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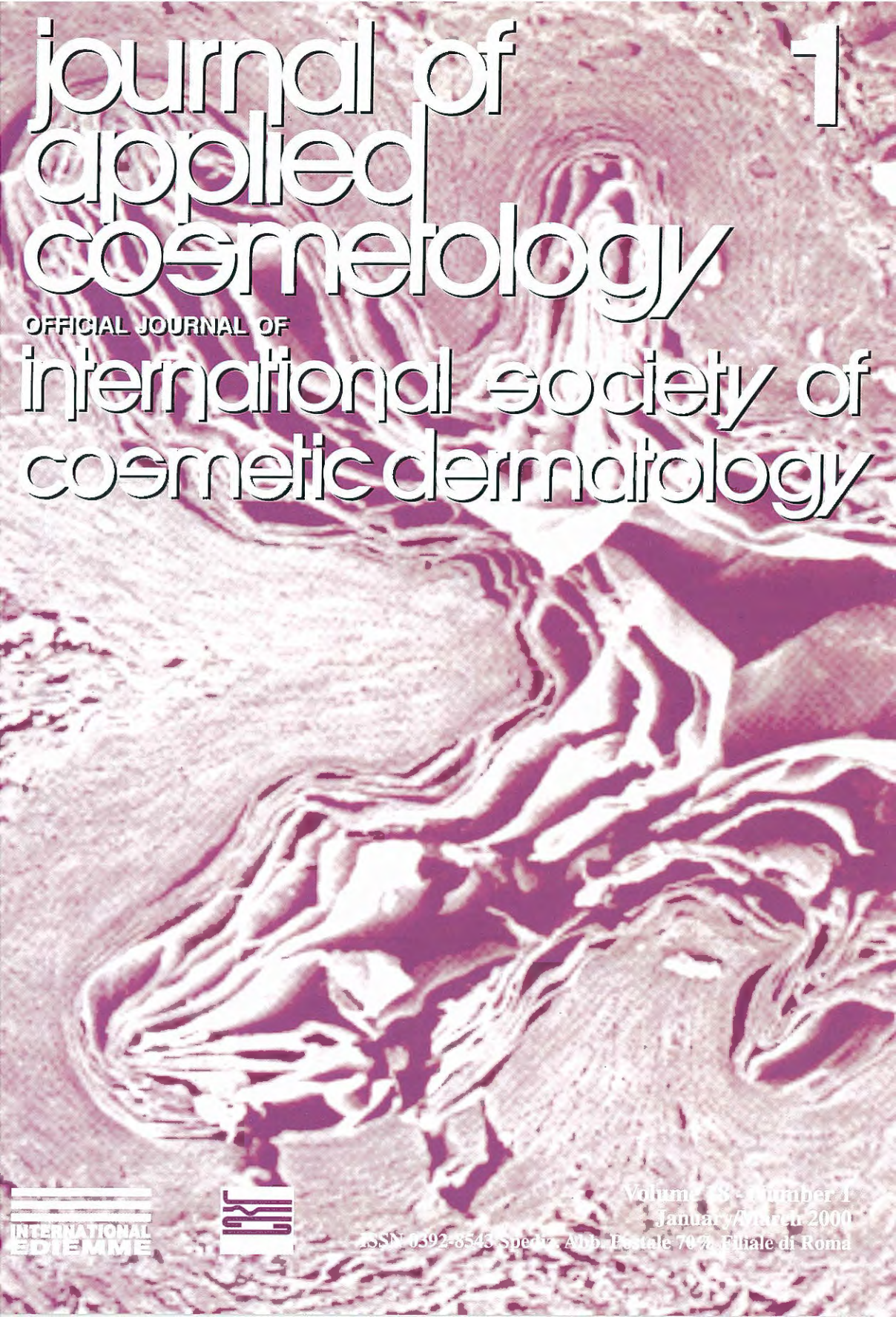

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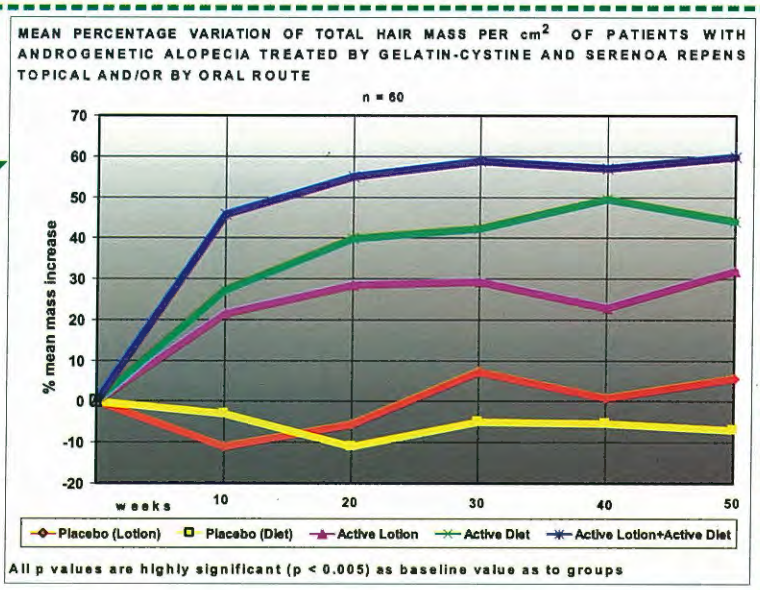
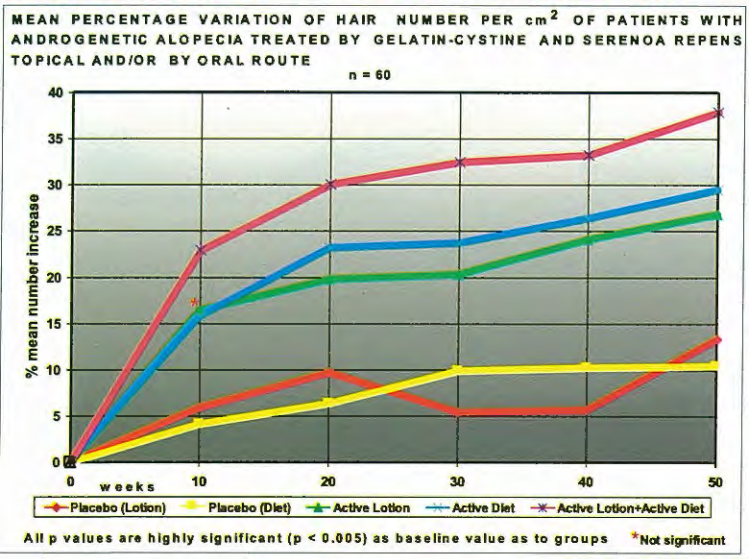
increase in hair mass





38%

increase in hair number

NO SIDE EFFECT WAS RECORDED

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1) Morganti P., Fabrizi G., James B., Bruno C. *J. Appl. Cosmetol.* **16**,57,1998

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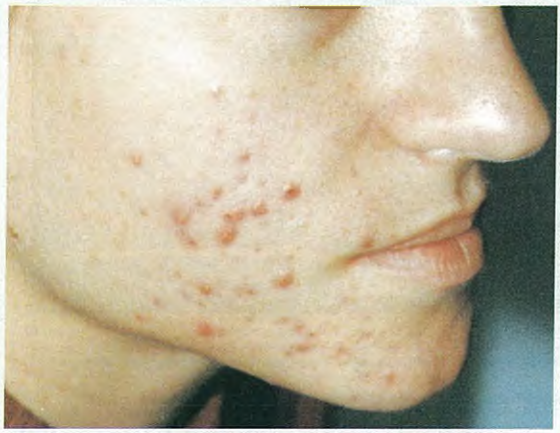

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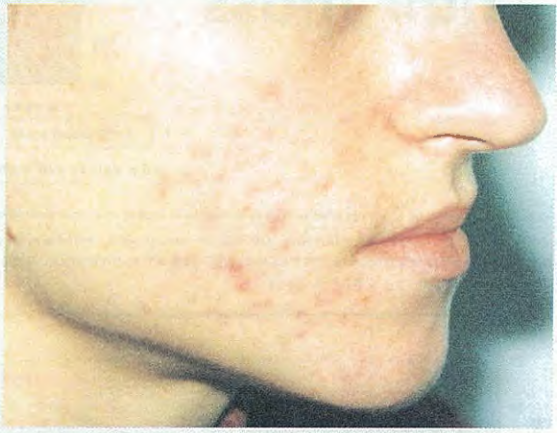

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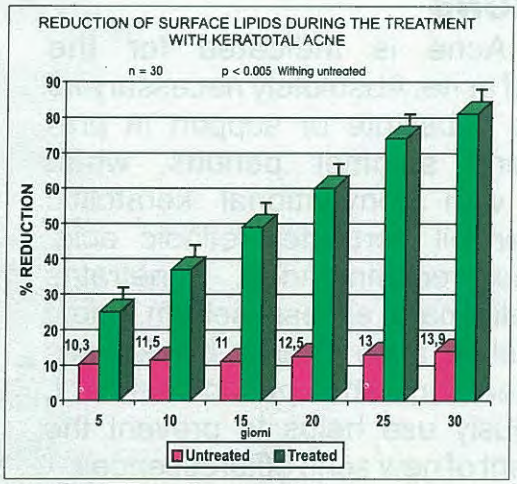

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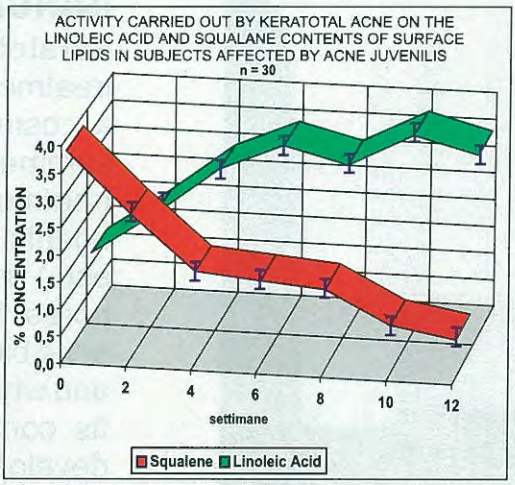
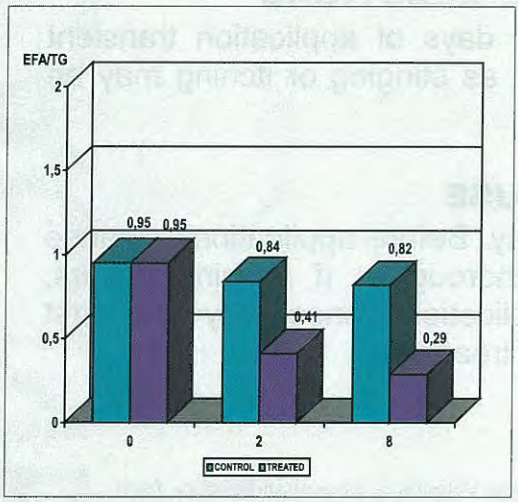


