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CENTRAL EUROPEAN VASCULAR FORUM

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1st Congress of the CENTRAL EUROPEAN VASCULAR FORUM

Ladies and gentlemen, dear colleagues,

I should like to inform you that the **„Central European Vascular Forum"** (CEVF) was officially established, in the presence of Mr.Domenico Zecca, notary public, on 24 October 1997 in Rome during the 11th Meeting of the European Chapter of the International Union of Angiology (IUA). The founding countries are: Austria (represented by Prof. H. Partsch), Czech Republic (Assoc. Profs. V. Puchmayer and K. Roztočil), Slovak Republic (Assoc. Profs. V. Štvrtinová, J. Kmec, P. Lesný), Hungary (Prof. C. Dzsinich), Poland (Prof. M. Szostek), Slovenia (Prof. P. Poredoš), Italy (Prof. C. Allegra). These countries, in fact, were the core of the former Austro-Hungarian Empire. It was decided that other countries, which in one way or another were connected with the empire, would be invited to join the new association. This does not, however, preclude personal membership of individual angiologists from any part of the world. The new association is open to specialists from all medical fields involved in angiological issues - internists, haematologists, surgeons, radiologists, rehabilitation physicians, dermatologists, neurologists, ophthalmologists, pathophysiologists and histopathologists. The purpose is an exchange of experiences from various areas, the goal a more comprehensive picture of various vascular disorders. It was decided to have English as the official language of the association, with German as a second language.

I have the great honour of having been elected first CEVF president. At the same time I was asked to organize the first congress of this new angiological association in the very heart of Europe, i.e. in Prague, from 26 to 28 November 1998. The second congress will be held in the year 2000 in Rome. The Prague congress should provide an opportunity for presenting new views about the pathogenesis, diagnosis and treatment of some diseases of the various vascular segments of the extremities. Actually, the congress should be a toouchstone of this new vascular forum.

As you all know, Prague has age-old traditions, countless historical monuments, a rich architectural past with almost all styles of architecture. Moreover, Prague boasts the oldest university in Central Europe, founded on 7 April 1348 by the king of Bohemia and Roman Emperor Charles IV. This year Charles University celebrates its 650th anniversary, an appropriate occasion for many international scientific congresses and symposia from all areas of human knowledge.

Dear friends, I hope that at our first congress you will learn many new and interesting things, while enjoying the beauties of our city and I wish the congress all possible success.

With best greetings,

Assoc. Prof. Vladimír Puchmayer, M.D., Ph.D.
President of the 1st CEVF Congress

GENERAL INFORMATION

CONGRESS VENUE
Radio Free Europe
Vinohradská Street No. 1
110 00 Praha 1
(underground station „Muzeum" – line A and C)

LANGUAGE
The official Congress language is English and Czech with simultaneous translation.

SECRETARIAT
„1st Congress of CEVF"
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Fax: +420-2-294610
e-mail: senderova@cls.cz
http://congress.cls.cz/vascularforum

EXHIBITION
Pharmaceutical exhibition will be held in the foyer of the Congress hall. Information about the exhibition available in the secretariat.

MAIN TOPICS

ARTERIES
- **Atherosclerosis-aspects of pathogenesis**
- **Coagulation changes and PAOD**
- **New diagnostic procedures in PAOD**
- **Asymptomatic carotid stenosis - to treat or not?**
- **Critical limb ischemia**
- **Criteria for invasive and conservative therapy of PAOD**
- **Systemic and local thrombolysis of PAOD**
- **PTA and stents**
- **Surgical reconstruction**
- **Conservative therapy of PAOD**

VEINS
- **Diagnostic procedures in phlebology**
- **Chronic venous insufficiency: pathogenesis, diagnostics and therapy**
- **Deep vein thrombosis**
- **Thrombolysis and/or Heparin therapy of DVT**
- **Surgical therapy and stents**

LYMPHATIC VESSELS
- **Pathogenesis of chronic lymphoedema and elephantiasis**
- **Therapy of chronic lymphoedema and elephantiasis**

VARIA

ACTA CHIRURGIAE PLASTICAE

No. 1, 1998

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LÉKAŘSKÁ KNIHOVNA V PRAZE 3 NÁRODNÍ

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LÉKAŘSKÁ KNIHOVNA V PRAZE NÁRODNÍ

SCOPE AND LIMITATIONS

Acta Chirurgiae Plasticae is an international journal with a long-standing tradition respected by the professional public worldwide. It is published in English four times per year. The journal contains clinical, experimental and theoretic studies from the discipline of plastic, reconstructive and aesthetic surgery, surgery of the hand, craniofacial surgery, treatment of burns and allied surgical disciplines (traumatology, orthopaedics, gynaecology etc.). In the journal you will also find reviews, case-histories, innovations, comments, reports from study trips and congresses, reviews of books and various announcements.

ACTA CHIRURGIAE PLASTICAE

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MICROSURGICAL RECONSTRUCTION DURING TREATMENT OF ONCOLOGICAL DISEASES OF HEAD AND NECK

J. Veselý[1], J. Kučera[1], J. Hrbatý[1], L. Dražan[1], M. Malantová[2], O. Bulik[2], E. Mannino[3]

[1]Clinic of Plastic and Aesthetic Surgery, St. Ann Faculty Hospital, Brno
[2]Second Stomatological Clinic, St. Ann Faculty Hospital, Brno
[3]Palermo University

SUMMARY

In 37 oncological patients where extensive resections of the face, maxilla, mandible or calva were necessary, microsurgical reconstructions were used in 27 cases as primary operations at the time of resection, and in 10 cases delayed or secondary operations were made. 49 flaps were used. In five cases two flaps were used in a single stage reconstruction, i.e. one flap for reconstruction of the mandible or buccal and on the other for facial side of the face. During operations a multidisciplinary approach of the surgical team comprising a maxillofacial surgeon, ENT and plastic surgeon is preferred.

ZUSAMMENFASSUNG

Die mikrochirurgischen Rekonstruktionen bei der Behandlung der onkologischen Kopf- und Halserkrankungen

J. Veselý, J. Kučera, J. Hrbatý, L. Dražan, M. Malantová, O. Bulik, E. Mannino

Bei 37 onkologischen Patienten mit dem Bedarf an eine ausgedehnte Resektion des Gesichtes, Unterkiefers, der Maxilla oder der Kalva wurden die mikrochirurgischen Rekonstruktionen in 27 Fällen primar in der Resektionszeit, in 10 Fällen verschoben oder sekundär angewandt. Es wurden 49 Lappen benutzt. In 5 Fällen wurden 2 Lappen in der einzeitigen Rekonstruktion angewandt, und zwar zur Rekonstruction des Unterkiefers und Gesichtes und der bukalen und fazialen Seite des Gesichtes. Bei den Operationen wird der multidisziplinare Zugang im Operationsteam des maxilofazialen Chirurgen, Otorinolaryngologen und plastischen Chirurgen bevorzugt.

Key words: free flaps, head and neck, oncology

Extensive malignant tumours of the head and neck are usually treated in maxillofacial surgical departments or ENT department and call for radical surgery with the necessity of primary or secondary reconstruction which under our conditions are usually implemented by plastic surgeons. Interdisciplinary collaboration on these medical problems provides positive therapeutic results as regards the successful cure of the oncological condition as well as from the aspect of functional and aesthetic reconstruction. As reconstructions of complex tissues are usually involved i.e. skin and subcutaneous layers of the head and face, buccal mucosa, and part of the skeleton of the jaws, microsurgery plays a large role.

A smaller proportion of patients are treated from the onset at departments of plastic surgery whose skin tumours relapse.

MATERIAL AND METHODS

Reconstructions were implemented by microsurgical transplantation for 37 or our patients, primary in 27 cases, i.e. at the time of resection of the tumour and in 10 patients in postponed or secondary operations. In a one-stage operation we prefer a multidisciplinary approach. The maxillofacial surgeon provides a radical resection of the tumour, the ENT surgeon a block resection of the lymphonodes and in most cases tracheostomy and the microsurgical team performes the reconstruction.

In 37 patients 49 flaps were used for the reconstruction, incl. 30 patients with one flap transferred and in seven patients several free flaps for an one-stage reconstruction or because of necrosis of previous flap.

Depending on the site and character of reconstruction in 23 cases soft tissues of the head incl. the vertex reconstructed, in nine cases the maxilla by transplantation of muscular or musculocutaneous flap and in five cases the mandible by using of vascularized fibula.

The most frequently used flaps were the following: latissimus, scapularis, serratus ant. sup., fibula, forearm flap.

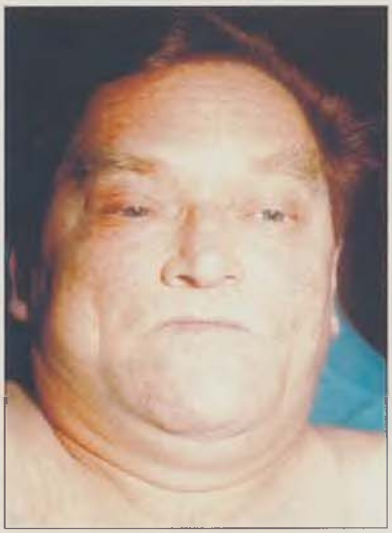

Fig. 1: A male patient aged 53 years with a poorly differentiated facial epidermoid carcinoma exulcerated into the oral cavity.

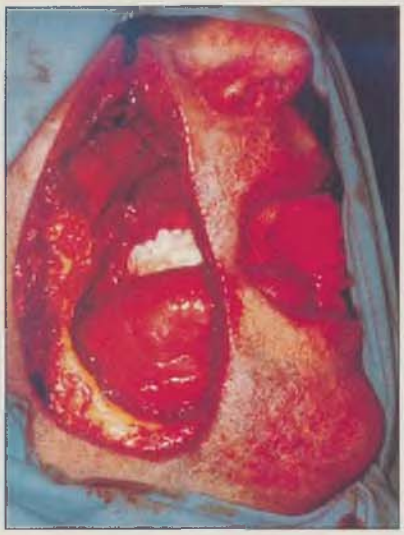

Fig. 2: The facial full-thickness radical resection with the simultaneous resection of cervical lymphonodes.

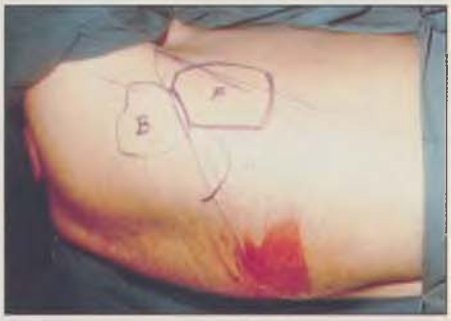

Fig. 3: The scheme of two independent flaps for the covering of a facial defect. B = scapular flap for the reconstruction of the bucal side of the cheek, F = a latissimus flap for the reconstruction of the superficial cover of the cheek.

