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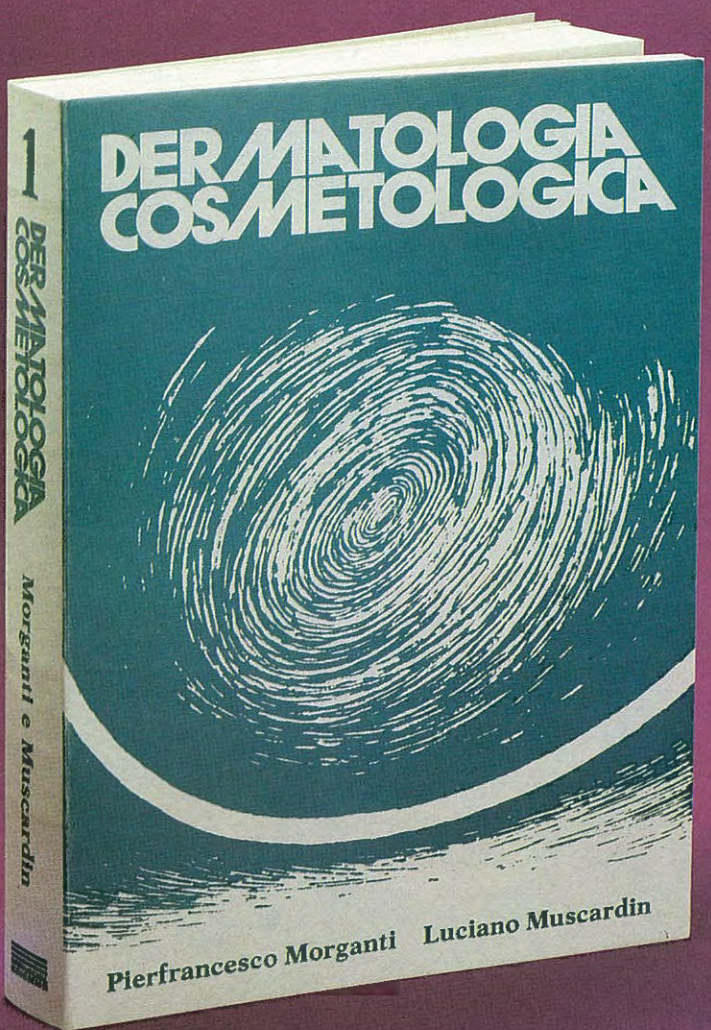

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DERMATOLOGIA COSMETOLOGICA

A cura di P. Morganti e L. Muscardin
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Trimestrale di Dermatologia Cosmetologica
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J. Appl. Cosmetol. 11, 107-112 (October-December1993)

NORMALIZING EFFECT OF GAMMA-LINOLENIC ACID ON ETRETINATE-INDUCED HYPERTRIGLY-CERIDEMIA IN PSORIATIC PATIENTS: PRELIMINARY RESULTS.

G.Vignati, C.Zaccone, G.P.Vignoli, G.Rabbiosi and G.Borroni
Dept. of Human and Hereditary Pathology, Institute of Dermatology CCS Policlinico "S. Matteo", P.le Golgi 2, Pavia

Receveid: *December 12, 1993.Presented at the "68° Congresso Nazionale SIDEV" Pisa, June 23-26, 1993*

Key Words: *Psoriasis; Etretinate; Gamma-linolenic acid; Hypertriglyceridemia.*

Synopsis

Retinoids are a group of synthesis compounds having vitamin A as their precursor. Among retinoids, etretinate is commonly used, alone or in combination with PUVA (8-methoxypsoralen+UVA), for diffuse and resistant psoriasis. However, eretrinate may induce local (severe skin dryness, flaking, cheilitis and fissures) and systemic side-effects. Among the systemic side-effects of etretinate, increased triglycerides, VLDLs, and cholesterol are frequently detected, which may cause treatment discontinuation. In the present paper 41 psoriatic patients undergoing Re-PUVA (Etretinate+PUVA) were considered. One month after the beginning of the therapy, 27 of them were additionally treated with gamma-linolenic acid, because of the dryness and itch induced by etretinate. During Re-PUVA treatment 11 out of these 27 patients showed increased triglyceride and cholesterol levels. A 2 month-treatment with gamma-linolenic acid induced an improvement of the cutaneous side-effects of eretrinate. Moreover, a statistically significant decrease of triglyceridemia ($p<0.01$) and cholesterolemia ($p<0.01$) was detected following the treatment with gamma-linolenic acid. These results demonstrate that association of gamma-linolenic acid is useful in contolling dyslipidemia if Re-PUVA treatment has to be continued to achieve clearing of psoriasis.

Riassunto

I retinoidi sono una famiglia di composti di sintesi che hanno il loro precursore nella Vit. A. I più diffusi in ambito terapeutico dermatologico sono l'etretinato, l'isotretinoina e l'acitretina. Questi farmaci agiscono promuovendo la differenziazione cheratinocitaria ed esercitano un effetto immunomodulatore. In particolare, l'etretinato trova indicazione, da solo o in associazione con PUVA-terapia (8-metossipsoralene+UVA), nel trattamento delle forme più estese e resistenti di psoriasi. L'etretinato, tuttavia, può indurre effetti collaterali sia locali (secchezza cutanea marcata, desquamazione, cheilite e ragadi) che generali. Tra gli effetti sistemici collaterali che l'etretrinato può indurre si rileva più frequentemente un innalzamento dei trigliceridi, delle VLDL e del colesterolo che possono indurre a sospendere la terapia prima del conseguimento di una risposta clinica soddisfacente. Nel presente lavoro vengono riportati i dati relativi al contollo dell' iperlipemia indotta da etretinato me-

diante l'impiego di acido gamma-linolenico per via generale. Tale acido grasso essenziale è stato impiegato in epoca recente per il controllo del prurito e della secchezza cutanea nei soggetti affetti da dermatite atopica; per questo motivo abbiamo ritenuto di utilizzarlo (480 mg/os/die) in un gruppo di 27 pazienti psoriasici che, in corso di trattamento con Etretinato (Etretinato 0,5 mg/Kg/os/die)+PUVA (Re-PUVA), avevano manifestato marcata secchezza cutanea e prurito, imputabili al retinoide. Ad un mese dall'inizio della terapia, 11 dei 27 pazienti affetti da secchezza cutanea e prurito avevano presentato anche anomalie del quadro lipidico, imputabili al trattamento con etretinato. Il trattamento con acido gamma-linolenico per 2 mesi, oltre a determinare un miglioramento degli effetti collaterali cutanei, ha indotto anche una riduzione statisticamente significativa della trigliceridemia ($p<0,01$) e della colesterolemia ($p<0,01$). Pertanto anche se gli innalzamenti di colesterolo e trigliceridi nella nostra casistica sono risultati, durante al terapia con etretinato, di moderata entità, l'utilizzo di acido gamma-linolenico ci ha permesso di continuare la terapia Re-PUVA con una certa sicurezza per il paziente. Come noto, infatti, la popolazione psoriasica risulta esposta ad un aumentato rischio di accidenti cardiovascolari, in associazione a diabete ed obesità, e l'ipertrigliceridemia iatrogena costituirebbe quindi un ulteriore fattore di rischio.