⇒ *Decreases the Squalene content of acne affected skin*



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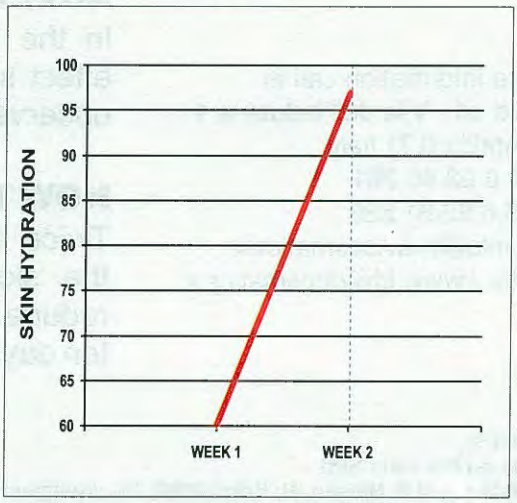

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DESCRIPTION

Keratotal Acne is a special fat-free lamellar phosphatidylcholine emulsion developed for the treatment of acne. It is delivered in a special phospholipidic-vehicle linoleic acid rich which contains glicolic acid and salicilic acid partially neutralized by a special patented blend of aminoacids

INDICATIONS

Keratotal Acne is indicated for the treatment of acne. Absolutely necessary as a cosmetic substitute or support in pre-summer and summer periods, when treatment with conventional keratolitic agents (benzoil peroxide, retinoic acid, ecc.) is not recommended. Penetrates pores to eliminate excess sebum, most acne blemishes, acne pimples, blackheads and whiteheads in a short period treatment. Its continously use helps to prevent the development of new acne efflorescences

ADVERSE REACTIONS

In the first days of application transient effect such as stinging or itching may be observed

HOW TO USE

Twice a day. Before applications cleanse the skin thoroughly; if stinging occurs, reduce application to once a day for the first ten days of treatment

REFERENCES:
1,2 - ***Data on file Mavi Sud***
3 - **M. Ghiczy, H.P. Nissen, H. Biltz (1996)** The treatment of Acne Vulgaris by phosphatidilcholine from Soybeans, with a high content of linoleic acid. *J. Appl. Cosmetol.* **14,** 137-145

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2) Strehler BL (1977) Time, cells and aging 2nd edn. Academic Press, New York
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Dear Readers

We would like to apologize for the inconvenience caused in delaying the publication of this issue, due to the substitution of the printing paper.
In fact, as you can see from now on, the journal will be print on a new environmentally friendly paper of higher quality.

Hoping you will understand our reasons sustaining us as in the past,

Yours

Pierfrancesco Morganti PhD
Editor-in-Chief

journal of applied cosmetology

Trimestrale di Dermatologia Cosmetologica
Quarterly Review of Cosmetic Dermatology

Contents

Questo articolo riporta una panoramica degli effetti collaterali provocati da farmaci o cosmetici, assieme ai relativi metodi di misurazione utilizzati, evidenziando i nuovi comportamenti dei pazienti riguardo agli effetti collaterali rilevati con metodologie elettroniche. Viene anche riportata l'influenza che tale metodologia di lavoro ha provocato a livello della ricerca dello sviluppo.

INTRODUCTION

Patient and consumer compliance has been studied for a long time and numerous studies provide evidence of the relationship between medical compliance and medical outcome. Since the introduction of the electronic monitoring device, many features of compliance could be observed and studied which were left undetected by conventional monitoring methods. So far, the impact of compliance has been mainly studied in psychiatric, hypertension and cardiovascular patients. For example, seizures are associated with missed doses of anticonvulsant drugs (2,4), and blood pressure control is less than optimum when antihypertensive regimens are not followed (2,5). In general, all patients and consumers have the potential to be noncompliant and thus noncompliance can be found in any medical, therapeutic field: When a therapy plan is not effective, it should be considered whether the treatment failed or whether the patient failed to take the medication as directed, before initiating alternative treatments and additional diagnostic tests.

Therefor, reliable distinction between noncompliance and nonresponse has become a new issue for the cosmetic industry. Accordingly, the influence of compliance habits on treatment efficacy should be considered in dermatologic therapy, cosmetic dermatology and the development and marketing of cosmetic products.

«COMPLIANCE» IN A NUTSHELL

The term «compliance» has been used to describe how a patient adheres to a recommended therapeutic regimen (7). More precisely it refers to the consent and ability of an individual to follow health instructions, to take medication as prescribed, to attend scheduled clinic appointments and to complete recommended investigations (25). It has long been recognized that patients often do not follow the instructions for the use of their therapy. For most diseases there is no «one shot' physician-administered therapy» Therefore, drug treatment relies on the cooperation of patients for self-administration (7). Compliance is regarded to be an intermediate part of the treatment process and is of clinical relevance when related to the simultaneous achievement of the treatment goal (3,2).

Poor compliance has been widely reported to be the most common cause for nonresponse to medication (25). Thus the problem of «compliance» is not only important for general practice, where practitioners are commonly faced with the problem of assessing whether failure to respond to treatment is the result of poor compliance or the failure of the treatment itself (25); «compliance» has also become an important issue in today's medical pharmaceutical and cosmetic research as well as for drug companies and public health authorities (27).

	TREATMENT GOAL	
COMPLIANCE	**Achieved**	**Not Achieved**
Hi	Ideal	Inadequate Therapy
Low	Wrong Diagnosis or Overprescribing	Clinically Important Noncompliance

Fig. 1 - *Treatment goal versus compliance. (Adapted from reference 2.)*

Condition	End Point	Non-Compliance (Controlled Study)
Epilepsy	Seizure	(33) (42) (44)
Hypertension	Blood Pressure	(5) (32) (34) (38) (39)
Contraception	Pregnancy	(28) (35)
Asthma	poor symptom control, acute severe asthma	(8) (41) (47)
Immunosuppressive therapy:	(31)	
- Organ transplant	-allograft function	(43) (45) (46)
Glaucoma	Intraocular pressure	(36) (37)

Fig. 2 - *Clinical Examples for compliance related outcomes.*

TRADITIONAL METHODS OF COMPLIANCE ASSESSMENT

The general method for assessing compliance in clinical practice has been the «patient interview» - during which the patient usually tells the physician what he or she thinks the physician wants to hear: that there is full compliance (1). The same problem occurs with «patients diaries'» and «- questionnaires», where patients are asked to keep records of their drug taking habits. The patients are supposed to hand in the records at their next appointment, which they often fail to do (26).

Assumably more objective data can be gained by «pill counts», «prescription refill surveys» and direct «measurement of serum drug concen-

Traditional Methods of Compliance Assessment	Disadvantage: «white - coat - compliance»
Patient interview	subjective,
Patient diaries	patients often only pretend to be
Patient questionnaires	fully compliant
Pill counts	semiobjective,
Prescription refill surveys	patients might dump left over medication
Serum drug concentration and other biological and chemical markers	quasi - objective, patients might try to make up for missed doses, taking an excessive amount, before the scheduled appointment

Fig. 3 - *Traditional Methods of Compliance Assessment*

tration» and other «biological -» or «chemical markers». But these approaches have significant drawbacks, as they also rely on patients' recall and candor: before scheduled appointments, patients dump their surplus medication or start taking an excessive amount trying to make up for the missed doses, pretending to be compliant («white-coat-compliance») (1, 26).
Using those techniques, apparently, compliance used to be greatly overestimated (12).

ELECTRONIC MONITORING

The state of the art in analyzing compliance is the use of sophisticated electronic monitoring devices: electronic medication event monitors.
Compared to the traditional methods of compliance assessment, electronic monitoring provides more reliable and detailed data about actual patient compliance.
Medication event monitors are drug packages with integral microcircuitry which records times and dates («timestamping») of medication events (12). For example, a microprocessor is placed in the cap of a standard medication bottle (6). Each time the bottle is opened the chip records the time, the date, and the interval since the previous bottle opening. Data are retrieved with a microcomputer using specially designed software (12). The data can be displayed immediately for presentation on screen and printed out, showing several aspects of medication-taking behavior of each individual patient:

- «Dose frequency»/ number of doses taken daily is displayed in a calendar plot;
- «Dose time» is displayed as a listing of the date and time of every bottle opening;
- «Dose interval» is displayed as the number of hours elapsed since the previous opening;
- «Dose timing» is displayed as a scatter plot showing the frequency of days on which a dose was taken at a specific hour, cluster of dots show the most common dose times, independent dots show dose times far from the usual schedule (26).

Previous assessing techniques left these details undetected (4,10).
As a prescribed regimen has two important qualities, quantity and time, a patient may appear to

Drug administration details	Compliance Assessment Methods	
	Traditional Methods	Electronic Monitoring
• **Dose Quantity**	only quasi-objective	objective data (if used correctly)
• **Dose Time**	-	registers every bottle opening
• **Dose Frequency**	-	numbers of doses taken daily
• **Dose Interval**	-	number of hours elapsed since the previous opening
• **Dose Timing**	-	continuity and regularity of dosing, time between doses

Fig. 4 - Compliance monitoring: Detection of drug administration details by conventional and electronic monitoring methods

be fully compliant with respect to quantity of medication used, but systematically introduces protracted intervals between doses. Electronic monitoring documents both, quantity and time.

The «bottlecap» was originally introduced in the 1980's (19,27) as the MEMS(r) (Medication Event Monitor Systems, Aprex Corporation, Fremont, California, USA, and Zurich, Switzerland).

Subsequent event monitoring has been applied to various packages (12,20): Eyedrop dispensers time-stamp the joint occurrence of cap removal and dispenser inversion. Vial-type containers for solid dosage forms time-stamp cycles of package opening and closing. Inhalers time-stamp aerosol release. Unit-dose («blister») packages time-stamp the removal of individual dosage forms. Treatment event monitoring can be applied to any type of package with minimal distortion because microcircuitry is only of the size of a large coin. It can record several thousand medication events over an 18-months period (12).

Feedback systems have been developed, for example the dDEM(tm) (electronic Drug Exposure Monitor, AARDEX Ltd./(USA), Inc.) (10, 26): Data recorded by the monitor can be transmitted any time via modem. Medication compliance records can be generated and immediate feedback is possible.

LESSONS FROM THE MONITOR

There is no perfect consumer. Although medication might be taken regularly, prolonged intervals between dose administration are the most common deviation from prescribed regimen (13). When the time comes, patients usually take the prescribed dose, but the intervals are frequently longer than prescribed and the timing of doses can vary considerably: by hours, days and even weeks (10,12).

The longer lapses (3 days or more) are called «drug holidays» (14,10).

