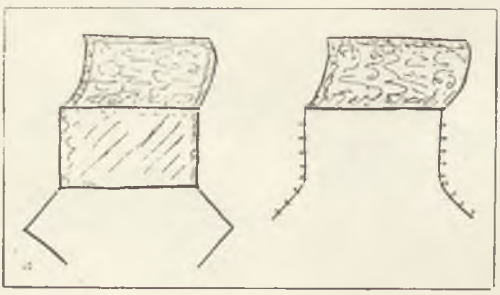

Fig. 4.

Fig. 1a. Lupus carcinoma of the face. — Fig. 1b. One-stage, partially tubed single-pedicle flap on the arm. Secondary defect covered with a dermatome graft. — Fig. 1c. Flap implanted into a defect after radical excision. — Fig. 1d. Five years without recurrence. — Fig. 2a. Radiation ulcer of the forearm, delayed flap transfer. — Fig. 2b. Flap raised on a broad pedicle, secondary defect covered with a dermatome graft. — Fig. 2c. Flap implanted into a defect on the forearm. — Fig. 2d. After severance of pedicle. — Fig. 3a. Chronic radiation ulcer. — Fig. 3b. Double-pedicle, one-stage, bridge flap. — Fig. 3c. After suture of pedicles. — Fig. 4. Closure of defect according to Kholevich.

tubed flap, whose shortest period of preparation is three weeks, the delay of the definitive implantation of the one-pedicle flap means a loss of only one week.

There are numerous therapeutic indications where delayed single-pedicle flaps can be used but where the nature of the pathological lesion, which is to be radically removed, does not permit a prolonged procedure, such being the case in cancer of the skin, chronic radiation ulcers, lupus and so on (Fig. 1).

Recent advances in free skin grafting and its combination further increase the versatility of the one-stage flap. The chief objection to the one-stage flap was the danger of sclerosis of the flap from infection of the pedicle or secondary defect which could not be closed because of tension. The severing and closure of the pedicle of the one-stage flap was taken over from the technique of tube flaps. This method of partial tubing is again most often possible with smaller flaps from the abdominal wall used for covering traumatic defects in the hand. The one-stage flap has become the method of choice not only in total loss of skin on the important fingers, such as the thumb and index finger, but also in the reconstruction of the entire thumb. The one-stage bridge flap is somewhat of a compromise between the one-stage, single-pedicle flap and the double-pedicle tube flap, wherein both pedicles are tubed and the middle section immediately placed in the defect. Gradual circumcision of the pedicle insures, as in tube flaps, nourishment for the transplanted skin and also considerable material from the original donor site is thereby acquired (Fig. 2).

The improvement in skin grafting, mainly the dermatome technique, which makes it possible to obtain extensive skin grafts, removes the danger of infection in the flap, after it is raised, by safely closing the secondary defect and raw surface of the pedicle (Fig. 3). Thus, the transplantation of a one-stage flap with a broad pedicle becomes successful and at the same time the size and shape of the flap can be made so that it fits directly into the defect. The method saves material since it is unnecessary to excise the flap in excess as is customary in partial tubing of the pedicle. Otherwise, it is also possible to close the defect, after raising the flap, by various skin shifting manoeuvers, such as the Kholevich procedure which is especially appropriate (Fig. 4).

The one-stage flap, particularly in the limbs, often fulfils the requirement of a biological flap graft. It has been observed that transplantation from an identical symmetrical region leads to better healing, better quality of skin, more adequate thickness, better distribution of the nerve supply and skin adnexa. The one-stage flap from a symmetrical region is therefore better than skin from a distant tubed flap. Most commonly this type of skin flap is used for many defects on the lower limbs (cross leg flap). Flaps from a neighbouring digit, which are the smallest flaps possible and biologically well suited, are also such cross flap. Agreement is expressed with Doc. Demjen that a flap transplanted from the forearm or arm to the fingers and hand, although aesthetically less pleasing, is much better, particularly on the tactile surfaces, than a flap from the abdominal wall.

In answer to the question when to use one-stage or two-stage tube flaps, it may be said that the former as well as the latter have their exact indications in present-day reconstructive surgery. After a period of suspicion when the tubed

flap dominated the field, the use of the direct, one-stage flap is once again coming into favour. The tubed flap is left for more complicated situations which require greater possibilities of modelling, relatively greater supply of material than can be supplied by a one-stage flap. The possibilities of the one stage flap, however, are constantly being increased with the perfecting of grafting techniques, particularly free skin transfer, and the use of delayed raising of the flap and partial tubing of the pedicle. The use of the quicker one-stage flap permits the plastic surgeon to intervene in an ever greater number of deep primary skin defects and much more safely than was the case before the era of tubed flaps. One-stage flap from a symmetrical region transplanted to an opposite limb has the value of a true biological graft which surpasses skin from a distant site.

SUMMARY

The combination of one-stage flap and free skin transplantation, delayed raising of the flap and partial tubing of the pedicle, removes the former disadvantages of direct flap surgery. The one-stage improved skin flap extends the field of plastic surgery, especially in traumatology and oncology.

ВЫВОДЫ

Одномоментный лоскут

В. Карфик

Сочетание техники одномоментного лоскута кожи с методикой перемещения свободных кожных лоскутов, откладываемого приподнимания и частичного свертывания ножки устраняет прежние невыгоды прямых лоскутных пластик. Одномоментный, усовершенствованный таким образом лоскут кожи расширяет использование пластической хирургии, главным образом, в травматологии и в онкологии.

RÉSUMÉ

Lambeau en un temps

V. Karfík

La combinaison de la technique du lambeau cutané en un temps avec la méthode des transplantats cutanés libres, du soulèvement différé et de la tubulisation partielle du pédicule écarte les désavantages antérieurs des plastiques directes du lambeau. Le lambeau cutané en un temps, ainsi amélioré, permet d'élargir l'utilité de la chirurgie plastique spécialement en traumatologie et oncologie.

ZUSAMMENFASSUNG

Einzeitige Stiellappenbildung

V. Karfík

Durch Verbindung der Technik der einzeitigen Stiellappenbildung mit der Methodik der freien Hauttransplantate, der abgelehnten Stiellappenhebung und teilweisen Tubulisation des Stiels werden die früheren Nachteile der lokalen Lappenplastiken beseitigt. Die einzeitige, in dieser Form vervollkommnete Stiellappenbildung erweitert die Geltendmachung der plastischen Chirurgie besonders in der Traumatologie und Onkologie.

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Fig. 8. Fig. 10. Fig. 13.

Fig. 8. X-ray of the hand of the patient J. E. K. — Fig. 10. X-ray of the hand of patient V. K. K. before treatment. — Fig. 13. X-ray of the hand of patient V. K. K. after operation.

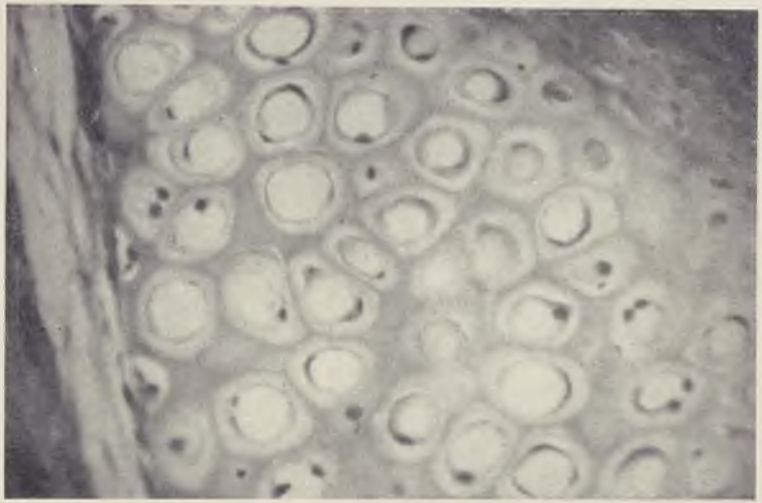

Fig. 4. A homotransplant of auricle cartilage of a rabbit transplanted with the perichondrium 113 days after transplantation. The surface of the cartilage is smooth, without signs of vascular or lacunar resorption. The chondrocytes are enlarged, contain vacuoles and all around them pericellular spaces are forming. Contact. Heamatoxylin. Magnified 200 times.

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FLAP VERSUS GRAFT

F. BURIAN

It is one of the weaknesses of the human race to wax enthusiastic over some object, idea or method and then to apply it indiscrimately. This is what is known as "fashion" and even surgeons are not exempt.

Fashions also appear in plastic surgery, including such curiosities as the injection of paraffin to fill out a withered face, or the insertion of plastic appliances into flabby breasts. These are naturally extreme examples, but it is nevertheless a fact that good operative techniques, which are excellent for certain specific purposes, have become the fashion and been used in cases in which other methods would have achieved far better results.

This has always been so. As far as we know, the Indians were the first to carry out plastic operations, many centuries before Christ. They conducted a flourishing line in noses and ears, since these parts were currently cut off as a form of punishment of criminals and prisoners of war. In the case of the nose, the cartilaginous part suffered, sometimes with a piece or the whole of the upper lip, according to the character and caprice of the executioner. As far as is known, in ancient times it was the fashion to carry out replacement by free skin grafts from the buttocks. The skin was beaten into a more suitable biological state with a slipper. In the days of Celsus, i. e. at the beginning of our own era, skin defects were covered by shifting strips from the adjoining parts. During the Middle Ages, the Italians carried out plastic surgery of the nose and ears by means of flaps from the arm only; these were prepared in successive stages, using a special ceremonial.

In the meantime the Indians abandoned free transplantation and carried out plastic operations on the nose by means of flaps from the forehead only. This method was introduced into Europe by English doctors at the beginning of the nineteenth century. It led in turn to the rebirth of the Italian method, which the German surgeons Gräfe and Dieffenbach improved and set up in rivalry against the Indian method as a German method.

Free skin grafts were not revived until about 1868 by the Swiss surgeon Reverdin. Reverdin transferred minute slips of skin about 2 mm. square from the surface of the skin to a granulating wound on the thumb which refused to heal. The slips of skin took, epithelium grew out from their edges and the wound healed

far sooner than had been anticipated. This operation was repeated several times and was frequently used during the Franco-Prussian war.

Ollier attempted to use larger sheets of epithelium, which he sliced off with a razor. This method was extended and technically improved by the German surgeon Thiersch. Another German, Wolffe, who was a naturalized British subject, succeeded in transplanting full-thickness skin grafts, thus reviving the oldest Indian method of transplantation.

All these methods of free transplantation and flap transfers and shifts were first used sporadically, opportunities being comparatively few, since great cultural progress had been made, noses and ears were no longer cut off and the motor-car had not yet been invented.

It was not until the First World War, with its perfected technique, caused innumerable injuries requiring replacement of the skin of the face in particular, that the demand for plastic operations suddenly and unexpectedly increased. Old methods often reappeared in new guises and many completely new operative methods were elaborated.

One of these was the tubed flap, introduced almost simultaneously by Filatov in Russia and Gillies in Britain. This method completely dominated the field of plastic surgery at the end of the war and during the ensuing years. It was adopted by every surgeon who wanted to keep up with the times. It was naturally used on every possible occasion, even when a different method would have produced quicker and better results.

In 1939, the Americans Padgett and Hood devised a dermatome for cutting sheets of epithelium to replace Thiersch's method of razor cutting. This instrument greatly simplified matters and made it possible to cut large grafts of even thickness throughout and to determine the thickness of the graft in advance, with an ad lib. thick layer of corium and auxiliary glandular formations and capillary and precapillary network if required, so that the covering obtained by this method was of far greater value than that obtained by the Ollier-Tiersch method. For a long time this method pushed flap plastic surgery into the background and was used particularly widely during the Second World War.

It was a long time before it was realized that one method is not suitable for every type of case and that exact indications must be worked out.

One of the basic principles in the evaluation of transferred tissue is recognition of the fact that full biological quality cannot be expected from any tissue, including skin, which has once been completely separated from its bed. Even in a 100% take, marked changes occur in the graft; a large part of its substance undergoes degeneration and destruction and regeneration is not absolutely complete, irrespective of the fact that a skin graft is not a whole biological unit like intact skin.

The quality of the covering obtained by free transplantation is dependent on a number of circumstances, chief among which is the general state of the patient at the moment when the graft is taken and transferred. Metabolic balance is a basic condition. If this in disturbed in some way, if the ratio of the blood proteins is altered, if acidosis of the tissues is present, the biological quality of

the skin itself is diminished. The wound to which the graft is applied is also in an unfavourable state and has less of the constructive energy required for the graft to take. This accounts for the failure of autoplasty in patients with very severe burns. Much research will be required before determining whether "autoaggression" participates in such cases, as assumed by Chytilová et al.

In an otherwise healthy subject, the biological quality of the site to which the graft is applied may also be diminished if that particular part of the body is diseased, e. g. in chronic varicose ulcers.

A graft completely separated from its vital environment undergoes basic changes even when transferred to an absolutely healthy fresh wound in a healthy subject. A certain degree of inflammation develops in every case, with all the attendant signs, i. e. small cell infiltration, exudation into the tissues, activation of fibroblasts producing collagen fibres. The exudate is slowly organized, the collagen fibres are converted into connective tissue fibrils, all of which results in shrinking of the tissue of the bed. The graft itself also shrivels as a result of regeneration and of invasion by inflammatory changes from the bed, including exudation and small cell infiltration, with the formation of sclerosis.

A further deficiency of free skin grafts is that they do not contain all the auxiliary skin formations. The thinner the graft, the fewer there are. Purely epithelial grafts do not exist, since all contain at least the tips of the papillae. Even full-thickness grafts do not contain all glandular and sensitive formations, however.

Free skin grafts are very differently denominated. There are three main types. One is the epidermal graft, i. e. a thin graft comprising the whole epithelial layer and the tips of the tactile papillae. This is applied as one coherent graft or in portions about the size of a postage stamp. Dermoepidermal grafts contain a more or less thick layer of corium, while a full-thickness graft lacks part of the skin adnexa which extend into the subcutaneous tissue. There are also the corium grafts which can be used for replacing skin by means of the epithelial elements, i. e. fat glands, sweat glands and the epithelial coverings of the hair follicles, the corium contains.

Grafts of Reverdin's type are equally unsatisfactory whether applied superficially or deep in the granulating tissue. This is a purely emergency measure, when there is no hope of any other method succeeding.

The value of skin grafts is also based on their microanatomical structure not simply on their thickness. Grafts of equal thickness from different parts of the body surface can have quite different characteristics and physiological value. A graft 0.1 mm. thick from the gluteal region will consist of epithelum only, whereas a graft of the same thickness from the volar surface of the forearm will practically constitute a full-thickness graft. Such a graft from the gluteal region mainly comprises the superficial epithelial layers, which are not capable of any great productive activity.

Dermic grafts were first used by Löwe in 1918 and were systematically elaborated by Rehn. They are used much oftener, and on a much larger scale, for deep reconstruction than for surface grafts.

It is obvious that the use of free grafts on any and every occasion is insuitable and non-physiological. These grafts have their own special indications and are very often be used as an emergency measure to close an open wound.

It is extremely important to handle grafts with the greatest care. They must not be immersed in a bath of physiological saline, which extracts important parts essential for a primary take. They must likewise not be allowed to dry. They should be folded with their cut surfaces together and wrapped in gauze moistened with physiological saline until they can be applied to the new bed, or returned to the site from which they were taken and covered with gauze moistened with physiological saline.

It is commonly assumed that cold reduces the metabolism of the graft and it is therefore recommended that no dressing should be applied to the operation site, so that the temperature of the graft should be lower than that of the body. This conflicts with the experience that skin-inlays, i. e. grafts inserted deep into the tissue, in a temperature higher than that of the body surface, take best. The most important factor is undoubtedly perfect contact with the whole surface of the bed at even, elastic pressure. This is best obtained by a gauze pad fixed in place by the suture-threads, and by an elastic bandage.

Another important factor in selection of the graft is the question of appearance, particularly where the face is involved. Only small defects can be covered with skin from behind the pinna or from the base of the neck, where the skin is similar in structure and appearance to the skin of the face. Grafts from any other part of the body differ considerably and usually permanently from the surrounding tissue at the new site. These circumstances associated with free skin grafts should all receive carefull consideration before deciding to adopt this method.

What is the situation with regard to flap grafts?

First consider the tubed flap, which for a long time held the field. This type transfers the full thickness of the skin together with an adequate layer of subcutaneous tissue containing all the accessory parts. It remains attached to the maternal site at both ends until the blood circulation is organized in a longitudinal direction, so that the nutrient tubing of the flap is ready for connecting up with the vascular network of the future bed. Theoretically the transferred tissue ought to be completely unchanged at the new site. That is not the case, however. The preparation of a tubed flap involves serious interference in the life of the tissue. Two deep parallel incisions are made and the skin is cut away from the base throughout its full extent through the layer of the subcutaneous fat. This involves considerable injury to the tissue, which is manifested in an inflammatory reaction and subsequent fibrosis. Sometimes simultaneously reflex vasoconstriction of a group of blood vessels occurs, with nutritional disturbance of part of the flap, the consequences of which are sometimes not manifested for two or three days. In case of doubt the operation must be interrupted, the strip must be resutured to its original site and transfer delayed. This means one more operation and a further degree of sclerosis.

In cases in which a sufficient amount of tissue for forming a flap for a certain defect cannot be obtained from a neighbouring part of the body, the flap must

be formed elsewhere and transferred by means of a temporary bearer. This means yet another operation, with further sclerosis. In plastic operations of the face, in which a satisfactory appearance must be achieved, the tubed flap requires a large number of additional modellings, each of which results in fresh sclerosis. This is manifested in thickening and hardening of the flap, with a disastrous decrease in the mass of transferred tissue. For plastic operations on the nose, the flap must be prepared from an area twice the size of the final nose, even when there are no complications - which is not, unfortunately, the general rule, even with the most skilled plastic surgeons.

Another disadvantage of the tubed flap on the face is the same as for free grafts transferred from other sites of the body to the face, i. e. differences in the properties of the skin, which are often not equalized for years.

In plastic surgery of the nose these circumstances constitute a considerable drawback for the Italian method, either in the direct form or on using the tubed flap. Plastic surgery of the nose necessitates a firm underlying support, which is provided by inserting small pieces of bone or cartilage. As the flap shrinks, it sometimes presses against the end of the resistant rod, with the result that at this site the skin becomes thin, the end of the support shows through, necrosis of the skin may occur and the whole operation may be ruined.