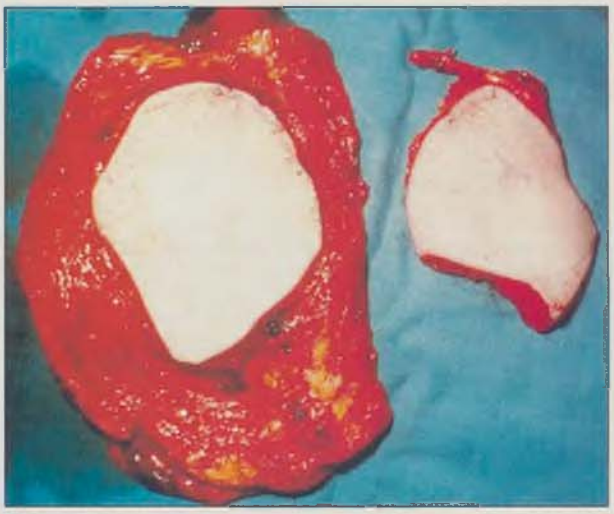

Fig. 4: Isolated flaps.

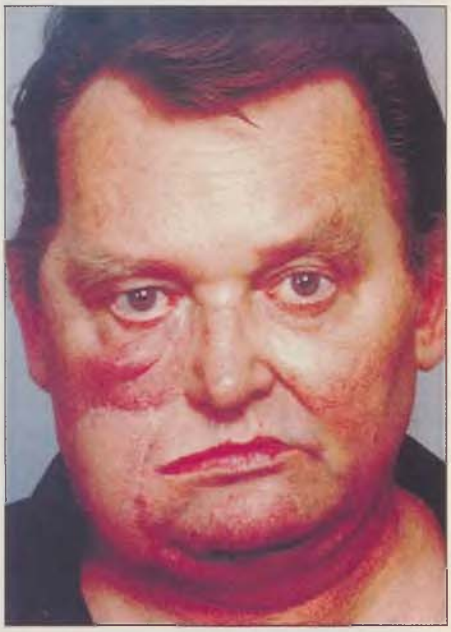

Fig. 5: Two years after the repair of a palatal fistula and fixation of the involved cheek with an active temporal muscle.

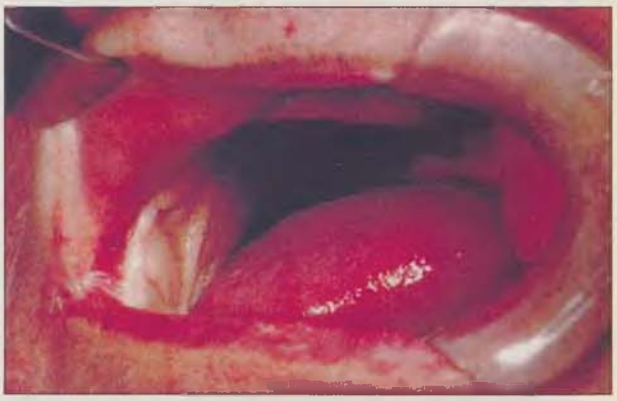

Fig. 6: A photo of a skin flap in the mouth.

RESULTS AND DISCUSSION

Regarding the survival of flaps and accomplishment of the function of reconstruction, the transplantation of one flap in oncological patients was accompanied by 11,5% of complications while two flaps in an one stage reconstruction were completely successful in 66%, in 34% one of two flaps failed. In those cases with failure of one free flap another one was transferred solving the problem of secondary defect. And as compared with other groups of free flaps transfers, e.g. in traumatology or in reconstruction of the penis these results have a much lower percentage of surviving flaps. There may be several reasons but complications are mainly due to irradiation of the tissues.

In the group of 37 patients operated in 1991-97 local relapses of cancer developed in three patients and generalisation in four patients. These results are comparable with those recorded abroad (Nakatsuka 1995).

Reuther (1991) reports a 10% increase in five-year survival of oncological patients treated by

microsurgical reconstructions, i.e. from 45-55% to 55-65%.

W. Millesi at the microsurgical course in Budapest (1997) reported relapses in 20-25% within three years and outlined the necessity of lymphonodes resection as follows:

Tumour without positive nodes - limited resection of supraomohyoid nodes

Tumour + suspect nodes - conservative block resection

Tumour + fixed nodes - radical block on affected side and anatomical resection of contralateral nodes.

CONCLUSION

In our opinion a multidisciplinary approach to such serious problems as malignant oncological diseases is an asset. The possibility of extensive reconstructions by microsurgical methods fundamentally alters views on the resection of the tumour. The demand of the plastic surgeon is a radical character of the operation regardless of the size of the defect on the skeleton and soft tissues. The maxillofacial surgeon who implements the resection is also relieved of stress associated with the size of the defect and its covering.

The use of two flaps in an one-stage reconstruction makes primary reconstruction of the mandible and soft tissues possible and a better cosmetic result when the buccal and facial portion of the face has to be reconstructed.

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TREATMENT OF A MAXILLARY DEFECT FOLLOWING RESECTION OF CARCINOMA

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[3]Neurosurgical Clinic, Faculty Hospital, Brno-Bohunice
[4]Palermo University

SUMMARY

A group of 37 oncological patients with tumours of the head and neck where extensive resection of the face, maxilla or mandible or calva was necessary, comprised five patients with a typical defect after resection of part of the maxilla including half of the palate and exenteration of the orbit. This extensive defect causes discomfort to the patient and his environment - functional i.e. impaired speech, and cosmetic.

A satisfactory solution during reconstruction of the maxilla without the need of skeletal reconstruction is microsurgical transplantation of a narrow flap of the latissimus dorsi, usually with two cutaneous islands - one to close the palate and the other to close the orbit and face.

ZUSAMMENFASSUNG

Die Lösung des Maxilladefektes nach der Resektion des Karzinoms

J. Veselý, J. Hložek, B. Krejčová, V. Smrčka, E. Mannino

Von 37 onkologischen Patienten im Kopf- und Halsgebiet mit dem Bedarf an eine ausgedehnte Hals-, Maxilla- oder Unterkieferresektion, oder Kalva waren 5 Patienten mit dem typischen Defekt nach der Resektion eines Teiles von Maxilla, einschließlich einer Hälfte des Gaumens und mit der Orbitexenteration. Dieser Defekt ist ein Diskonfort für den Patienten und seine Umgebung einerseits funktionell wegen der Behinderung des Sprechens und andererseits auch ästhetische.

Als eine gute Lösung bei der Maxillarekonstruktion ohne des Skelettersatzes bewertete sich die mikrochirurgische Versetzung eines engen Lappens Latissimus dorsi gewöhnlich mit 2 Hautinseln - die eine für den Gaumenverschluß und die andere für den Orbit- und Gesichtsverschluß.

Key words: free flaps, head and neck, oncology

One of the typical pictures after resection of the maxilla by otolaryngologists due to carcinoma is a defect of the face, half the palate and orbit after exenteration, while the alveolus is preserved. Usually the nasal septum is also preserved and there is either a separate opening into the nasopharynx or it is combined with the palatine defect.

These extensive resections raise great expectations in the patient that his oncological disease will be cured, on the other hand the operation is associated with devastation of the face which is depressing for the patient and his immediate environment. The patient must wear an obturator of the palate if he wants to speak comprehensibly and an epithesis or glued dressing across the maxillary defect.

MATERIAL AND METHODS

The authors resolved the described problem by microsurgical transplantation of a narrow muscle flap of the m. latissimus dorsi with two cutaneous islands. The more distal one in relation to the pedicle of the flap is used for reconstruction of the palate, the proximal cutaneous islet of this musculocutaneous flap is used to close the facial and orbital defect. The muscle is used to fill the maxilla. Only in one case the authors used three skin islands of the described flap: to close the palate, the nasopharyngeal choana and the orbit. In one case the cutaneous islets were joined to form the nasal septum resected during the primary operation. In another case where the defect after exenteration of the orbit was too small the

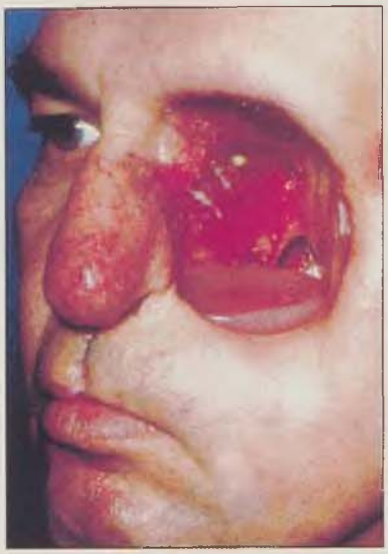

Fig. 1: Defect of maxilla with half the palate and obturator making rhinolalic speech possible.

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Fig. 3: Two years after reconstruction.

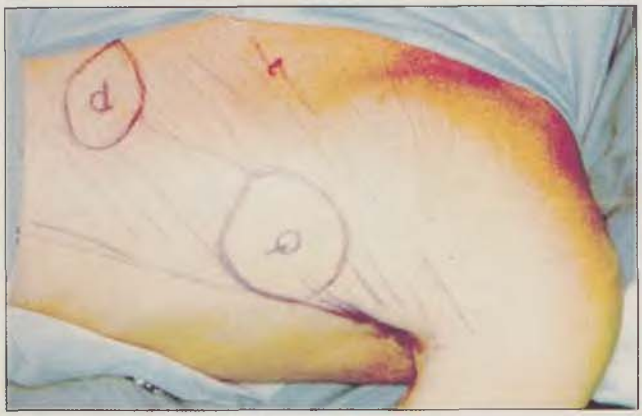


Fig. 2: Plan of flap of latissimus dorsi with cutaneous island for closure of palate and with island for closure of orbit.

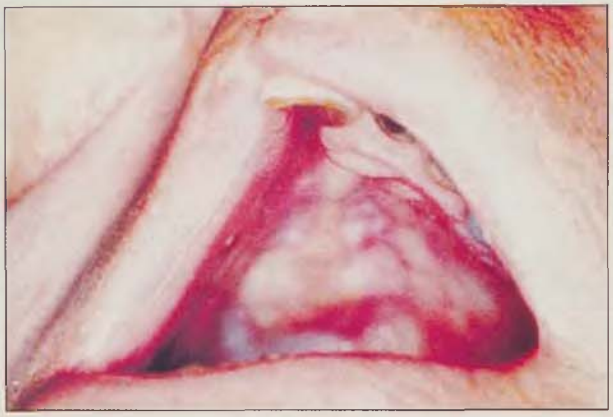


Fig. 4: View of closed palate.

cutaneous islet was resected because of an abundance of tissue and the muscle was covered by a split skin graft.

The recipient vessels were usually the vasa thyroidea superior, the pedicle of the flap of the m. latissimus was slipped subcutaneously to the recipient vessels on the neck. When it was necessary to prolong the pedicle to 10-15 cm, the vessels were prepared in the flap and the proximal part of the muscle was resected.

RESULTS AND DISCUSSION

In a group of 37 oncological patients admitted from 1991-97 five patients with the described defect were treated by the described type of flap. The survival of the flap as a whole was 100%, in one case a cutaneous island in the palate was too small and necrotized and the muscle covering the palate was covered within one month by epithelium of the oral cavity. The authors did not encounter any palatine fistulas nor any local relapses. One 71-year-old patient developed generalization of the process within a short postoperative period and one female patient developed another type of carcinoma on the affected side of the maxilla two years after reconstruction.

The described type of flap is an effective way of closing great facial and palatine defect without the necessity of skeletal reconstruction. Speech in all patients was comprehensible and thus satisfactory.