Treatment holidays occnr approximately monthly in 15-20% of ambulatory patients, and quarterly in a further 15-20% of patients. Usually they begin and end abruptly, followed by resumption of full-strength dosing (7, 13, 12). One third of all patients' are poor or partial compliers, usually unrecognized clinically. It is important to identify them because poor compliance has not only been associated with poorer treatment outcome but also with hazardous adverse drug effects: There can be rebound effects when dosing is suddenly stopped; excessive drug effects and recurrent first-dose effects when dosing suddenly resumes. And last but not least there are financial consequences. It has been suggested that hospitalization due to noncompliance accounts for 11 % of all health care expenditure in the USA and, when indirect costs are accounted for, the total costs of non-compliance are equivalent to 70% of healthcare expenditure on drugs (7, 11).

Variable dose timing confronts with variable treatment exposure, treatment action and outcomes. As drug holidays are common, testing for rebound and recurrent first-dose effects should become routine (10).

Monitoring reveals that a large number of clinically judged «nonresponse» is non-compliance (12).

Continuous electronic monitoring may therefore complement therapeutic monitoring. So health care providers could use data and when doses are taken in their attempts to understand therapeutic failure (12).

In contrast to previous assumption, monitoring studies show that partial compliance is pervasive and similar across all populations (12). Poor compliance occurs in virtually all fields of medical care, including organ transplant management, oral contraception, hormonal blockage to prevent recurrent breast cancer, anti-viral treatment of AIDS, blinding glaucoma, ... - fields where many assume that strong motivation

would ensure good compliance. Data contradict that assumption (10). Another myth disproved by electronic monitoring is that poor compliance is primarily caused by inconvenient dosing schedules or drug side effects as poor compliance occurs with once-daily schedules for drugs devoid of side effects. On average, patients take about three fourths of doses as prescribed (4). But nevertheless, inconvenient dosing regimens and side effects influence the patients' coping with recommended regimen (25).

Reminder schedules, pharmacy-generated refill reminders and special medication containers or packaging have been shown to significantly improve compliance (18, 25); though a few non-compliers may falsify monitor data.

Cramer suggested that compliance could be improved, if poor compliers were given specific feedback from health care providers about missed doses, doses taken too close together or too far apart and explaining possible side effects (1).

In general, the introduction of the electronic monitoring device is a breakthrough in the ability to differentiate between poor compliance and other pharmaco-kinetic and pharmaco-dynamic mechanisms leading to low serum drug concentrations and suboptimal clinical effects (12).

«FORGIVING» PHARMACEUTICALS AND SKIN CARE

It is now clear that poor compliance is more prevalent than previously recognized. In particular, poor compliance is often characterized by serial dosage omissions or drug holidays (7). Although the emphasis on improving compliance is important, it is more realistic and of greater clinical relevance to select drugs and dosage regimens which first do not exhibit the adverse events associated with drug holidays and, second, can provide good therapeutic coverage despite dosage omission (7). These kinds of drugs are called «forgiving pharmaceuticals».

«Forgiveness» is defined as the drug's duration of therapeutic action minus the recommended interval between doses (12). «Forgiveness» predicts the latitude that patients can have in dose timing without loss in therapeutic action. Thus « forgiveness», not dosing frequency, is the issue in designing new drug regiments of optimal outcomes.

Conversely, the concern with long-acting drugs is that they might be more likely to produce toxic effects in fully compliant patients. Therefore, the proper evaluation of forgiving drugs requires stratification by compliance (20).

Differences between drugs, in terms of both their concentration-time profiles and their duration of action, will lead to some agents being more effective than others in the face of dosage interruptions. Some otherwise good products can fail in many patients because they require extraordinarily punctual dosing in order to provide full therapeutic action and avoid therapeutic failure (7). Besides their medical benefit, products that can reliably minimize these problems have a much greater market potential (10).

For example a drug with an intrinsically long duration of action, such as the calcium antagonist amlodipine, will provide better therapeutic coverage than those with a shorter duration of action and therefore minimize effects generated by an intermittent pattern of dosing (7). Another example are oral contraceptives (28): The minipill loses contraceptive effectiveness at about the 27th hour after the last-taken dose; thus patients must take the once-daily dose within an exceptionally narrow time interval of 24 +/- circa 2 h. This brief margin for error in dose timing is the shortest of all once-daily products for which such limits are known. In contrast, the widely used, combined oestrogen-progestin oral contraceptives have a 12 - 24 h margin for error.

For the development of these pharmaceuticals

and the expansion of the related markets, a continuing hardware, software analysis, medical-economic interpretation and intervention are essential (10).

COMPLIANCE IN DERMATOLOGY AND COSMETIC THERAPY

Although more cross-field data would be useful to prove a consistent pattern of compliance, there is sufficient evidence to assume a similarity in the extent and range of compliance across therapeutic fields (12). Therefore we suspect that Dermatology patients and consumers of cosmetic products are not perfect compliers and non-compliance occurs within the previously shown patterns. Regarding the different treatment options, and here topical therapy in particular, «drug holidays» and missed applications are common just as well.

In Dermatology topical therapy is a primary tool in the treatment, supposedly delivering treatment quickly and directly to the diseased site (23, 48). However, the disadvantages of topical therapy are, that it can be laborious and time consuming and it often takes some time to work. Sometimes the topical agent might also be non-esthetic. Furthermore the application may also result in irritant reactions - erythema, peeling, burning/stinging or itching (9, 23). Patients frequently state that they would rather take a pill or receive an injection than perform topical regimen (23).

Another disadvantage is that the drug delivery effect can vary according to its preparation. Different vehicles have different properties and pharmacological qualities and bioeffects of the active agents are diverse (9, 48, 59, 65). Accordingly, the patient's failure to respond might be the result of a product substitution to a nonequivalent generic (9) or, much more often, non-compliance to the therapeutic regimen. Here as well, treatment failure is misinterpreted as the need for a more potent product, rather than as a bioequivalence or compliance problem. Thus topical therapy is occasionally ineffective (23). With topical therapy, patients apply their medication when it is convenient. From experience they are also known to reduce the amount of drug they use until side effects are diminished (2), if not taking a leave at all, at least for quite some time. They often return to the next appointment, stating the therapy hadn't worked. This is especially likely with irritating and slow acting drugs, for example tretinoin, in acne and anti-aging therapy.

The following is also true in topical treatment: When dosing lapses, drug concentrations and consequently drug action decline sooner or later, depending on the drug and its formulation (12) and the development of new medication relies on the knowledge about drug pharmacokinetics and pharmacodynamics (15, 48, 59, 61). The critical role of the vehicle to therapeutic efficacy and patient compliance is widely recognized (9, 65). But assessing bioavailability of topical agents is difficult (9). Reliable compliance measurements might help define the effectiveness of each preparation, examining the individual drug exposure hased on the actual dosing history. For example recalcitrant atopic dermatitis, psoriasis, tinea pedis and acne would be ideal study areas (55, 56, 57, 58). As a result, accurate estimation of exposure-response relationships can be obtained (15). And it might be possible to save time and resources in the appropriate management of patients and the development of new pharmaceuticals and products.

The future outlook seems promising for increasingly sophisticated formulations for cosmetics and skin care products. With a clear trend towards therapeutic cosmetics, dermatologists are required to obtain a better understanding of modern ingredients and assessment techniques and researchers and government regulatory agencies will meet new challenges as more chemicals with true biological activity are invented

and tested (61). Claim substantiation and premarketing testing must also evolve to accurately assess efficacy and safety issues with important implications for total body health (61). Finally, new vehicles and delivery systems combined with established ingredients will modify percutaneous penetration, requiring reevaluation of snbstances with already established safety profiles. This research aims to provide cosmetics and skin care products of superior quality and efficacy (61).

CONCLUSION

Drawing a reliable distinction between noncompliance and nonresponse is a key step towards the development of more appropriate patient management and more efficient pharmaceutical products (10). The new perspectives brought by a new method of compliance measurement, electronic monitoring, underscore the importance of pharmacological aspects of missed doses and drug holidays as a source of potential hazards and treatment inefficiency. The available data reveal patients ongoing dosing patterns and provide information about these pharmacodynamic triggers. They might be the basis for improvement: better drug delivery systems, better-designed regimens, molecular redesign, better information for prescribes, patients and consumers, and other means to achieve desired therapeutic actions (20).

The challenge now that the prevalence and extent of noncompliance have become clearer, is to design and select treatment for the imperfect patient, hoping to optimize the balance between benefit and risk (18). Important issues are the development of «forgiving pharmaceuticals» regarding the common lapses in dosing - answering the question «how much compliance is enough?» (20), and gaining more information on the implications of compliance pattern on cross-field therapies and product consumption. Good clinical outcomes come about through mechanisms determined by dose - and time - dependent drug actions (10) in medical treatment as well as in cosmetic therapy. On any instance, closer monitoring of compliance should increase the scientific rigor of cosmetic studies.

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ADORNMENT OF THE FOOT : THE FASHION SHOE AND ITS REPERCUSSION ON THE NAIL APPARATUS

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Key words: *nail, shoe, footwear, fashion*

Summary

The fashion shoe is slowly deforming device often taking years before the damaging effect appear. The toenail dystrophies may present in many ways: some are very obvious but others, more difficult to recognize, may perplex the physician. Their detection remains important in order to avoid prescription of useless, expensive and not always innocuous treatments.

Riassunto

Le scarpe deformano lentamente il piede anche se i danni si evidenziano soltanto dopo molti anni. Le distrofie delle unghie dei piedi possono evidenziarsi in diversi modi: molte sono evidenti ma altre sono difficili da riconoscere e lasciano spesso il medico nel dubbio. È quindi importante che il medico approfondisca questi problemi per evitare l'utilizzazione di trattamenti spesso inutili, costosi e non sempre innocui.

Footwear induced nail dystrophies may present in many ways: some are very obvious but others more difficult to recognise may perplex the physician. Their misdiagnosis often leads to prescriptions of useless and expensive treatments. ...

More than 80 % of women aged over 65 have foot pain (1). In this latter group, women outnumber men in chronic foot disorders with double the number of ingrown toenails and 13 times more bunions (2). Why such a female predominance? These toenail dystrophies are mostly seen in women who routinely wear ill fitting shoes: tight pointed shoes, high heels... The fashion shoe is a slowly deforming device often taking years before the damaging effects appear. For fashion victims, it is clear that the foot must adapt itself to the shape of the shoe and what could be worse than a square forefoot in a triangular space ? (3). Osteoarthritis, which is more prominent in women after menopause may also intervene in the pathogenesis of foot and toe deformities with subsequent toenail alterations. The latter may be aggravated in case of arterial insufficency. The weight of the body may also play a role in the etiology of the toenail abnormalities: in men, the whole body weight is located on the heel;in women wearing high heels a part of the body weight is transmitted to the toes thus increasing the toe/shoe interactions. The narrow pointed shoe will also increase the toe/toe interactions.