INTRODUCTION

Retinoids are a family of synthesis compounds having vitamin A as their precursor (1,2).
Among retinoids, etretinate (3,4), isotretinoin (5) and acitretin (6) are most commonly used in dermatologic treatment.
These drugs act on the keratinization process by enhancing the differentiation of keratinocytes and inhibiting their proliferation. In addition, they influence the immunomodule killer lymphocytes (7) and neutrophils (8) (chemotaxis reduction). The main field of use of retinoids includes psoriasis, some skin T-lymphomas, and other diseases characterized by keratinization changes, such as ichthyosis, Darier's disease, palmoplantar keratodermas, and acne cystica and conglobata.
Specifically, etretinate is recommended for diffuse and resistant psoriasis, and is used alone or in combination with PUVA or topical drugs (9). However, etretinate may produce systemic and local side-effects (severe skin dryness, flaking, cheilitis, and fissures). Among the possible systemic side-effects of etretinate, increased triglycerides, VLDLs, and cholesterol are most frequently detected (10,11,12). As a result, treatment must be discontinued before a satisfying clinical response is obtained.
This paper deals with data on the response of etretinate induced hyperlipemia to the systemic administration of gamma linolenic acid. This essential fatty acid was used in a group of patients treated with etretinate+PUVA (Re-PUVA) to reduce skin dryness due to etretinate.

MATERIALS AND METHODS

A group of 41 male patients with diffuse psoriasis was treated with Re-PUVA (Etretinate* 0.5 mg/kg/ orally given daily in combination with 8-methoxypsolaren (**) 0.6 mg/kg orally given three times a week.

Before treatment, all patients had normal hematochemical values, specifically for serum lipids (cholesterol < 200 mg/dl, triglycerides < 150 mg/dl). During treatment, 27 patients developed severe skin dryness and itching.
A further hematochemical examination, performed a month after the beginning of treatment, detected hypertriglyceridemia and hypercholesterolemia due to etretinate treatment in 19 patients. Specifically, 11 patients out of 27 with skin dryness and itching also showed lipid imbalance.
The maximun peaks for cholesterol and triglycerides were, respectively, 348 mg/dl and 322 mg/dl, while they exceeded 210 mg/dl and 150 mg/dl in all other patients (Tables 1 and 2).
Re-PUVA treatment had to be continued due to persistent psoriatic lesions. In order to control skin dryness and itching induced by etretinate, patients were orally given gamma linolenic acid (***) (480 mg/daily), which had been already used to control skin dryness and pruritus in Atopic Dermatitis. Gamma-linolenic acid 480 mg were orally used daily for at least two months in the patients considered.

(*) Tigason®, Roche
(**) Oxsoralen®, Lifepharma
(***) Efagel®, Mavi

RESULTS

Gamma linolenic acid proved effective in controlling skin dryness and itching in 15 patients out of 27. The statistical analysis of data revealed a statistically significant increase both in cholesterolemia ($p < 0.01$) and triglyceridemia ($p<0.01$) after a one-month treatment with etretinate (Table 3). An hematochemical examination, performed about three months after beginning of Re-PUVA and about 60 days after the beginning of treatment with gamma linolenic acid, revealed a decrease in cholesterolemia and triglyceridemia in 7 out of 11 patients (Tables 1 and 2). The overall analysis showed a statisti-

Table I.

BLOOD CHOLESTEROL CHANGES IN PSORIATIC PATIENTS AFTER TREATMENT WITH ETRETINATE AND AFTER ADMINISTRATION OF GAMMA LINOLENIC ACID (ANALYSIS DATA, MG/DL).

PATIENTS	BASIC LEVEL	AFTER ETRETINATE	AFTER ETRETINATE PLUS GAMMA-LINOLENIC ACID
1) F.F. 58ys	200	348	288
2) M.A.45ys	195	251	184
3) P.A. 25ys	185	221	190
4) C.A. 55ys	190	271	188
5) C.G. 44ys	190	292	280
6) R.G. 28ys	179	225	190
7) P.P. 58ys	200	295	245
8) S.G. 36ys	187	267	281
9) P.A. 59ys	182	232	185
10) G.V. 36ys	190	228	178
11) C.Z. 37ys	197	275	195

Table II.

TRIGLYCERIDEMIA CHANGES IN PSORIATIC PATIENTS AFTER TREATMENT WITH ETRETINATE AND AFTER ADMINISTRATION OF GAMMA LINOLENIC ACID (ANALYSIS DATA, MG/DL).

PATIENTS	BASIC LEVEL	AFTER ETRETINATE	AFTER ETRETINATE PLUS GAMMA-LINOLENIC ACID
1) F.F. 58ys	138	310	165
2) M.A.45ys	130	192	133
3) P.A. 25ys	135	322	145
4) C.A. 55ys	125	220	140
5) C.G. 44ys	132	195	189
6) R.G. 28ys	98	187	135
7) P.P. 58ys	145	195	175
8) S.G. 36ys	130	173	180
9) P.A. 59ys	100	196	139
10) G.V. 36ys	135	199	135
11) C.Z. 37ys	136	179	132

cally significant decrease in triglycerides ($p<0.01$), which had nearly returned to their normal level (Table 3). Cholesterolemia still exceeded its basic level ($p<0.02$), even though it was considerably lower than its average level measured after a one-month treatment with etretinate and before treatment with gamma linolenic acid ($p<0.01$) (Table 3).

(19). In addition, they are known as being able to play immunomodulating role on several cell populations (macrophages, langerhans cells, neutrophils, eosinophils, circulating lymphocytes), also by normalising the production of some cytokines (IL-2, leukocyte migration inhibition factor) (20,21). The increase in cholesterol and triglyceride levels is one of the side effects of

Table III.

CHANGES IN SERUM LIPID LEVELS (MG/DL) AFTER TREATMENT WITH ETRETINATE AND WITH ETRETINATE PLUS GAMMA LINOLENIC ACID..

	CHOLESTEROL	TRIGLYCERIDES
Basic level	190,45+7	127,64+15,05
After etretinate	264,09+38,52*	215,27+52,27*
After gamma linolenic acid	218,54+45,03	151,64+21,33

* $p<0.01$ increase after 30 days of etretinate compared to both the basic and final levels

DISCUSSION

All retinoids in general, and, specifically, etretinate are able to modulate keratinocyte growth and differentiation (14).

Retinoids are regarded being able to perform such regulatory functions by changing the genomic expression of target cells (15). They may exert an influence on the ribonucleic acid, which promote changes in the expression of specific proteins (16).

However, their effects on keratinocyte growth and differentiation do not seem to depend on a modified binding with EGF (17). Furthermore, auto radiographic investigations sbowed that, in psoriatic patients, etretinate causes a reduced incorporation of tritiated thymidine and an enhancement of DNA synthesis time in keratinocytes (18).