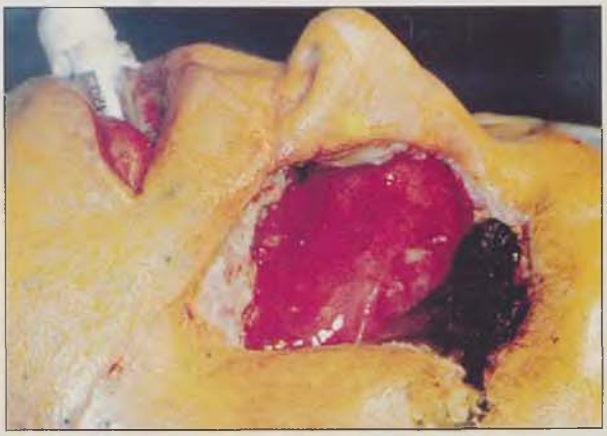


Fig. 5: After resection of maxilla with residual tumour in orbit.

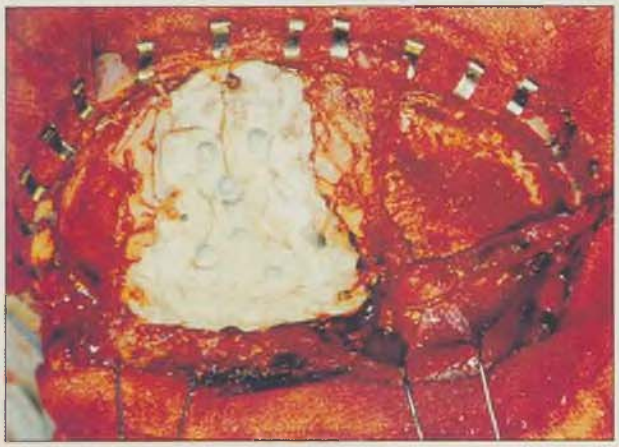


Fig. 6: After resection of orbital roof by a neurosurgeon the dura mater was covered by Palacost.

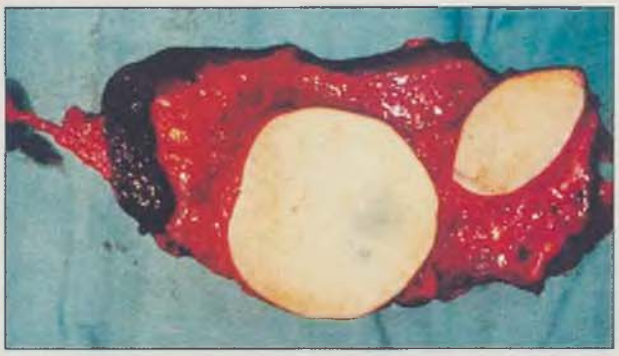


Fig. 7: Flap with cutaneous islands.

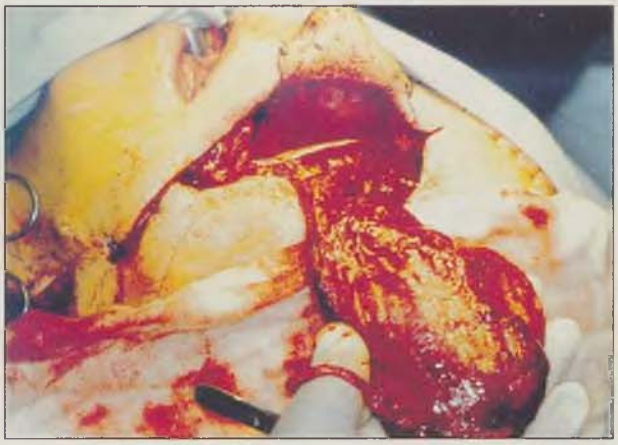
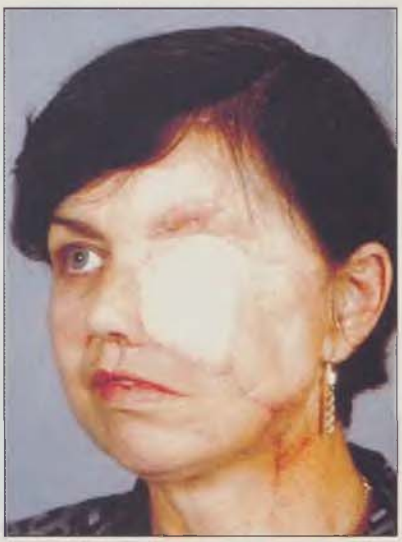


Fig. 8: During the operation first the skin flap was sutured to close palatine defect.

Fig. 9: Four years after reconstruction. →



CONCLUSION

The described type of reconstruction of an extensive defect of the maxilla with exenteration of the orbit and resection of the palate by a musculocutaneous flap of the latissimus dorsi with two cutaneous islands does not produce an ideal cosmetic appearance but satisfactory good functional result. Above all it closes the palate without the need of skeletal reconstruction and it covers the facial defect. Comprehensible speech was achieved in the patients. Some of the patients recovered after this operation to such an extent that they demanded reconstruction of the orbit including an ocular prosthesis to improve their appearance.

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FUNCTIONAL AND AESTHETIC CONSEQUENCES IN THE FOREARM AFTER HARVESTING THE CHINESE FLAP

C. Bravo, L. Dražan, E. Mannino

Department of Plastic and Aesthetic Surgery,
Medical School, Masaryk University, Brno, Czech Republic

SUMMARY

We have evaluated the donor site after harvesting the chinese flap in 40 patients operated at the Clinic of Plastic and Aesthetic Surgery of Brno between 1989 and 1994. We conclude that: 1 - The hand function is not oustandly altered after harvesting the flap, but in our study 11 patients (27.5%) indicated that they have some limitation or impairment of their hand function. 2 - Tolerance to forearm deformity is considerable, but it depends on degree of the defect for which the flap is transferred: 25 patients (62.5%) would like to elect a different flap. 3 - It is necessary to think about cosmetic consequences of the chinese flap and consider other possibilities of the flap choice. Secondary defect may be for the patient a problem even several years after operation.

ZUSAMMENFASSUNG

Die funktionelle und ästhetische Folge an dem Unterarm nach der Entnahme des chinesischen Lappens

C. Bravo, L. Dražan, E. Mannino

Wir haben bei 40 Patienten, die an der plastischen und ästhetischen Chirurgie in Brünn in den Jahren 1989-1994 behandelt wurden, die Stelle der Entnahme des chinesischen Lappens bewertet. Wir stellten dies fest:

1) Die Funktion der Hand ist nach der Lappentnahme nicht markant alteroviert. In unserer Studie führten 11 Patienten (27.5 %) ein, daß sie an einige Beschränkungen oder an die Verschlechterung der Funktion der Hand leiden.

2) Die Toleranz zur Deformation des Unterarmers ist groß, aber hängt vom Grad des Defektes, für den der Lappen versetzt wird; 25 Patienten (62.5%) würden einen anderen Lappen wählen.

3) Es ist notwendig über die ästhetischen Folgen des chinesischen Lappens nachzudenken und andere Möglichkeiten im Auswahl des Lappens in Betracht zu ziehen.

Der sekundäre Defekt kann für den Patienten noch viele Jahre nach der Operation ein Problem darstellen.

Key words: chinese flap, flap donor site

The radial forearm, so called chinese flap was first carried out in 1978 and described by Young et al. in 1981 (11). Since that time its use was quickly extended and it became one of the most popular flaps. Its advantages include thin and pliable skin, large and long vascular pedicle, sensibility, simplicity and safety of transfer. Necessity of skin grafting to cover the secondary defect resulting in cosmetic deformation of both forearm and skin donor area are some of the disadvantages of this flap. Controversial question remains occurrence of neuromas and scaring of the sensory branches of radial nerve under the skin graft (1, 10). Another objection represents impaired hand perfusion (5). The purpose of our study was the evaluation of the donor site according to subjective judgement of patient and objective physician's examination performed by non operating surgeon.

MATERIALS AND METHODS

The study was carried out on 40 consecutive patients, which were operated between 1989 and 1994 at the Clinic of Plastic and Aesthetic Surgery in Brno. Patient age ranged from 8 to 69 years (mean 43). There were 30 men and 10 women. The principal indications of the flap were: secondary defect or unstable scar after injury (30 patients - 75%), oncological defect (4 patients - 10%). Other indications were in 6 patients (15%). Size of the flap ranged from 1/3 (17 patients - 42.5%) to 2/3 (20 patients - 50%) of the volar forearm skin. Direct suture of the defect was possible

in 3 patients (7.5%). Any tissue expander or local flaps were used to close the donor site defect. Healing complications of skin graft used to cover the secondary defect were present in 6 patients (15%). We have developed five questions for subjective evaluation and 5 criteria for objective evaluation of forearm by examining doctor.

RESULTS

I. Subjective evaluation

1. How much appearance of your forearm matters you?
Significantly (7 patients - 17.5%)
Not at all (31 patients - 77.5%)
Partially (2 patients - 5%)

2. Do you feel limitation or impairment of the hand function?
Yes (11 patients - 27.5%)
No (29 patients - 72.5%)

3. Do you think that your hand is more sensitive to cold than the unaffected hand?
Yes (9 patients - 22.5%)
No (31 patients - 77.5%)

4. Would you prefer another flaps (groin flap, lateral arm flap, scapular flap) before operation if they were proposed to you?
Yes (25 patients - 62.5%)
No (15 patients - 37.5%)

5. Would you consider scar after skin graft harvest as a significant aesthetic defect?
Yes (3 patients - 7.5%)
No (37 patients - 92.5%)

II. Objective evaluation

1. Cosmetic appearance of the forearm.
Good (26 patients - 65%)
Minor deformation (10 patients - 25 %)
Serious deformation (4 patients - 10%)

2. Limitation of hand function (range of motion, grip strength).
Yes (4 patients - 10%)
No (36 patients - 90%)

3. Tinnel's test over the skin graft.
Positive (6 patients - 15%)
Negative (34 patients - 85%)

4. Allen's test (comparison with the other hand).
Positive (4 patients - 10%)
Negative (36 patients - 90%)

5. Thumb paraesthesia.
Yes (1 patient - 2.5%)
No (39 patients - 97.5%)

6. Cosmetic appearance of the skin graft donor site.
Acceptable (35 patients - 87.5%)
Questionable (5 patients - 12.5%)

DISCUSSION

The radial forearm flap is one of the most commonly used flaps on account of its qualities (2, 8). However, this flap has been questioned because its donor site morbidity (1, 3, 11). On the basis of our results the hand function is not oustandly altered after harvesting the chinese flap, but 11 patients (27.5%) indicated some limitation or impairment of their hand function. Boorman et al. (1987) reported 50% loss of power of grip and pinch and limitations of the other movements after harvesting the chinese flap containing bone. In our group of patients however no bone was harvested with the flap. The size of forearm flap seems to be an important factor to alter the hand function due to high tendency to cicatrix fixation when the donor site defect is covered by skin graft. Our 4 patients in which limitation of hand motion and grip strength occured were included in the group with a flap size 2/3 of the volar forearm skin.