The Indian method of plastic surgery of the nose has the advantage or reducing the number of stages of the operation. It uses skin with basically very similar properties to those of the normal skin of the nose. The abundance of blood vessels and great vitality of the skin of the forehead substantially diminishes secondary shrinking of the frontal flap. One unpleasant aspect of this method is that it leaves a permanent mark on the forehead. The secondary defect is covered by a free graft, which is always rather conspicuous, chiefly because of the absence of the movement of the frontal muscles throughout its full extent. For this reason many people prefer to undergo the far greater suffering of the Italian method.

Small facial defects do not cause any great difficulty and there are many ways of treating them without leaving noticeable traces.

In plastic surgery of the trunk many of the considerations which complicate facial plastic surgery can be dispensed with. Large portions of skin can be transferred, either at once or in stages, and free grafts also have a wide range of application.

In the upper limbs contractures of the large joints are a frequent problem, particularly after burns, as for example in scars in the axillary folds, with marked restriction of the movement of the shoulders, or the congenital contractures associated to defects of the large pectoral muscles. In such cases, local exchange of wedge-shaped flaps, elaborated geometrically by the Leningrad surgeon Limberg, produces excellent results. The same applies to acquired and congenital contracture of the knee.

The conditions for transplantation on the back of the hand vary according to the depth of the injury. If the tendons of the extensors are intact, thick dermo-epidermal grafts or full-thickness grafts are the most satisfactory. If the tendons are destroyed or severely injured, a flap graft must be used. The same method

should also be used on the forearm if replacement operations on the muscles and tendons are necessary. In this case direct flaps are very satisfactory, while the raw surface of the pedicles of these flaps can be covered with epithelial grafts, thus preventing infection and its resultant complications.

On the lower limbs flaps can sometimes be transferred from one limb to the other (cross-leg flaps), if the recipient and donor limb are both in biologically good condition. Otherwise the only alternative is the tubed flap, which is either migrated successively or transferred via a temporary bearer.

The exact therapeutic plan must be based on careful study of the task in hand, on an analysis of all the attendant circumstances and on thorough knowledge of the patient and his social background. The individual operations and treatment between operations must be based on careful study of the physiological requirements of the tissue.

SUMMARY

The author indicates on the basis of an historical survey of the development of skin transplantation that in plastic surgery fashion plays a role in influencing the preference for certain methods of operation. This has been shown most conspicuously in the preference for the tubulated flap graft after World War I and for the dermatome skin split graft after World War II. The article deals with the biological value of the individual types of skin grafts and with their indication determined after careful consideration of both the patient's general condition and the condition of the tisue at the site from which the graft is to be taken as well as the site where it is to be implanted. The decision is made according to the purpose the transplant is to serve.

The article also deals with technical details which must be observed if the operation is to be successful. The treatment must be planned precisely and carried out with every consideration for the physiological needs of the tissue.

ВЫВОДЫ

Стебельчатый лоскут или трансплантат

Ф. Буриан

На основании исторического обзора развития пересадки кожи автор доказывает, что и в пластической хирургии при применении некоторых способов операции играет роль мода. Наиболее ярко это выразилось в применении трубчатого лоскута после Первой мировой войны и трансплантата, отделяемого с помощью дерматома, во время Второй мировой войны. В работе разобран вопрос о биологическом значении отдельных видов пересадки кожи и о показаниях к ней, установленных на основании подробного обсуждения общего состояния больного и состояния кожи на месте, откуда будет взят трансплантат, и на месте, на которое он будет пересажен. Решающим является задание, которое трансплантат должен исполнять.

Разобраны технические детали, которые необходимо соблюдать для достижения успеха. Лечение необходимо точно планировать и проводить, принимая во внимание физиологические потребности ткани.

RÉSUMÉ

Lambeau contre transplantat

F. Burian

L'auteur déduit de l'évolution historique de la transplantation cutanée, que même en chirurgie plastique, la mode participe à l'emploi de certaines méthodes chirurgicales. Ceci a été le plus flagrant dans le lambeau tubulé après la première guerre mondiale et le transplantat de dermatome pendant la seconde. Dans ce travail, l'auteur traite de la valeur biologique des différentes espèces de transplantations cutanées et de leurs indications, déterminées d'après de soigneuses investigations sur l'état général du malade et sur l'état du tissu à l'emplacement duquel le transplantat sera prélevé de même que l'état de l'endroit où il sera placé. La rôle que doit remplir le transplantat est déterminant.

L'auteur traite également des détails techniques qui doivent être respectés pour atteindre au succès. Le traitement doit être planifié avec exactitude et pratiqué en tenant compte de tous les besoins physiologiques du tissu.

ZUSAMMENFASSUNG

Lappen versus Transplantat

F. Burian

An Hand einer historischen Übersicht der Entwicklung der Hauttransplantation zeigt der Verfasser, dass auch in der plastischen Chirurgie die Mode eine bestimmte Rolle bei der Anwendung mancher operativer Methoden spielt. Am auffalendsten trat dies beim tubulären Lappen nach dem ersten Weltkrieg und beim Dermatomtransplantat während des zweiten Weltkrieges in Erscheinung. Die vorliegende Arbeit befasst sich mit dem biologischen Wert der einzelnen Arten der Hauttransplantation; die Indikationen dieser Operationsarten sind auf Grund einer sorgfältigen Erwägung des Gesamtzustandes des Patienten, des Gewebezustandes am Ort, an dem das Transplantat entnommen werden soll, sowie des Zustandes des Gewebes dort, wohin es übertragen werden soll, zu stellen. Von entscheidender Bedeutung ist die Aufgabe, die dem Transplantat zufällt.

Die Arbeit befasst sich auch mit technischen Einzelheiten, die eingehalten werden müssen, soll die Operation von Erfolg gekrönt sein. Die Behandlung muss einem genauen Plan entsprechen und ist mit Rücksicht auf die physiologischen Bedürfnisse des Gewebes durchzuführen.

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LOCAL SKIN TRANSFERS

R. ERDÉLYI

Local skin transfers are of the greatest assistance in local plastic procedures, denoting closure of a skin defect with skin transferred from the immediate vicinity without disturbing the vascular and nervous connections. As opposed to techniques which use skin from distant sites of the body (free skin grafting, flap methods), in local plastic procedures the adjacent skin is utilized.

This type of plastic surgery has perhaps the oldest history in surgery. Historical records from the era before Christ show the technique of Egyptian, Indian, Arabian and Greek surgeons who even then used skin shifting. About 800 A.D. in his work Samhitá, the Indian Susrut described the local transfer of skin on the face. This method was later called the French technique.

Galenos (about 30 A.D.) and Celsus of the Alexandrian school should be regarded as among the originators of local plastic procedures on various parts of the body. The detailed elaboration of the individual methods of this type, however, was not undertaken until the 19th century by Dupuytren, Denonvilliers, Szymanowski, Graefe, Langenbeck, Blaskovics and Imre. Denonviliers was the first to describe, in 1847, the Z incision, indispensable in plastic surgery.

Skin transfer may be called the queen of plastic surgery, for its infinite number of variations and possibilities in any part of the body creates an almost unlimited field of action. Although techniques of this type have their firm basic features, new combinations are forever being created in plastic operations, combinations which the surgeon through his inventiveness must be able to utilize correctly. The Leningrad surgeon Limberg demonstrated, in his studies in 1929 and 1935, the mathematical treatment of the use of wedge flaps.

Local skin transfer is indicated whenever it is necessary to replace a defect with full-thickness skin, i. e. skin with subcutaneous fat, and whenever the size of the defect does not require grafting from a distant site. The condition for success with this procedure is a sufficient quantity of skin with a layer of fat which can be advanced into the defect without impairing the vitality of the implanted skin. At the same time, the secondary defect should not deform the neighbouring area.

It is, therefore, necessary to observe carefully the transplantability of the

skin, its physiological texture and possible changes in the surroundings. The basis for carrying out skin shifting is healthy tissue around the defect which must be present in sufficient amount and which, to a certain degree, must also be mobile. The shifting of skin and closure of the defect should not cause any marked changes in the surroundings or any undue tension and vascular impairment. It is

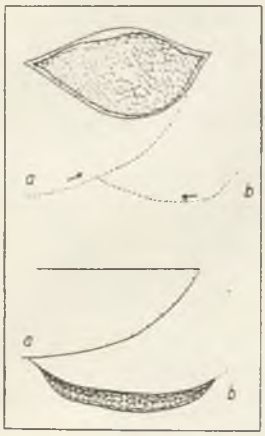

Diagram 1. Method of wound closure with incisions on one side of the defect.

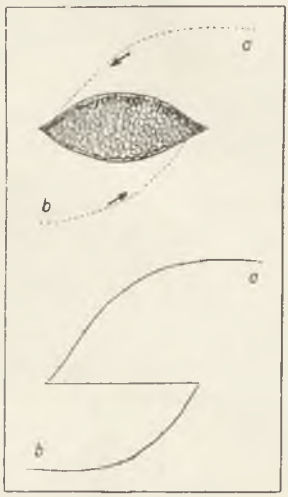

Diagram 2. Closure of defect by means of incisions on both sides.

necessary that the operative procedure be planned beforehand, but it often happens that the exact manner of closure must be decided upon during operation.

The most frequently used types of local skin transfer are the following: — The simplest and basic type of skin shifting is mobilization and approximation of the edges of the wound, usually spindle shaped, with subsequent linear suture. Celsus had already thought of the idea of closing the triangular defect by first suturing the corners of the triangle gradually toward the centre. Other workers describe — and we still find the descriptions in some textbooks — the closure of oval, rectangular and other defects by means of numerous, often unphysiological, supplementary incisions. These methods are generally not used today since defects of a precisely triangular or rectangular shape hardly ever occur. Even if they are encountered, a more simple shape can be obtained requiring less supplementary incisions. For example, the triangle can be transformed into a rectangle which is then sutured linearly after undermining the edges. The same may be done for oval defects. The closure of spindle-shaped defects appears to us to be very simple and usefull (Diagram 1): one of the longer sides of the defect is converted into a half-moon band of skin, the apex of which, as is seen in the drawing, is drawn into one corner of the defect. Then a second band of skin similar in shape and next to the first is mobilized, and the apex is sutured into the opposite corner of the defect. The advantage of this method is that the slight

tension is equally distributed between the two bands of skin — between a larger surface of skin — so that healing takes place under better conditions.

Alternatively, similar "flaps" may be produced (Diagram 2), but one from above and the other from below. The edges of the adjacent skin next to the incisions, however, must be thoroughly undercut (Fig. 1, 2, 3). Fig. 4 and 5

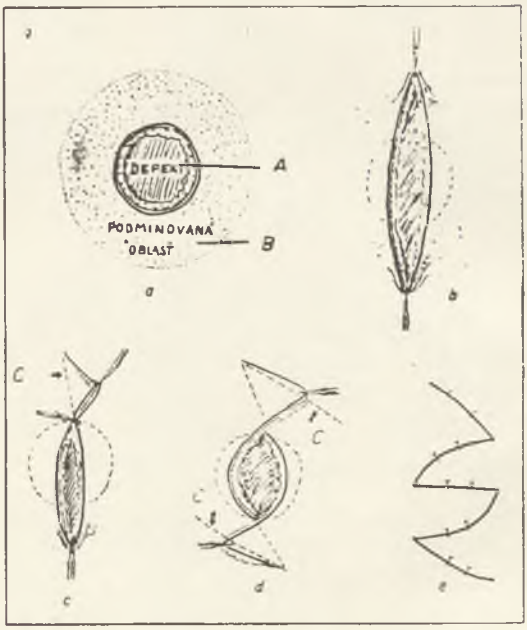

Diagram 3. Pick technique in circular skin loss.

show a patient with a radiation ulcer at the corner of his mouth which was treated by this method, but the skin flap was transposed from one side of the defect only. The same applies for Fig. 6 and 7.

The closure of circular defects, for example, following excision of benign and malignant tumours, represented the most difficult problem in plastic surgery. Their regular shape, however, is somewhat of an advantage in spite of the fact that previous methods (Szymanowski, Kirschner, Lexer, Hadjistamoff and others) treated these defects by sacrificing tissues and increasing their size. In addition, all of these methods have one disadvantage in common: all result in secondary defects of various shapes which are generally difficult to close either because of the shape or number. This difficulty is uniquely solved by the Pick technique: the edges of the circular defect (Diagram 3) are undercut in a circular manner for an adequate distance. Single-pronged hooks which are placed in the edges of the wound directly opposite each other are used to raise the skin in the form of a duplicature (c). The "pedicle" of one fold is severed by an incision in the skin so that a wedge-shaped flap is formed (D). The same procedure is repeated with the second hook, the incision, however, being made in an opposite direction to the first. After suture of the wound a zig-zag wound is formed (e).

An indispensable method for removing wrinkles or scar contractures in plastic surgery is represented by the so-called Z incision or exchange of wedge flaps. Its principle consists in the fact that the straight-line scar is transformed into a prolonged and zig-zag one which is deprived of the ability to contract. The incision is made directly in the scar (if possible it is better to extirpate it).

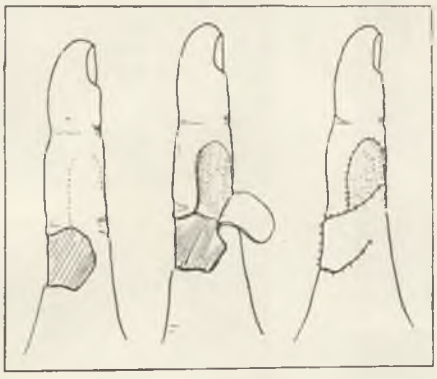

Diagram 4. Skin transposition with a proximal pedicle to the belly of a finger defect.

Both flaps of the mobilized skin are raised and freed by oblique incisions so that a triangular flap is formed on each side, resembling the letter Z (or reversed Z). After the flaps are raised they are rotated and placed into the bed in such a manner that the apex of each triangle falls into the angle of the oblique incision. Thus a shape opposite to the original incision is obtained (Fig. 8, 9, 10). By placing the flap on the level of the defect there is a shifting of skin from sites where there is an excess to sites where there is a shortage, but most important an extension of the entire section of the skin closure is thereby achieved. The size of the angle and the length of the sides of the triangular flap must always be modified in accordance with the conditions obtaining at the site.

The size of the angle which is formed between the middle and lateral sides of the Z incision (or reversed Z) depends on the condition of the adjacent tissue and on the blood supply. The best angle is one of 60^0. The two angles being of the same size. But this is practically impossible to achieve. In spite of the fact that the result could be satisfactory, the size of the angle should not be less than 30^0. At times it is necessary to transpose several pairs of wedge flaps, giving rise to saw-shaped scars. But the flaps and their sides are less drawn and shorter than in simple transposition of wedge flaps.

The purpose of flap transposition is briefly the following:

1. remove scar contractures (over joints, in the neck and so forth);
2. shift a dislocated section of skin into an anatomically correct site (eyebrows, corners of the mouth or eyes);
3. remove amniotic deformities;
4. perform Z incisions in those cases where the resulting increased tension could cause contractures at sensitive sites.

Fig. 1.

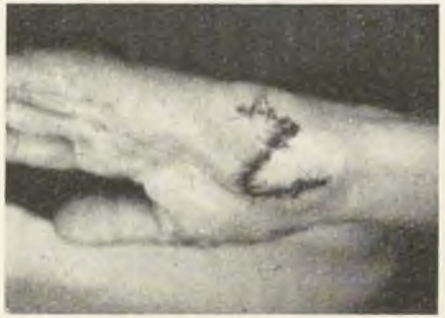

Fig. 2.

Fig. 3.

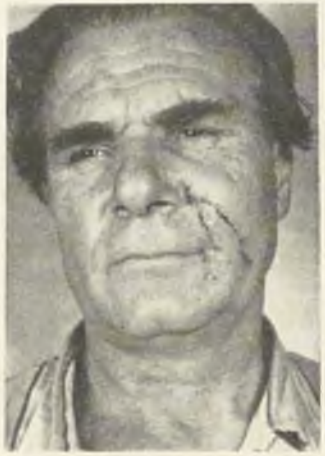

Fig. 4.

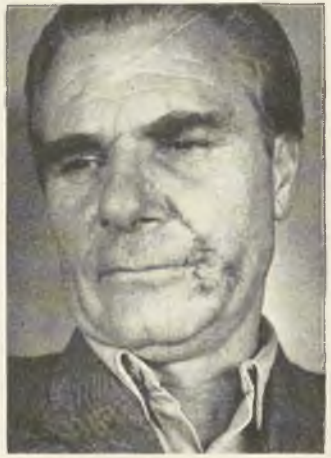

Fig. 5.

Fig. 6

Fig. 7.

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 11.

Fig. 12.

Fig. 13.

Fig. 14.

Fig. 15.

Fig. 1. Third degree electric burn on the antithenar. — Fig. 2. Closure by local skin shifting after primary excision of skin necrosis. — Fig. 3. Same wound as in Fig. 2, healed. — Fig. 4. Radiation ulcer in the left corner of the mouth with skin prepared for rotation. — Fig. 5. Immediate result. — Fig. 6. Skin defect on the cheek resulting from a horse kick. — Fig. 7. Shifting of adjacent skin by means of an incision in the wound edge. 10 days after accident. — Fig. 8. Contracting scar on the neck. — Fig. 9. Side view. — Fig. 10. Z incision. — Fig. 11. Ectropium and defect of the lower eyelid due to osteomyelitis. — Fig. 12. Bridge flap from the upper eyelid transferred to the lower. — Fig. 13. Immediate result. — Fig. 14. Shot-gun wound. — Fig. 15. Healed double-bridge flap where the secondary defect was covered with a free skin graft.

It is possible to use bridge flaps for the closure of larger defects in certain regions of the body (Fig. 11, 12, 13). The bridge flap is a band of skin which is raised from the donor bed and nourished by two pedicles. It is necessary to prepare it in the immediate vicinity of the defect and, usually, to cover the secondary defect with a free dermoepidermal graft. Double bridge flap is also useful (Fig. 14, 15).

Local skin transfer on injured fingers is of particular and invaluable assistance. This applies especially to defects on the belly of the fingers where in deeper wounds free skin grafting is contraindicated and where it is necessary to implant skin with a layer of fatty tissue. Transposition of skin with a proximal or distal pedicle from the dorsodateral surface of the finger to the defect offers complete replacement, from a qualitative point of view, so that complicated flap transposition from a distant site is unnecessary. Immobilization of the finger is simple and does not trouble the patient in the least. The resulting secondary defect must always be covered with a free skin graft (Diagram IV).