On clinical ground, this turns into a marked decrease in keratin production. Retinoids are thought to exert an anti-inflammatory effect and to influence the metabolism of arachidonic acid the systemic administration of retinoids, and of etretinate in particular.

Usually, the increased lipid level is persistent during the entire period of treatment with etretinate. Lipide are expected to return to their basic level 4-8 weeks after treatment is discontinued (22).

Studies on lipoprotein fractions during etretinate treatment may show an increase in both triglycerides and their VLDL fraction in some patients. As regards the changes in cholesterol during etretinate treatment, evidence is obtained of an increase first in the VLDL and then in the LDL fraction. Also, it should be taken into account that HDL cholesterol decreases slightly after treatment with etretinate, and with isotretinoin combined with acitretin. The above-mentioned changes in lipid levels due to etretinate may result from the following:

1) Increased VLDL synthesis or reduced catabolism of VLDL into intermediate and low density lipoproteins (23, 24).

2) Increased synthesis of these lipoproteins, as

occurs in diabetes hyperlipemia and familial hypertriglyceridemia. This hypothesis is also supported by the knowledge of the hypolipidemic effects of the eicosapentaenoic acid (omega-3 fatty acid) on retinoid-induced hypertriglyceridemia (25, 26).

Gamma linolenic acid (omega-6 fatty acid contained in borage oil) may be assumed to cause a considerable decrease in triglycerides (and in cholesterol) in psoriatic patients treated with etreninate, through the inhibition of VLDL production by the liver.

Despite, cholesterol and triglyceride slight increase during etretinate treatment, in the cases under consideration, Re-PUVA treatment was safely continued by using gamma linolenic acid. As is known, psoriatic patients are more exposed to cardiovascular disorders associated with diabetes and obesity (27-29). Further investigations are needed to elucidate these preleminary results through a more detailed analysis of the lipid metabolism of psoriatic patients treated with Re-PUVA and gamma linolenic acid.

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ORAL ADMINISTRATION OF BORAGO OIL IN ATOPIC DERMATITIS

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Key Words: *Gamma-linolenic acid; Borago oil; Atopic dermatitis; Skin dryness.*

Synopsis

Borago, evening primrose, and blackcurrant oils are all well known for their richness in gamma-linolenic acid (G.L.A.), but borago oil is characterized by the highest G.L.A. content of all, up to 25%.
Normally, dietary linoleic acid is converted to G.L.A. by the enzyme delta-6-desaturase and the following biological pathway leads to synthesis of eicosanoids and prostaglandins.
A defect in the function of delta-6-desaturase has been observed in atopic dermatitis and G.L.A. has been reported of value in the treatment of this disease.
A borago oil oral supplementation in a group of 24 atopic dermatitis patients improved their clinical conditions after 4-8 weeks, with significant reduction in inflammation, dryness, scaliness and itch and without side effects.

Riassunto

L'olio di semi di borragine, quello di enagra e quello di ribes nero sono noti per il loro alto contenuto in acido gamma-linolenico (A.G.L.), ma tra tutti il più ricco è l'olio di borragine che ne contiene fino al 25%.
Nel soggetto sano, l'acido linolenico assunto con la dieta è convertito dall'enzima delta-6-desaturasi in A.G.L., che rappresenta un passaggio chiave nella sequenza metabolica che porta alla sintesi finale di eicosanoidi e prostaglandine.
Numerose osservazioni sperimentali suggeriscono che una carenza di delta-6-desaturasi e di acidi grassi essenziali svolga un ruolo patogenico nella dermatite atopica e che l'A.G.L. possa essere utile nel trattamento di tale malattia.
Uno studio controllato condotto in 24 pazienti affetti da dermatite atopica ha permesso di dimostrare che una dieta arricchita di A.G.L. per somministrazione giornaliera di 2 g di olio di borragine è in grado di migliorare in 4-8 settimane le condizioni cliniche dei pazienti, con effetti particolarmente evidenti sul prurito nonchè su congestione, xerosi e desquamazione della cute.
Non sono stati osservati effetti collaterali indesiderati.

Normally, dietary linoleic acid is converted by the enzyme delta-6-desaturase to gamma-linolenic acid (G.L.A.), a key intermediate essential fatty acid in the biological pathway leading to synthesis of eicosanoids and prostaglandins PGE1 and PGE2.
This desaturation may be inhibited by several clinical conditions such as diabetes, alcoholism, stress etc. with a reduction of G.L.A. formation and risk of pathological consequences (1). The G.L.A. bio-deficiency may be avoided by the dietary intake of G.L.A. from a natural origin. Common dietary fats and oils from vegetable or animal origin are known for not containing this particular essential fatty acid, but several research teams working in Northern America and Europe have selected new seeds containing a good percentage of oils with a high G.L.A. content.
Today, borago, evening primrose, and blackcurrant oils are well known for their richness in G.L.A., but borago oil extracted from mature seeds of Borago Officinalis, is characterized by the highest G.L.A. content of all, up to 18-26% of total fatty acid composition (2) (Table I).

Borago Officinalis, a plant native to West Asia, is distributed in the Mediterranean basin. It has recently been grown commercially in France (with success) and its oil is in widespread use.

Wright and Burton (3), have observed that in patients with atopic dermatitis (A.D.) the plasma levels of G.L.A., dihomogammalinolenic acid (DGLA) and arachidonic acid were lower than in healthy control subjects, whereas the level of cis-linoleic acid was higher. The same difference in the plasma levels of essential fatty acid N=6 with a more consistent variation was described by Strannegard et al. (4) in children affected by A.D.. The AA. also observed a positive correlation between plasmatic high concentration of linoleic acid and serum IgE increase in newborns with a familial anamnestic risk to develope AD.
Moreover, several comparative studies in humans and animals (5,6) demonstrated that a diet deficiency in EFA is followed by several pathological modifications mainly located on the skin.

Cutaneous alterations due to lack of EFA
- Thinned hair or alopecia
- Wrinkled and finely scaling skin
- Eczematic dermatitis similar to AD
- Fragility of superficial vessels
- Slow cicatrization of injuries
- Susceptibility to cutaneous infections
- High trans-cutaneous water loss
- Itching

Table I.

FATTY ACID COMPOSITION FOR MAJOR G.L.A.-RICH OILS

Fatty acid	Borago	Ev.Primrose	Blackcurrant
Palmitic Acid	9-12	5-6	6-7
Stearic Acid	3-4	1-2	1-2
Oleic Acid	15-19	8-12	9-10
Linoleic Acid	34-39	70-79	45-50
Alfa linolenic Acid	0,1-2	0,1-0,4	12-15
Gamma linolenic Acid	18-26	8-12	12-17
Stearidonic Acid	0,1	-	2-4

All these observations suggest a pathogenic role for metabolic alterations in EFA and delta-6-desaturase enzyme in AD and GLA has been reported of value in the treatment of that discase (7).
Good therapeutic results have been reported following oral treatment with evening primrose oil or blackcurrant oil in patients with AD (8,9).