It has been accepted that no ischaemic complication manifest after harvesting the chinese flap (2, 10). However, Jones and O'Brien (1985) reported a case of acute ischaemia after elevation of the forearm flap. In our study only in 4 patients (10%) the blood circulation of the affected hand after timed Allen's test was retarded in comparison with the other hand. In 9 patients (22.5%) the affected hand was more sensitive to cold. The results are similar to that obtained by Timmons et al. (1986). Boorman et al (1987) reported absolutly no cold intolerance in a group of 27 patients. In 12 (44.4 %) of those patients however the reconstruction of radial artery was made.

The percentages of thumb paraesthesia (1 patient - 2.5%) and positive Tinnel's test over skin graft (6 patients - 15%) were in accord with the literature (1, 6). It has been emphasized the importance of the skin elevation from the volar surface of the forearm to avoiding the radial nerve (1). The principal negative characteristic of the Chinese flap is the scar deformation of the forearm. Some report concludes that it is not prudent to use the flap in younger patients and children because the possibility of hypertrophic forearm cicatrization. In elderly patients, the skin of the forearm is lax, permitting advancement of the skin for primary donor site closure, in many instances (5). The traditional method to cover the donor site is the split skin graft. At our Department we have used these grafts with relatively low healing complications (6 patients - 15%), overall, in our study 14 patients (35%) had some grade of scar deformity. Patients tolerance to this deformity is considerable, but it depends on degree of the defect for which the flap is transfered: 25 patients (62.5%) would like to elect a different flap. Tissue expanders (7), island skin flaps from the ulnar aspect of the forearm (6) and fullthickness skin grafts (4, 9) have been proposed for

closing the radial forearm flap donor site and to improve its morbidity.

Simplicity and swiftness are some of the great advantages of the chinese flap, but they should not be the only criteria for its choice. Before indication of the radial forearm flap it is necessary to think about its cosmetic consequences and according to possibilities to prefer other flap. Secondary defect may be a problem even several years after operation.

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SOME THOUGHTS AND OBSERVATIONS CONCERNING THE PREVENTION OF NEUROMA

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SUMMARY

Reliable prevention of neuroma is a problem the solution of which is still outstanding. Compared to earlier methods, which mostly consisted in attempts to stop axonal proliferation abruptly, it is now coming to be generally accepted that the regenerative potential of the axons needs to be reduced gradually. The methods most in accord with this view - centro-central anastomosis and capping of nerve ends with a nerve or vein graft - are considered, adding personal observations. A new variant that has shown special promise in animal experiments involves using a nerve and a vein graft in combination. The method still requires clinical verification.

ZUSAMMENFASSUNG

Gedanken und Beobachtungen zur Prävention der Neurombildung

J. Šmahel

Eine zuverlässige Prävention der Neurombildung stellt ein ungelöstes Problem dar. Im Gegensatz zu den älteren Methoden, die meist versuchten, die Axonproliferation abrupt zu stoppen, kristallisiert die Meinung, daß das Regenerationspotential der Axone stufenweise abgeschwächt werden müßte. Die Methoden, die dieser Auffassung am ehesten entsprechen, wie centro-centrale Anastomosen und capping des Nervenendes mit einem Nerventransplantat oder mit einem Venentransplantat, werden analysiert und mit eigenen Beobachtungen ergänzt. Als besonders perspektiv zeigte sich im Tierexperiment eine neue Variante, die die Anwendung eines Nerventransplantates mit einem Venentransplantat kombiniert. Die Prüfung dieser Methode bleibt der klinischen Praxis vorbehalten.

Key words: development of neuroma, prevention of neuroma, suppression of axonal proliferation, centro-central anastomosis, capping of nerve end, nerve and vein grafts

The development of a painful neuroma following severance of peripheral nerves has always been a problem for both patients and surgeons. Efforts to eliminate this unwelcome complication have been correspondingly great. It is estimated that well above a hundred different techniques have been proposed to prevent neuroma (8, 10, 15, 16).

Biologically, neuroma development reflects a disproportion between the regenerative potential of axons and related nerve structures. The proliferation of Schwann's cells and neurofibroblasts responsible for the development of new guiding structures cannot keep pace with the enormous regenerative potential of the axons. Lack of guidance cause chaotic axon growth with connective tissue intervention putting the final seal on the pathological condition.

There is little point in attempting to analyze the proposed methods of preventing neuroma, as not one of them has gained full acceptance in clinical practice. It seems more important to consider a change of opinion in this area. With earlier methods the aim was generally to stop axonal proliferation abruptly. Various, often drastic measures such as crushing, and heat or chemical coagulation of the proximal nerve stump were the means employed. Failure of these attempts has led to the realization that axonal proliferation cannot be stopped abruptly. It is now coming to be generally accepted that the regenerative potential of the axons needs to be reduced gradualy.

Centro-central anastomosis

Gradual reduction of axonal regenerative potential appears to be most likely to be achieved

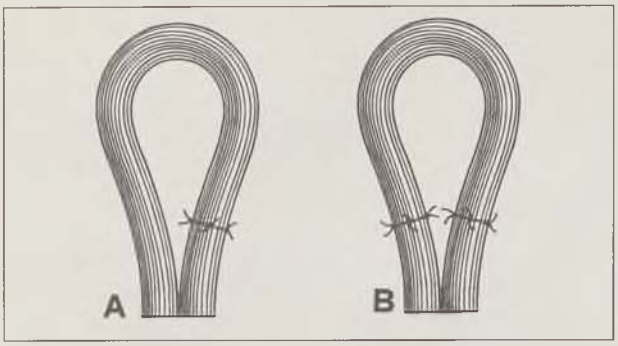

Fig. 1: Diagram to show variants 'A' and 'B' of centro-central anastomosis.

Fig. 2: Centro-central anastomosis variant 'A'. Rat sciatic nerve, 6 months after the operation.

with centro-central anastomosis. The method consists in anastomosing the fascicles in the proximal nerve stump. A definite precondition is the presence of at least two fascicles in the stump. Centro-central anastomosis may be achieved in two ways. The first method is to shorten one fascicle, turn the other one back and suture the two together (Fig. 1A). The second consists in shortening both fascicles and using one of the segments thus obtained as a free nerve graft to bridge the shortened fascicles (Fig. 1B).

Centro-central anastomosis was first discussed by Langley and Anderson (7) and by Bardenheuer (1). One of the experimental variations given by Langley and Anderson (7), who were not doing the work with the aim of preventing neuromas, was to anastomose the central ends of two peripheral nerves. This failed to give a functional link, with axons at most growing into the anastomosed nerve stumps for a short distance. Wood and Mundge (18) have recently used what is in principle the same technique to treat 5 patients who had developed painful neuromas following amputation of the hand. An anastomosis between the median and ulnar nerves resulted in marked pain relief. Bardenheuer (1) called centro-central anastomosis „neurincampsis" and gave 4 techniques for achieving it. The method proved successful in clinical use. Petropoulos and Stefanko (10) tested a number of measures, including Bardenheur's (1) method, to prevent neuroma in experiments on dogs, but with little success.

More recent work on centro-central anastomoses, (4-6, 12) with most authors testing method B, shows that this may limit or completely prevent neuroma. It also confirms that one effect of the method is to inhibit axon proliferation. Seckel (13) and Whipple and Unsell (16) have discussed the possible mechanisms involved in detail. Mechanisms under consideration are isolation of central nerve ends from target-derived factors, and central axon suppression caused by the approaching nerves.

Personal experience with centro-central anastomosis was gained in rat sciatic nerve experiments (Fig. 2). Clinical and histological observation 6 months after the operation has shown that method A requires careful coaptation of the nerve fascicles and meticulous suturing of the perineural sheath. The proliferating axons meet in the suturing site with this method, and axons will use any technical imperfection to escape from a crowded situation into surrounding areas. A tendency to neuromatous proliferation was noted in the suture (Fig. 3). The distinct advantage of method B is that the proliferating axons are provided with guiding structures, and that the axons meet in the graft. The graft has an intact perineurium, which is known to present an impenetrable barrier to axons. Histological stud-

Fig. 3: Neuromatous proliferation in suture site of centro-central anastomosis, variant 'A'. Rat sciatic nerve, 6 months after the operation. Silver impregnation, x 110.

ies have confirmed complete neurotization of the grafts, with endoneural tubes showing „double" axon colonization in some areas. Axon frequency was remarkably high in those areas, and they would be in pairs (Fig. 4, 5). Gorkisch et al. also spoke of axonal overlap in the graft (5). The overlap was 2 - 5 mm in their experiments, with axon growth ceasing after this.

Fig. 4: Neurotization of graft used for centro-central anastomosis, variant 'B'. Note 'double' neurotization of the graft in the upper third of the figure. Sciatic nerve of rat, 6 months after the operation. Silver impregnation, x 110.

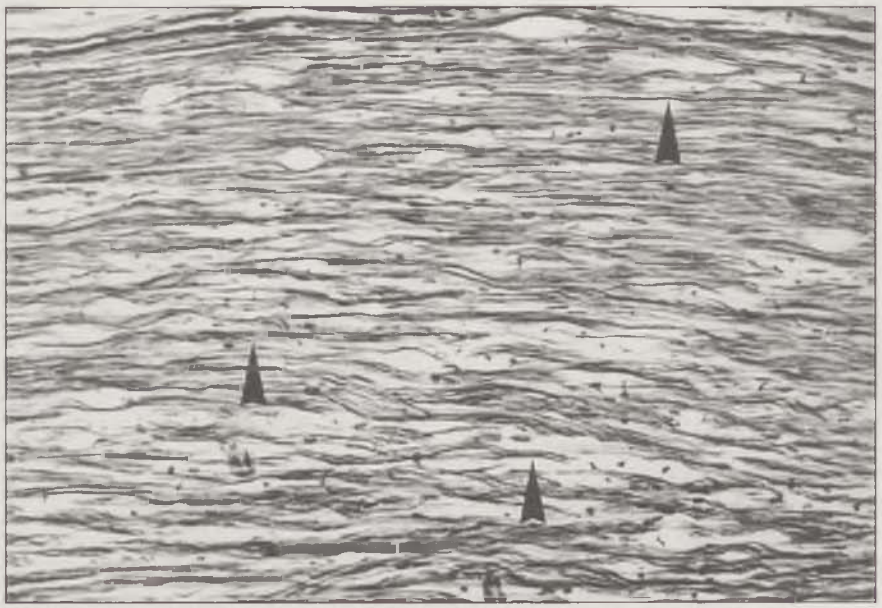

Fig. 5: Detail of 'double' neurotization shown in Fig. 4. Some axons running closely together marked by arrows. Silver impregnation, x 220.

Capping with a nerve graft

Another method designed to limit axons by reducing regeneration potential is to cap the nerve end with a nerve graft (Fig. 6A). Biologically the method bases on the realization that crossing the suture site and neurotizing the graft go hand in hand with axon reduction and a weakening of axon regeneration potential (9, 14, 16). Opinions on the efficiency of the method in preventing neuroma differe. Martini (8), who has studied the capping method in detail in animal experiments, always observed neuroma developing at the free end of the graft. No neuroma would develop when he used lyophilized homografts. In my own investigations on the rat femoral nerve and rabbit peroneal nerve, neuromas would develop on the end of the graft, but were not very marked (Fig. 7). The graft also showed fibrotic changes. Sunderland (15) was skeptical about the method. Robbins (11), on the other hand, spoke of substantial relief in the treatment of painful neuroma with the method in clinical use. The length of the graft seems to be important; according to Robbins it must be at least 2,5 cm.