From the preceding discussion it follows that the reason for closure of defects by local skin transfer is most frequently loss of skin, after trauma, tumour resection or after X-ray radiation. All these types of defects cause functional disorders of the affected region and not simply cosmetic deformities. The skin defects should always be covered with full-thickness skin since the defects are dangerous in that the pathological changes extend far beyond the visible area of the deformity and their typical endarteritic processes are progressive and lead, after transitory improvement and healing, to disintegration. In this century of radioisotopes it is also to be expected that even greater sequelae will occur from radiation on the surface and deeper parts of the body. This means that the number of injuries from isotopes will be substantially higher ten years hence than it is now. The local conditions in fresh loss of skin are somewhat different from those obtaining after removal of more extensive blocks of scar tissue. Here the surroundings are not pathologically altered and the results are therefore very favourable.

It is possible, in general, to close defects of a more limited size by local flap transfer. Its use is dictated solely by local conditions, that is, on the possibility of skin transfer by means of variously shaped incisions.

Although this type of plastic procedure may be used anywhere on the body, it is of the greatest importance in plastic surgery of the face, for skin lying in the immediate vicinity, which far surpasses skin from other parts of the body in regard to quality and colour, is used to repair the deformity. The closer the skin used is to the defect, the more satisfactory is the functional and esthetic effect. Consequently, the necessity is always stressed of performing skin transfer on the face even if it is very complicated, in order to refrain from grafting skin of a different character from more distant parts of the body.

The mobility of the skin is dependent on its flexibility and thickness, on the thickness of the fatty tissue and, to a considerable extent, on the age of the individual. The skin of children and old people shows extraordinary good mobility. In children this is due to the thin skin and the thick layer of fat, out

of proportion to the skeleton and muscle. In older persons the skin is flaccid due to the loss of elasticity.

If the incisions on the body are made in the direction of the Langer lines, that is, in the direction of skin tension, the edges of the wound may be approximated to each other without tension or pressure. However, this does not apply on the face since here it is necessary to be guided by the physiological wrinkles and grooves which, for the most part, run at right angles to the direction of muscular pull.

The advantages of skin transfer over the free skin grafting consists mainly in the fact that in the former case skin is used with a layer of fatty tissue which practically never succumbs to contractures and has a substantially better esthetic appearance. Full replacement of skin from the immediate vicinity of the defect with preservation of vascular and nervous continuity guarantees favourable conditions for healing and formation of satisfactory surfaces. In contrast to distant transplanted skin, local transfer is less time consuming, more satisfactory with regard to skin colour, does not require any immobilization in the necessary position, and, above all, does not require modelling which in flap procedures considerably prolongs the period of treatment. As with every operative method local skin shifting has its shortcomings also. Its greatest disadvantage is that it may be used only for smaller defects, as adherence to the principle of preservation of vascular and nervous connection of the shifted skin with the surroundings is possible only in smaller deformities. In certain parts of the body (soles of the feet) where the skin is only slightly mobile and not in any abundance, this procedure is difficult. The need to close the resulting secondary defect in some cases (bridge flap) with free skin grafts is its further disadvantage. But in spite of these shortcomings it may be said that the unquestionable advantages of local skin shifting exceeds the disadvantages.

CONCLUSION

On the basis of an analysis of the possibilities of skin transfer is should be emphasized that it is one of the most versatile operative techniques in plastic surgery. Skin shifting can be used for defects of the skin of various etiology, of limited extent anywhere in the body, and guarantees a good functional and esthetic result. The technical simplicity and the fact that it is not time consuming exceed certain disadvantages of the plastic procedure.

SUMMARY

Local transfer of skin is the most commonly used in local plastic procedures which denote the repair of defects with skin from the immediate vicinity without disturbing the vascular and nervous connection. This method is indicated wherever it is necessary to replace the skin defect with skin containing a layer of subcutaneous fat and wherever the size of the defect does not require the use of skin from a distant site. Various types of surgical techniques are explained and documented: mobilization of the edges and suture of the wound, mobilization

of the edges with relaxing incisions around the defect and beyond. Transposition of wedge flaps is also discussed.

The advantages of local plastic procedures consist mainly in the fact that the shifted skin practically never contracts, it is more suitable in colour and texture, and it does not require modelling so that the period of treatment is considerable shortened. Its disadvantage is that it cannot be used for large defects and in regions with very little mobile skin.

ВЫВОДЫ

Местные смещения кожи на целом теле

Р. Эрдели

Местные смещения кожи являются самым частым методом при т. наз. местной пластике, которая означает закрытие кожного дефекта кожей с непосредственной близости без нарушения сосудистой и нервной связи. Она показана везде там, где необходимо кожный дефект закрыть кожей с подкожным жиром и где обширность дефекта не требует произвести пересадку кожи с отдаленных мест тела. В статье объяснены и рассмотрены разные виды местной пластики; мобилизация краев и сшивание раны, мобилизация краев с разрезом на краю дефекта и с разрезом в отдаленных местах. Должное внимание посвящено также пластике при помощи перемещения встречных треугольных лоскутов.

Преимущества местной пластики заключаются, главным образом, в том, что смешенная кожа практически не сморщивается; она лучше всего подходит в отношении цвета, не требует применения моделировочной пластики, ввиду чего срок лечения значительно сокращается. Невыгодой ее является то, что ее нельзя применить при больших дефектах и в областях с малоподвижной кожей.

RÉSUMÉ

Déplacement cutané local sur le corps entier

R. Erdélyi

Les déplacements cutanés locaux sont les auxilliaires les plus fréquents dans la „plastique locale“ qui consiste à masquer un défaut cutané avec les environs immédiats, sans interrompre les liaisons nerveuses et vasculaires. Il y a indication partout où il faut remplacer un défaut cutané par de la peau avec de la graisse sous-cutanée et ou l'étendue du défaut ne réclame pas la transplantation cutanée d'un endroit du corps éloigné. L'auteur explique et documente diverses sortes de plastiques locales: mobilisation des bords et suture de la plaie, mobilisation des bords avec incision au bord du défaut et incision à des endroits plus éloignés. L'auteur attache également son attention à la plastique avec lambeaux triangulaires (zet-plastique).

Les avantages de la plastique locale reposent dans le fait que la peau déplacée ne ride pratiquement pas, convient le miex du point de vue de coloration et ne nécessite pas de modelage plastique, de sorte que la période de traitement est notoirement réduite. Ses désavantages sont les suivants: elle n'est pas employable dans les défauts cutanés étendus et dans les régions où la peau est peu déplaçable.

ZUSAMMENFASSUNG

Lokale Hautverschiebungen am ganzen Körper

R. Erdélyi

Lokale Hautverschiebungen sind das häufigste Hilfsmittel bei der sog. Lokalplastik, die eine Deckung des Hautdefektes aus der unmittelbaren Umgebung ohne Unterbrechung des Gefäss- und Nervenbahnen bedeuten. Sie sind überall dort indiziert, wo es notwendig ist den Hautdefekt durch Haut und subcutanes Fettgewebe zu ersetzen und wo die Ausdehnung des Defektes keine Hauttransplantation aus entfernteren Körperstellen erfordert. Es werden verschiedene Arten von Plastiken erklärt und dokumentiert: Mobilisation der Ränder und Wundnaht, Mobilisation der Ränder mit Einschnitt am Defektrand Einschnitt an entfernteren Stellen. Der Plastik durch Austausch von Z-Lappen wird ebenfalls eine entsprechende Aufmerksamkeit gewidmet.

Die Vorzüge der Lokalplastik beruhen hauptsächlich darin, dass die verschobene Haut nicht schrumpft, am besten der Farbe nach entspricht, keine Modellationstechnik benötigt, sodass die Behandlungsdauer wesentlich verkürzt wird. Ihre Nachteile: Unbrauchbarkeit bei grossen Defekten und in Teilen mit wenig verschiebbaren Haut.

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NEUROPLEGICS AND HORMONES IN THE TREATMENT OF BURNS

R. DOLEČEK, J. KALINA, L. KLABUSAY

In addition to local changes, every serious case of burns can also produce extensive general reactions, which are often exaggerated and disproportionate and may cause considerable harm or even death. There are many different indicators of these reactions (blood pressure, pulse, ionic changes in the urine or serum, changes in the erythrocyte or leucocyte count or the haematocrit, the behaviour of eosinophils, steroid excretion, ADH values in the serum, etc.).

If the central nervous system — hypothalamus — pituitary — adrenal cortex system reacts normally, steroid excretion values, particularly of glucocorticoid catabolites, are an almost direct indicator of the action of the stress. The same also applies, with certain reservations, to eosinophil (EO) values and also perhaps, to some extent, to antidiuretic hormone values (ADH). Under the action of stress, the amount of ADH in the serum appears to increase before normovolaemia and isoionia are disturbed (Charvát 1956).

Earlier studies by the present authors (Doleček 1956, 1958) and by others Sevitt 1951, 1954, Wight et al. 1953, Wilson et al. 1955, Hume et al. 1956, Moore 1957) show that functional hypercorticalism of varying duration develops in most cases of burns. The level of 17-hydroxycorticoids (17-OH) usually remains raised for a particularly long time, occasionally for as long as several months. Values of 17-ketosteroids (17-KS) are not generally raised for as long as 17-OH values. An increase in the aldosterone level in the urine was found on some occasions (maximum 20 gamma/day), but low values were also found (Doleček et al., in press). Raised ADH values were likewise found in the serum of all patients with burns, during the first days and weeks (maximum 110 microunits/ml.) — see table 13. In the papers cited above (Doleček 1956, 1958) mention was made of the possible harm caused by exaggerated, disproportionate reactions to burns on the part of the adrenal cortex (osteoporosis, poor healing of the wounds, the development of psychotic reactions, worsening of diabetes, ulceration of the alimentary tract, etc.). High ADH values could have an adverse effect by worsening oliguria; they might also endanger the patient indirectly

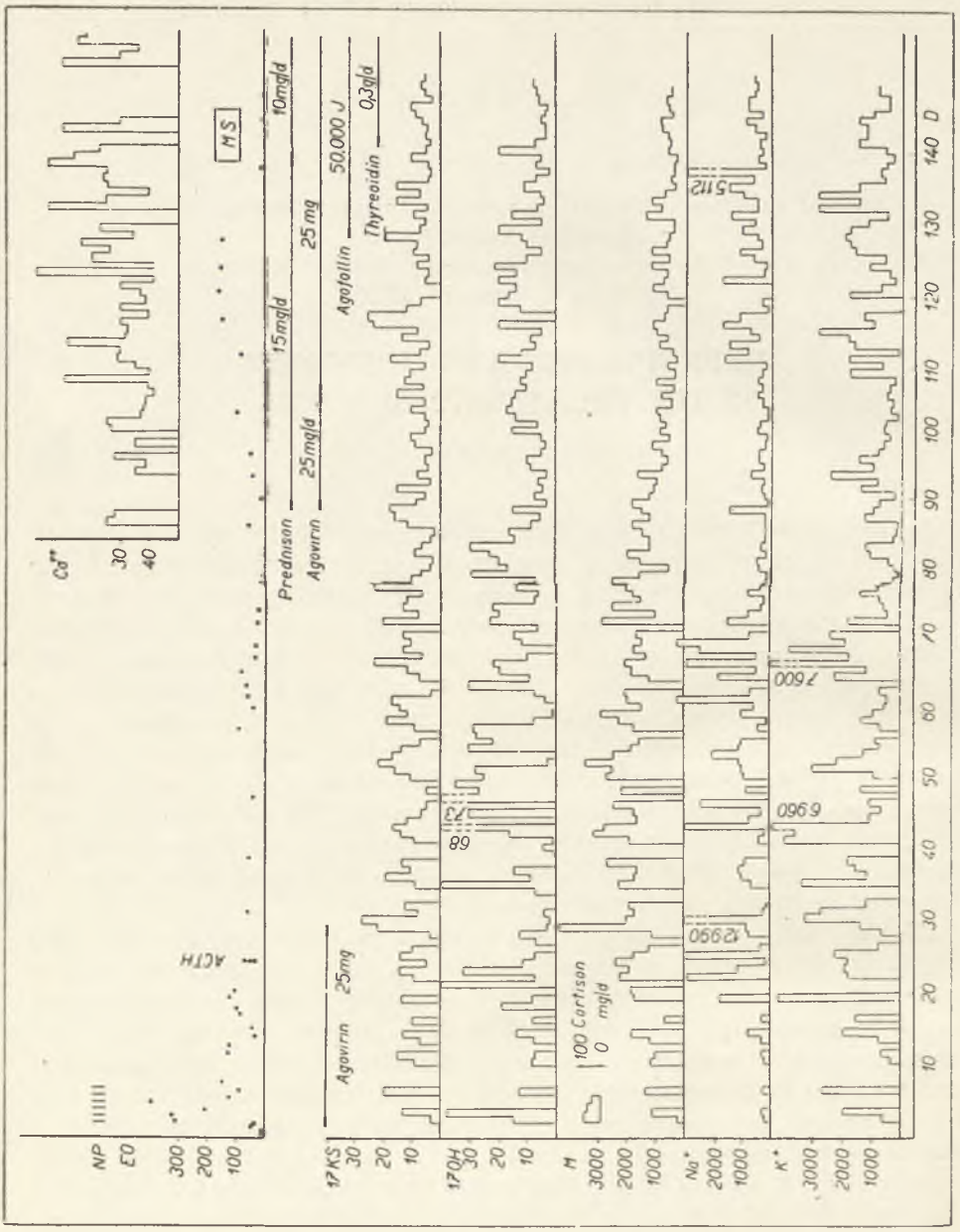

Fig. 1.

by causing retention of a large part of infusions of electrolyte-free water (e.g. 5% glucose), resulting in an increase in the total amount of water in the body, with a consequent decrease in ion concentration. The experiments of Dudley et al. (1954) and of Moore (1957) on this subject are particularly interesting.

For the inhibition of exaggerated reactions by the organism after burns, the authors, since 1956, have begun using the modified mixture M_2 (Caithaml),

which contains Hydergine (= DH-Ergotoxin-Spofa), Sandosten-calcium and Panthesine (the Hydergine, Sandosten-calcium and Panthesine were kindly supplied by Sandoz, the DH-Ergotoxine by OIS Spofa). In order to verify the success of inhibition of the reaction of the adrenal cortex after burns, and hence, to

Fig. 1. Patient B. K., aged 43. Burns involving 65% of body surface (45% third degree, 20% second degree). Treated with neuroplegics (NP). Also given hormones.

some extent, the reaction of the organism as a whole, indicators of the function of the adrenal cortex and other tests were studied over long periods in almost half the patients treated with the above neuroplegics. Excretion of 17-KS, 17-OH, Na, Ca and K in the urine and EO values were studied daily. Recently, aldosterone has also been determined in the urine and ADH in the serum. In some patients with burns, free and conjugated 17-OH were also determined in the plasma.

The patients were naturally treated at the same time in the classic manner (local treatment, infusions, antibiotics, nutrition, etc.).

The use of neuroplegics and hibernation in the treatment of severe burns has been described by Chippaux (1954), Huguenard (1956), Stüttgen (1955, 1957),

Tab. 1. Survey of all burned patients treated with neuroplegics in 1956—1959.

Percentage of body surface involved	Number of patients	Number of deaths	Mortality %
10—19	8	0	0
20—29	7	0	0
30—39	17	0	0
40—49	11	4	36
50—59	9	4	44
60—69	8	2	25
70—79	3	2	67
80—	4	4	100
	67	16	

The patients included 47 adults and 20 children. All were from second to fourth degree.

Kaloud (1958) and others. The Vishnevsky block and morphine are also intended to serve a similar purpose. An account of laboratory experiences in the long-term study of steroid excretion in the urine of patients suffering from burns treated with neuroplegics has already been given elsewhere (Doleček 1958, 1958a).

The use of cortisone and ACTH in the treatment of burns has been discussed by a number of authors, whose results are not, however, always in agreement (Crassweller 1950, Whitelaw 1951, Adam et al. 1951, Olsen 1952, Heinzel 1953, Martin 1955, Frank 1957 and others). In the course of their investigations, the present authors attempted to elaborate rational indications for the administration of these substances in cases of burns and also to determine indications for the administration of other hormone preparations during different phases of the illness. Longterm study of the function of the adrenal cortex in patients with burns enabled these indications to be established.

METHODS

The neuroplegic mixture was administered to patients with burns over a period of several days. The duration of this treatment and the daily number of doses were determined by the clinical condition and laboratory findings.

One dose contained 0.6 mg. Hypergine, 5 ml. 5% Panthesine and 10 ml. Sandosten-calcium. For the first two to three days the patient usually received two to four doses daily. In most cases the average period of treatment was five to six days.

After the patient was admitted, the saphenous vein was usually exposed 10—15 cm. from the inguinal ligament, a polyethylene tube was inserted and one dose of neuroplegic mixture in 5% glucose and physiological saline was administered intravenously. One dose diluted with the same amount of physiological saline was usually administered

Tab. 2. Survey of all burned children treated with neuroplegics in 1956—1958.

Percentage of body surface involved	Number of patients	Number of deaths
10—19	7	0
20—29	4	0
30—39	2	0
40—49	3	2
50—59	1	0
60—69	3	1
	20	3

intramuscularly at the same time. The doses for children were smaller, comprising 0.1 mg. Hydelrgine, 0.8 ml. 5% Panthesine and 1.6 ml. Sandosten-calcium per 10 kg. body weight. When "stepping out" of neuroplegia, Hydergine linguets or DH-Ergotoxine in drops were used. No side-effects from the neuroplegic mixture were observed.

Ketosteroids were determined in the urine by a modification of Matys' method (Matys 1951), total 17-OH were determined in the urine by Reddy's method (Reddy 1954, Doleček and Novák 1956), free plasma 17-OH by the Porter-Silber method (1954) and conjugated 17-OH by the methods of Reddy (1956) and of Doleček and Endryáš (1959).

Moolenaar's method (1957) was used for aldosterone estimation and ADH in the serum was determined by the method of Holeček et al. (1954). Normal urine 17-KS values are 15 ± 5 mg./day for men and 10 ± 5 mg./day for women. Average urine 17-OH values are 5—6 mg./day, the upper limits of normal values being 10—12 mg./day. ADH in the serum of normal subjects, without an osmotic load or exposure to stress, should be below 15 microunits/ml. serum.