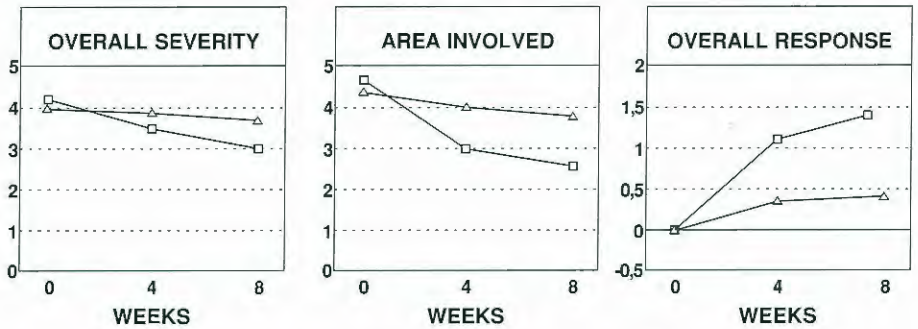
To analyse the effects of borago oil, (the oil with the highest concentration of GLA) in AD, a borago oil oral supplementation was adopted in a group of 24 patients with AD in comparison with placebo.
24 young adults (13 males and 11 females), aged 12-27 years with atopic dermatitis (AD) were studied (Table II). The diagnosis was based on a typical dermatological picture and, in addition, the patients also had a family history of atopy or suffered from atopic respiratory symptoms.
The patients were randomly divided into two groups, 14 patients receiving borago oil and 10 patients receiving placebo, in a double-blind trial. The borago oil was provided in capsules each containing 500 mg of oil (EFAGEL) and 35 mg of lipids, 26% /70 of linoleic acid and 17,6% /70 of GLA. The placebo capsule contained 500 mg of liquid paraffin. Four capsules were taken twice a day for 8 weeks. The patients were instructed to keep diet unchanged during the study period. Only in case of severe skin symptoms a mild topical corticosteroid cream or oral antihistamine was adopted, whereas an emollient cream was at the patient's disposal in unlimited quantities.
The extent and severity of the AD was assessed at the beginning of the trials and every 4 weeks thereafter, always by the same dermatologist. The overall severity of the AD was estimated on a linear scale from 0, no symptoms, to 100, worst possible. In addition, the percentage of the body surface involved was recorded, and the degree of inflammation, dryness and itch graded on a scale of 0, none; 1, mild; 2, moderate, and 3, severe. The overall response to the treatment was estimated on the following scale: -1, worse; 0, no change; 1, improved; 2, much improved; 3, cured.
No patient dropped out of trial and no side-effects due to borago oil were observed.
During the 8-week period, only one patient in the borago oil group consumed about 20 g. of topical not alogenate steroid, whereas in the placebo group the same topical steroid was used by three patients and in 2-3 times larger quantity.
In the borago oil group (Table III), a statistically

Table II.

BASAL FEATURES OF THE TWO GROUPS OF TREATMENT

Basal features		Borago oil	Control	P
Sex	MALE	8	5	n.s.
	FEMALE	6	5	n.s.
Age (years)	MEAN	17.7±5.1	16.1±6.8	n.s.
	RANGE	13-26	12-27	n.s.
Weight (Kg)	MEAN	56.4±15.1	51.3±13.6	n.s.

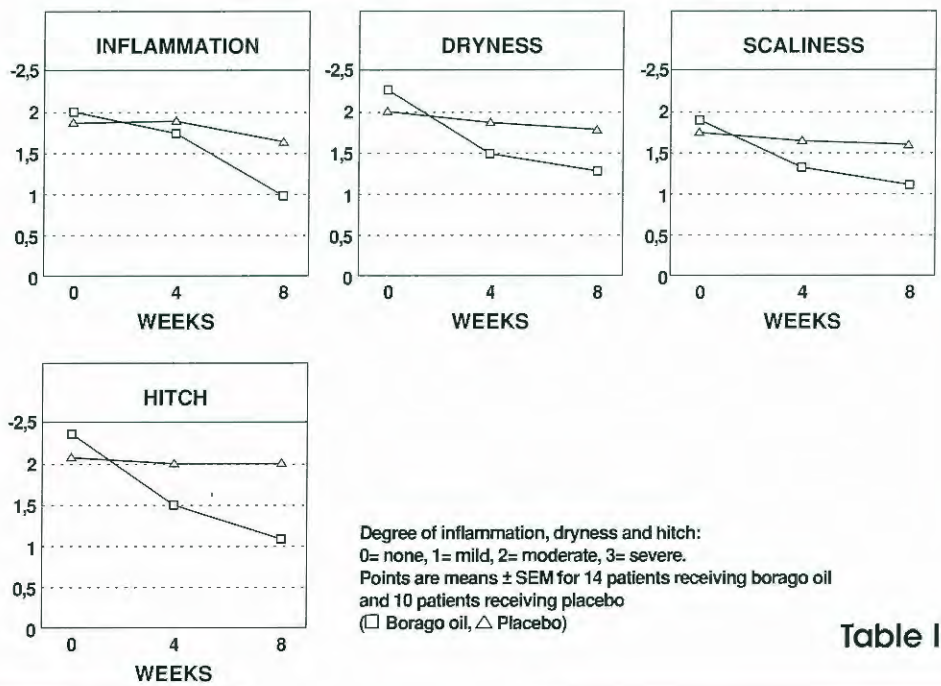
Effects of treatment with oral borago oil or placebo on the clinical status of atopic dermatitis



Overall severity of atopic dermatitis and extent of cutaneous area involved on a linear scale from 0 to 10.
Estimation on overall response to treatment:
-1 = worse, 0 = no change, 1 = improved, 2 = much improved, 3 = cured.
Points are means ± SEM for 14 patients receiving borago oil and 10 patients receiving placebo
(□ Borago oil, △ Placebo)

Table III.

Effects of treatment with oral borago oil or placebo on the different symptoms of atopic dermatitis



Degree of inflammation, dryness and hitch:
0= none, 1= mild, 2= moderate, 3= severe.
Points are means ± SEM for 14 patients receiving borago oil and 10 patients receiving placebo
(□ Borago oil, △ Placebo)

Table IV

significant improvement was observed at the end of treatment in the overall severity and in overall response ($p<0.01$).
A significant reduction in surface of the area involved was also observed in the same group.
Patients in the placebo group showed a small insignificant improvement. At the end of treatment the borago group also presented a significant reduction of all clinical parameters and in 5 patients, these results were mantained in an open longterm treatment without side effects. The same symptoms were not influenced by the placebo (Table IV).
In conclusion, in this study only the patients receiving borago oil showed significant improvement in their AD with respect to all the clinical parameters assessed.

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DRY SKIN: PATHOPHYSIOLOGY AND TREATMENT

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Key Words: *Dry skin; Cosmetic treatment; PCA; Collagen; Hydroxyacids; Vitamin A derivates; Pharmacosmetics.*

Synopsis

Dry cutis is found in different conditions, both hereditary and acquired due to general or local factors, and the condition is also found in old people as a result of natural skin aging.
The mechanisms accounting for this alteration of the eudermic state are complex and not always clear. As well as the involutionary changes of dermo-epidermal structures and functional components, particular attention must be drawn to the changed water/lipids/NMFs ratio.
From the standpoint of treatment, action must be directed towards the elimination of the specific causes in the case of cutaneous dehydration from acquired general factors. In the other cases, along with the local or general "cosmetic" treatment, action is needed to try and prevent damage.
We believe that the corrective cosmetic treatment must take into account that the principal of the cosmetic can have a replacing activity (collagen, PCA, urea) or restoring activity (glycine, hydroxyacids, vitamin A derivatives).