Capping with a vein graft

Bridging a nerve defect with a tubular structure became the preferred model for the study of different aspects of nerve regeneration over the last ten years. Veins, preformed mesothelial tubes and silicone chambers of different design have been used. All authors found that the regeneration potential of the peripheral nerves of small laboratory animals was such that defects of up to 10 mm could be made up. Another observation made by all was that the distal nerve stump plays a crucial role by stimulating nerve regeneration. Without this stimulation - if the distal nerve stump is not connected - regeneration ceases after a few millimeters (2, 17). Danielsen et al.

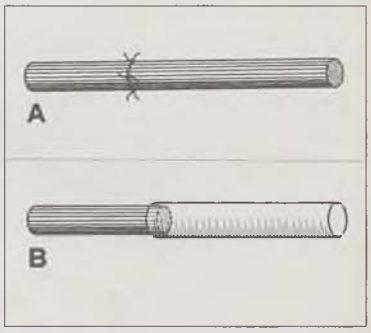

Fig. 6: Diagram showing capping using a nerve graft ('A') and venous

Fig. 7: Moderate degree of neuroma at the end of the graft used to cap the nerve end (Fig. 6A). Rat femoral nerve, 6 months after the operation. Silver impregnation, x 70.

(2, 3) found that the nerve fibers in an „open chamber" do not show ongoing activity. They surmised that putting a tube over the proximal nerve end might serve to prevent neuroma. I tested the method, using veins on the rabbit peroneal nerve (Fig. 6B). Histological examination confirmed that nerve structure development soon ceases in the vein, but there was a distinct impression that the regeneration potential was not easily suppressed. This was evident from the relatively high axon frequency and the tendency for chaotic axon growth (Fig. 8).

Combined method

The results seen when capping nerve ends with a nerve graft or vein led to the assumption that neuromas might be fully prevented by combining the two methods (Fig. 9). The method would weaken the axon regeneration potential by crossing the suture site and passing through the graft and then bring it to an end in the vein, without a target organ. The 10 mm distance is considered critical for nerve regeneration, and care was taken to ensure that both nerve graft and vein segment were not less than 15 mm in length. Histological examinations done as part of these trials with the combined method applied to the rabbit peroneal nerve indicated that the assumption had been correct. Nerve regeneration in the vein was limited to the development of a short cone in which the axons showed reasonably orderly arrangement and only rarely grew in whorls (Fig. 10).

Comments

My trials with the methods under discussion were not part of a systematic study, the aim being rather to complement the observations of other authors. Every variant was, however, tested four times at least. In my view, there is no point in setting up a systematic trial because animals provide no direct information on the subjective response to the measures taken to prevent neuroma. Animal experiments only enable us to make assumptions in this respect. The animals showed normal behavior during the experimental period, they were gaining weight and made no serious attempt to interfere with the surgically treated area. This suggests that either there were no unpleasant sensations or that these were not enough of a nuisance to provoke a reaction.

The main purpose of the present study was to draw

Fig. 8: Axonal activity in nerve stump with venous graft (Fig. 6B). Rabbit peroneal nerve, 6 months after the operation. Silver impregnation, x 70.

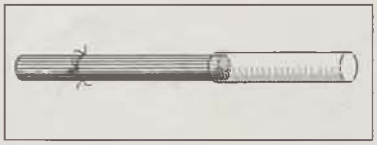

Fig. 9: Diagram to show method of combining nerve graft and venous graft.

Fig. 10: Axonal activity at the end of the nerve graft with venous segment connected (Fig. 9). Rabbit peroneal nerve, 6 months after the operation. Silver impregnation, x 70.

attention to the combined method of neuroma prevention. This gave promising results in animal experiments and would be easy to implement, especially with amputations. The ultimate assessment of the method must of course be in clinical practice.

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COMBINED APPLICATION OF ALPHA-TOCOPHEROL AND FC- 43 PERFLUOROCARBON EMULSION SUPRESSES EARLY POSTBURN LIPID PEROXIDATION AND IMPROVES DEFORMABILITY OF ERYTHROCYTES

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SUMMARY

The effect of FC-43 perfluorocarbon emulsion and α-tocopherol on lipid peroxidative damage and deformability of erythrocytes was evaluated in rats (full skin thickness burns over 15-20 % of total body surface) at third hour after burns. The animals were divided into five groups: (1) non-burnt non-treated (controls); (2) burnt non-treated; (3) burnt but treated with α-tocopherol („Serva", Germany, 20 mg/kg b.m. i.p.) (4) burnt treated with FC-43 emulsion („Green Cross Corp.," Japan, 5 ml/kg, i.v.); (5) burnt treated with combination of α-tocopherol (20 mg/kg) and FC-43 perfluorocarbon emulsion (5 ml/kg). In the burnt non-treated group the concentration of α-tocopherol decreased by 38% ($p < 0,05$), the levels of malonyl dialdehyde (MDA) and fluorescent damaged products raised by 32% ($p < 0,001$) and by 52% ($p < 0,001$) of the controls, respectively, whereas the deformability of red blood cells diminished by 34% ($p < 0,001$). Both the accumulation of MDA and fluorescent lipid peroxidation products and the decrease in deformability of affected cells were suppressed significantly by α-tocopherol treatment which also prevented the decrease in erythrocyte α-tocopherol content. FC-43 emulsion lowered the level of MDA but did not restrain the reduction in erythrocyte deformability significantly. The combined application of α-tocopherol and FC-43 emulsion immediately after thermal skin injury decreases peroxidative membrane damage and improved erythrocyte deformability more significantly than α-tocopherol at the third hour after thermal skin injury.

ZUSAMMENFASSUNG

Die kombinierte Application von Alfa-tocopherol und FC-43 perfluorocarbon Emulsion unterdrückt die frühe Peroxidation der Lipiden nach Verbrennungen und vermindert die Deformation der Erythrozyten

G. Bekyarova, T. Yankova, I., Kozarev

Die Wirkung der FC-43perfluorocarbon Emulsion und des Alfa-tocopherol auf die peroxidative Schädigung und Deformation der Erytrozyten wurde im Tierversuch an Ratten mit Verbrennungen der gesamten Hautdicke an 15-20% des Körpes drei Stunden nach der Verbrennungen gewertet. Die Tiere wurden in fünf Gruppen verteilt. (1) ohne Verbrennung, unbehandelt (Kontrollgruppe), (2) mit unbehandelten Verbrennungen, (3) mit Verbrennungen und behandelt mit der Alfa-tocopherol („Serva" Germany, 20 mg/kg b.m.i.p.), (4) mit Verbrennungen und behandelt mit FC-43 Emulsion („Green Cross. Corp." Japan, 5 ml/kg, i.v.), (5) mit Verbrennungen und behandelt mit der Kombination von Alfa-tocopherol (20 mg/kg) und der FC-43 perfluorocarbon Emulsion (5 ml/kg). Bei der unbehandelten Gruppe erfolgt eine Herabsetzung der Konzentration von Alfa-tocopherol um 38% ($p < 0,5$). Bei der Kontroll-gruppe steigen der Spiegel der Malonyl-dialdehyd (MDA) und schädlichen durch eine fluoroscensis auszeichnenden Produkte um 32% ($p < 0,001$) und 52% ($p < 0,001$), und zwar dort wurde die Deformationfähigkeit der roten Blut-Körperchen um 34% ($p < 0,001$) herabgesatzt war. Die Behandlung mit Alfa-tocopherol herabsetzt sowohl die Anreichung von MDA und der fluoroscenten peroxidativen Produkten der Lipiden, wie auch der Deformationen der betroffenen Zellen. Diese Terapie hindert ferner die Herabsetzung des Alfa-tocopherol spiegels in der Erytrozyten. Die FC-43 Emulsion herabsetzt den MDA Spiegel hindert jedoch nicht in bedeutender Weise der Deformation der Erytrozyten. Die kombinierte Applikation von Alfa-tocopherol und FC-43 Emulsion unmittelbar nach der thermalen Verletzung der Haut vermindert die peroxidative Membranschädigung und in significanter Weise die Deformation der Erythrocyten im Vergleich zur Verabreichung der Alfa-tocopherol drei Stunden nach der Verbrennung.

Key words: lipid peroxidation, erythrocyte deformability, thermal trauma, alpha-tocopherol, FC-43 perfluorocarbon emulsion

Clinical and experimental studies reveal that burn injury induces oxidative damages and erythrocyte haemolysis, abnormal shapes and loss of deformability in the early phase (1-3). Oxygen radical burst from polymorphonuclear neutrophil leucocytes following thermal injury is closely

linked with erythrocyte alteration (4). Vitamin E (α-tocopherol) is well known as an important chain-breaking antioxidant and may protect erythrocytes against membrane peroxidative damage and rheological impairments (5).

Perfluorocarbons, known as oxygen carrying blood substitutes have been reported to improve microcirculation and rheological blood properties (7, 8). Perfluorocarbons have low viscosity and very small emulsion particles (1/70 of the size of erythrocytes) and can penetrate deeply to the hypoxic tissue vasculature bypassing sludged red cells. They are also able to reoxygenate them and to reverse the stiffening of the erythrocyte membrane occurring under conditions of hypoxia and acidosis (9). It has been reported that perfluorocarbons inhibit superoxide radical production from activated leucocytes (10). Previous data showed that Pluronic polyols, the main compounds of perfluorocarbon emulsions, have protective effect against heat damage of erythrocyte membranes and vascular endothelium and improve microcirculation after burns (11, 12). However, no information is available about perfluorocarbon effect on erythrocyte deformability after thermal skin injury.

The aim of the present study was to examine lipid peroxidation, the levels of α-tocopherol in erythrocytes and their deformability at the third hour after thermal skin injury and to evaluate the effect of treatment with α-tocopherol and FC-43 perfluorocarbon emulsion alone and in combination.

MATERIAL AND METHODS

Male Wistar rats weighing 225 ± 33 g (mean ± SD) were subjected to a 15-20 % of total body surface area full thickness burn over the back by immersion of 90 °C water for 10 s under anaesthesia with thiopental (30 mg/kg body mass). The animals were divided into five groups: (1) Non-burnt non treated; (2) Burnt non-treated (n = 8); (3) Burnt but treated with α-tocopherol (20 mg/kg, i.p., „Serva", Germany) (n = 8); (4) burnt treated with FC-43 emulsion (5 ml/kg, i.v., „Green Cross Crop", Osaka, Japan) (n = 9); (5) burnt treated with the combination of α-tocopherol (20 mg/kg, i.p.) and FC-43 emulsion (5 ml/kg, i.v.) (n = 9). α-tocopherol and FC-43 emulsion were injected immediately after thermal skin injury. Non-treated healthy rats served as controls.