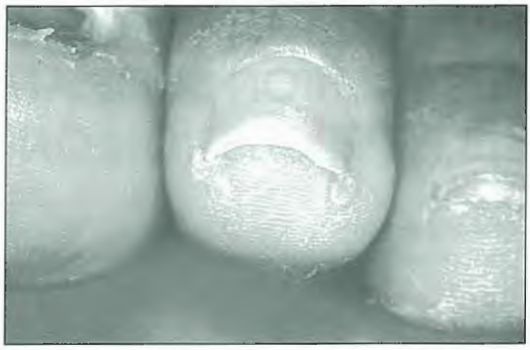

Fig. 1 - Onychophosis : hyperkeratosis of both lateral nail folds secondary to pressure of adjacent toes.

1. LATERAL CONSTRAINTS:

Friction of the shoe against the medial part of the great toenail leads to an hyperkeratosis of the distal part of the lateral nail fold called **onychophosis.** The same condition may be observed on the lateral part of the fifth toe and may also result from pressure from adjacent toes and is therefore located on both lateral nail folds (Fig. 1). Rubbing of the proximal nail fold against the shoe may be responsible for a **frictional melanonychia** (4) that commonly involves the fifth toe, often associated to subungual hyperkeratosis of the nail, but that may also be observed on the fourth and even the third toe (Fig 2). Tight pointed shoes enhance the lateral

Fig. 2 - Frictional melanonychia of the fifth, fourth and third toes.

deviation of the great toenail resulting in hallux valgus, often forcing the second toe to override the first one with subsequent **frictional onycholysis** (5) (Fig 3). This onycholysis occurs in an anatomical zone where the nail plate is loosely attached to its nail bed (6). Secondary fungal contamination is frequent;systemic antifungal therapy will lead to mycological cure;a normal nail will only be achieved with the suppression of the overriding. The same mechanism is responsible of **subungual haematomas,** almost always of triangular shape. A major factor that

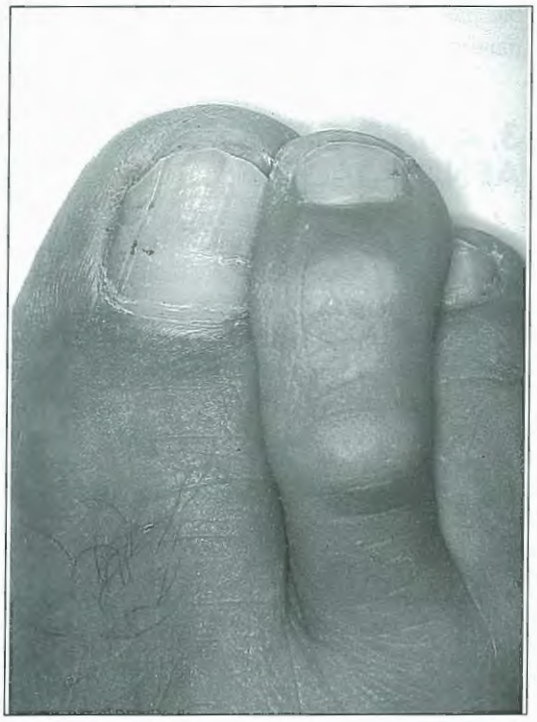

Fig. 3 - Disto-lateral frictional onycholysis of the great toe due to overriding of the second toe.

encourages haematomas is the lack of cushioning subcutaneous fat deep to the nail bed (7). Rarely, the second toe might override the great toenail with similar consequences: onycholysis, frictional melanonychia, subungual haematomas. Permanent pressure of tbe second toe on the lateral part of the great toenail, on which the former is imprinted, may account for the arising of a **pincer nail** (8). Pressure from the shoe box and/or from the adjacent toe may in some instances be responsible from an hypertrophic nail fold of the great toenail, also called **hypertrophic lip**, that may precipitate an ingrowing toenail. Seams running over the distal part of the shoe have an irritating effect on the proximal nail fold, which added to rubbing against the shoe, are responsible for the arising of a **chronic frictional paronychia** with potential acute episodes.

2. ANTEROPOSTERIOR CONSTRAINTS:

During walking, the foot has a forward and backward motion within the shoe. When the great toenail is long, its repeated buffeting against the tip of the shoe may be responsible for disto-lateral **nail fractures** (Fig 4). The same mechanism may lead to **transversal leukonychias** (9) (Fig 5) that may in some rare instances also be observed on the lesser toes. When the great toenail is cut, one may however observe **lamellar splitting** (onychoschizia) of the nail plate at its longest part: this particular aspect is common in sportsmen in which the foot is subjected to frequent sudden starts and stops as in tennis, squash, soccer, basket ball.... Friction of the upper part of the shoe against the nail plate may induce an byperkeratotic reaction that manifests as a subungual horn, called **onychoclavus or heloma**, located under the distal

Fig. 4 - Nail fractures on the medial part of the great toe nail.

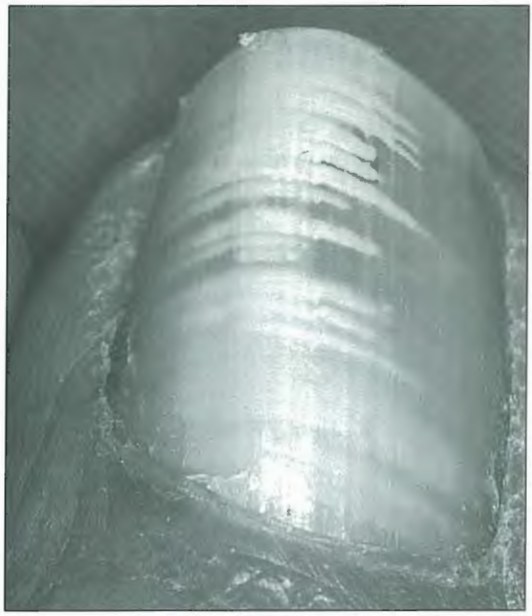

Fig. 5 - Transverse leukonychias. Note the location facing the longest part of the nail plate.

part of the nail plate, mostly the great toenail (10) (Fig 6). It may be very painful and may impair walking. Its clinical presentation is very discrete exception made of the subjective symptoms: a black or sometimes a pinkish red patch is seen through the nail plate on which pressure with the rubber of a pen gives causes considerable pain. Avulsion of the distal part of the nail plate reveals the lesion which is easily excised.

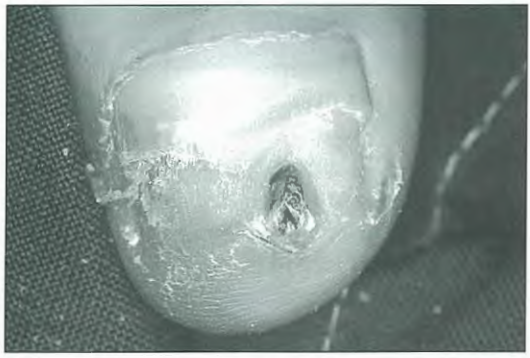

Fig. 6 - Onychoclavus (or heloma). The subungual horn is revealed by partial nail avulsion.

3. ADDED ORTHOPAEDIC ABNORMALITIES:

Chronic trauma to the nail unit can result from added faulty biomechanics (11). Most of the orthopaedic abnormalities are acquired and precipitated by long-standing footwear (especially high heels) and / or underlying osteo-arthritis which accounts for their occurrence in the elderly. Some of them are congenital such as Morton's toe. Accidental trauma and surgery may also be responsible for these deformities. Occupational factors should also be taken in account: the amount of time a patient spends in his shoes may affect the severity of his nail problems: an orthopaedic abnormality will more rapidly affect the nail apparatus in a sportsman than in a sedentary person. Occupational footwear, such as steel toe cap shoes, may also act as a precipitating factor.

Morton's toe is a second toe longer than the first one, but the trouble is in fact a shorter great toe. Therefore, this second toe performs a plantar rotation when the shoe is worn. The amplitude of this downward flexion is modulated by the length of the toe: the longer it is, the greater the rotation. According to the degree of rotation and the duration of the condition, several nail alterations may be observed: a slight rotation leads to an hyperkeratosis of the hyponychium, due to the repeated buffeting of the tip of the toe against the shoe. In time, the hyperkeratosis may affect the distal portion of the nail bed leading to onychauxis often associated to splinter haemorrhages. When the rotation is severe, the whole distal phalanx will rub against the shoe. Hyperkeratosis of the hyponychium and hyperkeratosis of the nail plate (onychauxis) may be observed. Onychomycosis has always to be ruled out (12). Rubbing on the proximal nail

fold may also result in frictional melanonychia often associated with a callosity facing the pigmented band. Subungual haematomas due to repeated stubbing are common.

Hammer toes result from a muscular imbalance between the extensor and flexor muscle group. As in the Morton's toe, several deformities may be observed according to the severity of the plantar rotation: hyperkeratosis of the hyponychium, onychoclavus, onychauxis, frictional onycholysis, subungual haemorrhages.

Hallux valgus is characterised by an enlargement of the metatarsal head and a general stiffening of the joint; over time, this leads to a fixed dorsiflexed distal phalanx. The nail often protrudes dorsally and is then exposed to rubbing and stubbing against the shoe, resulting in *onychauxis* or *onychogryphosis* often associated with *hyperkeratosis of the medial nail fold*. The gradual lateral deviation of the great toe forces the second to override the first one. Progressively, the lateral nail fold becomes hyperkeratotic due to friction, achieving an *onychophosis* or an *hypertrophic lip*; pressure of the second toe on the lateral portion of the great toenail is a precursor of the development of *pincer nail*. Overriding of the second toe on the first one may lead to *frictional onycholysis* of the lateral part of the great toenail which may be subsequently contaminated by fungi. *Subungual haematomas* due to overriding are common and mostly always show a triangular shape.

Lateral rotation of the fifth toe is precipitated by osteo-arthritis and footwear. The toe is orientated such that the patient ambulates on the lateral part of the nail plate. The frictional forces occurring between the shoe and the nail apparatus will result in hyperkeratotic reactions such as *heloma* or *onychophosis*. *Subungual haemorrhages* are very common and must be distinguished from *frictional melanonychia*.

Hallux erectus is due to an exaggerated tension of the extensors with a laxity of the flexors. This diagnosis is often missed because dermatologists examine the nail apparatus from the front. Examination from the side reveals that the nail protrudes dorsally which exposes it to rubbing and stubbing against the top of the shoe. This can lead to distal *onycholysis* and to a progressively shortened and thickened nail due to a constant pressure against the upper part of the shoe (Fig 7). The patient often spontaneously acknowledges that he does not trim this nail anymore or is persuaded that this nail never grows out !

Fig. 7 - Hallux erectus on a side view : note that the nail protrudes dorsally being thus constantly worn out against the top of the shoe.