Riassunto

La cute secca si riscontra in diverse condizioni condizioni sia ereditarie che acquisite per fattori generali o locali, oltre che nell'anziano in seguito all'invecchiamento naturale del sistema cutaneo. I meccanismi con cui tale alterazione dello stato di eudermia si verifica sono complessi e non sempre del tutto chiari. In aggiunta alle modificazioni involutive delle strutture e delle componenti funzionali dermo-epidermiche occorre considerare in particolare il modificato rapporto acqua-lipidi-NMF.
Dal punto di vista del trattamento, l'intervento deve essere rivolto alla eliminazione delle cause specifiche nel caso degli stati di disidratazione cutanea da fattori generali acquisiti. Negli altri casi, accanto al trattamento "cosmetologico" di tipo locale o generale, occorre anche intervenire per cercare di prevenire il danno.
Riteniamo che nell'intervento cosmetologico correttivo occorre considerare che il principio attivo del cosmetico può svolgere attività sostiutiva (collagene, PCA, urea) o attività ricostruttiva (glicina, idrossiacidi, derivati della vit. A).

PATHOPHYSIOLOGY

From a clinical point of view, we all know that dry skin (1) appears rough, stiff, thin, fragile, inelastic, dull and grey-yellow. Under these conditions, skin is more easily exposed to external attacks and aggression, and the frequent concomitant itch often produces typical injuries due to scratching.

Dry skin can affect the whole body or be more evident in some areas (legs, hands, face).

This change in the eudermic state is caused by many factors which are not always completely clear, and is found in both hereditary and acquired conditions. Besides natural aging, it is due to either general or local factors.

Hereditary conditions include mainly early skin aging such as progeriae, and especially the Werner syndrome (2), as well as xeroderma pigmentosum (3), and several forms of ichthyosis (4). In addition, dry skin conditions are found in particular dermatoses such as atopic dermatitis (5).

General acquired conditions (6) include prolonged fasting, persistent vomiting, unrestrainable diarrhoea (typical of dry cholera and Mouriquand syndrome), low sodium diet, prolonged use of diuretics, etc. As a result of these situations, the water contained in the skin - which is a major reservoir - is used by other parts of the organism, which leads to skin dehydration.

The conditions acquired due to local factors (6) which determine the clinical pictures of dry skin include:

- the negative influence of climate and environment (wind, cold, sun, reduced air humidity), which is particularly evident in certain areas and in subjects performing certain professions (farmers, sailors, etc.) especially if they have little natural photoprotection (pheomelanins);
- chemical attack linked to professional conditions (use of solvents, paints, detergents), incorrect hygienic habits (frequent washing, often with not very mild detergents), prolonged use of certain treatments (topical corticosteroids).

Finally, dry skin is a characteristic of old people due to the physiological involution of the cutaneous systems (6). The clinical picture first appears around 40 and becomes evident around 60. However, it originates around 25 with natural involutionary changes in dermo-epidermal structures and functional components.

Cutaneous aging, which is particularly evident in the senescence, generally presents (7-9):

* at dermal level:
- reduced fibroblast activity with decreased collagen production and altered ground substance due to the reduction of glycosaminoglycans (GAGs) and hyaluronic acid;
- reduced angiogenesis and consequent reduced vascularization with degeneration of elastic fibers and collagen;

* at epidermal level:
- strong reduction of the particularly fragile and rough horny layer, with altered barrier function;
- reduction of melanocytes resulting in reduced photoprotection;
- decrease in the number of Langerhans cells and consequent reduced local immunity defenses;
- flattening of dermal ridges and dermo-epidermal junction with minor adherence at this level and functional alteration;
- slow passage of keratinocytes into keratocytes with reduced horny lamellae balance.

In addition, the functional activity of sweat and sebaceous glands decreases.

Under these conditions, however, water, lipids and NMF (natural moisturizing factor) change their values (10).

Water travels to the epidermis from the dermis, which contains 70% of cutaneous water (equivalent to 10-20% of the total water in the organism). Water is reversibly bound to GAGs and mostly to hyaluronic acid (11). The mechanism regulating its passage through the basal membrane is not yet perfectly known. In the horny layer, water changes in physical state and evaporates in the form of perspiratio insensibilis when it exceeds the maximum imbibition gra-

dient. Water is bound in the horny layer (12) by certain substance: NMF (a complex of hydrophilic substances) and especially its constituent, PCA (2-pyrrolidon-5-carboxylic acid). These substances have a great water-retention capacity.

The presence of water in the horny layer can, thus, be reduced since less water is supplied by the dermis (reduced bond with GAGs), NMF water retention capacity is decreased, as well as the functional activity of the horny layer which is between 15% and 10%. This results is dryness.

Sebum is another factor which contributes to horny layer hydration (its secretion is highly reduced in old subjects). It prevents water loss at transepidermal level, and helps to keep a barrier function. This function is also ensured by bilayer phospholipids, whereas Odland lamellar bodies offer the possibility to bind water at deep horny layer level (14).

The surface hydrolipidic film is an W/O emulsion where the oily continuous phase is made of sebum and apocrine sweat lipids, and the dispersion aqueous phase is made of water and eccrine sweat salts. Its insulating effect prevents water from being lost by the epidermis, and, under conditions of integrity and in synergy with other structures and substances, it allows skin to maintain optimum hydration.

An undamaged keratocyte protein strnctnre and resistant horny lamellae play a considerable role in water retention at the cutaneous level. These conditions depend on involucrin and filaggrin. Filaggrin produces natural moisturizing factors (15) and is found only in small quantities in conditions of compromised cutaneous hydration, such as during ichthyosis vulgaris and psoriasis.

On the other hand, excessive hydration of the horny layer (a prolonged bath) determines permeability in the skin surface, as well as alteration of the barrier function and imbalance in the eudermic state.

Treatment

Skin dehydration due to general factors (fasting, vomiting, diarrhoea, etc.) requires actions which aim at eliminating the specific causes. In the case of "cosmetic treatment" for dry skin - be it local or general - prevention plays a significant role.

It is therefore necessary to start from clothing, which must be appropriate in terms of age, work, climate and environment. For example, profuse perspiration is detrimental since it involves a considerable loss of water and trace elements, and prolonged and repeated exposure to solar radiation accelerates skin aging.

Individuals with fair skin, blue eyes and reddish hair who are not protected with melanin (in addition, pheomelanins favour free radicals and consequent genetic mutation), and some professional categories which are repeatedly exposed to the sun, need to apply moisturizing day creams, containing long-lasting sun filters or sun screens with total protection over the exposed areas. This is to be associated with the administration of photoprotection substances (beta carotene) (16).