Venous blood was drawn at the third hour after burns. Malonyl dialdehyde (MDA) and fluorescent products were used as markers for the presence of lipid peroxidation. MDA was assayed as thiobarbituric acid (TBA)-reactive substances by the method of Porter et al. (13). Fluorescent products of lipid peroxidation were measured by the method of Dillard and Tappel (14), using „LS-5 Perkin Elmer" luminescent spectrofotometer. The content of erythrocyte α-tocopherol was determined fluometrically as described by Taylor et al. (15). The deformability of red blood cells was assayed by the method of Tannert and Lux (16).

The values of lipid peroxidation products, α-tocopherol of red blood cells and deformability were given as percent of controls, accepted to be 0 (100) %. The statistical significance of the differences was evaluated by the Student's *t*-test, assuming a significance level of $p < 0,05$.

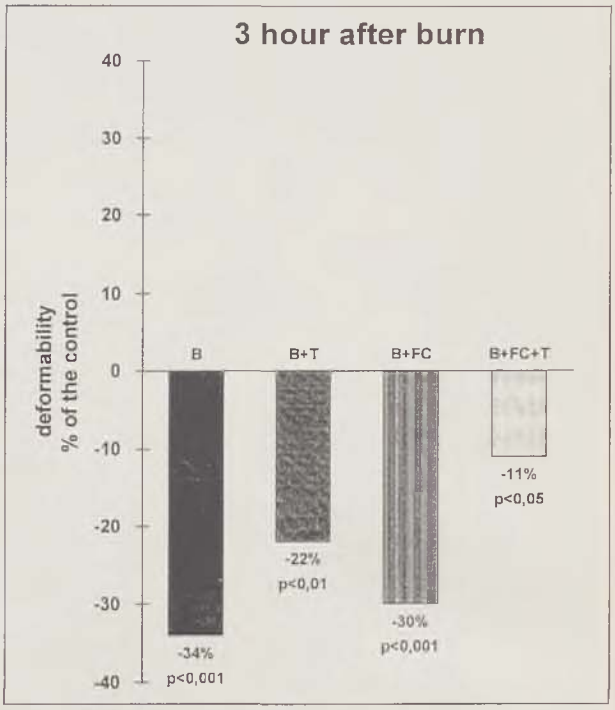

Fig. 1: Changes in erythrocyte deformability after thermal skin injury of rats and treatment with α-tocopherol and FC-43 perfluorocarbon emulsion; B-burnt-non-treated; B+T-burnt but treated with α-tocopherol; B+FC-burnt treated with FC-43 emulsion; B+FC+T-burnt treated with α-tocopherol and FC-43 emulsion. Data were given as percent of the controls.

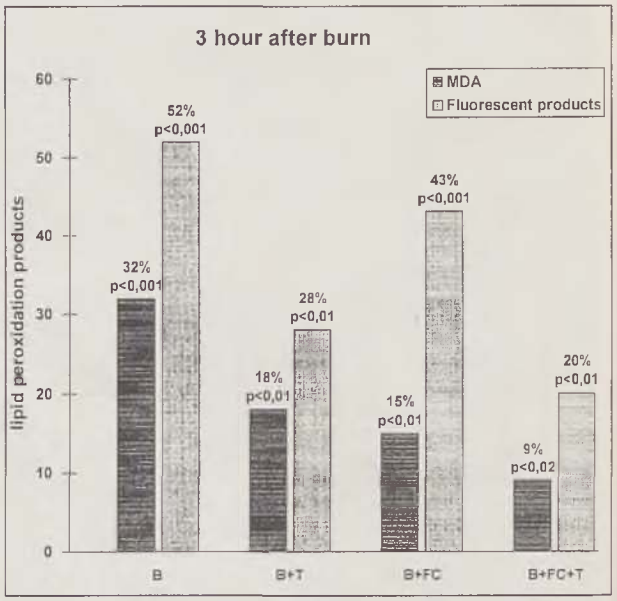

Fig. 2: Changes in the levels of MDA and Fluorescent lipid peroxidation products in erythrocytes after thermal injury of rats and treatment with α-tocopherol and FC-43 emulsion. Data were expressed as percent of the controls.

RESULTS

At the third hour after thermal skin injury the erythrocyte deformability decreased by 34% ($p < 0,001$) as compared to that of the controls (Fig. 1). The deformability of thermally affected red blood cells lowered by 22% ($p < 0,01$) of the control values after treatment with α-tocopherol and by 30% ($p < 0,001$) after administration of FC-43-emulsion. After combined application of α-tocopherol and FC-43 emulsion the deformability of red blood cells decreased by 11% ($p < 0,05$) of the control values.

The levels of MDA and fluorescent damaged products elevated as a results of thermal injury by 32% ($p < 0,001$) and by 52% ($p < 0,001$), respectively (Fig. 2). The concentrations of MDA and fluorescent products increased by 18% ($p < 0,05$) and by 28% ($p < 0,01$) from the control values after α-tocopherol treatment. FC-43 emulsion increased the levels of MDA by 15% ($p < 0,05$) and fluorescent products-by 43% ($p < 0,001$) in comparison with that of the controls. The levels of MDA and fluorescent products exceeded the control values by 9% ($p < 0,02$) and by 20% ($p < 0,01$) respectively, after combined treatment with α-tocopherol and FC-43 emulsion.

The concentration of α-tocopherol in red blood cells decreased by 38% ($p < 0,05$) of the controls after burns (Fig. 3). After application of FC-43 emulsion the content of α-tocopherol in thermally damaged erythrocytes decreased by 29% ($p < 0,05$) in comparison with that of controls. At the same time the concentration of erythrocyte α-tocopherol in burnt rats treated with vit E overrided significantly (by 20%) the control values. After combined application of α-tocopherol and FC-43 emulsion the concentration of α-tocopherol excceded by 31% ($p < 0,02$) the control values.

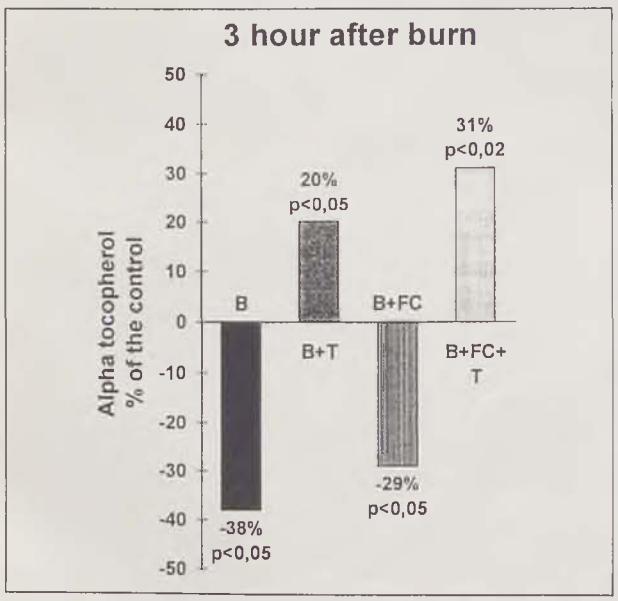

Fig. 3: Changes in the concentration of erythrocyte α-tocopherol after thermal skin injury of rats and treatment with α-tocopherol and FC-43 emulsion of rats. Data were given as percent of the controls.

DISCUSSION

The results of the present study demonstrate that erythrocyte deformability is markedly decreased on the third hour after thermal skin injury. They are consistent with previous data which support the observation that reduced deformability of red blood cells contributes to microcirculatory complications, progressive tissue ischemia and organ dysfunctions in the early post-burn period (1, 3).

The enhanced concentrations of MDA and fluorescent products suggest that the rate of oxygen free radicals overrides erythrocyte scavenging and antioxidant system capacity. Both the complement - activated neutrophils and the hypoxic damaged vascular endothelium via wanthine oxidase have been shown to be the main sources of oxygen free radicals after burns (4). Reactive oxygen species attack directly polyunsaturated fatty acids of the membrane phospholipids, which leads to the formation of lipid breakdown products. These products such as MDA may be involved in polymerization of membrane components and cause peroxidative damage of erythrocyte membranes (17).

Liposoluble vitamin E, as an important component of biological membranes and an chain-breaking antioxidant protects membrane polyunsaturated fatty acids from radical mediated lipid peroxidation (18). The decreased concentration of α-tocopherol can increase susceptibility to peroxidative membrane damage of affected erythrocytes under the conditions of activated lipid peroxidation, which is in agreement with other data (19).

The enhanced levels of fluorescent products indicate peroxidative damage and crosslinking of MDA with membrane proteins and lipids (20). MDA can also cross-link haemoglobin to cytoskeletal proteins (especially spectrin) (21). Oxidative cross-linking of cytoskeletal proteins increases the stiffness of erythrocyte membrane and reduces the deformability of red blood cells. Oxidative modification of erythrocyte membranes decreases Ca^{2+} ATP-ase activity with subsequent accumulation of intracellular Ca^{2+}, which controls deformability through calmodulin and cytocalbin (22).

The lowered activity of scavenging enzymes such as superoxide dismutase and glutathione peroxidase, detoxifying the oxygen reactive metabolites and the deficiency of glutathione which protects SH-groups of membrane spectrin and haemoglobin facilitates the oxidative membrane alteration and the impairment of erythrocyte deformability (23-25).

The treatment with α-tocopherol reverses the levels of erythrocyte α-tocopherol to control val-

ues and suppresses both the accumulation of lipid peroxidation products and the decrease in deformability of erythrocytes. Vitamin E scavenges peroxy, hydroxy, superoxide radicals and singlet oxygen and thus restrains radical-mediated alterations of erythrocyte membranes (18). It also exerts membrane stabilizing properties (26).

The application of FC-43 emulsion causes reduction in the MDA levels, but does not restrain the decrease in erythrocyte deformability significantly. These results are not in agreement with the data reported by other authors (7). The mechanism of these changes is not clear. It has been reported that Pluronic F-68, one of the main components of FC-43 perfluorocarbon emulsion, and its homolog F-127, increase the resistance of red blood cells and improve the microcirculatory blood flow, including the burn area (12). Small particles of perfluorocarbon emulsions can promote the diffusion of oxygen across the endothelial membrane even in the absence of oxygen enriched inhaled air (27) and can exert protective effect on endothelial structures and functions after burn injury (12). The early postburn injury of endothelium can enhance the adherence of activated leucocytes via wanthine-oxidase (4). Two perfluorocarbons and F-68 inhibit neutrophil activation and superoxide production (10) through elevation of intracellular cAMP in white blood cells (28).

It could be postulated that FC-43 emulsion suppresses oxygen radical overproduction from activated leucocytes and damaged vascular endothelium probably by improving the microcirculation, erythrocyte resistance and tissue oxygen supply in the early postburn period, but there are no data about antioxidant effect of FC-43 emulsion.

The combination α-tocopherol and FC-43 emulsion protects erythrocytes from peroxidative alteration and reduction of their deformability more significantly, than α-tocopherol when used alone. The mechanism of FC-43 emulsion protective effect remains unknown. A homolog of F-68, Pluronic F-127 has been used as drug'delivery vehicle in burns (29). It is possible that lipofilic perfluocarbon emulsion particles act as transporters of α-tocopherol molecules to erythrocytes. The direct antioxidant activity and membrane stabilizing effect of α-tocopherol, the ability of FC-43 emulsion to improve microcirculation and oxygen delivery to tissues and to suppress free radical overproduction, might contribute to this effect.