4. TREATMENT:

Treatment of such dystrophies has to be appropriate in order to allow these patients to ambulate with greater efficiency and minimal pain thus keeping their independence. But most of the orthopaedic abnormalities of the foot in the elderly are irreversible as well as their consequences on the nail apparatus. Treatment must be therefore conservative. Moreover, when conditions are operable, the patients may not be candidate for surgery due to associated systemic diseases (diabetes, cardiac failure...) or concomitant therapy such as anticoagulants. In these instances, podiatric care is the most useful approach to maintaining mobility. Several techniques are available:

- Drilling with an electric drill or a burr is helpful in almost every type of hyperkeratosis. If

such a treatment is contraindicated (eg. diabetes) partial or complete removal of the nail plate may be achieved with 40 % urea ointment under occlusive dressing for 3 to 8 days.

- Silicon prosthesis is probably the most useful technique in such dystrophies and is indicated to avoid or reduce friction and rubbing from the shoe box or from toe-toe interaction.
- Surgery may however be indicated in some patients with pincer nails or onychoclavus i.e.

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UVR PROTECTION IN SHANGHAI

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Summary

The highest means UVR irradiate value at noon is observed in July (UV-420, 7325 μW/cm2; UV-365, 3317 μW/cm2) or August (UV-297, 34.7 μW/cm2) at Shanghai. The trend showed that radiation power of summer > that of autumn > that of spring > that of winter. The highest means UVR of a day appeared around noon. The UVA is nearly 100 times higher than UVB.

There are more than 315 brands of sunscreens in China to date. The quantities of sunscreens in China are increasing every year and the quality of sunscreens is also improved greatly. The most of commercial available sunscreens are broadband. The largest producing area is Shanghai. More and more Chinese people are using the sunscreens every day.

Though majority of students realized the harmful effects of UVR, a lot of them neglected to protect themselves from exposure to UVR. In summer outdoor activities, 16.4% of students applied sunscreens every day, 20.3% used sunscreens between times, 66.3% did not use any sunscreens. 61% female think it is necessary to use sunscreens regularly, but only 23% male agree with that. It is urgent to take some propaganda against UVR in China.

Riassunto

A Shanghai la maggior intensità dei raggi solari si registra a mezzogiorno nei mesi di luglio (UV-420, 7425 (W/cm2; UV-363, 3317 (W/cm2) o di agosto (UV-297, 34.7 (W/cm2). In queste ore gli UVA sono circa 100 volte di più degli UVB. L'intensità radiante diminuisce passando dall'estate all'autunno, alla primavera ed all'inverno.

Oggi in Cina sono presenti circa 100 marchi diversi di prodotti solari. Sia la quantità venduta che la qualità aumenta di molto ogni anno e la maggior parte dei protettivi solari commercializzati sono ad ampio spettro e prodotti principalmente nell'area di Shanghai. Numerosi sono i cinesi che usano i filtri solari ogni giorno e pur essendo noti i danni provocati dal sole. Questo problema viene sottovalutato dagli studenti. Infatti soltanto il 16% degli studenti utilizzano regolarmente prodotti solari, ma solo il 20.3% li utilizzano saltuariamente ed il 66,3% non li usano. Il 61% delle donne pensano che è necessario utilizzarli ma solo il 23% li usa abitualmente.

È necessario, quindi, incrementare i messaggi sull'uso di questi prodotti.

The level of living in China has been improved greatly since Chinese opening door policy was executed in 1978. Not only do Chinese satisfy with the common daily life, but also we want to be looked younger and more active, especially the women hope themselves more beautiful and attractive. The most of Chinese become more and more interested in nutrition, exercise and anti-aging. There are more and more commercial available cosmetics in China. In this paper, we mainly discussed the sunscreens and UVR protection at Shanghai.

SOLAR UVR MEASUREMENTS IN SHANGHAI

The sun is the main source of ultraviolet radiation (UVR). The stratospheric ozone layer prevents almost all UVR of wavelengths less than 290 nm and a substantial proportion (70%-90%) of UVB radiation from reaching the earth. Recent public and scientific concern about ozone depletion and increased UVR have lead to the establishment of many UVR monitoring centers in the last few years. Measurements of solar UVR have been made worldwide for many years. Generally, however, these measurements have not been coordinated and provide only a limited database for assessing personal exposure to solar UVR at ground level [1]. There are few UVR measurement reports in China to date. We started to measure ground-level solar UVR in Shanghai area in 1995 and carry it on to now.

We use the broadband radiometer of UV-A and UV-B (Light and Electric Instruments Factory of Beijing Normal School). UV radiation was measured in sunny days, from AM 9.00 to PM 3.00, sometimes from AM 7.00 to PM 7.00, total three days in a month. One day is among the first ten days of a montb, another day is among the middle ten days of a month and the third day is among the last ten days of a month. There are no any reflective objects or shadow around monitoring point.

The highest means UVR irradiate value at noon is observed in July (UV-420, 7325 (μW / cm2; UV-365, 3317 (μW / cm2) or August (UV-297, 34.7 (μW / cm2) at Shanghai. The trend showed that radiation power of summer > that of autumn > that of spring > that of winter. The highest means UVR of a day appeared around noon. The UVA is nearly 100 times higher than UVB.

It is a very important work to monitor the ground level UVR, especially for a long time. It can be to provide information to the public on UVR levels and variations and to establish a basic UVR climatology. It can also study cause and effects of UVR transmission and detect long term variability [2]. We cooperated with Shanghai Meteorology Association to set up an automatic monitor station in 1997 and forecast the UV index by TV, radio, newspaper and Internet.

SUNSCREENS IN CHINA

In history, the life style of Shanghais was influenced heavily by western culture. The Shanghai people are eager to know the new things and the fashion in the world. There were not more than 10 types of commercial available cosmetics before 1978 and most of them were produced at Shanghai. At that time, the Shangbais cosmetics were famous in China. After the Chinese opening door policy was executed in 1978, the prodnction of cosmetics increased year by year.

The first commercial available sunscreens appeared at Shanghai in 1980, which was imported from Europe. Since then, more and more sunscreens were imported. The first sunscreen made in China launched in1990 and then the increases of new brand is almost 100% each year (Table 1). The proportion of sunscreens in special cosmetic also increases very rapidly (Table 2).

Table 1 Net Increase of Sunscreen Each Year

Year	Sunscreen	Percent
1991	10	3.2
1992	19	6.0
1993	11	3.5
1994	32	10.2
1995	67	21.3
1996	97	30.8
1997	79	25.0
Total	315	100

Table 2 Proportion of Sunscreens in Special Cosmetics

Year	Special Cosmetics	Sunscreens	Percent
1991	132	10	7.6
1992	252	29	11.5
1993	319	40	12.5
1994	425	72	17.0
1995	563	139	24.7
1996	798	236	29.6
1997	1004	310	30.9

There are several types of formulation of sunscreens in China (Table 3). The most of sunscreens are cream and lotion.

The producing areas of sunscreens in China are listed at table 4. The largest producing area is Shanghai. The second is Guangdong. The third is Beijing.

The quantities of sunscreens in China are in-

Table 3 Types of Sunscreens

Type	Sunscreens	Percent
Cream	134	42.5
Lotion	117	37.1
Liquid	33	10.5
Cake	18	5.7
Oil	8	2.5
Lip Stick	4	1.3
Shampoo	1	0.3
Total	315	100

Table 4 Production Area of Sunscreens		
City/Province	Sunscreens	Percent
Shanghai	102	32.4
Guangdong	99	31.4
Beijing	31	9.8
Zhejiang	23	7.3
Jiangsu	22	7.0
Tianjin	13	4.1
Sichuan	5	1.6
Liaoning	4	1.3
Fujian	3	1.0
Hunan	3	1.0
Hainan	2	0.6
Others	8	2.5
Total	315	100

creasing every year and the quality of sunscreens is also improved greatly. The most of commercial available sunscreens are broadband, not only protect the UVB, but also protect the UVA [3]. More and more Chinese people are using the sunscreens every day.

Epidemiological Studies of Sun Protection in Undergraduates

Sun exposure and sunburn, particularly in childhood, are important risk factors for skin cancer. In order to find out whether the students are aware of the harmful effects of UVR and whether they know how to protect themselves from UVR. We carried out a series of investigation in undergraduates. In Chinese university, the new students must take part in one month (September) military exercises before their classroom studies. Using these opportunities, we investigated the new students from 1996 to 1998 and the total students were 1058 in all together. We used the questionnaires to obtain the general conditions, history of sunburn, diseases associated with sunlight, the awareness of UVR harmful effects and how to protect oneself from UVR [4].

Of 1058 students, male is 518 (49%) and female is 540 (51%) respectively, averages of age is 18.8 years old, range from 16 to 21 years old, 14 (1.3%) had light allergic, 112 (10.6%) had sunburn. 92.6% people are aware of UVR harmful effects. 75.8% consider that UVR can lead to skin aging, 95.2% agree with that UVR is risk factor of skin cancer. But only 37.8% take care of themselves away from UVR. 89.6% know about sunscreens, but only 24.4% understand the meaning of SPF. In summer outdoor activities, 16.4% of people applied sunscreens every day, 20.3% used sunscreens between times, 66.3% did not use any sunscreens. In military exercises, 21.4% of people applied sunscreens every day, 36.7% used sunscreens between times, 41.9% did not use anything. There is a significant difference between the male and female on the using of sunscreens. 61% female think it is necessary to use sunscreens regularly, but only 23% male agree with that.

The investigation shows that though majority of people realized the harmful effects of UVR, a lot of them neglected to protect themselves from exposure to UVR. The result was similar to that of early investigation in western country. It is urgent to take some propaganda against UVR in China.

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THE RADICAL PROTECTION FACTOR FOR INNOVATIVE NUTRICEUTICALS

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Summary

Oxidative stress is defined as a molecular alteration generated by oxidant molecules.

This oxidative damage can occur by direct chemical oxidation, or it can involve a more insidious chain reaction in molecules that are oxidatively reactive for the presence of a single unpaired electron: the free radical.

Since free radicals are essentially caused by UV and environmental oxidants, the free radical-induced oxidative damage is always present.

Moreover, the oxidative stress is characterized by both reversible and irreversible cell damage and can, with time and sufficient severity, lead to cell death.

Biological systems are protected from the oxidative assault by a diversity of mechanism designed to suppress pernicious oxidative pathways.

Among these mechanisms there are the antioxidant systems represented by carotenoids.

The object of the study was to control the efficacy against free radicals of a dietary supplement based on carotenoids and antioxidant vitamins, determining also its real activity "in vivo" together with its radical protection factor (RPF) according to Herrling et al.

The radical oxygen species (ROS) before, during, and after the diet supplementation was determined by the new Ros-meter-system (Dermotech - Italy) at 505 nm. on the blood serum of 36 smoker volunteers (women and men) aged between 30 and 45.