Too-frequent washing is to be avoided, as well as the use of highly aggressive detergents such as syndets (especially solid ones, which have a great quantity of snrface-active agent) (17). The daily toilet should remove dirt from the skin surface, but respect the hydrolipid film and the integrity of the horny layer. This is why traditional soaps should be used such as Marseilles soap - less irritant than synthetic soaps (20) - enriched with collagen protein hydrolysates. They have, in fact, the property of counteracting the irritant action of the snrface-active agent (18).

The skin acid pH, which is temporarily lost when using alkaline soaps, returns to the original values within one hour from rinsing (19). In addition, 5-10 minute baths with water dispersible oils at 34° - 35°C create a protective film and have a soothing effect.

The professional categories which make great use of detergents, paints, solvents and similar materials, are recommended to wear white-cotton gloves under rubber gloves. This should not be done over a long period, however, in order to avoid excessive insulation.

As well as prevention, corrective intervention is also deemed necessary for the clinical imbalance of the xerotic condition.

The corrective cosmetic can:

1) replace altered or lacking mechanisms or conditions; its rapid effect is not long-lasting, especially if the cosmetic is O/W rather than W/O emulsion;

2) have a restoring property; its curative effect lasts some days.

The principles with **replacing activity** can have:

a) a structure which is inadequate to penetrate the epidermis, such as collagen which, however, has a great capacity to bind water (2000-3000% of its weight) and tends to stratify on the cutaneous surface, when applied;

b) a structure which is able to penetrate the epidermis, creeping into the lamellae of tbe stratum corneum, such as NMF components (PCA and urea: we recall that continued and prolonged use of urea-based preparations can provoke the disgregation of lamellae and the alteration of the barrier). In this regard, some substances with a globular sub-microscopic structure and functioning as carriers (liposomes, niosomes, nanospheres) prove to be very useful (21). They are able, in fact, to transfer the principle in the epidermis, where it will be released in time (chronocosmetic effect). This is a remarkable break-through of scientific research which is present at the implementation stage.

The principles with **restoring activity**, assuring a more lasting curative effect, consist of amino acids, such as glutamic acid (precursor to PCA) and glycine (stimulating PCA production), as well as hydroxyacids (glycolic, citric, lactic, malic, tartaric, etc.) which are able to affect the quality of the forming horny layer. A restoring function is performed also by vitamin A. Retinol, however, is scarcely effective at cutaneous level. Retinoic acid, on the other hand, which is classified as a pharmaceutical product and not as a cosmetic, can favour angiogenesis and the synthesis of new elastic fibers and collagen at dermal level, following percutaneous absorption.

The general treatment suggested includes a diet rich in vegetable oils containing essential fatty acids (EFA or vit. F) mainly represented by linoleic and linolenic acids contained in borage, soy and serotine primrose oils in high percentages. EFA deficiency results in the incapability of membranes and cutis to retain water; cutis thus becomes dry and squamous.

Other vitamins (A, E, C, PP, B1, B2, B6, B12, H, D) are also important in order to maintain orthokeratinogenesis (22).

The per os administration of glycine - an amino acid contained in large quantity in gelatin - has been recently (23) introduced. Gelatin enriched with glycine, in fact, increases skin hydration by 12% after 15 days, and by 30% after 30-45 days of treatment (24). The substance is postulated to promote the synthesis of collagen and activate one or more enzymatic systems needed for PCA production. Even if the glycine dose is reduced, the hydrating activity can be increased by 10-15%, by enriching the preparation with trace elements (iron, manganese, copper, and calcium) and vitamins (C and B6). Trace elements are, in fact, cofactors in forming bonds of collagen and elastin molecules, while vitamins activate enzymatic processes (24-25).

Supplementing the diet with zinc can be suggested to fight mineral deficiency (poor absorption, incorrect diets), since zinc is a constituent of enzymes, which are responsible for the development of different metabolic processes. It is important to recall, in this respect, that vitamin PP favours zinc digestive absorption, whereas fibers and phytates prevent it during a vegetarian diet. For functional needs, even low doses of zinc supplement are sufficient (50 mg/die).

Final remarks

Facing the complex physiopathological mechanism which leads to the beginning of the clinical picture of dry skin, our intervention can follow different lines: from the removal of the general pathology to prevention, from local to systemic therapy.
From a cosmetic standpoint, corrective preparations can contain principles with a replacing activity, whose effects are rapid but not long-lasting, and principles with restoring activity whose effects last longer (in this case, we should speak of "pharmacosmetics" rather than cosmetics).
The dermatologists' task is to diagnose and treat dry skin in order to relieve, as far as possible, the anguish of patients complaining of this condition of eudermic imbalance.

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Fourth International Course on
Occupational Dermatoses

7-11 June 1994, Hotel Naantali Spa, Naantali, Finland

Background

Three international courses on Occupational Dermatoses have so far been arranged by NIVA, in 1982, 1986 and in 1991. Each course was attended by about 100 participants. Occupational dermatoses cause a significant percentage of industrial disabilities and a great number of lost work days. It has proven difficult even for an experienced dermatologist to determine the agents causing an occupational skin disease.

Objectives

The aim of the course is to provide the participants with detailed up-to-date knowledge on occupational dermatoses.

The course will comprise the latest knowledge on the progress of occupational dermatology of practical importance.

Each lecture is followed by in-depth-discussion. Group-work teaching will take place daily tutored by a faculty member. The groups will discuss problems brought in by the participants, and will review and solve questions that have come up during the lectures. Active participation of the participants is highly encouraged. Report related to occupational dermatology can also be presented as posters.

Target group

Occupational dermatologists, dermatologists and clinicians in industrial medicine with a good basic knowledge of occupational dermatology.

Main topics

- Allergic contact dermatitis
- Irritant contact dermatitis
- Immunology of contact dermatitis
- Epidermiology of occupational dermatoses
- Contact urticaria
- Immediate allergy skin testing
- Patch testing problems
- New allergens

Faculty members

D. Belsito, USA; M. Bruze, Sweden; T. Diepgen, Germany; A. Dooms-Goossen; Belgium, P. Elsner, Switzerland; T. Estlander, Finland; T.Fischer, Sweden; A. Fransway, USA; P. Frosch, Germany; K. Kalimo, Finland; A. Lauerma, Finland; H. Maibach, USA; T. Menne, Denmark; R. Rycroft, UK; J. Taylor, USA; K. Turjanmaa, Finland; J. Wahlberg, Sweden.

SKIN PERMEATION: FUNDAMENTALS AND APPLICATION

Edited by Joel L. Zatz, PhD
Hardback, 300pp - US $ 115 (Add 20$ for all international orders)

Researches are becoming more aware of the ability of drugs, cosmetic ingredients, and other topicals to pass through the stratum corneum barrier. Those who work in these research areas should read Skin Permeation: Fundamentals and Application. The book covers the philosophy and methodology of evaluating skin permeation and its applications to product formulation. Chapters cover in-vivo and in-vitro methods of testing sorption, biological factors affecting sorption, drug delivery, and instrumental monitoring. Sixteen authors have come together to share their expertise on the subject.