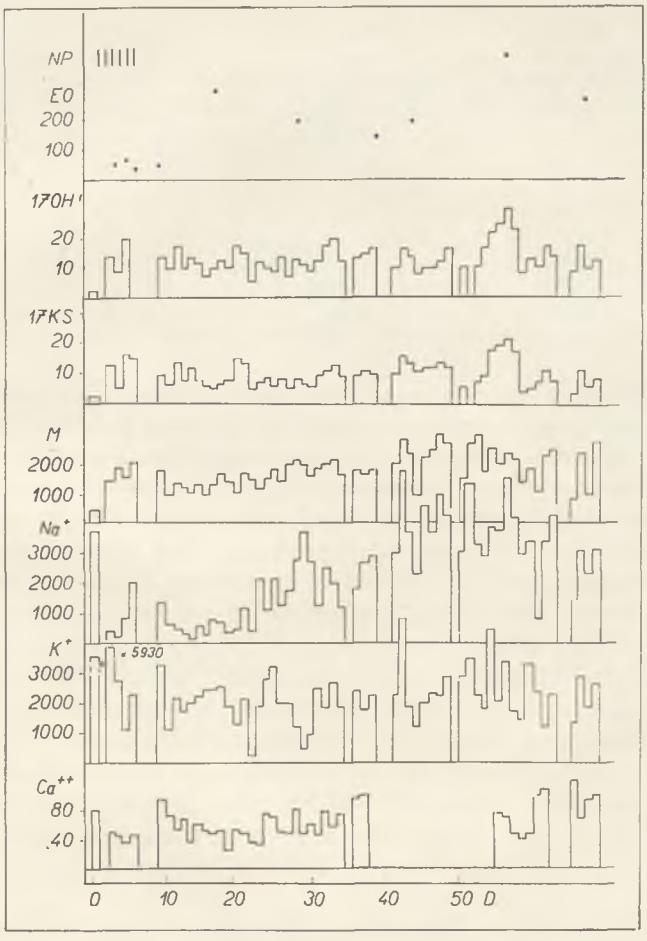

Fig. 3. Patient B. V., aged 50. Burns involving 69% of body surface (39% third degree, 30% second degree). Treated with neuroplegics. Discharged cured, after 67 days.

RESULTS

To date, 67 patients with burns (adults of both sexes and children) have been treated with neuroplegics in addition to the normal treatment. Tab. 1 gives details on the extent of the burns and on survival in all the patients concerned.

while Tab. 2 gives the same details for children only. Of the 67 patients treated with neuroplegics, a long-term study was made of 17-KS, 17-OH, sodium, potassium and calcium values in the urine (for a maximum of 10 months) in 25 patients. Tab. 3 and 4 compare the results with the results obtained in an English burns unit (Evans 1957) and in a children's university clinic in Austria (Kaloud 1958).

Tab. 3. Results of treatment of burned patients in an English Unit (A. J. Evans, Brit. Med. J. 1957, 5018, 547—551).

Percentage of involvement	Number of patients	Number of deaths	Mortality percent
10—19	98	0	0
20—29	40	0	0
30—39	21	5	23.8
40—49	9	2	22.2
50—59	9	4	44.4
60—	7	6	85.7

The patients in this table were all under 60.

Tab. 5 and 6 give the averages of the lenght of stay in hospital, the number of doses of neuroplegics and the amount of infusion solutions in adults and children who survived. The amount of infusion solutions required for patients treated with neuroplegics is strikingly small. For pursposes of comparison. Tab. 7 shows the scheme of Baxter Lab. Inc., copyright 1954, for fluid consumption.

Tab. 8 and 9 show the doses of neuroplegics used for one adult patient (B. B., 25 years, burns over 63% of the body surface (20% second degree, 43% third degree) and in one child [P. G., 2 years, burns over 60% of the body surface (50% second degree, 10% third degree)].

The neuroplegic mixture used by the authors inhibits ADH secretion. This was verified experimentally. After intravenous administration of 20 ml. 10% NaCl, ADH values in the serum of the 16 subjects investigated rose in the course of one hour to 28.4 microunits/1 ml. If the experimental subjects received a dose of the given neuroplegics one day and 1½ hours before administration of the same dose of NaCl, ADH values rose only to 22.2 microunits/1 ml. serum. The difference is statistically significant (p between 0.05 and 0.02).

Tab. 4. Survey of all patients treated for burns at Children's University Clinic, Graz, 1950—1955 (H. Kaloud 1958).

	Area of burns as a percentage						
	—10	11—20	21—30	31—40	41—50	51—60	over 60
Cured	163	40	1				
Died	12	17	14	5	1	1	1
Number of deaths as a percentage	6.8	29.8	93.3	100	100	100	100

Neuroplegics were not used in the treatment of these patients.

Tab. 10 and 11 give the absolute and relative indications for the administration of cortisone or cortisol during the first days after sustaining burns. Tab. 12 gives the indications for the administration of hormone preparations during different phases of the illness.

Fig. 1 illustrates the results of long-term observation of 17-KS, 17-OH, sodium, potassium and calcium in the urine and of EO in a female patient with

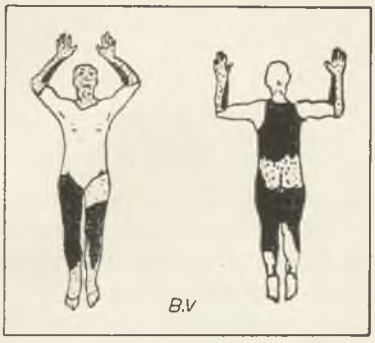

Fig. 4. See fig. 3.

severe burns, who in addition to classic surgical treatment was also treated with neuroplegics and hormones.

The patient, B. K., aged 43, suffered burns of the face, both upper and lower extremities and the back, involving 65% of the body surface, 20% being second degree and 45% third degree burns (Fig. 2). The burns were caused by exploding benzine. Prior to the accident the patient had been treated for anaemia.

On the first four days the patient received a total of 8,000 ml. fluid, administered parenterally, including 6,300 ml. blood and plasma. Intensive neuroplegic treatment was given on the first six days. In view of her extremely serious condition, in addition to the usual treatment and administration of neuroplegics, the patient was also given cortisone, administered intramuscularly in amounts of 100—50 mg. daily, and Agovirin (testosterone propionate), administered intramuscularly in amounts of 25 mg. daily, for the first four days (Fig. 1). The rapid appearance of EO, normal 17-KS values and, except for one day, practically normal 17-OH values in the urine were striking. These was marked sodium retention (functional hyperaldosteronism?). After six weeks a marked increase occurred in the 17-OH level in the urine, with a subsequent decrease in EO to low and almost zero values; the erythrocyte count was slightly over 1,000,000 and considerable respiratory difficulties developed. Marked sodium retention was again observed. At this stage, osteomyelitis of the sternum, which developed during the first days after admission, became worse. An attempt was made to block catabolic reactions by prednisone and Agovirin. As seen from Fig. 1, the 17-OH level in the urine decreased, EO increased and the urine flow diminished. In view of presumed inhibition of the other endocrine glands possibly as a result of a pituitary "shift" (Selye 1949, 1950), small doses of Ago-

Tab. 5. Survey of adult burned patients treated with neuroplegics.

Extent %	Total number	Survived	Died	Neuroplegia		Admin. in 4 days		Av. no. of days in hosp.
				Days	Dose/day	Plasma, blood	crysta-loids	
10—19	1	1	0	3	1	500	950	52
20—29	3	3	0	1.5	1.5	690	400	23.5
30—39	15	15	0	3.8	2.7	1,789	1,350	54
40—49	8	6	2	5	2.8	3,118	3,158	103
50—59	8	4	4	4.6	2.4	2,474	2,610	86
60—	12	5	7	6	2.4	3,278	2,940	119

*) Patients who died not included.

follin (oestradiol-benzoate) and of dessicated thyroid were administered. The patient's condition showed marked improvement (healing, a more cheerful mood, appetite, blood picture); 17-KS and 17-OH values remained permanently normal or even low. Slight menstruation occurred twice.

It is now more than two years since the accident and the patient feels well. In the interval she has had repeated attacks of cholelithiasis, from which she did not suffer previously. Metastatic calcifications appeared in the axillae at the site of previous abscesses. Osteoporosis was found in some bones, as a consequence of increased mobilization of calcium during prolonged stress. Bone changes in burned patients have been described in other communications (Štěpánek and Doleček 1959, Doleček and Štěpánek 1959).

See also fig. 3, 4, 5 and 6. On figures *M* means: urine in ml./day, *D* means days. Na,K and Ca are given in mg./day in urine. On figures 2, 4 ad 6 the black areas mean the III^0 burns, the dotted areas the II^0 burns.

DISCUSSION

Although the 67 patients with burns who were treated with neuroplegics in addition to the classic treatment do not constitute a very large series, the authors are of the opinion that this series is not too small. They particularly stress the fact that more than 50 of these patients had severe burns involving over 30% of the body surface, that the patients were kept under observation

Tab. 6. Survey of burned children treated with neuroplegics.

Extent %	Total number	Survived	Died	Neuroplegia		Admin. in 4 days		Av. no of days in hosp.
				Days	Dose/day	Plasma, blood	crysta-loids	
10—19	7	7	0	2.1	1.2	256	183	32.5
20—29	4	4	0	2.0	1	690	510	61
30—39	2	2	0	3.0	1	670	300	67
40—49	3	1	2	4.0	2	2,145	3,650	74
50—59	1	1	0	4.0	2	1,000	800	61
60—	3	2	1	3.0	2	810	600	61

*) Patients who died not included.

Tab. 7. Fluid consumption for second degree burns in ml. (according to American authors).

Extent %	Plasma and blood	Electrolytes	Glucose
20—29	—	2,500	2,000
30—39	500	3,500	2,000
40—49	1,000	4,500	1,500
50—59	1,250	6,000	1,500
Fluid consumption for third degree burns in ml.			
20—29	500	2,000	2,000
30—39	1,000	3,000	2,000
40—49	1,500	4,000	1,500
50—59	1,500	6,000	1,000

The amounts are calculated for a body weight of 70 kg., from the scheme of Baxter Laboratories Inc., Copyright 1954.

for long periods and that numerous tests were carried out in the course of treatment. In the discussion the authors wish to reemphasize some of their observations and to attempt to explain some of the results.

Some of the clinical signs in burned patients treated with neuroplegics are worth mentioning. One feature was the relatively quiet course of stages which are normally stormy. The patient was quiet and cooperated better, the usual vomiting was absent, the care of such patients was generally easier than of patients not treated with neuroplegics and rehabilitation could be commenced sooner. A favourable effect on tachycardia was often observed. The blood pressure could be measured in a few cases only, since in most cases the upper extremities were also burned. During the first days, temperatures were almost always below or about 36^0 C; the toxaemia phase was mostly free from septic swinging of the temperature, rigors and profuse sweating and the temperature rarely exceeded 38^0 C.

Sixteen of the patients treated with neuroplegics died. Most of these were cases of very severe burns, usually involving more than 50% of the body surface

Tab. 8. Average doses of neuroplegics for one patient (The given doses are for the whole day. (See text).

Days	Hydergine in mg.	Sandosten-calcium in ml.	5% panthesine in ml.	Remarks
1	1.8	30	15	In three doses (2× i. v., 1× i. m.)
2, 3, 4	1.2	20	10	In two doses (1× i. v., 1× i. m.)
5, 6	0.6	10	5	I. m. in one dose

(Tab. 1 and 2). Encouraging results were obtained in children. Of a total of 20 children treated with neuroplegics, only three children with severe burns died. On comparing these results with other series of cases of burns not treated with

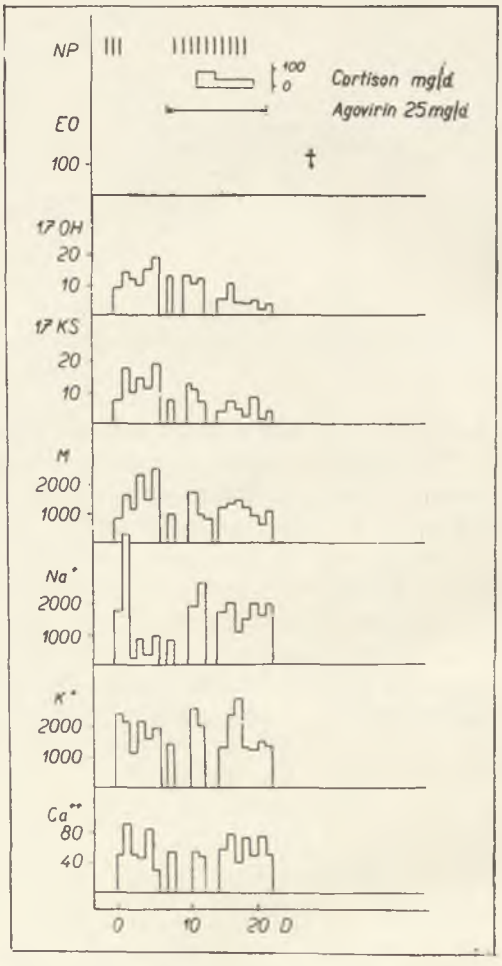

Fig. 5. Patient S. J., aged 59. Burns involving 65% of body surface (55% third degree, 10% second degree). Treated with neuroplegics for first three days; intensive neuroplegic treatment repeated during toxaemic phase because of high temperatures not responding to antipyretics. It is interesting to note steady decrease in 17-KS and 17-OH, despite the administration of cortisone and testosterone propionate, with constant zero eosinophil values. The patient died on the 22nd day.

neuroplegics (Tab. 3 and 4), they are seen to be very favourable. No neuroplegic-treated patients in which the burns involved less than 40% of the body surface died in this series. The somewhat higher percentage of deaths in the

40—49% group in the present series as compared with the English series can be explained on the basis of the particularly severe degree of burns in this group. Another striking feature is the much lower consumption of infusion solutions in the patients of the present series. This is best seen from a comparison of Tab. 5 and 6, which show the average consumption of infusion solutions according to the degree of the burns in the present series, with Tab. 7, which shows the scheme of an American firm. Healing takes place much more rapidly in patients treated with neuroplegics (better blood supply? decrease in hypersecretion of glucocorticoids? action via the central nervous system?), as seen from the relatively short stay in hospital (Tab. 5 and 6).

The influence of prolonged administration of neuroplegics on the function of the adrenal cortex is quite marked. It results not only in the early appearance of EO, but also in a pronounced decrease in steroid excretion (first part of Fig. 1, Fig. 3 and papers from Doleček 1958, 1958a). Extensive burns are often accompanied by almost normal (not raised) 17-KS and 17-OH values, without any signs of hypocorticism (e. g. Fig. 3). Such states were observed repeatedly. It thus seems that increased excretion of 17-KS and 17-OH in the urine is not essential to satisfactory recovery even in patients with very severe burns. Plasma 17-OH values likewise need not always be greatly raised. Although the possibility of increased utilization of cortical hormones must be borne in mind, it is nevertheless also important, in this connection, to take into account the conception of the permissive role of cortical hormones (Ingle 1951).

In patients with severe burns it was sometimes necessary to combine neuroplegic treatment with cortisone, so as to inhibit hyperpyrexia, which cannot be controlled by any other means. In such cases prednisone is a satisfactory substitute for cortisone. Fig. 5 illustrates the case of S. J., who suffered severe burns, and in whom toxaemia was accompanied by marked hyperpyrexia. It shows a pronounced decrease in 17-KS and 17-OH to low values, with permanent aneosinophilia. The 17-KS and 17-OH level fell despite the administration of cortisone and Agovirine. This is another interesting example of the interrelationships and differences in the regulation of EO and the cortical hormones.

It is impossible to state exactly by what mechanism neuroplegics interfere in neuroendocrine reactions, but it is almost certainly a mechanism which affects not only the pituitary-adrenal system, but also other organs, via the

Tab. 9. Doses of neuroplegics used in the case of a two-year-old child (v. text), which can be regarded as average (in relation to weight).

Days	Hydergine in mg.	Sandosten-calcium in ml.	5% panthesine in ml.	Remarks
1	0.2	3.2	1.6	In two doses (1× i. v., 1× i. m.)
2, 3	0.1	1.6	0.8	In one dose i. m.

The given doses are for the whole day.

central nervous system. Under the influence of the neuroplegic, the organism became less stormily "perceptive" of the stress, if such an expression can be used, and its exaggerated reaction ceased. In the given doses, *the neuroplegic mixture damps down adaptation mechanisms before the pituitary.* This explains why *it is possible to block the reactio to stress, but not to the administration*

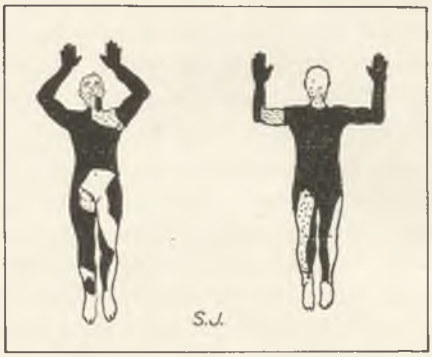

Fig. 6. See fig. 5.

of ACTH (Doleček 1958, 1958a). Similar results were obtained by American authors (Christy et al. 1956, Ohler 1956, etc.).

It is very probable that in the present case the neuroplegics interfered successfully in the exaggerated catabolic reaction of the organism, which under their influence did not react disproportionately to the severe stress. A very favourable indicator in this association is the early, gradual increase in EO, which usually appeared sooner in patients treated with neuroplegics than in others. The authors do not claim that the early appearance of EO is always a sign that all is well, but prolonged low and zero EO values were always an indication of a grave condition (e. g. Fig. 5).

Neuroplegia also seemed to have a favourable effect on the urine flow in patients with burns. It is possible that, in addition to other functions (e. g. the renal blood flow), the neuroplegics also interfered in hypersecretion of ADH, excretion of which was raised after burns (Tab. 13).

Apart from selection of the preparation (e. g. mixture M_1 or M_2), an important question in the administration of neuroplegics is the dosage and the duration of treatment. In the authors' view, the Modified M_2 mixture, i. e. Hydergine (= DH-Ergotoxine), Sandosten and Panthesine, is more satisfactory than mixture M_1. Hydergine is not known to produce unpleasant side effects like chlorpromazine (tachycardia, liver involvement, etc.). Patients are not so sleepy after M_2 as they are after M_1 — a very important condition for cooperation.

The authors' own experimental results in rats (Klabusay), which were related directly to the problem of clinical observations, and the experimental results of other authors (Špaček et al. 1957) confirm these views. As a result of their experiences, the authors have ceased in the main to use mixture M_1 and

Tab. 10. Indications for the administration of cortisone or cortisol in the treatment of burns during the first days after the accident. — I.