The obtained results proved that the carotenoids based dietary supplement is able to reduce the oxidative stress of about 30/40 % during the first week of treatment, and the methodology used is also useful to determine, in a quite fast way, the RPF of the diet supplement used.

This way it seems possible to label the diet by RPF values strictly depending on the different needs, as it already happens with the sun products. At the same time it is possible to classify diet supplements as "nutriceuticals" and to demonstrate their efficacy.

Riassunto

Lo stress ossidativo è dovuto ad un'alterazione molecolare provocata da molecole ad attività ossidante. Il danno ossidativo può verificarsi per un'ossidazione chimica diretta o può coinvolgere una serie di reazioni provocate da molecole particolarmente reattive per la presenza di un elettrone

spaiato: il radicale libero.
Siccome i radicali liberi sono provocati essenzialmente dai raggi UV, dalla luce e dagli ossidanti presenti nell'ambiente, il danno ossidativo indotto dal radicale libero è sempre presente. Inoltre lo stato di stress ossidativo è caratterizzato dal danno cellulare sia reversibile che irreversibile; danno che se molto grave, può portare alla morte della cellula.
I sistemi biologici sono protetti da diversi meccanismi necessari per eliminare tali danni. Tra questi meccanismi vi sono i sistemi antiossidanti rappresentati dai carotenoidi. Controllare l'efficacia contro i radicali liberi di un dietetico basato su carotenoidi e vitamine antiossidanti, determinando "in vivo" sia l' attività che il fattore di protezione "antiradicale libero" (RPF) secondo la metodica di Herrling et al.
La presenza di radicali liberi (ROS) prima, durante e dopo la dieta è stata determinata utilizzando il ROS-meter-system a 505 nm sul siero di sangue di 36 fumatori volontari (uomini e donne) di età compresa tra 30 e 45 anni. I risultati ottenuti hanno dimostrato che la dieta basata sui carotenoidi è in grado di ridurre lo stress ossidativo di circa il 30/40 % durante la prima settimana di trattamento.
In questo modo sembra possibile caratterizzare il prodotto dietetico con valori di RPF strettamente collegati con le diverse necessità, come già si verifica con i prodotti solari.
È così possibile classificarli, ad esempio, come veri e propri nutriceutici, dimostrandone anche una loro eventuale efficacia protettiva.

BACKGROUND

Radicals are among the most important intermediates in the mechanism of toxicity for a vast number of chemicals. Oxygen-derived radicals are obligatory intermediates in the mechanism of toxicity for a vast number of chemicals.
Biologically speaking, oxidative stress is defined as a molecular alteration generated by oxidant molecules.
This oxidative damage can occur by direct chemical oxidation, or it can involve a more insidious chain reaction in molecules that are oxidatively reactive for the presence of a single unpaired electron: the free radical.
Since free radicals are essentially caused by UV light and by environmental oxidants the radical-induced oxidative damage is always present (1-3).

INTRODUCTION

The strong reactivity of free radicals makes their determination difficult.
The most popular methodology is spin trapping, whereas a diamagnetic organic molecule, called the spin trap, reacts with the radical to be identified to produce a secondary more stable radical called spin adduct, which is more readily detectable by Paramagnetic Resonance Spectroscopy (EPR) (4).
This method, though difficult to apply "in vivo", provides direct information regarding the identity of free radicals generated in a system (5, 6).
A big limit of this method is that free radicals, being too unstable, practically react topically where they are produced, that's why the "ubiquitary diffusability" of the "traps" should be assured, thing not at all demonstrated.
It has been tried to solve the problem differently, by using the hydroperoxides.
The fact that lipids in presence of free radicals, easily oxidize, has to be considered natural target; among these, the essential fatty acids (EFA), for their own characteristic, are gradually oxidized in the so-called reaction of propagation that leads to the formation of a hydroperoxide radical L00°, surely more stable than the OH° radical beginning the process of oxidation (7).
This hydroperoxide could be defined as "marker" of the oxidative stress in the biological systems, since its increase is proportional to the production of OH°.
Differently to other ROS (Reactive Oxygen Species), the hydroperoxide L00° is relatively stable and, in order to produce other radicals, it must react with an iron ion.

AIMS

The object of this study was to control the efficacy of a diet supplement based on carotenoids, antioxidant vitamins, and polyphenols against free radicals determining also its real activity "in vivo" together with its Radical Protection Factor (RPF) according to Herling et al. (8).

MATERIAL AND METHODS

Before, during ,and after, the dietary supplementation was detected by the new ROS-meter System (Dermotech-Italy) at 505 nm., on the blood serum of 60 smoker volunteers (women and men) aged between 30 and 45, according to Morganti P. and Fabrizi G. (9).

ROS MEASUREMENT

As it is known free radicals are extremely reactive and have a very short life. Because of its unopposed electron, a radical is slightly attracted to a magnetic field; it is paramagnetic. This unique physical property allows for its detection and analysis by electron paramagnetic resonance spectroscopy (EPR). But only a small num-

ber of radicals are stable enough to be detected by such spectroscopy in aqueous solution at room temperature. Fast flow techniques are used to detect short-lived radicals. The most popular methodology is spin trapping, in which a diamagnetic organ molecule, called the spin trap, reacts with the radical to be identified, to produce a secondary but more stable radical called a spin adduct which is more readily detectable by EPR.
One U. CARR is equal to a hydrogen peroxide concentration of 0,08% mg.
The methodology has been controlled and validated by the Electronic Spin Resonance (ESR) (10-12).

Table I

MEAN ASSESSMENT OF ROS IN STRONG SMOKERS

SMOKERS	N	Average ROS mg% ± SD*
20 Cigarettes/day	20	27.04 ± 0.81
30 Cigarettes/day	20	30.43 ± 0.74
40 Cigarettes/day	20	43.84 ± 0.66

Standard deviation on 3 different analysis for each of the 20 subjects controlled

SCREENING PROCEDURE

Before starting the study, the ROS present in the blood serum of different groups of volunteers (men and women) smoking from 20 up to 40 cigarettes a day were controlled.
A small quantity of blood was sampled from each volunteer, whose serum has been tested through three different determinations using the ROS-Meter System (Dermotech-Rome, Italy) (9).
The obtained results are reported on Table I.
The blood sampling was effected in a medical office always at 10.00 a.m. and on fasting.

TEST PROCEDURE

Sixty healthy smoker volunteers age range 30 and 45 (35 women and 25 men), were selected for the study. Each volunteer smoked at least 40 cigarettes a day. The subjects were randomly divided into 6 groups of 10 people and to each group were given sufficient capsules for 1

month of treatment. Neither the operator nor the subjects were able to identify the product. Eight weeks before starting the study, the subjects suspended all drugs or diet supplements taken by oral route.
The groups were subdivided in:

I	group	1 capsule/day	PRODUCT A[1]	(betacarotene 6 mg.)
II	group	2 capsule/day	PRODUCT A	(betacarotene 12 mg)
III	group	3 capsule/day	PRODUCT A	(betacarotene 18 mg)
IV	group	1 capsule/day	PRODUCT B	(carotenoids 10 mg.)
V	group	1 capsule/day	PRODUCT C	(carotenoids 15 mg.)
VI	group	1 capsule/day	PRODUCT D[2]	(carotenoids15mg + C and E vitamins and polyphenols)

Each subject took 1, 2 or 3 capsules per day for one month, according to the group of affiliation. The ROS were photometrically evaluated in the blood serum at week 0 (baseline value) and respectively at week 1, 2, 3 and 4 by ROS-meter System at 505 nm, according to Carratelli et al. methodology (10), formerly used by our group (9).

The RPF provided by the tested products, were determined by calculating the ROS reduction obtained with the diet supplement used, and interpolating those values in the standard curve determined at different concentrations of carotenoids taken by oral route (Fig. 1).

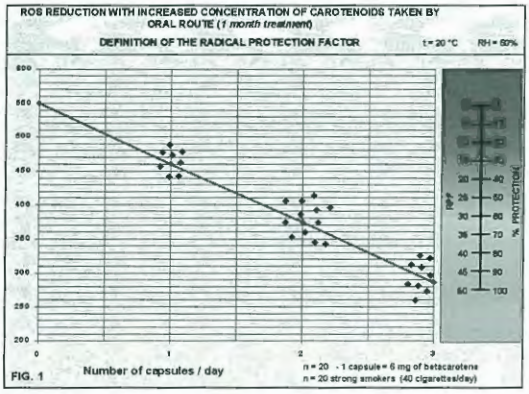

Fig. 1

RESULTS AND COMMENTS

As it is possible to see from Tab. I, the values of ROS, found in the smokers, seems to change from mg 27.04 ± 0.81 to 30.43 ± 0.74 up to mg 43.84 ± 0.66 ($p<0.05$) in depending of the number of cigarettes smoked during the day: 20, 30 or 40.

In fact, as it is known, the presence of carotenoids, found in the smokers' blood, decreases over 50% for the ROS provoked by the combustion of the tobacco substances.

Moreover, it can be observed an increasing of free radicals that seems to be directly proportional to the cigarettes smoked (9).

These data perfectly agree with what Carratelli (10) set in evidence, underlining how the smoke and the stress, or the beginning of different pathologies, can influence, in a remarkable way, the presence of free radicals in the blood serum. From that, the possibility to classify the different pathologic conditions, or the simple stress condition, in relation to the ROS checked (Tab. II) in the serum (10, 11).

What is interesting to observe is the positive influence, towards the ROS, not only of carotenoids but also of polyphenols, and vitamin C and E.

Table II

BASELINE VALUES: U.CARR	
300 to 320 CARR U.	Borderline value
320 to 340 CARR U.	Slight oxidative stress
340 to 400 CARR U.	Oxidative stress
400 to 520 CARR U.	Heavy oxidative stress
Above 500 CARR U.	Very heavy oxidative stress

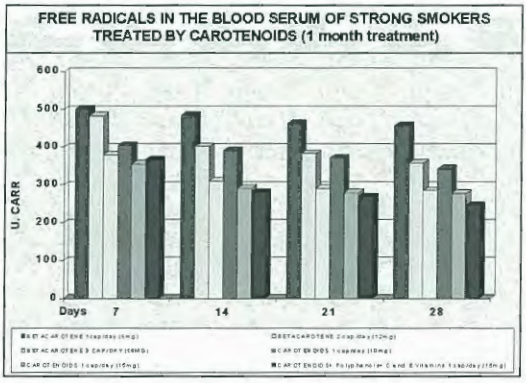

Fig. 2

1 Trade name Betaeffe Plus
2 Trade name Betaeffe Complex

In fact, from the Tab. III and Fig. 2, it can be easily observed how the assumption by oral route of an antioxidant, such as Betacarotene, at the dosage of 6 mg/day for a month, can reduce of about 16% ($p < 0.05$) the ROS content in the serum blood of strong smokers (RPF 15).
The above reduction is even higher in a daily intake of 12 mg (RPF 30) and reaches values of 50%, if increasing the dosage at 18 mg per day (RPF 50).
What is interesting to underline is that, even with just 15 mg/ day of carotenoids is possible to obtain a reduction of the ROS of about 50 % ($p< 0.05$), reduction increasing in a remarkable way ($p < 0.05$), when the carotenoids are added with polyphenols, vitamin C and E (RPF 60) (Tab. III).
In conclusion by means of this study, following the suggestion of Herling et al. (8), it has been tried to determine the RPF of the dietary supplements in order to classify their activity towards the ROS in the serum.
It was defined a conversion table through which it seems possible to pre-determine the RPF in depending of the more or less activity they solve towards free radicals present in the blood serum (Fig. 1).
This way it seems possible to label the diet by RPF values strictly depending on the different needs, as it already happens with the sun products. At the same time it is possible to classify diet supplements as "nutriceuticals" and to demonstrate their efficacy.