The literature on skin permeation of drugs and other substances has grown amazingly in recent years. Skin Permeation aims to provide ideas and techniques that will be of immediate use to both researchers new to the field and those needing a comprehensive review of developments. The information presented should also be helpful to medical personnel, drug and personal care product formulators and other interested in the techniques and results of skin permeation studies.
References accompanying each chapter direct readers to additional sources of information, including mathematical treatments and models not covered in detail in this book.

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THE PARALIZED FACE

Leonard R. Rubin, M.D., F.A.C.S.
Mosby - Year Book, Inc. - 11830 Westline Industrial Drive, St.Louis, Missouri 63146
©1991 Format 21,5x28,5 cm, 280 pages, Hard-bound, 312 illustrations.

Facial palsy issues are topical and relevant not only for plastic surgeons, but also for other specialists, such as neurologists, ophthalmologists, and otorhinolaryngologists.
This book aims at thoroughly outlining the results of a multidisciplinary approach to facial palsy diagnosis and treatment.
This book, with contributions from distinguished specialists in the various surgical and medical branches concerned, was intended as an ample and up-to-date account of this issue for the general audience, and as a sound technical guidebook for specialists, who aim at social reintegration of individuals affected with facial palsy.
The book is divided into two sections. In the first part of the book, the author thoroughly describes face anatomy, physiopathology, and semeiotics, the instrumental examinations for proper diagnosis, as well as facial palsy etiology.
The second part exhaustively deals with the different reconstructive techniques introduced by contributors, as a sound tecnical and scientific reference for readers.
Schemes, drawings, and reported case-studies clearly show advantages and limits of current reconstructive techniques.
Finally, the author analyses issues concerning post-operative rehabilitation which has proved essential to improve the muscular mobility and expression of the face in patients with facial palsy.
This book gives an exhaustive and multidisciplinary account of the complexity of facial palsy diagnosys and treatment. In addition, it is easy to understand and tecnically and scientifically interesting, which makes it a good and up-to-date digest on the international scientific scene.

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Vice Chief Department of Plastic and Reconstructive Surgery
S. Eugenio Hospital - Rome - Italy -

YEAR BOOK OF PLASTIC, RECONSTRUCTIVE, AND AESTHETIC SURGERY 1991

Editor: Stephen H. Miller, M.D.

Mosby-Year book, inc.-11830 Westline Industrial Drive, St. Louis, Missouri 63146
©1991. Format 15,5x23,5 cm, 325 pages, Hard-bound.

This book can be rightly considered as a thorough and up-todate collectoin of articles, wich have been written on the most significant issues of plastic surgery between 1989 and 1990.
Dr. Miller and his assistants selected the most interesting and significant articles from 63 international journals and divided them into seven chapters. Each chapter deals with a main branch of surgery, as follows: congenital defects; neoplasias, inflammations, and degenerative diseases; reconstructive surgery in traumas; reconstructive surgery; breast diseases and reconstruction; flaps, grafting, and tissue expanders; and tissue reconstruction.
This book, with its excellent graphic layout, is a handy, multidisciplinary up-date on plastic surgery. In addition, considering the large number of its sources, it gives a wide scientific account of current issues, approaches, and studies in branches related to plastic surgery.
Each article is commented on by the editor or one of his assistants, and is followed by questions and answers by its author. These give exhaustive information on the issue dealt with. The chapters on neoplasias, infiammations, and degenerative diseases, which are surgically treated with satisfying results, are extremely interesting.
The same applies to the chapters on reconstructive surgery and hand surgery, thanks to their careful description of special surgical techniques.
The chapter on breast reconstructive surgery includes few, but extremely significant articles.
A considerable effort has been made by the authors to select those articles from international literature which have the most appeal from the technical and scientific point of view. The outcome is a pratical and up-to-date guide to the major books in the field of international plastic surgery.

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Pharmacology/Pharmaceutics, Medicine (all fields)

LIPOSOMES: FROM PHYSICS TO APPLICATIONS

By D.D. Lasic, Liposome Technology Inc., CA, USA

©1993 580 pages
Price: Dfl. 475.00 (US$ 271.50)
ISBN 0-44489548-5 Hardbound
Pubblication: July 1993

After their discovery, liposomes rapidly spread into various sciences and applications. This volume critically reviews the applications of liposomes (some for the first time), including theoretical physics, chemistry, energy conversion, ecology, genetic engineering, food industry, cosmetics and medicine, as well as their characteristics and properties. It presents the most recent developments, such as Stealth liposomes (which are invisible to the immune system and have shown encouraging results in cancer therapy). Rather than being presented in a "catalogue" style, the data is logically explained, and fundamental models and mechanism are reviewed and proposed. All of the seemingly unrelated phenomena in various methods and applications are defined using simple laws of physics, chemistry and biology. The volume will be invaluable to pharmacists and pharmacologists as to all those involved in liposome research.

Contents:

I. General Introduction to Liposomes.

Introduction. 1. Chemistry of lipids and liposomes. 2. Structure of amphiphilic aggregates. 3. Preparation of liposomes. 4. Mechanism of liposome formation. 5. Liposome characterization methods. References.

II. Applications of Liposomes in Basic Sciences.

Introduction. 6. Applications of liposomes in theoretical sciences. 7. Applications in biophysics. 8. Liposomes in the studies of the evolution of life. 9. Application in chemistry. 10. Reconstitution of proteins. References.

III. Applications of Liposomes in Pharmacology and Medicine.

Introduction. 11. Liposomes as a drug delivery system. 12. Liposomes in the treatment of infectious diseases. 13. Liposomes as immunoadjuvants. 14. Liposomes in anticancer therapy. 15. Liposomes and inflammations. 16. Other medical applications of liposomes. 17. Other administration routes of liposomes. 18. Site specific drug delivery. References.

IV. Other Applications of Liposomes.

Introduction. 19. Cosmetic Applications of liposomes. 20. Liposomes as a carrier system in genetic engineering. 21. Liposomes in diagnostics. 22. Liposomes in food industry. 23. Liposomes in ecology and other applications. 24. Industrial manufacturing of liposomes. References.

The book is available from the Amsterdam address, or in the USA/Canada from Elsevier Science Publishing Co. INC., P.O. Box 945, Madison Square Station, New York, NY 10159 USA.

BLAUE LISTE
Cosmetic Ingredients
Second, revised and enlarged edition

Editors: H. P. Fiedler, H. Ippen, F. H. Kemper, N.-P. Lüpke, K. H. Schulz, W. Umbach

© 1993. Format 17,2 X 20,5 cm, 352 Pages, Bound, Price: 148,-DM.
ISBN 3-87193-136-5

Recognizing and avoiding undesired side-effects of substances with which people come in contact is a task that has aquired increasing importance.
This applies particularly to hypersensitivity reactions ("allergies").
The "Blaue Liste" considers cosmetic ingredients, which can be significant causing allergic reactions.
It offers the producers a proposed format for ingredient declaration, and likewise addresses the physician providing him with the information on cosmetic ingredients necessary to investigate allergic reactions. Simultaneously, however, a binding concept is submitted how allergy-prone users can be protected from the particular materials. In order to make an EC-wide usability possible the text is bilingually written in German/English.
Two allergen lists indicating test concentrations for patch testing, classifying characteristics for each substance on the allergy rate, toxicity and toxicological characterisation are additionally included in the new edition.
In an clearly arranged presentation (a sample reduced in size is shown on the reverse side) the "Blaue Liste" includes:
106 Preservatives (Code P) - 207 Colourants (Code C) - 27 Ultraviolet Filters (Code UV) - 127 Other Compounds (Code O).
Several detailed indices render a quick access to a particular substance searched for possible.