Absolute indications	Time of administration	Doses
Patients treated for primary or secondary hypocorticism	Throughout	100—200 mg./day, according to extent of burns, clin. state and lab. findings
Potential hypocorticism (if diagnosed previously)	Throughout	50—100 mg./day and more, as required
Patients taking adrenal hormones (glucocorticoids) for a long time previously	Preferably throughout*)	50—100 mg./day and more, acc. to clinical state
Adrenogenital syndrome with low 17—OH	Throughout	50—100 mg./day and more
Very low steroid excretion values after injury, with generally normal urine flow. Considerable sodium loss via urine (perhaps better to give aldosterone or deoxycorticosterone)	Acc. to clin. state and lab. findings	50—100 mg./day, according to clinical state and laboratory findings**)

*) Gradually reduce doses if required, occasionally administer ACTH (either by i. v. infusion or long-acting i. m.)

**) This may be a functional or organic disturbance or only a temporary condition at adrenal level or higher. Preferably give cortisone or cortisol and gradually reduce doses, occasionally administering ACTH.
The doses are approximate and it is important always to follow the patients' general condition and the laboratory findings. In severe cases it is preferable to administer cortisol intravenously (100 mg. cortisol in 5% glucose for 2—4 hours). The doses are given for cortisone; 25 mg. cortisone = approx. 20 mg. cortisol.

even in animal experiments they found that chlorpromazine did not favourably influence survival of animals with burns or hasten the healing of skin burns. In large doses it has an unfavourable stressor effect on the pituitary-adrenal regulatory system. Small doses of M_2, which proved more satisfactory in clinical practice, also proved satisfactory in experiments. They gave the highest survival results and healing was also more rapid (see Doleček et al. — in press). In cases of extensive burns, over-large doses of M_2 are harmful, as the authors found from their own expericence and as stated in the literature. Over-inhibition of defence reactions does not have a good effect either. *All that is necessary is to inhibit "overshooting" of these reactions.* Simultaneous experimental treatment with hibernation and neuroplegics did not produce good results; on the contrary, the condition tended to deteriorate (Kochetygoff 1957).

The duration of treatment and gradual "stepping out" of neuroplegia are also very important, so as to avoid "overshooting" of the reaction following sudden interruption of the administration of neuroplegics.

The use of neuroplegics in the prevention of the consequences of severe shock and in the treatment of shock due to burns is important not only for individual cases, but also *when dealing with mass burns* (e. g. lower consumption

of infusion solutions). The administration of a suitable neuroplegic mixture at the outset of treatment could be of great significance for the further fate of the patient. The authors themselves use neuroplegia when transferring patients with burns to hospital. *Neuroplegics are naturally not a panacea for the treatment of burns as a whole and the usual forms of treatment must also be used at the same time* (local treatment, infusions, antibiotics, vitamins, nutrition, etc.), but the authors found from their own practice that neuroplegics improve the course and prognosis of cases of burns. *Treatment must be comprehensive and must be directed not only against the specific effect of the pathogenic agent, but must also be aimed at controlling any more or less nonspecific responses of the organism.*

On the basis of experiences gained hitherto it can be said that neuroplegia is a good and useful method for the treatment of burns. It helps to steer the patient over the reefs of the illness in an incomparably better state than would otherwise be possible. It permits the infusion of smaller amounts of fluid and the patient is able to eat. It has a marked effect on temperature and on the patient's general mental state. States of delirium, restlessness and anxiety do not occur in patients to whom neuroplegics are administered. Tachycardia is often abolished. All these factors ensure better cooperation, which is so important for the healing process.

Neuroplegia can therefore be recommended as a useful method in the treatment of severe burns. Attention is drawn, however, to the great importance of careful clinical and laboratory control and to the need for *dealing with each case on a strictly individual basis.*

If disturbances in the production of different "peripheral" hormones (e. g. adrenals, gonads, thyroid, etc.) last for a particularly long time, they can have different consequences for the organism as a whole (resistance to infection, fat deposits, growth, stimulation of arteriosclerotic changes, healing of wounds, etc.). On undertaking comprehensive treatment of a patient in whom these numerous disturbances may be present, it is important, therefore, to determine their extent and to abolish them, for instance, by administering for some time preparations of the different hormones of which there is an absolute or relative deficiency.

Unfortunately it is not known exactly what can be regarded as a normal reaction (e. g. after a burn) and it is thus not known what constitutes an exaggerated and a lowered reaction. If this were known, it would be far easier to talk, for example, of substitution. In patients with burns, this applies mainly to the excretion of adrenal steroids, which were studied in the present series of experiments for different periods. It is possible that an exaggerated reaction may sometimes have beneficial results. Extensive injury and destruction of the skin as a result of burns may give rise to the development of different antibodies, including non-specific antibodies, which can have an adverse effect on the taking of skin grafts, It is possible that a marked increase in glucocorticoid production, while harmful in other respects, may reduce and restrict this antibody formation. It is also possible that raised glucocorticoid values may have

Tab. 11. Indications for the administration of cortisone or cortisol in the treatment of burns during the first days after the accident. — II.

Relative indications	Time of administration	Doses
Menstruation period (possibility of potential functional hypocorticism)	3—4 days, under careful observation	50—100 mg./day
Some allergic patients with high eosinophilia (possibility of partial glucocorticoid hypocorticism)	3—4 days, under careful observation	50—100 mg./day
Sudden increase in EO	3—4 days, under careful observation	50—100 mg/day/
Marked oliguria*)	1—2 days	100—200 mg/.day
After severe injuries or infectious diseases	3—4 days, keeping check on condition; longer if required	50—100 mg./day or more
Severe conditions not controlled by usual treatment and neuroplegics, the severity of which does not absolutely correspond to the degree of burning (can include patients with potential hypocorticism or inadequately reacting defence mechanisms)**)	3—4 days, keeping check on condition; longer if required	100—200 mg./day

*) 100 mg. cortisol in 5% glucose administered intravenously in an attempt to improve the urine flow when other methods failed (novocaine block, neuroplegics, novocaine i. v., adequate supply of fluids).

**) I. v. administration of cortisol most satisfactory in severe cases.
If the adrenals are not severely affected, the doses can gradually be reduced. With large doses, on the last two days, 40—80 units of long-acting ACTH are given daily, divided into two doses. After completing long-term administration of corticoids, it is necessary to pay the patient increased attention for a few days. The same applies to tab. 10. The doses are given for cortisone; 25 mg. cortisone = approx. 20 mg cortisol.

a favourable effect on certain processes in the central nervous system (the development of phase states). As already mentioned, many authors have already discussed the use of cortisone and ACTH in the treatment of burns, not always with the same results. This is because the type of preparation, and possibly the duration of administration, were not always correctly indicated. It is also possible that more was expected of cortisone than it was capable of accomplishing.

A very important role in the development of post-traumatic reactions after burns is played by the central nervous system — hypothalamus — pituitary — adrenal system. Without accurate and prompt intervention by this system the patient soon dies. Many *different localizations of disturbance* are possible — at the level of the central nervous system (?), hypothalamus (?), pituitary or adrenals. There are also *two possible types of involvement — organic or functional*. Disturbances of this system result in deficient production of corticoids — chiefly glucocorticoids and possibly mineralocorticoids — essential to a favourable course of defence reactions. It is therefore logical to administer these "peripheral hormones" where necessary, since there is usually too little time to determine the site of the disturbance. In patients with burns, a marked increase

in the activity of the adrenal cortex, i. e. functional hypercorticism, almost always occurs at the outset. Further stimulation by the administration of exogenous ACTH might injure the already fully stimulated adrenal cortex (e. g. by the development of tubular necrosis). On the other hand, excessive doses of exogenous cortisone, administered over a long period, might lead by a backfeed mechanism to a blocking of ACTH production, the cessation of which could result in manifestation of hypocorticism. It is known, however, that back-feed relationships are somewhat different under the action of stress than under resting conditions.

The administration of *cortisone or cortisol has two types of action: specific* (substitutional) *and non-specific.* In hypocorticism its specific action consists in replenishment of endogenous production, while if the function of the adrenal cortex is normal, it acts non-specifically on the general reaction of the organism. This non-specific activity may be manifested against shock, possibly by favourably influencing, or limiting, the development of phase states (Vvedenskij) in neuroendocrine reactions, by increasing glomerular filtration, probably by stimulating ADH break-down, by influencing the reaction of the mesenchyma. The importance of the time factor in the administration of adrenal hormones can be seen from a study of some of the graphs from the authors' previous studies. On the first two to three days, 17-KS and 17-OH values (especially the latter) were usually raised, although sometimes they were normal and occasionally low. This was followed by a period sometimes lasting several weeks, during which 17-KS and 17-OH values were raised: this applied especially to 17-OH values, since 17-KS values were sometimes lowered. During the phase of toxic cachexia, both 17-OH and 17-KS values were low, particularly the latter; 17-OH values rose only as a result of some complication or following stimulation by ACTH. In patients with burns, therefore, 17-OH values in the urine are mainly raised, i. e. metabolites of glucocorticoids (catabolic "hormones"); 17-KS values are sometimes lowered for long periods, so that it is possible to speak of partial hypocorticism of their precursors, i. e. anabolic hormones.

Determination of aldosterone was introduced only recently and it is not possible, from the first results, to venture an opinion on their behaviour and therapeutic use for cases of burns. (Aldosterone for intramuscular administration was supplied kindly by Ciba.) (Tab. 13.) The first results, however, show that aldosterone values are sometimes raised. Llaurado (1957) also recorded raised aldosterone values in surgical patients. In two patients with severe burns, low to zero aldosterone values and relatively very low sodium retention were found. The possibility of functional hypoaldosteronism can therefore not be excluded. In addition to their effect on electrolytes and water, low aldosterone values could also have an unfavourable influence on vascular reactions (Raab et al. 1950, 1956). In the authors' view, the therapeutic administration of aldosterone would be fully justified in such cases. As yet, little is known of the therapeutic administration of aldosterone in cases of burns. In the authors' opinion, however, it has a place in the treatment of selected cases, with special reference to the large shifts and losses of water and electrolytes which take place in the organism after sustaining burns.

Tab. 12. Survey of administration of hormone preparations in different phases of the burns illness

Hormone preparation	Phase of shock, onset of toxaemia	Toxaemia	Toxic cachexia
Cortisone	50—200 mg./day and more, reduced as required. Indications as in tab. 10 and 11	V. tab. 10 and 11. In hyperpyretic reactions, poss. together with neuroplegics	Small doses: 12.5 to 25 mg./day, except where larger doses are indicated or where contraindicated
Anabolic hormones	Testosterone propionate, 25 mg./day or alternate days. Methyl androstenediol 25 to 50 mg./day	2—3 times weekly in same doses as for previous phase	2—3 times weekly, as before
Aldosterone	Marked excretion of sodium in urine and low serum sodium level on first days after burning (?)	?	?
Thyroid preparations	—	—	Thyreoglobulin mite, 1 dragee daily, acc. to tolerance

The administration of the above preparations is always determined by the clinical condition and laboratory findings and can be used only in a limited number of cases.

In Tab. 10 and 11 the authors attempt to determine *the indications for the use of cortisone or cortisol during the first few days after the accident.* On the first days it is preferable to administer cortisone or cortisol intramuscularly rather than perorally. In states of shock, however, the best method is by intravenous infusion (e. g. cortisol — free alcohol). Synthetic preparations like prednisone or prednisol one were not used on the first days.

The authors emphasize that the tables and schemes are only a partial guide. It is essential always to proceed according to the given situation and to follow carefully the clinical condition and the laboratory findings.

As already stated, it is better to administer cortisone or cortisol during the early phase rather than ACTH. ACTH requires a normally functioning adrenal cortex, not overloaded by its own endogenous stimulation. In the presence of deficient activity of the adrenal cortex (organic or functional disturbance), or of overstimulation by endogenous ACTH, the administration of exogenous ACTH has no or little effect and under unfavourable conditions can even be injurious by causing over-stimulation. ACTH is indicated in cases of failure of the adenohypophysis or of higher situated trigger mechanisms (e. g. the corticotropin-releasing factor); in patients with severe burns, however, there is no time to diagnose this state. The administration of cortisone or cortisol, in suitable doses, circumvents the danger of blocking endogenous production. It is true that ACTH has a wider action than cortisone (or cortisol), since it increases production of N-hormones as well, but in severe cases it is necessary to indicate the "peripheral" hormone, if it is not known how the gland concerned will react. In the authors' opinion, this view is absolutely correct.

The administration of anabolic hormones to patients with burns on the first days is entirely justified. The authors know from their own experience that the doses used (25 mg. testosterone propionate daily or on alternate days, or 50 mg. methylandrostendiol daily or on alternate days) do not cause blocking of the adrenal cortex, and in view of occasional partial hypocorticism of 17-KS precursors, i. e. mainly of androgens (N-hormones), they act as a kind of substitution, particularly if the massive production of catabolic glucocorticoids is taken into account.

The situation during the *phase of toxic cachexia,* which often develops after extensive burns, is quite different. This phase is characterized to some extent by inhibition — usually functional — after exhaustion during the catabolic phase. Values of 17-OH and 17-KS are usually low, especially the latter, but generally rise after stimulation by ACTH. EO values can be raised or normal; in cases in which some complication is present they may be low (Fig. 1). In this phase, which is frequently accompanied by poor healing, the formation of weak granulation, poor taking of skin grafts (increase in antibodies against the patient's own skin?), deterioration of digestion, progressive cachexia and anaemia, substitution by hormone preparations is completely justified. During this phase, therefore, different "peripheral" hormones are administered (glucocorticoids, anabolic hormones, oestrogens, thyroid extract), keeping a careful check on the patient's general condition. Small doses are therefore recommended, especially in the case of glucocorticoids, since they probably also have a stimulating effect on tropic hormones. The authors have not as yet any wide experience of the administration of tropic hormones, although they may well be satisfactory. As mentioned above, the phase of toxic cachexia is characterized by poor healing and poor taking of grafts. A "loss of priority" seems to occur in the supply of substances necessary for healing. The administration of ACTH or cortisone sometimes resulted in recovery of this priority (v. also Moore 1957).

During this phase anabolic hormones were administered over long periods in the form of tetosterone--propionate (2—3 times weekly, intramuscularly, in amounts of 25 mg.) or of methylandrostenediol (25 mg. daily or on alternate days); glucocorticoids were administered as cortisone in daily doses of 12.5—25 mg., except where there were special contraindications or where it was not necessary, for other reasons, to increase the dose. In such cases it was sometimes an advantage to give prednisone. Thyroid extracts were administered in the form of Thyreodin (dessicated thyroid), in amounts of 0.3 g. (0.18 mg. iodine), or of Thyreoglobulin mite (thyroglobulin with 0.2 mg. iodine), in doses of one dragee daily, according to tolerance. This treatment frequently led to a striking improvement in the patient's condition. Tab. 12 gives a concise survey of the doses and times of administration of the various hormones. The simultaneous administration of several types of hormones cannot be regarded as polypragmasia; it merely replenishes absent, "sluggish" or relatively deficient production in the phase of toxic cachexia in selected cases.

The use of hormone preparations in the treatment of burns is justifiable. It is necessary, however, to be fimiliar with the pathophysiological processes of the illness and to use these highly effective substances correctly, i. e. not to give

Tab. 13. Aldosterone and antidiuretic hormone (ADH) values in some burned patients.

Name	Extent and degree of burns	Aldosterone in gamma/day	ADH in microunits/ 1 ml. serum
Č. J.	90%, mainly III°	0	34
D. K.	51% III°	4	26
B. A.	10%, mainly III°	8	20
B. O.	30%, II—III°	9	26
P. L.	30%, II—III°	20	24
N. M.	39%, II—III°	12 7*	28 36*
V. L.	35%, II—III°	—	48
J. J.	63%, mainly III°	18 16*	110 54*

* The values are for two consecutive days.

them superfluously and to administer them at the proper time and in the proper dose. Only in this way can unnecessary or harmful consequences be avoided.

As with neuroplegia, the authors again emphasize that suitable hormone treatment in cases of burns partially improves the course and prognosis of the illness, shortens the stay in hospital and may sometimes even save life. It only forms part of the treatment, however. Local treatment, infusions and antibiotics are still the main part.

SUMMARY

The authors discuss their more than three years' clinical and experimental experiences with burns. They concentrated mainly on the study and therapeutic control of the more or less non-specific response of the organism (reaction signs) to burns. Their chief object of study was the function of the adrenal cortex, which is of primary importance in adaptation mechanisms. Attention was repeatedly drawn to the great importance of the central nervous system as the controlling organ in these adaptation mechanisms.

The stress effect of burns on the organism evokes different types of reactions, which are often exaggerated and disproportionate and may be very harmful to the patient. The inhibitory effect of a neuroplegic mixture on different levels of the nervous system sometimes depresses these exaggerated reactions.

The neuroplegics selected were Hydergine (DH-Ergotoxine), Sandosten and Panthesine, i. e. a modification of mixture M_2. The need for individual determination of the dosage is stressed and the doses for adults and children are given. Neuroplegics were administered for several days, in combination with classic methods of treatment (local treatment, infussions, antibiotics, etc.).

From 1956 to 1959, the authors treated 67 patients suffering from burns (adults and children) with neuroplegics; in over 50 of these second and third degree burns involved more than 30% of the body surface. Sixteen of these patients died. Not one death occurred among cases in which less than 40% of the body surface was involved (second and third degree burns). Among eight patients in which second and third regree burns covered 60—69% of the body

surface, only two died. Strikingly low consumption of infusion solutions was found in patients treated with neuroplegics, as seen from the relevant tables. The stay in hospital was also shorter. The illness took a quieter course without hyperpyrexia, eosinophils appeared sooner and 17-ketosteroid (17-KS) and 17-hydroxycorticoid (17 OH) values in the urine were lower than in patients not treated with neuroplegics. Severe burns were often accompanied by almost normal 17-KS and 17-OH values. Tables of results from other places are given for comparison. The results of treatment with neuroplegics are seen to be substantially more favourable. The neuroplegic mixture used by the authors also inhibits secretion of the antidiuretic hormone.

The discussion again gives the advantages of the use of neuroplegics in the treatment of burns and analyses a number of interesting observations, such as the lack of agreement between the behaviour of eosinophils and 17-KS and 17-OH. Neuroplegic mixtures have an inhibitory effect before the pituitary. Excessive inhibition of defence reactions has an adverse effect. The importance of the correct selection of the preparation, dosage and duration of administration is stressed. Neuroplegics could be particularly important in the treatment of mass burns. They do not resolve the problem of the treatment of burns as a whole, and must be combined with the usual forms of treatment, but they improve the course and prognosis of the illness. The authors emphasize the need for individual treatment, based on the clinical state and laboratory findings.