We might conclude that thermal skin injury in rats leads to α-tocopherol deficiency, enhanced peroxidative membrane damage and reduced deformability of red blood cells. The combined application of α-tocopherol and FC-43 perfluorocarbon emulsion immediately after thermal skin injury suppresses free-radical mediated alteration of erythrocytes and improves their deformability and could be a novel approach in the therapy of patients in the early postburn period.

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THE TISSUE ADHESIVE INDERMIL AND ITS USE IN SURGERY

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There are agents in nature able to make bodies stick together by very strong attraction and it is the business of experimental philosophy to find them out. Sir Isaac Newton, 1718

SUMMARY

Indermil, in relation to the tissue adhesives described remains the state of the art with regard to function and clinical outcome. The advantage of an inventory sterile tissue adhesive that is to say one that is in the clinic or operating theatre ready for immediate use on demand is the requirement of modern surgical practice. Cost factors are also an important consideration in today's environment. A research study by the Department of Health Economics at the University of York found the cost of the Indermil tissue adhesive system equivalent to absorbable sutures and produced projected savings per patient in relation to conventional sutures with respect to theatre time and return patients' visits (6). In parallel a survey of patients showed 90% would prefer wound closure by an adhesive in relation to traditional sutures.

There are few areas of surgical practice which cannot find some application for tissue adhesives. The growing international interest in adhesives and their application would confirm their importance and potential in surgery.

ZUSAMMENFASSUNG

Gewebs-adhesivum Indermil und seine Anwendung in der chirurgischen Praxis

Alan C. Roberts

In der Gruppe ist das geschriebene Gewebs-adhesivum besonders gut geeignet wegen seiner guten klinischen und funktionellen Wirkungen. Die Vorteile dises Mittels, welches an der Klinik oder im Operation-saal stets zur Verfügung steht ist unbenigt notwendig für die moderne chirurgische Praxis. In der heutigen Zeit müssen auch die Preise in Erwänung gezogen werden. Die Studien an dem Zentrum der Ökonomik der Universität in York zeigten, dass der Preis den Adhesivum Indermil den Preisen der anderen bei Suturen angewandten Erzeugnissen gleicht. Dabei bringt es für den Patienten weitere Vorteile sowohl was die Dauer der Operation wie auch die nachvolgenden Kontrollbesuche des Patienten anbetrifft. Gegenwärtig möchten 90% der Patienten der Sutur der Wunde mit dem Adhesivum vor anderen traditionellen Mitteln bevorziehen.

In der chirurgischen Praxis gibt es nur wenige Gebiete, in der ein Gewebs-adhesivum nicht zur Anwendung gelangen könnte. Die ständige Vergrössung das internationalen Interesses für die Anwendung der Adhesiva bestätigt ihre Wichtigkeit und Potential für die Chirurgie.

Key words: tissue adhesives, Indermil, surgery

The practical importance of being able to make things bond together is appreciated by almost everyone. From the engineer needing to join parts during construction processes or the carpenter needing to place together panels in a piece of furniture.

Adhesives have in fact become increasingly part of our working environment and a wide range are now available for industrial uses.

Adhesive technology has in many ways outpaced adhesion science in recent years. The ground rules for industrial adhesives are well established and meet our current needs.

There is however an area of immense application and need where adhesion is a particular object of desire but where the ground rules are almost impossible to obey and where industrial adhesives are non-starters. That is the application of adhesives in surgery.

Over a period of several centuries the union and closure of human tissue has been achieved by means of needle and thread. Many types of suture materials have been employed with varying success. Primarily there have been natural products such as cotton wood-fibre, linen and animal sinews.

In modern surgical science synthetic materials such as nylon and dacron have gained importance. The culture and convention of wound closure by suturing have been therefore the standard method for generations of surgeons and clinicians. However the past twenty-five years have

seen surgeons become increasingly interested in replacing and augmenting conventional sutures by means of adhesive bonds (1)

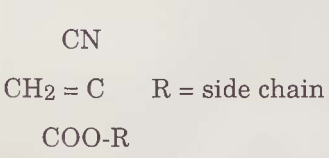
There are several reasons for this clinical interest:

1. The potential rapidity with which tissue union can be achieved.
2. The ability of a bonding substrate to effect complete tissue closure, thus preventing seepage of body fluids.
3. The advantage of forming bonds without deformation of the tissue.
4. The possibility for improvement in the repair of tissue affected by age and disease where suture methods are difficult.
5. The ability to effect tissue closure in inaccessible areas of the body.
6. To reduce infection.

A further point is that conventional suture of facial skin can cause the „Zipper effect" (due to the needle puncture pattern on either side of the wound) with the consequential poor aesthetic results. This effect is absent when adhesive closure is used and is of obvious value in facial surgery.

Chemistry

Indermil Tissue Adhesive is the result of a novel formulation of a homologous series of liquid monomers termed cyanoacrylates which polymerise when applied to a moist tissue surface and have the ability to bond human tissues together. The alkyl 2-cyanoacrylates were first recognised to have adhesive properties by Coover et al. in 1959. The cyanoacrylates have the general formula:



The number of alkyl groups in the side chain may be increased from one (methyl cyanoacrylate) up to any number but usually no further than eight (octyl cyanoacrylate) providing a series of adhesive compounds.

Cyanoacrylate adhesives differ physicially to meet the defined application. The main distinguishing feature between the esters is the size of the molecule.

Methyl, the original cyanoacrylate ester is the smallest. A large number of molecules from adhesives with this ester can be applied over a given area. Consequently a larger number of polymer chains can be formed resulting in bonds with high tensile strength. Methyl cyanoacrylate adhesives are by formulation recommended for rigid structures.

The **Ethyl** ester is slightly larger than the methyl, although adhesive properties are very similar. However, because of their larger size the number of molecules per given area is less than that for methyl adhesives. This results in a less rigid adhesive and is used for bonding polymers.

The **Butyl** ester is considerably larger than the methyl or ethyl ester. Because of this butyl cyanoacrylate adhesive when compared with methyl and ethyl based adhesives are slower curing, relatively weaker and less volatile. Whilst a slower cure speed has obvious advantages to some surgical applications such as an alignment of bone and soft tissue, it is its low volatility which gives butyl cyanoacrylate adhesive its main advantage.

The larger molecule is less volatile than the other two esters. A particular feature of this ester is that „blooming" is eliminated. Blooming is the term describing a white stain on the bond line caused by the rapid condensation of cyanocrylate vapours. This is of importance in surgical procedures.

Indermil is formulated from butyl ester and provides a novel range of mechanisms which meet the needs of wound closure. In keeping with cyanoacrylate adhesive chemistry Indermil polymerises due to reaction with moisture on the surface of the tissue to be bonded.

Surface Phenomena

Indermil is maintained in a liquid state by an acidic stabiliser which has the action of inhibiting the molecules from cross linking. This phenomena is of considerable advantage to surgery.

Partly ionised molecules of water normally found on all surfaces exposed to the atmosphere have the action of neutralising the inhibitor. On the surface of human skin the normal exodate can be as much as 700ml. When Indermil is applied to the tissue surface the inhibitor is eliminated and the chemical action allows the molecule to join and polymerisation is completed in some 10 seconds. The polymerisation of Indermil is effected by phenomena which relate to good practice. Good tissue approximation will complement the results achieved and in areas of fine closure minimal amounts of adhesive will achieve maximum results which is the reason for the Indermil precision applicator for operating theatre use. The adhesion mechanism of Indermil is achieved by attraction between molecules both adhesive and skin surfaces. The adhesive strength is in relation to the approximation of the molecules attracted to each other. A physical locking is also a factor by virtue of the penetration of the adhesive into the irregularities of the tissue surface. Therefore Indermil penetrates into the interstices of the tissue resulting in immobilisation or ligation by polymerisation. Bond strength responds to tissue morphology and the preparation of the interface i.e. approximation. Provided that the wound site is not under excessive tension Indermil will function in comparison to conventional sutures. In a tension site it may require a supporting suture with Indermil forming the principle bond. Indermil also can be used

as a suture seal and clear dressing resulting in reduced infection rates and valuable saving in wound dressing time and reduced hospital episodes.

Clinical Properties

Indermil has been found to act as a fast and effective haemostatic agent. Slow bleeding over a surface area can be a problem in surgery. Indermil has proved a useful topical haemostatic agent. The role of cyanoacrylate in the Vietnam was in the form of propellant sprays is credited as a life saving agent in first line treatment of critically wounded servicemen with severe haemorrhage and soft tissue damage.

The mechanism by which Indermil achieves haemostasis is still a matter for laboratory conjecture at the present time. The hypothesis is that the ester forms a macrofilm causing mechanical blockage to slow blood flow providing a surface agent to activate the clotting cascade. There is evidence that the film forms a porous mass which becomes invaded with blood with subsequent clotting within the pores of the adhesive.

Patients report a mild anaesthetic effect with the use of Indermil. Again, the film phenomena described may cause nerve ending occlusion resulting in reduced pain. A number of surgical procedures completed with Indermil and without a surface anaesthetic have been completed in hand and facial surgery.

Indermil is biodegradable and its rate of removal from the application site is by polymer degradation and surface sloughing. Research indicated that the rates of degradation **in vitro** are analogous to the **in vivo** results. The rate of degradation in relation to cyanoacrylate monomers indicate that methyl ester degrades much faster than other esters and the rate is reduced for higher groups of the series. As the homologous series is ascended the inflammatory responses in tissue are decreased. Butyl derivative and higher homologs are well tolerated by soft tissue comparing well with sutures. The conclusion from data (3) is that length of the alkyl chain determines the toxicity rate with methyl ester being most toxic hence its industrial intention and butyl being the tissue acceptable ester for medical application.

Indermil in its present form is presented as a topical solution of low viscosity in a polyethylene bottle and is gamma radiation sterile. Two kits are available. The clinic kit is presented within a sealed foil pouch before being terminally sterilised by gamma radiation. The kit is intended for clinic and field use with particular reference to accident and emergency. Military and veterinary application are also applicable to this Indermil pack. Disposable cannula are included in the sterile pack. These are located on the bottle to enable Indermil to be placed on the surgical site.

The Indermil Theatre kit is as the name describes intended for operating theatre procedures. The foil pack of Indermil is again a sterile sealed unit terminally sterilised by gamma radiation. Each pack contains the adhesives and supporting items for connection to the Indermil precision applicator unit. This smart system provides the surgeon with precision control in the delivery of the adhesive to the surgical site. The unit will at the programme selection of the surgeon dispense metered volumes of Indermil through a range of drop size from large medium and small to continuous flow. This range of application gives the surgeon total control. A foot switch provides a simple means of transmitting the selected volume via a silicone tube to a cannula ended handpiece.

This precision unit will provide a wide range of procedures to be attempted that have previously been impossible or difficult to complete.

Many fields of surgery have areas which are difficult to access for tissue closure. The precision applicator can be used to exploit remote sites via its flexible cannula. The new field of minimal invasive surgery (4, 5) will benefit from a precision delivery system in its continuing development.

Alternative Adhesives

The current status of alternative tissue adhesives to Indermil have presented various problems both biological and technological.