The Coding
Codifying is the easiest method to identify and classify definitively and clearly the often complex cosmetic ingredients regardless of their various chemical or trivial names. It is simpler for the interested consumer to memorize a short name in the form of a code than a long, incomprehensible, and often confusing chemical nomenclature.

From the physician's point of view the code possesses additional advantages over other ingredients descriptions:

1. Ingredient classification according to four classes of active substanees: preservatives (Code P), colourants (Code C),Ultraviolet filters (Code UV), and other ingredients (Code O).

2. Group classification of related substances with regard to chemical and allergological aspects. In regard of the phenomenon of cross- or group-allergies this point is of special importance.

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Kerth (12), McKinney (13), Rudolph (14) and Vogel (15) suggest performing the rhytidectomy of the upper third of the face (frontal face-lift) in all cases where ptosis of the eyebrows, deep wrinkles of the root of the nose coexist, determining the typical frowning expression.

Blepharoplasty is indicated for patitnts with dermatochalasis of the adipose tissue underlying the musculus orbicularis.

Kamer (16) illustrates his own experience on the "preexcision pinch lower lid blepharoplasty", whether associated or not with upper blepharoplasty and rhytidectomy. Only 5 patients out of 1017 treated over 15 years shown postoperative ectropion.

Mc Graw (17) suggest careful evaluation of the patient's local conditions before the operation and the performance of conservative surgical techniques, in order to avoid this unpleasant complication.

The routine lower blepharoplasty with a transconjunctival approach carried out by Zarem (18), in cases where the excision of excess cuties is not necessary, seems to reduce the risk of ectropion. Out of 104 patients treated over the last two years, there were no cases resulting in this complication. However, the actual need to excise the excess cutis is not always precisely assessed. As qa matter of fact, the author reports 5 cases in which it has been necessary to intervene again at cutaneous level.

As regards rhinoplasty, there is an interesting remark by Sénéchal (19) on the psychological effects of this operation on elderly patients. In addition, Daniel (20) underlines the importance of systematically establishing a relation between the anatomy, in particular that of the alar cartilages, and the shape of the nose, thus being ahle to operate with greater control and forecast of results.

One of the major problem of fat accumulation and the resulting excess of skin on flanks and thighs. Lockwood (21) proposes to use first the liposuction and after 3-4 months the excision of the excess cutis by incising transversally, within the covered area of a two-piece bathing suit, peeling off upward and downward, pulling the superficial fascial system in such a way that the tension does not affect the cutaneous scars. He reports an experience of 10 cases with few complications,j and good client satisfaction.

In the field of additive mastoplasty with prostheses, many works have been published mainly regarding silicone polyurethanc biocompatibility, as well as any risk connected with the use of prostheses. A study was carried out in Los Angeles (22) on 3112 women who had undergone implants between 1959 and 1980. The follow up lasted 10.6 years as an average, and revealed that the risks of developing cancer had not increased following the prosthetic implant with silicone gel or polyurethane.

In addition, Jennings (23) shows that the greater concentration of silicone transudated from a prosthesis is not responsible for a greater risk of capsular contractures.

As regards mammary reduction, none of the scientific works published over the last years has brought actual changes to already standardized techniques. Hang-fu L (24) has compared 6 different reductive mastoplasty techniques (free nipple, Robbins, Mc Kissock, modified Strombeck, Regnault and modified Regnault techniques), used in 410 patients, analyzing their morbidity and the results with reference to preoperative expectations. The modified Regnault technique seems to be the procedure which is closest to the ideal, although there is no perfect operation for the needs of every patients. The free nipple implant syhould he reserved for patients with gigantomastia or older patients with reduced tolerance to anaesthesia.

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YEAR BOOK OF PLASTIC, RECONSTRUCTIVE AND AESTHETIC SURGERY 1993

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As every year, the US publication "Year Book of Plastic, Reconstructive and Aesthetic Surgery" has been issued.

We are going to deal with the section on Aesthetic Surgery, which is increasingly popular.

Among the articles of a general nature, the ones written by Goin and Rees (1), Edgerton et all. (2) and Julliard (3) are very in interesting. They concern the psychological aspects of this kind of surgery, which are crucial in establishing optimum doctor-patient relationships.

Méau (4) points out a major problem: is it right to carry out surgical operations of an aesthetic nature on HIV-positive patients? Can the stress they undergo speed up the passage from HIV positiveness to overt AIDS?

Although no official lines of conduct exist in this concern, the author suggests to warn patients of the possible risk of carrying out surgical operations for purely aesthetic reasons, as well as to carry out a routine Western Blot test. In the section on the scalp, Uebel (5) describes the micro-implant technique to solve baldness problems, which gives encouranging results, but requires very long periods of surgery. Chajchir et all (6) describe the use of a bitemporal bipedicled flap based on the Gillies flap for the reconstruction of the forehead area and in the juri J flap (7) for the surgical treatment of baldness.

Let us examine the section on the face.

Aiache (8) describes a simple technique to increase the thickness of lips by making an incision in the shape of a "W" and then a suture in the shape of a double "Y" on the mucosa, while making a plication in the midline at the level of the orbicularis. The increase in thickness is moderate. It is certainly an alternative to use the use of liquid silicone qand of fat infiltrations. However, achieving acceptable results in the static and in aspect of lips and their thickness is still a problem.

Stuzin proposes a detailed anatomic description in planes of the structures involved in the formation of flesh on the face (i.e. cutis, subcutaneous Lissue, fascia superficialis, mimetic muscles and deep fascia) under which lie the rami of the facial nerve and the parolid duet. Furthermore, he underlines the existence of support structures, the zygomatic and mandibular osteocutaneous ligaments running from the periosteum to the derma. With the passing of years, the support provided by these ligaments tends to give way thus causing the appearance of muscular flaccidity of the cheeks and of the submandibular region, as well as the accentuation of the sulcus nasolabialis.

Ramirez (9) and Maillard (10) boast wonderfurl results with the subperiosteal rhytidectomy, describing the wide peeling off of the upper two thirds of the face in a very deep plane. The case study they present is almost without complications. However, the great risk of neurological damage and the appearance of the considerable postoperative edema greatly extend postoperative periods. De La Plaza (11) replaces the subperiostal face-lift with a less traumatic technique which provides for the peeling off of two thirds of the face between the musculoaponeurotic plane and the periosteum. He also presents a follow-up without complications, though still performing a method at risk from a neurological standpoint.

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