Table III

EFFECT OF 1 MONTH TREATMENT REGIMEN ON RPF VALUE IN STRONG SMOKERS (40 cigarettes/day)

TREATMENT (1)	REGIMEN	GROUP	ROS	RPF
6 mg Betacarotene	1 cap/day for a month	I	36.56 ± 0.072	15
12 mg Betacarotene	2 cap/day for 1 month	II	26.84 ± 0.081	30
18 mg Betacarotene	3 cap/day for 1 month	III	22.30 ± 0.059	50
10 mg Carotenoids	1 cap/day for 1 month	IV	27.30 ± 0.034	35
15 mg Carotenoids	1 cap/day for 1 month	V	21.80 ± 0.046	55
15 mg Carotenoids + C and E Vitamins + Polyphenols	1 cap/day for a month	VI	16.30 ± 0.018	60

(1) All treatments consisted of a diet supplement containing BETACAROTENE or various concentrations of CAROTENOIDS or/and vitamins and polyphenols

Tab. II

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SURGICAL TECHNIQUES FOR CUTANEOUS SCAR REVISION

By Marwali Harahap
1999. 495 pages, illustrated
$195.00
ISBN 0-8247-1973-5
Marcel Dekker, Inc. - New York -USA
Fax: +212 685-4540
E- mail http://www.dekker.com

This interesting book of my friend Prof. Marwali Harahap is focused on the best way "to avoid the scars and, once they are there, how to repair or remove them".
As matter of fact, scars deform many patients and generally they are anxious to normalize them. To remove and/or hide these scars they try all the means at their disposal and, not finding a complete solution through the doctor, turn to physicians and attorneys to solve their problem.
The first five chapters of the book are dedicated to fundamental principles, such as biomechanical properties of the skin, wound healing and scar formation. In theory cutaneous wound repair should involve regeneration of the skin bringing all the anatomical and physiological capabilities back to normal, but practically it does not happen. In fact, the cutaneous wound healing can result either in a normal scar or an abnormal scar formation. Abnormal scarring leads to hypertrophic scar or keloid formation, therefore "the ability of a cutaneous surgeon to camouflage and revise scars defines his/her ability as a surgeon".
At present many are the obscure sides linked to scar formation. However availability of highly sophisticated molecular and cellular biology techniques has given the opportunity to better understand the complex mechanisms involved in wound healing.
It was verified that type III collagen is the major type of collagen synthesized by wound fibroblasts and the dermis in the wound returns to the normal pre-injury state containing type I collagen, over a long period of time.
The whole first chapter describes the problems linked to wound healing at cellular level and the consequent scar formation, such as the increased matrix production by dermal fibroblasts, and its remodeling. Successful treatment of wounds and favorable scar formation require an understanding of the biomechanical properties of the skin. This is the subject of the second chapter.
Collagen molecules, cross-linked with lysine residues to form fibrils, provide most of the mechanical strength of skin.
Elastin, that forms a mesh like network in dermis, seems to function as a type of energy storage device. It stretches collagen back to a relaxed position, having an effect on the directionality of skin tension. Glycosaminoglycans, hyaluronic acid, and chondroitin sulfate, make up the ground substance and, with water, contribute to the viscoelastic nature of skin. The viscous properties of connective tissue are strongly correlated with the type and the amount of glycosaminoglycans.
In evaluating wound closure and scar revision, the biochemical properties that are most pertinent are related to the directionality of resting skin tension, tensile and elastic properties, plasticity and expandability of skin. Moreover the biomechanical skin properties offer cellular and structural basis

for the qualitative differences in skin according to site, age, and state of hydration. Skin viscoelasticity and expandability together with scar maturation explain long-term results in wounds and flaps.
Chapter three describes the factors increasing the probability that a larger scar will result from a wound.
A healing wound is the result of several major processes: inflammation, angiogenesis epithelization, and collagen production and remodeling. Contraction plays also an important role especially in open wounds. When one of more of these processes are hindered, non-healing wound results that frequently gives more scarring.
Factors that impair healing can be classified into intrinsic causes, such as age, immune status, stress etc. and extrinsic causes such as malnutrition infection, smoking etc.
The stress-mediated mechanism that influences wound healing seems to be directed through the immune system.
Vasoconstriction and higher levels of carboxyhemoglobin, which limits the oxygen-carrying capacity of blood seems to delay wound healing as well as to decrease skin flap survival in smoking people.
Many other local factors, such as infection, hematoma and seroma but also the excessive wound cleansing or the excessive pressure over the surgical site, may cause cellular damage increasing the like-hood of scarring. With careful preoperative planning, meticulous surgical technique and research to improve scar-reducing therapy, the control of cutaneous scarring may be possible in the future.
The fourth chapter focuses on the cultural and psychological aspects of patients with scars, giving an historical excursus on scars wished for cultural, religious and ethnic reasons, also highlighting how the unsatisfactory results claimed by the patients is often caused by false promises of media-promoted miracles or follow the advice of unqualified physicians.
Chapter five "discusses prevention, and minimization of scars by proper management of the initial wound".
A correct planning of the excision orientation and a good postoperative care may prevent unsatisfactory scarring, ensuring the best final result.
Of course, the key of the preoperative discussion is the patient informed consent that make possible to take a decision on the procedure chosen by the doctor. As matter of fact the procedure's indications, the alternative treatment options, the risks, and the potential adverse outcomes, need to be discussed with the patient.
In fact, not all the ethnic groups have the same post-operative effects. Africans and Americans patients, for example, have a higher incidence of keloid. Being aware that a patient has a history of keloid formation can facilitate post-operative planning. A preoperative history must also include an inquire about previous difficulties with bleeding and the use of medications, such as aspirin, retinoids coumarin derivatives or diet supplement as vitamin E or fish oil, may increase the risk of bleeding or scar formation. The patient must also be questioned about possible allergic reactions to any topical antibiotics such as neomycin or dressing materials.
Hence follows the description on orientations of the incision. What are the preferred sites for incision placement and which are the intraoperative techniques often used. The cutaneous surgeon should be familiar, for example, with the location of the skin tension lines, resulting from the repeated contraction of the underlying muscles. These lines vary in dependence of the cutaneous areas.
As well known, on the forehead, the lines are transverse because of the underlying frontal muscle. In the glabellar area they are vertical, meanwhile in the perioral region, the lines are radial. The unsatisfactory results to prevent the principle of free margins need to be taken into account also when

planning an excision or repair.
In this chapter, there are also sections dedicated to suture problems related to scar formation, the technique regarding the flap or the graft closure, and all the complications leading to scarring, such as bleeding, infection, necrosis and dehiscence.
At the end, there's a note on the problems related to hypertrophic scars and the keloids as well as to pigmentary changes that may occur. Deeper epidermal damage is more like to result in hypopigmentation of the skin as a result of destruction of the majority of the melanocytes. More superficial epidermal damage is more like to result in hyperpigmentation as the remaining melanocytes proliferate in the injured area. All the other 19 chapters are about the clinical applications of scar revision and all the known scar removal techniques.
Furthermore, the resurfacing techniques from dermabrasion, to Luminar Dermal Reticulotony or Scalpel sculpting are described, and it's given room also to the recent clinical techniques connected with the cryosurgical or the laser methodologies.
Chapter six is of fundamental importance to understand the whole book. The goal of this chapter is to show how to accomplish the greatest scar improvement through the "geo-topographic approach". This is a new conceptual tool for analyzing scars, their treatment, and prevention in order to achieve satisfying results. In this regard fundamental is the general approach to the scar and to the patient.
By means of the topographic approach of the scars, the elevation, depression and texture changes are described. The geologic approach examines the characteristics of superficial and deep tissue strata in a scar, the tissues contiguous to them in adjacent anatomic units, and passive and dynamic stresses. Integrating the "geo" and the "topographic" into a "geo-topographic" helps maximally in analysis and planning.
Naturally significant questions to know are how old is the scar, the age and the personality of the patient, the anatomic location of the scar. Local skin tension, previous treatments or injuries, medications, nutrition, and general health affect also the selection of a scar revision technique.
Big room is given to the correction of depressed scars and wrinkles by use of fillers like the collagen Zyderm and Zyplast or hyaluronic acid and the lyophilized collagen Fibrel. It's reported also the description of different other techniques such as the use of the antologous fat, the punch transplant technique for pitted scars or the dermal overgrafting.
This book is surely innovative nothing is left out. Also a new technique as "recollagenation" used for the acne scars, and unusual ones as the Z-plasty and W-plasty techniques are reported and remarkably described. All the operative techniques are always well illustrate and explained in a very "easy" step-by-step way.
This book would be of great help for dermatologists as well as for plastic surgeons because of wealth of details and news reported. It can be used also by young Ph.D. students in dermatology and plastic surgery and by all the specialists in aesthetic medicine.