In three of the tables the authors give the absolute and relative indications for the administration of steroid hormones (cortisone, testosterone, aldosterone) and other hormone preparations in the treatment of burns. The comprehensive treatment of burns by neuroplegics and hormone preparations is illustrated from the case of one female patient with severe burns. The advantages of the administration of a "peripheral" hormone (cortisone, cortisol) as compared with ACTH, in some phases of the illness, are explained. Steroids have a "specific" (substitutional) action and a "non-specific" action, modifying the reactions of the organism. The significance of the time in the administration of different hormone preparations is stressed.

Special attention was paid to the phase of toxic cachexia, in which correctly indicated hormone treatment frequently improves a serious condition.

Like neuroplegics, hormone therapy also improves the course and prognosis of the burns illness, but it is necessary to be familiar with the pathophysiological processes which occur in the course of the illness, so as to avoid doing more harm than good by incorrect treatment.

ВЫВОДЫ

Применение нейроплегических средств и гормонов при лечении пострадавших от ожогов

Р. Долечек, И. Калина, Л. Клабусаи

Авторы докладывают о своем более, чем трехлетнем клиническом и экспериментальном опыте с пострадавшими от ожогов. Работа направлена, главным образом, на исследование и лечение неспецифического ответа организма (т. наз. признаков, вызванных реакцией) на ожог. В первую очередь исследовалась деятельность коры надпочечников, которые в при-

способительных механизмах имеют первостепенное значение. Повторно указывалось на большое значение ЦНС, как высшего органа этих приспособительных механизмов.

Действие балластной нагрузки ожога на организм вызывает разные виды реакций, которые часто могут быть преувеличены, несоответственны и могут причинить много вреда у пострадавших. Нейроплегические смеси своим угнетающим влиянием на разные расстройства нервной системы могут иногда тормозить эти преувеличенные реакции.

В качестве нейроплегических средств были избраны гидергин (дигидроэрготоксин), сандостен и пантезин, следовательно, модифицированная смесь M_2. Была подчеркнута необходимость индивидуализации дозировки и приведены дозы для взрослых и детей. Нейроплегические препараты назначались в течение нескольких дней. Кроме нейроплегических препаратов были; пострадавшие от ожога лечены классическим способом лечения (применялось местное лечение, вливания, антибиотики и т. п.).

С 1956 г. до начала 1959 г. было лечено при помощи нейроплегических препаратов 67 обожженных взрослых и детей, из которых было более 50 с площадью ожогов II—III степеней, занимающей более 30 % поверхности тела. Из общего числа больных, леченных при помощи нейроплегических препаратов, умерло 16 людей. Ни одного смертного случая не было при ожогах II—III степеней, занимающих менее 40 % поверхности тела. Из восьми больных с ожогами II—III степеней, занимающих 60—69 % поверхности тела, умерли только двое. У нейроплегированных больных было значительно понижено потребление растворов для вливаний, как это видно из прилагаемых таблиц. Был также сокращен срок госпитализации. Наблюдалось более покойное течение без высоких температур, эозинофилы появлялись раньше, величины 17-кетостероидов и 17-гидроксикортикоидов в моче были меньшими, чем у пострадавших от ожогов, у которых не применялись нейроплегические препараты. Часто тяжелые ожоги сопровождались почти нормальными величинами 17-кетостероидов и 17-гидроксикортикоидов. Для сравнения результатов были приведены также таблицы результатов, достигнутых в других лечебных учреждениях. Результаты, полученные при помощи нейроплегических средств были гораздо более благоприятными. Применяемая авторами нейроплегическая смесь тормозила также секрецию антидиуретического гормона.

В обсуждении было снова указано на преимущества применения нейроплегии у пострадавших от ожогов и разобраны некоторые интересные наблюдения, как, например, несогласие между поведением эозинофилов и величинами 17-кетостероидов и 17-гидроксикортикоидов. Нейроплегические смеси оказывают угнетающее действие перед гипофизом. Слишком большое торможение защитных реакций оказывает неблагоприятное действие. Подчеркнуто важное значение правильного выбора препарата, дозировки и длительности применения препарата. Нейроплегические смеси могли бы иметь большое значение особенно в лечении массовых ожогов. Нейроплегия не решает лечения пострадавших от ожогов в целом, необходимо одновременно лечить их и обычно применяемым до сих пор способом, однадо, нейроплегия улучшает течение и прогноз ожоговой болезни. Подчеркнута необходимость индивидуализации в лечении, согласно клиническому состоянию и данным лабораторных исследований.

Авторы привели на трех таблицах абсолютные и относительные показания к назначению у обожженных стероидных гормонов (кортизона, тестостерона, альдостерона) и других гормональных препаратов. На примере больной с тяжелыми ожогами показано комплексное лечение ожогов при помощи нейроплегических и гормональных препаратов. Объяснено преимущество дачи «периферического» гормона (кортизона, кортизола) в сравнении с АКТГ в некоторых фазах ожоговой болезни. Стероиды оказывают «специфическое», заместительное действие и «неспецифическое», которое модифицирует реактивность организма. Подчеркнуто значение фактора времени в даче разных гормональных препаратов.

Большое внимание посвящено фазе токсического истощения организма, где правильно назначенное лечение при помощи гормонов часто сможет излечить тяжелое состояние.

Как применение нейроплегических препаратов, так и гормональное лечение, улучшают течение и прогноз ожоговой болезни, однако, необходимо всегда хорошо знать пато-физиологические процессы, происходящие в течение ее, чтобы неправильным лечением не было причинено больше вреда, чем пользы.

RÉSUMÉ

Neuroplégiques et hormones dans le traitement des brûlures

R. Doleček, J. Kalina, L. Klabusay

Les auteurs exposent leurs expérineces cliniques et expérimentales sur les brûlures, acquises pendant plus de trente ans. Le travail est dirigé surtout vers l'examen et la maîtrise thérapeutique des réactions non-spécifiques de l'organisme (appelés symptômes de la réaction) à la brûlure. En premier lieu, les auteurs ont suivi l'activité des cortico-surrénales qui présentent un intéret de premier ordre dans les mécanismes d'adaptation. Ils attirent à nouveau l'attention sur la grande importance du système nerveux central en tant qu'organe irrité dans ces mécanismes d'adaptation.

L'action de la surcharge de la brûlure sur l'organisme provoque diverses sortes de réactions qui peuvent souvent être exagérées, non-proportionnelles et provoquer de nombreux dommages au sujet atteint. Les mélanges neuroplégiques, avec leur effet amortisseur à divers étages du système nerveux, peuvent quelquefois amoindrir ces réactions exagérées.

Comme neuroplégique, les auteurs ont choisi l'hydergine (DH ergotoxine), le sandostène et la panthésine, donc le cocktail M_2 modifié. Ils soulignent la necéssité qu'il y a à individualiser la posologie et indiquent les doses pour adultés et pour enfants. Les neuroplégiques ont été appliqués pendant plusieur jours. Outre les neuroplégiques, les brûlures ont été soignées de façon classique (soins locaux, infusions, antibitoques etc). De 1956 jusqu'au début de 1959, 67 brûlés, adultes et enfants ont été soignés aux neuroplégiques; dans ce groupe, plus de 50 sujets ont souffert de plus de 30 % de surface brûlée au II^e et III^e degré. Du nombre total des malades traités aux neuroplégiques, 16 sont morts. Il n'y a pas eu une selue mort chez les brûlés jusqu'à 40 % de surface au II^e et III^e degré. De 8 sujets atteints sur 60—69 % de la surface du corps par des brûlures du II^e et III^e degré, deux seulement sont morts. Chez les malades traités aux neuroplégiques, la quantité de liquide nécessaire aux infusions a été nettement diminuée, comme on le voit sur les tableaux. La durée d'hospitalisation a également été diminuée. Le cours du traitement a été nettement plus calme, sans hyperpyrexie, les éosinophiles sont apparus plus tôt et les valeurs des 17-cétostéroides et 17-hydroxycorticoides dans l'urine ont été plus basses que chez les sujets brûlés et sans neuroplégie. Les auteurs ont souvent observé de graves brûlures accompagnées de valeurs presque normales de 17-CS et 17-HO. Pour comparer les résultats, les auteurs présentent également les tableaux de résultats d'autres centres de travail. Les résultats obtenus avec les neuroplégiques ont été de loin plus favorables. Le cocktail neuroplégique employé par les auteurs réussit à inhiber même la sécrétion d'hormone antidiurétique.

Dans la discussion, les auteurs présentent à nouveau les avantages de l'emploi de neuroplégie chez les brûlés et analysent certaines observations intéressantes, telle que la dissociation entre l'attitude des éosinophiles et des 17-CS et 17-OH.

Le cocktail neuroplégique a une action inhibitrice avant l'hypophyse. Une inhibition trop grande des réactions de défense agit défavorablement. Les auteurs insistent sur le choix adéquat des produits employés, sur la posologie et la durée d'application. Les

cocktails neuroplégiques auraient une grande importance spécialement dans le traitement de brûlures en masse. La neuroplégie ne résout pas le traitement des brûlures en général et il faut continuer d'appliquer le traitement habituel mais celle améliore le cours et le pronostic de ces brûlures.

Les auteurs insistent sur la nécessité d'une individualisation du traitement d'après l'état clinique et les résultats de laboratoire. Les auteurs proposent en trois tableaux l'indication absolue et relative de l'application d'hormones stéroides (cortisone, testostérone, aldostérone) et d'autres produits hormonaux chez les brûlés. Dans les cas de brûlures graves, les auteurs proposent le traitement complexe aux neuroplégiques et aux hormones. Ils expliquent l'avantage qu'il y a à appliquer une hormone „périphérique" (cortisone, cortisol) par rapport àl'ACTH, dans certaines phases de la maladie. Les stéroides ont un effet „spécifique", de substitution, „non-spécifique" qui modifie la réactibilité de l'organisme. Les auteurs soulignent l'importance du facteur temps dans l'application de diverses hormones.

Ils attachent une grande attention à la phase de cachexie toxiue où un traitement hormonal adéquat peut souvent guérir un état grave. De même que la neuroplégie, le traitement hormonal améliore le cours et le pronostic des brûlures; il faut toutefois toujours être parfaitement au courant des processus pathophysiologiques afin de ne pas provoquer par le traitement, plus de mal que de bien.

ZUSAMMENFASSUNG

Neuroplegica und Hormone bei der Behandlung von Verbrennungen

R. Doleček, J. Kalina, L. Klabusay

Die Verfasser berichten über ihre mehr als dreijährigen klinischen und experimentellen Erfahrungen mit Verbrennungen. Die vorliegende Arbeit befasst sich hauptsächlich mit der Untersuchung und Behandlung der unspezifischen Reaktion des Organismus auf die Verbrennung (den sogenannten Reaktionssymptomen). In erster Reihe wurde die Tätigkeit der Nebennierenrinde, die bei Adapatationsmechanismen eine erstrangige Bedeutung hat, verfolgt. Wiederholt wird auf die grosse Bedeutung des Zentralnervensystems als übergeordneten Organs bei diesen Adaptationsmechanismen hingewiesen.

Die Stress-Wirkung der Verbrennung auf den Organismus ruft verschiedene Arten von Reaktionen hervor, die oftmals übertrieben und unangemessen sein und viel Schaden bei den Betroffenen bewirken können. Durch ihren hemmenden Einfluss auf verschiedene Etagen des Nervensystems können neuroplegische Kombinationen diese übertriebenen Reaktionen manchmal dämpfen.

Als Neuroplegica wurden Hydergin (Dihydroergotoxin), Sandosten und Panthesin gewählt, also eine modifizierte Kombination M_2. Die Verfasser betonen die Notwendigkeit einer individuellen Dosierung und führen die entsprechenden Dosen für Erwachsene und Kinder an. Die Neuroplegica wurden mehrere Tage hindurch verabreicht. Abgesehen von der Verwendung neuroplegischer Präparate wurden die Verbrennungen auf klassische Weise behandelt (lokale Behandlung, Infusionen, Antibiotica und so weiter).

Von 1956 bis Anfang 1959 wurden mit neuroplegischen Medikamenten 67 Erwachsene und Kinder mit Verbrennungen behandelt, davon mehr als 50 mit über 30 % verbrannter Oberfläche und Verbrennungen II.—III. Grads. Von allen mit Neuroplegicis behandelten starben insgesamt 16 Patienten. Nicht ein einziger Todesfall entfiel auf Verbrennungen bis zu 40 % der Körperoberfläche II.—III. Grads. Von 8 Patienten mit Verbrennungen von 60—69 % der Körperoberfläche II.—III. Grads starben bloss 2. Bei den mit neuroplegischen Präparaten behandelten Patienten war der Bedarf an Infusionslösungen auffallend vermindert, wie aus den beigefügten Tabellen hervorgeht; auch die Dauer des

Krankenhausaufenthalts war kürzer. Der Verlauf der Krankheit war weniger dramatisch, entbehrte der Hyperpyrexie, die Eosinophilen traten früher auf, die Werte für 17-Ketosteroide und 17-Hydroxykortikoide im Harn waren niedriger als bei Verbrennungen ohne neuroplegische Behandlung. Oftmals waren schwere Verbrennungen von fast normalen Werten für 17-Ketosteroide und 17-Hydroxykortikoide begietet. Zum Vergleich der Ergebnisse werden auch Tabellen mit an anderen Arbeitsstätten erzielten Resultaten angeführt. Die Ergebnisse bei neuroplegischer Behandlung sind bedeutend günstiger. Die von den Verfassern benützte neuroplegische Kombination vermag sogar die Sekretion des antidiuretischen Hormons zu hemmen.

In der Diskussion werden nochmals die Vorzüge der Verwendung neuroplegischer Präparate bei Verbrennungen hervorgehoben und einige interessante Beobachtungen analysiert, wie zum Beispiel der Wiederspruch zwischen dem Verhalten der Eosinophilen und dem der 17-Ketosteroide und 17-Hydroxykortikoide. Neuroplegische Kombinationen bringen ihre hemmende Wirkung bereits vor der Hypophyse zur Geltung. Eine übermässige Hemmung der Schutzreaktionen wirkt ungünstig. Die Verfasser betonen die Wichtigkeit einer richtigen Wahl der Präparate, deren Dosierung und Verabreichungsdauer. Neuroplegischen Kombinationen fällt eine hervorragende Bedeutung besonders bei der Behandlung massenmässiger Verbrennungen zu. Die neuroplegische Therapie löst nicht die gesamte Problematik der Behandlung von Verbrennungen — es ist unerlässlich, die Behandlung auch auf bisher übliche Weise durchzuführen — sie erleichtert jedoch den Verlauf und bessert die Prognose der Verbrennungskrankheit.

Die Notwendigkeit einer individuellen Behandlung je nach klinischen und Laboratoriumsbefunden wird unterstrichen.

An Hand von 3 Tabellen führen die Verfasser die absoluten und relativen Indikationeń für die Verabreichung steroider Hormone (Cortison, Testosteron, Aldosteron) und anderer hormonaler Präparate bei Verbrennungen an. Am Falle einer schwer verbrannten Patientin wird die komplexe Behandlungen der Verbrennungen mit neuroplegischen und hormonalen Präparaten demonstriert. Die Vorzüge der Verabreichung eines „peripheren" Hormons (Cortison, Cortisol) gegenüber der von ACTH während mancher Phasen der Verbrennungskrankheit werden aufgezeigt. Die Steroide haben einen „spezifischen", das heisst Substitutionseffekt und eine „unspezifische" Wirkung, die die Reaktivität des Organismus modifiziert. Die Bedeutung des Zeitfaktors bei der Verabreichung der verschiedenen hormonalen Präparate wird betont.

Erhöhte Aufmerksamkeit widmen die Verfasser der Phase der toxischen Kachexie. bei der eine richtig indizierte hormonale Behandlung oftmals den schweren Zustand beheben kann.

Gerade so wie die neuroplegische, vermag auch die hormonale Behandlung den Verlauf und die Prognose der Verbrennungskrankheit zu bessern; es ist jedoch immer notwendig, mit den pathophysiologischen Vorgängen im Verlaufe dieser Krankheit vertraut zu sein, damit durch eine unrichtige Behandlung nicht mehr Schaden als Nutzen gestiftet wird.

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A MANOMETRIC STUDY OF THE VIABILITY OF CARTILAGE GRAFTS

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In plastic surgery increasing use is made of cartilage grafts. That was one of the reasons why we decided to make a closer study of the viability of implants particularly of this tissue. The second and main reason for the investigation was the actual nature of the tissue, namely its relatively simple structure and its homogenity (it does not contain any connective tissue, vessels or nerves). It consists merely of its own parenchymatous cells and of the intercellular substance. It takes, therefore, a characteristic place among other tissues and is particularly suitable for biochemical investigations, since errors in measurement deriving from the presence of other elements are excluded.

Among the multitude of histological studies on the transplantation of cartilage there are only a few which deal in more detail with the problem of the viability of grafts. Thus Leopold (1881) and Dupertuis (1941) assessed the growth of young grafts in experimental animals as a manifestation of their viability. Peer observed unfixed, unstained sections of cartilage grafts, and after treating them with supravital dyes.

Burian and Soraluce (1937) investigated the fate of viable autotransplants of cartilage in man from the aspect of the physiological changes as described by Wolf, changes which the cartilage undergoes *in situ* during the maturing and aging of the individual. Samples and controls were obtained by operation mainly during subsequent surgical adjustments of the grafts from patients under long clinical observation. The authors ascertained that after autotransplantation the cartilage remains viable in 97.5% and unaltered in quality. Only the physiological manifestations of aging are accelerated: a greater number of cartilage cells perishes, more asbestos foci and fissures as well as more clustres with less stained basic substance and groups of lacunae without cells appear. These are signs of the stage preceding arrosion which can also be found beneath the perihondrium in aging, not transplanted cartilage. Part of the graft covered with perichondrium fuses with the connective tissue of the bed which itself takes on the character of perichondrium. A graft from rib cartilage remains, therefore, viable, and only the degenerative processes of aging are accelerated.

Any impediment to the nutrition of the graft (e. g. a haematoma of the bed) gives rise to a further series of degenerative changes.

In order to study the viability of a cartilage graft by methods other than histological, the knowledge of the metabolism of this tissue is a necessary prerequisite: that knowledge has long been neglected and became important only with the development of plastic surgery. Bywaters (1936), Dickens and Weil-Malherbe (1936) first investigated the metabolism of cartilagenous tissue by a manometric method. They found a predominantly anaerobic type of metabolism with a comparatively low oxygen consumption. Hills (1940) in his detailed paper arrives at a similar conclusion. Lutwak-Mann (1940) carried out a detailed study of the enzymatic system of young beef cartilage, dealing with glycolysis and oxidoreductive processes. Laskin, Sarnat and Bain (1952) compared the metabolic activity of fresh auto- and homotransplants of cartilage in rabbits manometrically.