Fibrin tissue adhesives have been used in surgery since 1909; the bond strength of Fibrin adhesives are minimal and have more tack than adhesion. Commercial exploitation of pooled blood products have found restrictions due to possible HIV infection transmission hazards. The potential risk of human pooled blood base adhesive has therefore immense limitations. It is possible to produce Autologuos Fibrin in the operating theatre using the patient's own blood.

Autologuos Fibrin tissue adhesive (AFTA) has the disadvantage that the procedure is complex, time consuming and only limited amounts can be produced. Again although this process has the benefit of the patient's own infection free blood, the bond strength in comparison to liquid suture such as Indermil is minimal.

Attempts have been made to exploit the biohesive properties of mussels and similar marine organisms noted for their tenacious adherence to underwater surfaces. An active agent in this phenomenon is an unusual polyphenolic protein.

This polyphenolic protein is secreted by the mussels phenol gland and combines with other protein to form an adhesive disc at the attachment site. Research attempts to develop a surgical adhesive from mussel polyphenolic protein have been difficult and disappointing. The problem of isolation useful amounts of protein from mussels has shown that some 100,000 mussels must be extracted to yield just one gram of protein. Synthetic proteins have been produced but

as yet do not have the required adhesive properties.

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SOUHRNY

Mikrochirurgické rekonstrukce při léčení onkologických onemocnění hlavy a krku

J. Veselý, J. Kučera, J. Hrbatý, J. Dražan, M. Malantová, O. Bulik, E. Mannino

Na 37 onkologických pacientech s potřebou rozsáhlé resekce tváře, maxily nebo mandibuly či kalvy byly uplatněny mikrochirurgické rekonstrukce, ve 27 případech primárně v době resekce, v 10 případech odloženě nebo sekundárně. Bylo použito 49 laloků. V pěti případech byly užity 2 laloky v jednodobé rekonstrukci, a to k rekonstrukci mandibuly a tváře a bukální a faciální strany tváře. Při operacích je dávána přednost multidisciplinárnímu přístupu v operačním týmu maxilofaciálního chirurga, otorinolaryngologa a plastického chirurga.

Řešení defektu maxily po resekci karcinomu

J. Veselý, J. Hložek, B. Krejčová, V. Smrčka, E. Mannino

V souboru 37 onkologických pacientů v oblasti hlavy a krku s potřebou rozsáhlé resekce tváře, maxily nebo mandibuly či kalvy bylo 5 pacientů s typickým defektem po resekci části maxily včetně poloviny patra a s exenterací orbity. Tento rozsáhlý defekt je diskomfortem pro pacienta i okolí jak funkčním s postižením mluvy, tak i estetickým.

Jako uspokojivé řešení při rekonstrukci maxily bez potřeby náhrady skeletu se osvědčil mikrochirurgický přenos úzkého laloku latissimus dorsi s obvykle 2 kožními ostrovy - jedním pro uzávěr patra a druhým pro uzávěr orbity a tváře.

Funkční a estetický následek na předloktí po odběru čínského laloku

C. Bravo, L. Dražan, E. Mannino

U 40 pacientů operovaných na klinice plastické a estetické chirurgie v Brně v letech 1989 - 1994 jsme hodnotili místo po odběru čínského laloku. Zjistili jsme:

1) funkce ruky není významně alterována po odběru laloku, v naší studii uvedlo 11 pacientů (27,5 %), že mají některá omezení nebo zhoršení funkce ruky,

2) tolerance k deformaci předloktí je značná, ale závisí na stupni defektu, pro který je lalok přemísťován, 25 pacientů (62,5 %) by rádo volilo jiný lalok,

3) je nezbytné se zamyslet nad estetickými důsledky čínského laloku a zvážit jiné možnosti ve výběru laloku.

Sekundární defekt může být pro pacienta problém ještě mnoho let po operaci

Úvahy a pozorování týkající se prevence neuromů

J. Šmahel

Spolehlivá prevence neuromu je problém, jehož řešení je stále nedokončené. Ve srovnání s dřívějšími metodami, které se většinou skládají z pokusu ostře zabránit anoxální proliferaci, je nyní všeobecně přijímáno, že obnova potence axonů musí být omezena postupně. Zvažovány jsou metody ve shodě s následujícím postupem - centrocentrální anastomóza a překrytí konce nervu nervovým nebo venózním štěpem, včetně osobního pozorování. Nová varianta, která se osvědčila v pokusech na zvířatech, se skládá z užití kombinace nervového a venózního štěpu. Tato metoda potřebuje klinické ověření.

Kombinovaná aplikace alfa-tocopherolu a FC-43 perfluorokarbonové emulze potlačuje časnou popáleninovou lipidovou peroxidaci a zlepšuje deformaci erytrocytů.

G. Bekyarova, T. Yankova, I. Kozarev

Efekt emulze FC-43 perfluorokarbonu a alfa-tocopherolu na lipidové peroxidativní poškození a deformaci erytrocytů bylo hodnoceno u krys s popálením celé tloušťky kůže na 15 až 20 % povrchu těla ve třetí hodině po popálení. Zvířata byla rozdělena do pěti skupin: (1) nepopálená, neléčená (kontrola); (2) popálená, neléčená; (3) popálená a léčená alfa-tocopherolem („Serva" Germany, 20 mg/kg b.m.i.p.); (4) popálená a léčená emulzí FC-43 („Freen Cross. Corp." Japan, 5 ml/kg, i.v.); (5) popálená, léčená kombinací alfa-tocopherolu (20mg/kg) a emulzí FC-43 perfluorokarbonu (5 ml/kg). V popálené neléčené skupině se snižuje koncentrace alfa-tocopherolu o 38 % ($p < 0,05$), hladiny malonyl-dialdehydu (MDA) a škodlivých fluoroscentních produktů se zdvihají o 32 % ($p < 0,001$) a o 52 % ($p < 0,001$) u kontrol, respektive tam, kde deformace červených krevních buněk byla zmenšena o 34 % ($p < 0,001$). Jak hromadění MDA a fluoroscentních lipidových peroxidativních produktů, tak snížení deformace postižených buněk bylo signifikantně posíleno léčbou alfa-tocopherolem, která také pre-

ventivně brání snižování obsahu alfa-tocopherolu v erytrocytech. FC-43 emulze snižuje hladinu MDA, ale významně nezabrání redukci deformace erytrocytů. Kombinovaná aplikace alfa-tocopherolu a emulze FC-43 bezprostředně po tepelném poranění kůže snižuje peroxidativní membránové poškození a zlepšuje deformaci erytrocytů, a to významněji než alfa-tocopherol ve třetí hodině po tepelném poranění kůže.

Tkáňové adhesivum Indermil a jeho použití v chirurgii
Allan C. Roberts

Ve skupině popsaných tkáňových adhesiv je Indermil obecně používán s ohledem na funkci a klinické výsledky. Výhoda skladovaného sterilního tkáňového adhesiva, které by bylo na požádání okamžitě k dispozici na klinice nebo operačním sálu, je požadavkem moderní chirurgické praxe. V dnešní době je důležité brát v úvahu i faktory cenové. Výzkumná studie provedená na Ústavu zdravotnické ekonomie Univerzity v Yorku prokázala, že cena adhesivního systému Indermil je ekvivalentní s absorbovatelným šicím materiálem a přináší u nemocného další úspory ve srovnání s konvenčními materiály vzhledem k době na operačním sálu a k opakovaným návštěvám pacienta. Při současném sledování by dalo 90 % nemocných přednost uzávěru rány adhesivem před tradičními materiály.

V chirurgické praxi je málo oblastí, kde by se nenašly nějaké aplikace pro tkáňová adhesiva. Zvětšující se mezinárodní zájem o adhesiva a jejich aplikace potvrzuje jejich důležitost a potenciál v chirurgii.

BOOK REVIEW

NASAL NEOPLASIA

Dennis H. Kraus, Howard L. Levine
Thieme 1997, New York - Stuttgart

The monograph belongs into the series of publications devoted to the problem of rhinology and sinusology published by Thieme Verlag.

During the last twenty years revolutionary advances were made in diagnosis and possible therapeutic approaches in many medical disciplines. The development of CT, MRI, the possibility of 3/D imaging permit accurate visualisation, assessment of the size of a tumour and its relationship with adjacent structures. Concurrently with diagnostic possibilities developed also progressive advances of firm and flexible endoscopic instruments for further extension of diagnostic possibilities and the development of new therapeutic procedures.These technical advances had also a significant impact on the treatment of tumours of the nose and paranasal sinuses. The monograph deals with present knowledge of the treatment of nasal neoplasms, as implemented in different major centres in the USA. Pathological units which develop at this anatomical site are analyzed in detail in the chapter on pathology. These findings are supplemented by adequate information on the clinical development and a very detailed chapter on X - ray examination.

The authors emphasize the necessity of reconstruction of defects and rehabilitation procedures in the chapters on reconstructive surgery and maxillo-facial prosthetics. The purpose is to restore shape and function and to improve the quality of life. The part played by a multidisciplinary approach in patients with advanced tumours is emphasized in the chapter on radiation treatment and chemotherapy. A very instructive and comprehensive account is presented in chapter five devoted to juvenile angiofibroma. Also the chapter dealing with the surgery of the orbit is very detailed and supplemented by diagrams. In the chapter devoted to surgery of the anterior cranial fossa a due part deals with reconstruction by means of a pericranial flap. Plastic surgeons will be interested in the chapter on skin tumours of the nose which mentions all therapeutic methods used and briefly also principles of reconstruction.

The monograph has 276 pages, every chapter is supplemented by a list of references, incl. very recent ones. Twenty-four authors from different departments in the USA participated in the preparation of the book. The publication is supplemented by 137 photographs, X-ray pictures and microscopic findings and several summarizing tables. It will be found useful and helpful not only by residents and ENT specialists but also by surgeons, maxillo-facial and plastic surgeons.

J. Kozák

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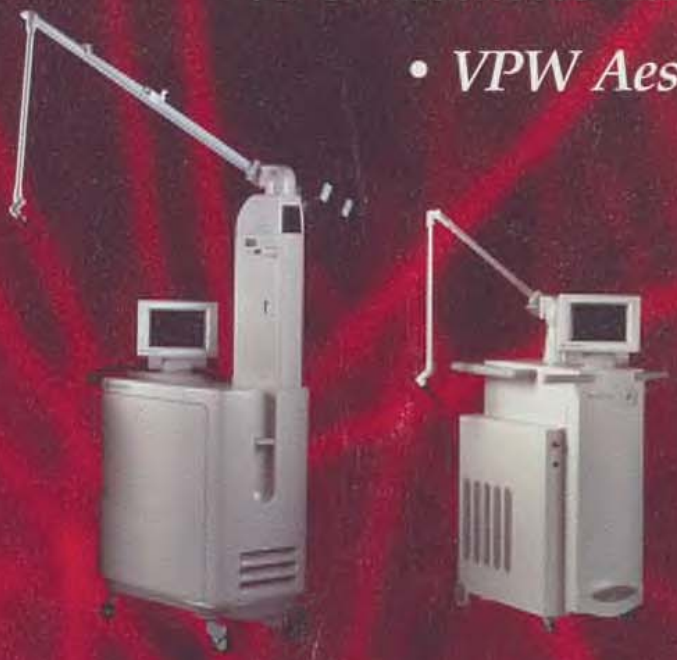

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