In order to gain an insight into the metabolism of cartilage, both fresh and transplanted, a number of authors (Boström and Manson 1952, Pelc and Glücksmann 1955, Wyburn and Bascich 1955 and others) also used isotopes, mainly sulphur S^{35} as sulphate. Musil and Kluzák (1959) used labelled phosphorus for studying the metabolism of cartilage and investigated above all the metabolic relationship between the graft and its bed (Kluzák and Musil 1959).

In this work the author has used a manometric method supplemented by histological and macroscopic observations to deal mainly with the following problems: a) the influence of transplantation on the metabolic activity of the tissue in its aerobic as well as anaerobic component after auto- and homotransplantation; b) the change in the level of metabolism of the grafts in the course of a long-term experiment and with regard to this — the difference between an auto- and a homotransplant; c) the influence of preservation or removal of the perichondrium on the metabolic activity of the graft; d) the influence of the quality of the blood supply to the bed.

MATERIAL AND METHODS

In 26 Chinchilla rabbits, of the same age (6 months at the start of the experiment) and approximately of the same weight, a study was made of the following main types of grafts: auto- and homotransplants of cartilage from the ribs or auricles grafted under the skin with and without perichondrium. A smaller series of grafts implanted into muscle was also observed. Each animal was used as donor as well as recipient. Each recipient received a large number of grafts (of course, from the same donor) so that it could become the source of several samples. Controls of fresh, not transplanted, cartilage were taken from the same animal.

On taking the samples the grafts were easily found by palpation, extracted from a small incision and treated immediately. Homotransplants were sampled for measurement of respiration at intervals of 26,48 hours, 8, 14, 61, 113,127 and 282 days; for measurement of anaerobic glycolysis at universals of 26,48 hours, 5, 19, 61, 127, 190 and 382 days after transplantation. In the samples of rib cartilage — because of shortage of material one of the pair of intervals, linked by a bracket, was sometimes left out. Main attention was paid to homotransplants; samples of autotransplants — because survival

was taken for granted — were taken for aerobic and anaerobic measurements only at intervals of 26 hours, 19, 61 and 190 days.

Preparations of the tissue: Immediately after removal the samples were rinsed with physiological saline, all adherent tissue, the remnants of the bed and the perichondrium carefully cut off so as to eliminate an error of measurement deriving from the presence of another kind of tissue. Transverse slices 0.3 mm thick were cut with a microtome of our own design. After wiping the slices dry they were weighed on a torsion balance and placed at once into the manometric containers filled with the pipetted medium. Approximately 200 mg. of slices were placed into each container.

Media: a) The liquid phase: The suspension medium for tissue slices under aerobic measurement was 2 ml. of Krebs-Ringer phosphate physiological solution, pH 7.4, 0.2 ml. of 10% glucose and 0.2 ml. 0.001 M aqueous solution of methylene blue in each container. 0.2 ml. of 2N KOH were pipetted into the absorption cup to absorb the freed CO_2, the surface of absorption being increased by a folded piece of filter paper. Methylene blue was added on account of its constant catalytic influence on the consumption of oxygen as confirmed by all authors. The suspension medium for anaerobic measurement consisted of 2 ml. of Krebs-Ringer bicarbonate physiological solution (pH 7.4) and 0.2 ml. of 10% glucose.

b) The gaseous phase: For aerobic measurements the manometres were filled with pure oxygen bubbling up through water. For anaerobic measurements a mixture of 95% nitrogen and 5% CO_2 was prepared by mixing the gases in a cylinder. The introduction of the gaseous phase into the manometer was realized by means of packing, using a distribution system of tubes and a safety valve.

Actual measurement: After connecting them to the manometers the manometric containers were put into a water bath whose temperature was kept at 38^0 C; the speed of shaking (of the system) was 140 swings per minute, the amplitude 40. The manometers were considered balanced 15 minutes after having been placed into the water bath. Individual readings were then taken at intervals of 10 to 15 minutes for 2 to 7 hours. After respective calculation the results were expressed by the metabolic quotient $Q_{O_2}^{O_2}$ for respiration — in microlitres of consumed oxygen per hour, and by $Q_G^{N^1}$ for anaerobic glycolysis — in microlitres of freed CO_2 per hour. One g. of the moist weight of the fresh slices was considered as the basis.

Method of histological controls: Simultaneous histological examinations had only the significance of controls, e. g. to find out whether any transformation from the bed had taken place. Sections for histological investigation were made only of some samples and the grafts were treated together with their beds. The tissue was fixed with Gendre solution or 10% formol. Staining of the sections was carried out with haematoxylin-eosin for orientation, contact haematoxylin according to Wolf, haematoxylin-Sudan for fat, Masson's stain for collagen and by the method Hale-PAS according to Ritter-Oleson for mucopolysaccharides and glycogen.

RESULTS AND DISCUSSION

Macroscopic findings: It was always possible to recover each graft; none underwent complete resorption. The grafts were placed into the subcutaneous tissue, i. e. without functional strain and without contact with homologous tissue. The transformation of the bed during long-term observation, as ascertained macroscopically, corresponds to the histological findings of Peer (1955). Arrosions, though found histologically in older homotransplants, were

not visible macroscopically. The adherence of the graft to the bed was firmer in those with perichondrium than without.

The findings on grafts with perichondrium 127 days and more after transplantation were interesting; whereas the transplanted perichondrium adhered firmly to the bed so that the border between both was macroscopically indistinguishable, the connection of the perichondrium to its own cartilage was markedly loosened. On preparation for measurement the cartilage freely slipped out of its perichondrium, whereas preparation of fresh or recently transplanted cartilage required considerable force and sharp raspatories.

In the sparse subcutaneous tissue the grafts often migrated: when implanted in the flank of the animal the grafts were frequently found in the ventrolateral inguinal fold of skin, a number close together but each with its own bed. This was obviously due to the uniform movement of the hind limbs causing continual shifting of the skin.

After transplantation of pure perichondrium no regeneration of cartilage was ever observed. This confirms the statements of other authors (Craigmyle 1955, Bisgard already in 1934, in dogs). Peer (1955) found that cartilage does not regenerate even from the perichondrium sheath left *in situ*. Dupertuis (1941) on the contrary maintains that young grafts of perichondrium do produce cartilage. The majority of authors, however, denies regeneration of cartilage from perichondrium. It is more likely that metaplasia takes place as described by Knobloch (1934) or in regeneration of the meniscus after meniscectomy as described by Becker and Stieve (cit. Schaefer, 1953).

The importance of the perichondrium for the firm union of the graft with its bed in human autotransplants was stressed by Burian (1937); a similar favourable influence of the perichondrium was observed in the animals of the above experiments. The loosening of the connection of the perichondrium to its own cartilage in the later stages after transplantation as mainly observed in homotransplants cannot yet be explained with certainty; probably a gradual substitution of the homologous perichondrium by the connective tissue of the bed takes place.

The metabolic activity of the transplants: During the first hours and days after implantation marked changes in the metabolic activity of the grafts were observed. In the majority a substantial decrease took place so that the average readings of $Q_{O_2}^{O_2}$ in grafts of auricular cartilage decreased from the original —168 μl O_2/g/hour to —148 down to —88; in grafts of rib cartilage from the original —60 to —44; otherwise (in grafts without perichondrium) the level of metabolism remained approximately unaltered.

The main readings of Q_G^N — the same as fresh tissue — were constantly higher than the corresponding readings of $Q_{O_2}^{O_2}$. They did, however, change markedly after transplantation. In the majority a decrease took place from the original +231 μl CO_2/g/hour in auricular cartilage to +151, from the original +70 in rib cartilage down to +51.

The intensity of the changes varied in different types of grafts. The most evident decrease was registered in homotransplants with perichondrium.

A smaller decrease could be seen in bare homotransplants and in autotransplants with perichondrium. An exception was formed by the anaerobic phase of the metabolism of autotransplants without perichondrium which in the first hours and days after transplantation showed an increase of metabolic activity (from the original +231 μl. CO_2/g/hour up to +273 in auricular cartilage and from the original +70 up to +93 in rib cartilage).

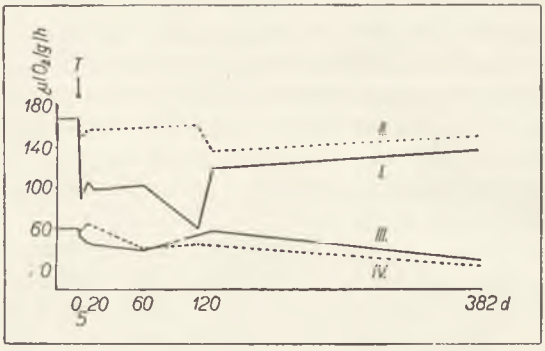

Fig. 1. Course of aerobic phase of metabolic activity of homotransplants of auricle cartilage (curves I and II) and of rib cartilage (curves III and IV). The full line indicates grafts transplanted with perichondrium, the dashed line grafts transplanted without perichondrium, *x* number of days after transplantation, *y* number of μl O_2/g hours.

In the further course of the long-term experiment levelling of the readings, which deviated immediately after transplantation, was observed. The metabolic activity of autotransplants at the period around 61 days and that of homotransplants from the period of around 127 days did not show any marked deviation. The metabolic quotient again rose slightly, but never reached the level of activity prior to transplantation. In the aerobic phase it remained at —120 to —150 in auricular cartilage and at +45 to +60 in rib cartilage; in the anaerobic phase at +160 to +210 in auricular and at +45 to +60 in rib cartilage.

Because of the large numbers of figures graphs were used for the detailed analysis in the registration of all results (see Fig. 1, a and 3).

Transplantation is a significant interference into the life of a tissue. In this the removal of the tissue from its natural environment and the surgical preparation play a certain part. This, however, is decidedly not the main part, as Laskin et al. assert, because before measurement the same surgical treatment is suffered by the fresh tissue serving as control; the tissue must always be excised, freed from its perichondrium, cut into slices and put into the instrument for measurement. All samples were taken and prepared in the same way and by the same person. Important diferences were noted in the type of transplants as well as in the method of transplantation.

In nearly every case a marked decrease in metabolic activity was registered in homotransplants within the first hours or days of implantation, whereas in autotransplants this decrease was always smaller, or practically nil, or even — in samples implanted without perichondrium — a slight increase could be ob-

served (see Fig. 1, 2 and 3). The effect of the transplantation on the metabolic activity of homotransplants as compared with autotransplants is best shown in grafts of auricular cartilage with perichondrium (curve I): the decrease in the aerobic phase of metabolism in the first days after transplantation amounted in homotransplants to 47.6%, in autotransplants only to 17.8%; in the anaerobic phase the decrease in homotransplants was 34.6%, in autotransplants only 21.6%.

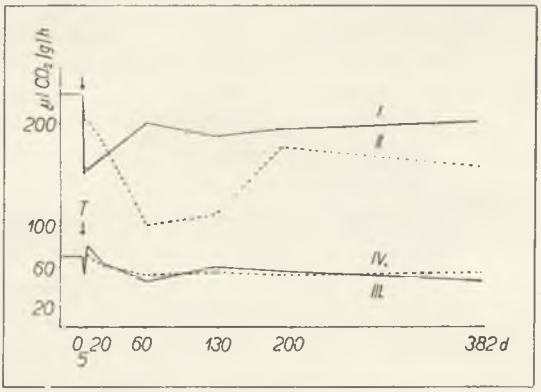

Fig. 2. Course of anaerobic phase of metabolism in homotransplants. Detailed specification as in Fig. 1 (y number of μl CO_2/g/hour).

Regarding the results it seems that the biochemical character of the new environment into which the tissue was implanted has an influence on the metabolism of the graft. The differences, as described above, were observed already in the first hours and days after transplantation; therefore, it is impossible to ascribe their cause to immunological processes.

The decrease in the metabolic activity of the grafts is not to be regarded as an irreversible damage to the tissue. It is rather a manifestation of the varying changes in the relationship between the graft and its new environment. Borst (already in 1913) assumed that each individual is to be regarded as a specific biochemical system. Later Loeb (1945) based on this conception, elaborated his broad theory of the individuality of tissue. In line with these theories the apparent differences in the metabolic activity of the various types of transplants can be taken as manifestations of the altered condition under which metabolites reach the grafts and under which they are metabolized by its tissue. A more detailed analysis of this problem is given elsewhere (Kluzák and Musil, 1959).

From the manometric results it is evident that the viability of grafts is affected not only by the surgical treatment of the tissue, but also by the circumstance that the tissue is placed into auto- or homoplastic bed; both being valid for the first days after transplantation.

A further important factor having an influence on the metabolic activity of the graft in the first days after transplantation is the preservation or removal of the perichondrium before implantation. This influence of the perichondrium has not hitherto been described in world literature.

It was ascertained that in grafts implanted together with their perichondrium a marked decrease in the metabolic activity a l w a y s occurs after transplantation. In grafts without perichondrium this decrease was considerably smaller, in autotransplants without perichondrium even an increase in the anaerobic phase was registered. As can be seen from Figs. 1, 2 and 3 this influence of the presence of the perichondrium on the level of metabolic activity is clearly shown in all observed transplants (full line — curves I, III — transplants with

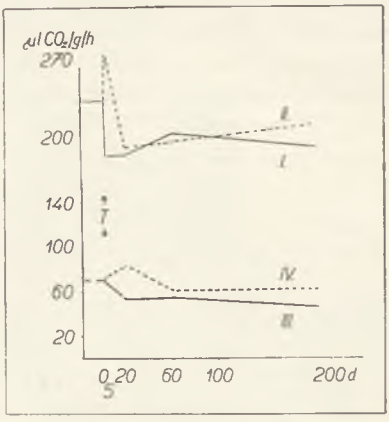

Fig. 3. Course of anaerobic phase of metabolism of autotransplants. Detailed specification as in Fig. 1 and 2.

perichondrium; dashed line — curves II, IV — transplants without perichondrium).

Table 1 compares the changes in the metabolic activity of grafts with perichondrium and without perichondrium during the first 48 hours after transplantation. The figures give the percentage of the original readings. The symbol — (minus) stand for decrease, + (plus) for increase in the metabolic activity as compared with controls of fresh tissue. The comparison between the two was always carried out in tissue of the same doon transplanted into the same recipient.

The results attained prove that the preservation of the perichondrium lowers the metabolic activity of grafts in the first hours and days after transplatation.

Table 1.

Transplant of cartilage	Aerobic phase		Anaerobic phase	
	with perichondrium	without perichondrium	with perichondrium	without perichondrium
Auricle homotr.	−47.6%	−11.9%	−34.6%	−11.2%
Rib homotr.	−13.3%	−5.0%	−27.1%	−4.3%
Auricle autotr.	−17.8%	−6.5%	−21.6%	+18.1%
Rib autotr.	−10.0%	+18.3%	−2.8%	+4.2%

It seems that in these first stages after transplantation, when the nutrition of the graft is guaranteed by diffusion from the bed and not — as *in situ* — by diffusion from the perichondrium normally supplied with blood, the simultaneously transplanted perichondrium has turned into a sort of barrier against the osmotic forces.

A further factor having an influence on the degree of change following transplantation, is the original metabolic activity of the transplanted tissue. On comparing curves I, II (upper part of figs. 1, 2 and 3) with curves III, IV (lower part of the figs.) the different intensity of the changes in auricle and rib cartilage becomes clear when expressed by absolute figures. This is quite understandable since rib cartilage shows a low degree of metabolism already *in situ.* However, if relative figures, i. e. percentage in relation to the original readings of the not transplanted tissue is used (separately for auricle and for rib cartilage, the deviation in auricle cartilage is higher than in rib cartilage (see table 1 and compare pairs vertically). These registered differences support the view that the shock to a tissue on free grafting is the more intense the higher its original metabolism.

Measurements of later and the latest stages of the grafts (up to 382 days) did not show any marked deviation. A levelling of the curves takes place; the readings which had shown a marked decrease, have somewhat increased. The metabolic activity of the grafts never reaches the level of fresh tissue, but the percentage decrease is not exceedingly high even in transplants under observation for long periods. This indicates that cartilage grafts remain permanently viable as a biologically active tissue.

In old grafts — from 120 days after implantation, — no marked differences between auto- and homotransplants could be detected. The histological controls (see below), however, showed early absorption from the periphery in older homotransplants. It seems, therefore, that the immunological reaction, commonly regarded as the cause of absorption from without, has no influence on the metabolic activity and, because of that, on the viability of the remaining tissue. This would indicate that humoral antibodies — if there are any at all — do not cause damage to the graft as a whole. They only act on the surface of the graft and do not penetrate by diffusion into the depth of the tissue of the transplant.

Interesting is the gradual equalizing of the readings of the metabolic quotient in old transplants with and without perichondrium. As can be seen from the figs. 1, 2 and 3 this levelling takes place to the detriment of the metabolic activity of the grafts without perichondrium as well as by a slight increase in the readings in grafts with perichondrium, considerably lowered before. In the majority of homotransplants the approximate equalizing is reached in the period about 127 to 190 days after transplantation (figs. 1 and 2), in autotransplants earlier, i. e. in the period about 19 to 61 days (fig. 3). This would indicate that the perichondrium of autotransplants integrates comparatively earlier with the metabolic condition of the bed (probably by the joining up of vessels of the perichondrium with those of the bed or by revascularization of the perichondrium), and in this way the inhibitory effect of the perichondrium on the metabolism of the tissue is annulled. In homotransplants the equalizing of the curves

takes place much later; here it is necessary to take into consideration the gradual absorption of the transplanted perichondrium and its substitution by the connective tissue of the bed. This interpretation coincides with the macroscopic findings in samples of homotransplants which long after implantation almost spontanously "slipped" out of their own perichondrium — or rather of the connective tissue of the bed. The connective tissue of the bed had probably already absorbed the transplanted perichondrium and was now immitating it macroscopically. It remains, however, unexplainable why a late decrease in the metabolic activity occurs in grafts without perichondrium mainly during the period between 19 and 69 days after transplantation. May be this is due to the connective tissue capsule around the transplant which just at that time reaches the height of its development.

It remains to deal with the influence of the blood supply of the bed on the metabolic activity of the grafts. Only a few experiments devoted to this problem were carried out in order to obtain a general survey. No difference in the metabolism of transplants was observed whether implanted into muscle (i. e. into a bed with a very good blood supply) or into the sparse subcutaneous tissue (i. e. into a bed with a poor blood supply). It seems that cartilage with its low level of metabolism, predominantly of an anaerobic type, does not require a bed well supplied with blood. It should, however, be stressed that this conclusion does not apply to a bed formed of pathologically altered tissue, such as scar tissue. It is a well-known clinical experience that grafts of human cartilage implanted into scar tissue decrease in size and as a whole and by absorption from without, whereas the same grafts, when implanted into healthy tissue, maintain their volume (Peer). No satisfactory explantation of these observations has hitherto been offered. From the immunological point of view just the contrary would be expected: a bed well supplied with blood should attack the graft by cellular infiltration, proliferation of absorbing tissue and also by the richer supply of antigens, beter than the scar. The author, however, explains this finding on the basis of his own metabolimetric experiments — including those described elsewhere (Kluzák and Musil, 1959) — by the theory of autoresorption: If placed into the scar tissue the grafts — in the majority of cases they were autotransplants under clinical observation — are not sufficiently supplied with nutrients. A similar situation arises as in hetero- or homotransplants, where the insufficient or lowered supply of nutrients is obviously caused by the disharmony between the biochemical systems of the graft and the bed. The cells of the transplant, while on the whole preserving their metabolic activity unchanged, consume their own intercellular substance. A graft thus debased can then easily be liquidated even by the inferior scar tissue of the bed.

Histological controls: These controls were of secondary importance for the experiments reported above, since these were centred mainly on metabolism. They were, nevertheless, necessary for the morphological evaluation of the biochemical examination mainly in order to estimate the degree of surface arrosion, to exclude substitution from the bed, and, finally, to ascertain the morphological changes which had taken place in the graft itself.

The majority of the histological findings made by the author during his

experiments do not differ at all from the results of the detailed histological studies (Craigmyle, Burian, Peer and others). They will, therefore, not by analysed here in detail. Attention is drawn only to the more interesting changes which take place within the homotransplants and which have not hitherto been described.

In older homotransplants changes were observed within the tissue which were almost indistinguishable two months after implantation, but already well marked after four months and which were as follows: enlargement of chondrocytes with the formation of large central vacuoles, widening of lacunae, formation of projections by the cartilage cells, and the appearance of a space between the cell and its capsule filled with a PAS positive substance without definite structure (fig. 4). A series of similar phenomena was described recently by Zástava and Titlbach (1957) in the enlargement of cells of ossifying hyaline cartilage (not transplanted) and termed *endogenous resorption.*

This endogenous resorption indicates that chondrocytes themselves can dissolve and consume the basic substance. The similarity between these changes and those found in older homotranplants may support the opinion that the surviving cells of the graft consume their own intercellular substance.

In view of the fact that this paper was not concerned with histological research it is perhaps understandable that the histological material produced here is rather meagre and cannot be regarded, therefore, as reliable evidence. Work continues on this subject. The actual purpose of the histological study in this work was much more simple: to make quite certain that the tissue taken for manometric measurement was that of the transplant and not tissue from the bed.

CONCLUSION

By repeated and simultaneous manometric and histological examinations of transplants observed for long periods it was proved that the cartilage remains a viable and biologically active tissue after auto- and homotransplantation. The grafts survive without contact with homologous tissue or the need for functional use. It seems that survival depends neither on the blood supply of the bed so long as the bed does not consist of pathologically altered tissue, nor does it depend on the presence of factors causing absorption from without. On the other hand the viability of the graft is evidently affected by the transplantation itself, the degree of these changes depending on the preservation or the removal of the perichondrium, on the character of the new environments (auto- or homo-), and on the original metabolic activity of the transplanted tissue.

SUMMARY

1. A long-term observation of auto- and homotransplants of rib and auricle cartilage in rabbits, with and without perichondrium, by a manometric method supplemented by macroscopic and histological examinations, was carried out. These grafts remained viable and biologically active without contact with homologous tissue in the bed and without necessity for functional loading. Survival

of the graft is evidently not affected by the blood supply of the bed so long as the latter is not formed by pathologically altered tissue.

2. From the analysis of the changes in the metabolic activity of the grafts during the first hours and days after transplantation it follows that:

a) the simultaneously transplanted perichondrium lowers the metabolic activity of the graft probably acting as a barrier to the osmotic forces;

b) the biochemical character of the new (auto- or homo-) environment exercises an influence on the metabolism of the graft. This influence is already noticeable at a period when no immunological processes can be taken into account;

c) the higher the original metabolism of transplanted tissue, the more intense is the shock to the tissue after free transplantation.

3. From the analysis of the changes in the metabolic activity a long period after transplantation it can be deduced that

a) the grafts remain a biologically active tissue with a slightly lowered metabolic level;

b) the perichondrium of autotransplants relatively soon integrates with the nutritive source of the bed whereas the perichondrium of homotransplants is evidently replaced by the connective tissue of the bed;

c) factors effecting absorption from without do not cause damage to the viability of the graft as a whole, but act only on its surface.

4. No cartilage tissue regenerates from transplanted pure perichondrium.

5. The results of the histological controls of cartilage homotransplants support the assumption of autoresorption (described elsewhere), i. e. that the cells of these grafts consume their own intercellular substance.

RÉSUMÉ

Etude manométrique de la viabilité des greffes de cartilagineux

R. Kluzák

1. Par méthode manométrique complétée d'observations microscopiques et histologiques, l'auteur a étudié pendant une longue période, les auto- et homogreffes de cartilage costal et du pavillon de l'oreille chez les lapins, d'une part avec périchondre, d'autre part sans. Ces greffes restent un tissu vivant, biologiquement actif sans qu'il y ait nécessité de contact avec un tissu homologue dans le lit et de surcharge fonctionnelle. Sur la viabilité, le degré d'irrigation sanguine n'a apparement pas d'influence, pour autant qu'il ne s'agisse pas d'un lit formé d'un changement pathologique de tissu.

2. Il découle de l'analyse des changements dans l'activité métabolique des greffes au cours des premières heures et journées après transplantation que:

a) le périchondre transplanté en même temps diminue l'activité métabolique des greffes, agissant vraisemblablement comme une digue aux forces osmotiques;

b) le caractère biochimique du nouveau milieu (auto- ou homo-) influence le métabolisme des transplantats et ce, déjà à la période où on ne peut compter sur des processus immunologiques;

c) plus le métabolisme du greffe est élevé, plus est grand le choc que le tissu ressent après transplantation libre;

3. Il découle de l'analyse des changements dans l'activité métabolique des greffes après une période plus longue suivant la transplantation que:

a) les greffes restent un tissu biologiquement actif avec un métabolisme légèrement diminué;

b) dans les autogreffes avec périchondre, les foyers se relient relativement rapidement à la source nutritive alors que dans les homogreffes on observe apparamment un remplacement du périchondre transplanté par le tissu conjonctif du lit;

c) les facteurs, provoquant l'absorption de l'extérieur ne lèsent pas le greffe dans son entité mais ont tout au plus une action sur sa surface.

4. Le tissu cartilagineux de périchondre transplanté seul ne régénère pas.

5. Les résultats des contrôles histologiques des homogreffes de cartilage appuient la conception d'autorésorption (développée dans d'autres travaux) c'est à dire que les cellules de ces greffes emploient leur propre structure intercellulaire.

ZUSAMMENFASSUNG

Manometrische Studien über die Lebensfähigkeit von Knochentransplantaten

R. Kluzák

1. Mittels manometrischer Methodik, ergänzt durch makroskopische und histologische Beobachtungen, wurden Auto- und Homotransplantate von Rippen- und Ohrmuschelknorpeln bei Kaninchen, einerseits mit Perichondrium, anderseits ohne Perichondrium langfristig verfolgt. Diese Transplantate bleiben ein lebendes, biologisch aktives Gewebe ohne Notwendigkeit eines Kontaktes mit gleichgeartetem Gewebe in der Empfangsstelle und ohne Notwendigkeit einer Funktionsbelastung. Auf das Überleben hat der Durchblutungsgrad der Empfangsstelle wahrscheinlich keinen Einfluss, soweit es sich nicht um eine Empfangsstelle mit pathologischen Gewebsveränderungen handelt.

2. Aus der Analyse von Veränderungen in der Stoffwechselaktivität in den ersten Stunden und Tagen der Überpflanzung geht hervor, dass

a) das mitüberpflanzte Perichondrium die Stoffwechselaktivität des Transplantates herabsetzt, wahrscheinlich als Schutzwall gegen osmotische Kräfte;

b) der biochemische Charakter des neuen Mediums (Auto- oder Homo-) den Stoffwechsel des Transplantates beeinflusst und dies bereits im Zeitabschnitt, wo mit immunologischen Prozessen nicht zu rechnen ist;

c) je höher der Stoffwechsel des überpflanzen Gewebes ist, desto grösser, ist die Gewebserschütterung nach der freien Transplantation.

3. Aus der Analyse von Gewebsveränderungen längere Zeit nach der Überfplanzung kann geschlossen werden, dass

a) Transplantate biologisch aktives Gewebe mit einem mässig herabgesetzten Stoffwechselgrad bleiben;

b) bei Autotransplantaten sich das Perichondrium relativ rasch in die Ernährungsquellen der Empfangsstelle einschaltet, wogegen es bei Homotransplantaten wahrscheinlich zu einem Ersatz des überpflanzten Perichondriums durch Bindegewebe der Empfangsstelle kommt;

c) Faktoren, die eine Absorption aus dem Äusseren verursachen, die Lebensfähigkeit des Transplantates als Ganzes nicht schädigen, sie wirken demnach höchstens an der Oberfläche.

4. Aus dem transplantierten Perichondrium allein, wird das Knorpelgewebe nicht regeneriert.

5. Die Ergebnisse der histologischen Kontrollen von Knorpel-Homotransplantaten unterstützen die Vermutung einer Autoresorption (in einer anderen Arbeit ausführlich behandelt) — dass Zellen dieser Transplantate ihre eigenen intercellularen Strukturen verbrauchen.

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ELECTRIC CONDUCTIVITY AS A MEASURE OF THE VITALITY OF TISSUE

J. KRYŠPÍN, Z. HARANTOVÁ

At the present stage of development of transplantation, a quantitative criterion for evaluating the vitality of tissue would be not only of theoretical importance, but also of practical value, e. g. for determining the effect of preservation methods or changes in transplanted tissues. Present criteria are of a mainly qualitative character and in the given situation they cannot be expected to make any basic contribution to resolving the involved problem of tissue vitality. The authors therefore consider it right that new methods should be introduced in clinical research on transplantation.

One method which fulfils requirements of accuracy is the determination of the electric conductivity of tissue. Experiments attempting quantitative evaluation of tissue and cell permeability, as a test of vitality, by measuring electric conductivity have been carried out by a number of authors (Galeotti 1901, Kodis 1901, Osterhout 1922, Brooks 1923, Tarusov 1938, Vávra and Mělka 1942, Kryšpín and Klen 1956). Their results can be summed up as follows: 1. The normal cell (i. e. the cell membrane) possesses marked specific resistance, which is related to its selective permeability for certain ions. 2. Stimulation causes a decrease in resistance of the membrane. 3. Injury to the tissue is manifested in a decrease in resistence to very low values, which is first reversible, but after death is irreversible.

It is no longer possible to interpret some of these changes as changes in the state of the cell membrane. The latest research shows that the conduction of an electric current in tissue is influenced by polar macromolecules and by changes in their physical and chemical structure. These findings can, however, provide a good basis for dynamic research on the molecular structure of living matter in relation to survival and death.

On the basis of these findings the authors evolved a method of their own and modified measuring methods in current use today with regard to the requirements of transplantation, particularly in plastic surgery.

METHOD

The electric conductivity of grafts was measured in a resistance vessel, in which the tissue was fixed by two contiguous rings. This formed a partition between the two sections containing the conduction medium and the non-polarizable electrodes. The current passing between the electrodes was thus obliged to pass through the tissue. This method permits the measurement of the electric properties of any tissue, e. g. skin,

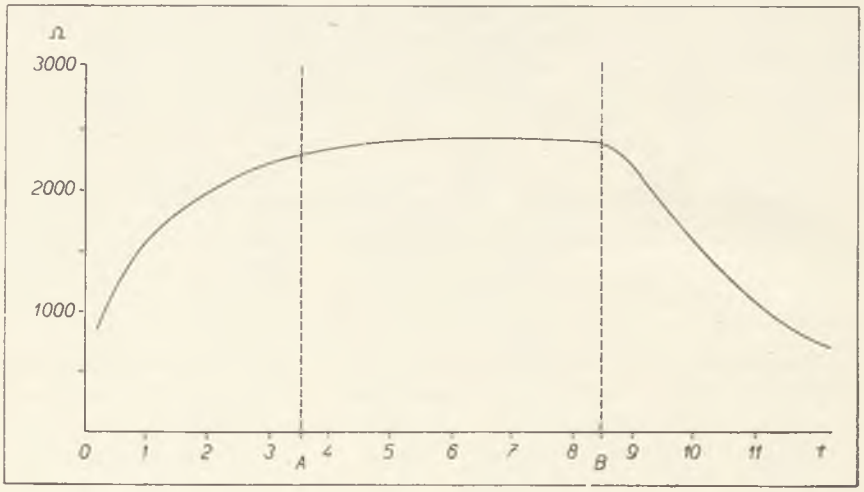

Fig. 1. Changes in ohmic resistance of tissue during survival. *x:* time from commencement of survival in arbitrary units; *y:* tissue resistance values in ohms. O — beginning of survival (in most cases the moment of extirpation of the tissue). A — approximate commencement and B — end of steady state.

cornea, kidney and liver sections, etc. The resistance of the tissues was measured by constant direct current (transient phenomenon method, Vogel and Kryšpín 1956, Kryšpín and Klen 1958) and by alternating current with a frequency of 500 to 50.000 Hz, using a Wheatstone bridge.

RESULTS

Under constant conditions (the same method of tissue preparation, medium, temperature), the authors found that changes in the electric conductivity of surviving skin, cornea, liver, kidney and brain took a similar course. For each tissue it was biphasic (Fig. 1). Resistance first increased; a steady state then developed, i.e. a period during which tissue resistance remained constant, followed by an irreversible decrease in resistance. This decrease is regarded as the manifestation of an irreversible disturbance of tissue permeability and hence of death of the tissue. The ascending curve and the steady state, which can be of varying duration, are the manifestation of a still active reaction of surviving tissue. The duration of the steady state depends on the type of tissue. In the present experiments it was shortest for liver tissue (minutes) and longest for skin (up to several dozen hours). It also depends on all the factors known to influence tissue vitality. Exchanging the medium and provision of an oxygen

supply prolonged the duration of the steady state, while a reduction in the pH of the medium, irradiation of the tissue with X-rays or the addition of metabolic poisons shortened it.

The changes described were most marked when measuring with direct current. When the frequency was raised they decreased in extent and from frequencies of 50.000 Hz upwards they could not be demonstrated at all under the given experimental conditions.

DISCUSSION

Most of the older authors only describe a decrease in the resistance of surviving tissue; in the present experiments a biphasic reaction with a steady state of varying duration was observed. In tissue with active metabolism the steady state was of relatively short duration and an irreversible decrease in resistance soon occurred. In the case of skin, cornea and cartilage, i. e. tissues important from the aspect of transplantation, the steady state usually lasted for hours. The authors assume that the steady state which precedes an irreversible decrease represent the borderline where the decisive changes resulting in death of the tissue take place. Its duration in surviving tissue can therefore be regarded as a measure of its vitality. The advantage of this method is that the tissue is not damaged by measuring.

SUMMARY

Using a precise electrophysiological method, the authors followed on from earlier findings and studied the relationship between the electric conductivity of tissue and its vitality. The normal cell membrane possesses high resistance, which on death of the tissue falls to the values of physiological saline. Before this occurs, however, a steady state of varying duration is observed in every type of tissue, during which electrical resistance is higher than under physiological conditions, and during which the processes leading directly to death of the tissue probably take place. Resistance changes are most marked when measured by means of direct current.

ВЫВОДЫ

Электропроводность в качестве показателя жизнеспособности ткани

Я. Крышпин, З. Гарантова

При помощи точного электрофизиологического метода можно, продолжая прежние исследования, найти объясиение взаимосвязи электропроводности тканей с их жизнеспособностью. Нормальная клеточная мембрана обладает высоким сопротивлением, которое при отмирании понижается даже к величинам физиологического раствора. Перед этим понижением, однако, в каждой ткани наблюдается период устойчивого состояния, разной продолжительности, когда сопротивление ткани по сравнению с физиологическим состоянием бывает повышеным, и когда, вероятно, происходят процессы, приводящие непосредственно к отмиранию ткани. Изменения сопротивления бывают найболее выраженными при измерении постоянным током.

RÉSUMÉ

Conductibilité électrique comme critère de la viabilité des tissus

J. Kryšpín, Z. Harantová

A l'aide d'une méthode électrophysiologique précise, il est possible de se rattacher à certains résultats antérieurs et d'éclaircir le rapport de la conductibilité électrique des tissus et de leur viabilité. Une membrane cellulaire normale présente une forte résistance qui en mourant diminue jusqu'à des valeurs de solution physiologique. Avant cette diminution, nous observons toutefois sur chaque tissu une période de stabilisation de durée différemment longue, présentant une résistance tissulaire augmentée contre l'état physiologique et pendant laquelle ont vraisemblablement lieu des processus qui conduisent directement à la mort du tissu. Les changements de la résistance sont les plus accentués avec des mensurations au courant continu.

ZUSAMMENFASSUNG

Die elektrische Leitfähigkeit als Maßstab der Gewebsvitalität

J. Kryšpín, Z. Harantová

Mit Hilfe einer genauen elektrophysiologischen Methode ist es möglich, in Anknüpfung an einige frühere Befunde den Zusammenhang zwischen der elektrischen Leitfähigkeit der Gewebe mit deren Vitalität weiterhin zu erhellen. Die normale Zellmembran bietet einen hohen Widerstand, der beim Absterben der Zellen bis auf Werte, die physiologischer Kochsalzlösung zukommen, absinkt. Vor diesem Absinken kann man jedoch bei jedem Gewebe ein verschieden lange dauerndes Stadium eines ausgeglichenen Zustandes beobachten, wo der Gewebewiderstand gegenüber den physiologischen Verhältnissen erhöht ist und wo sich wahrscheinlich jene Processe abspielen, die unmittelbar zur Gewebsnekrose führen. Die Veränderungen des Widerstands sind am deutlichsten bei Messung mit Gleichstrom zu verzeichnen.

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