P. MORGANTI PH.D
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CHITIN AND CHITINASES

By P. Jollès and R.A.A. Muzzarelli
1999. 360 pages. Hardcover, SFR 188.
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This book approaches chitin from an original stand point describing in the first part all it is known at present on chitin biosynthesis; in the second part are discussed all the structural and evolutionary aspects concerning the enzymes chitinases, and the third part is devoted to chitosan derivatives.
Chitin, (1-4)-linked 2-acetamido-2-doxy-b-D-glucan is an insoluble polymer of N-acetylglucosamine, widely distributed among invertebrates and ubiquitous in fungi. The nitrogen present in chitin imparts unique properties to this class of polysaccharides that may be considered as an ecocompatible and environment friendly raw material. For these reasons chitin and its derivatives play a pivotal role in many industrial fields, cosmetic included. That because it was possible to obtain by new biotechnological processes more soluble polymers modifying the intractable biopolymer chitin and chitosans under mild conditions.
What is interesting is that chitosans may be derived from the animal world of crustacean shells or from insect exoskeletons but they can also be obtained from fungi, easily cultured on simple nutrients. Moreover chemically modified chitins, important in the light of their biochemical significance in medicine and crop protection, are easily recycled by biodegradation operated by microbial genera present in the environment surrounding.
Therefore, chitin oligosaccharides represent a widely distributed organic compound of nitrogen environmentally important.
The first part provides up-to- date information on the state of knowledge and understanding of chitin synthesis and degradation in vitro and in vivo. The basic mechanisms of the chitin synthesis are important to understand properly the defending functions chitin performs. As matter of fact, many organisms utilize chitin as a structural component of the protective cell walls or exoskeletons, wbich surround them. Moreover, the polysaccharides chitin is also an important structure component of the cell walls of many fungi. These structures are light and resistant composites with specific structural and mechanical properties, which allow them to fulfill their protective role. Chitin, in the form of microfibils, is immersed in a matrix of proteins and other polysaccharides.
These cementing compounds protect chitin from chemical attack, keep the microfibrils separate, preventing fracture, and provide support to tensions. Hence chitin is degraded by three different chitinases and its synthesis can be blocked during the various steps by a variety of antibiotics, metabolic inhibitors, hormone analogs etc. All these synthesis inhibitors as well as inhibitors of chitin degradation, are also pursuing agents for controlling insects parts, fungal pathogens and helminthic parasites.
The second part of the book formed by 10 chapters, is devoted to chitinases, which split the ß-1,4 glucosidic bonds of chitin just as in a less pronounced manner, lysozymes also do. In general these chitinases act through a retaining mechanism in which ß linked polymer is cleaned to release a ß monomer product. These enzymes found primarily in plants but in bacteria also have a bilobal struc-

ture with a high α-helical content and their properties seem to be closely related to their biological function. As matter of fact, chitinase, produced by a wide variety of phatogenic and parasitic microbes and invertebrates during their attack on chitin-containing organism, play an important role in penetration of fungal cell walls, and of exoskeletons and peripheric membranes of arthropods. Moreover these enzymes play a major defensive role in all plants against attack by fungi, and perhaps also against attack by insect pests.
At least some vertebrates, including fish and humans also may utilize chitinases in their defense against pathogenic fungi and some parasites.
This knowledge gave a remarkable impulse to the study and the relative production of special chitinolytic enzymes to be used as biopesticides or as chemical defense proteins in transgenic plants and microbial biocontrol agents.
As matter of fact, the public concern over the harmful effects of chemical pesticides on the environment and human health. Therefore control of plant pests by the application of biological agents environmentally friendly holds great promise as an alternative to the use of chemicals. The discovery of chitinases allows us to have novel strategies for biological control. Further work on cloning and characterization of chitinases will also provide us the tools and understanding for making better use of these genes. Genetic engineering allowed us to verify that the potential of chitinases is likely to be enhanced by combining them with other bioactive peptides and lytic enzymes such as glucanases, as in natural systems. This, special emphasis should be make of the use of combinatorial strategies.
As previously said chitin and chitinases play important roles in the life cycle of several protozoon and metazoan parasites but may be also useful as preventive or therapeutic agents. Moreover a considerable number of medically important parasites shown to possess chitinase-like activities. The enzyme is produced at a particular stage of the parasite's life and seems to be important in lifetime. This implies that the blocking of the chitin production or the chitinase activity in these parasites may block their development to maturity and their transmission to the next host. Hence the possibility to use a chitinase as a transmission-blocking vaccine for humans.
The third and last part of the book is devoted to chitosan derivatives that, for their biodegradability, biocompatibility and capacity to promote the synthesis of hyaluronan are administered to humans in the form of dressings for wounded soft and bone tissues or are used as anticholesterolenic dietary foods, cosmetic items for the controlled delivery of drugs.
The biological significance of these modified chitins depends on the actions that certain hydrolases exert on them. The resulting chitooligomers stimulate various cells, while the released monomers are phosphorylated and incorporated into the intracellular matrix and connective tissue, such as hyaluronan and keratan sulfate.
Therefore in comparison with conventional therapy with irrigation and antibiotic administration to wound, the treatment with chitin and chitosan allows a substantial decrease in treatment frequency with minimum scar formation.
Chitosan through their amino groups, seems also to be recognized by the immune system and able to activate the macrophages. Moreover chitosan developing a competitive inhibition of lipases, seems to be effective to control overweight when associated to a diet, even if it could deprive the diet of liposoluble vitamins. Chitosan is also proposed as a drug carrier for mucosal administration based on its bioadhesive properties. Finally chitin /chitosan shows antimicrobial activity on a wide variety of microorganism including fungi, algae and some bacteria. However, the antimicrobial action is influenced by intrinsic and extrinsic factors such as for example the type of chitosan, its gra-

de of polymerization or the substrate chemical and/or nutrient composition used.
In conclusion, the biological significance of chitin and chitosans in human body depends on the action that certain human hydrolases exert on it and the experimental results obtained from many worldwide studies highlighted how these polysaccharides offer genuinely valuable and interesting items for agriculture, food, cosmetic and pharmaceutical industries.
This interesting book provides a stimulating background for who wants to know better all the aspects connected with the production and the present and future use of chitin/chitosans compounds as new category of polysaccharides.
It would be useful for the medical class, chemists or marketing specialists whose aim is to create innovative biocompatible products, but it would be of great help also for the students of pharmacy, biology, medicine and agriculture.

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CHITOSAN PER OS
From Dietary Supplement to Drug Carrier

By R.A.A. Muzzarelli
2000. 334 pages. Softcover
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This interesting book is the latest the author has dedicated to chitin / chitosan derivatives.
Chitosans, deemed generally safe, when administered per os , are generated by the activities of the food industry, and it should not be surprising that they find a place in the food chitosan. By the way, the polymeric nature of chitosan justifies also its different use. The polycationic chitosan, able to form polyelectrolyte complexes with a number of anionic substances, is filmogenic, undergoes the hydrolytic activity of lysozyme and other hydrolyses, and it's used, for example, as drug-carrier or for bone regeneration and tissue healing. Thus chitosan is used as vehicle for parental drug delivery device or as a direct tableting agent in oral formulations, in the forms of microparticles, liposomes, chitosan-gelatin coacervates and interpenetrating polymer networks. Nicotinic acid was therefore combined with chitosan in the preparation of chitosan alginate beads and used to study the uptake of bile acids. As matter of fact, the existing data indicate that the reaction of bile acids with aminated polysaccharides such as chitosan, is the fundamental step in the treatment of hypercholesterolemia and overweight. For obese patients, the orally administered chitosan leads to overweight reduction after a few week treatment assessing a lipid-lowering effect. Moreover, it is able to form complex salts that bind also triglycerides, fatty acids and cholesterol, and a great portion of these bond lipids are excreted. In analogy with other polysaccharides, chitosan inhibits also the putrefactive activity of the intestinal microbiota thus reducing the risk of diseases.
This book is divided in four sections for a total of nineteenth chapters. The *first section*, in four chapters, is dedicated to dietary supplements. The introductory chapter describes the hypocholesteromic action of chitosan, covering all the technical explanations that justify its use in the body weight control. In a study that has involved for 12 weeks 1000 volunteers with a body mass index over 25, it was observed a significant decrease of the body weight, even if some subjects did not respond to the chitosan treatment. In order to obtain positive results, the chitosan administration has to be associated to a diet. It is recognized as a safe compound, and seems to have a hypoglycemic and hypolipidemic effect; immunopotentiating and anticancer /antistatic actions have also been documented. Moreover, chitosan provides a sustained-release form of glucosamine and, therefore, may be orally administered in the treatment of patients with osteoarthritis. Finally it has mucoadhesive properties and enhances the penetration of macromolecules across the intestinal, the vaginal and nasal barrier. In the next three chapters, the basic molecular mechanism of the chitosan interactions with dietary lipids are reported. In the *second section* constituted by eight chapters, drug delivery methodologies are described.
Chitosan increases the penetration of hydrophilic macromolecules across epithelia in acid environ-

ments; it displays also mucoadhesive properties, due to the interaction of the positively charged chitosan microspheres with the negatively charges mucus glycoproteins. These mucoadhesive properties and the great biocompatibility of chitosan suggest that it may be a suitable drug carrier for peroral peptide drug delivery. In the research devoted to more and more active derivatives, it has been demonstrated how the trimethyl chitosan (TMC) chloride polymers may be considered as a novel class of permeation enhancers, which are able to open the paracellular pathways of mucosal epithelia in a safe and a reversible way. Their absence of cyto-and systemic toxicity is very advantageous, making TMC polymers promising excipients for drug delivery systems of peptide and protein drugs. Therefore, chitosan is good excipient for oral drug delivery systems because of its biocompatibility, biodegradability, low costs, and ability to open intercellular tight junctions between epithelial cells in the gastrointestinal tract.

At this purpose there are many studies and it has been demonstrated how chitosan can be used to prepare microparticulate carrier systems to be added with drugs. As matter of fact, incorporation of the drug in macroparticles makes them less vulnerable to enzymatic degradation in the gastrointestinal tract. These characteristics also make these particles promising candidates as carrier for oral vaccine delivery system to determinate costs of vaccines worldwide.

By the way, it has to remembered that to succeed they should not exceed 10mm in size, should be resistant to low pH values and capable to associate with various antigens. It was found that chitosan with a high degree of deacetylation (DA) and polymerization >50 induce the greatest effect on opening tight junctions, Low molecular weight chitosan appear also to cause slightly more cell damage and protein release than high molecular weight chitosans.

Moreover, the low degree of deacetylation, the high molecular weight and the short exposure time, contribute to reversibility of chitosan-induced opening of tight junctions.

Chitosan cross-linking represents a further approach to the control of drug release from solid oral dosage forms providing insoluble, swellable matrices whose release properties may be influenced by the nature of the cross-linking agent and the cross-linking degree.

Chitosan's ability to swell and form a hydrogel in the acidic gastric juice makes this substance suitable also as excipient in the preparation of floating dosage forms. As a matter of fact, a dosage form that exhibits, for example, slow-release of a drug in the stomach fluid, may improve the bioavailability of substances released or absorbed only in the stomach. In addition to these uses, chitosan is also reported to have several direct parapharmaceutical properties. As polymer glucosamine, it seems to be useful in the treatment of osteoarthritis, by enhancing the synthesis of glycosaminoglycans, by inhibiting their degradation and by scavenging reactive oxygen species, such as superoxide anion, hydrogen peroxide and hydroxyl radical. Chitin containing preparation are also promising treatment of diseases with complicated genesis, especially those followed by infection, intoxication, allergy and immune compromised conditions.

The *last part* of the book is dedicated to dentistry and related topics. Applications of chitosan in gel and film form for the delivery of chlorhexidine gluconate, as a film enriched with the antioxidant agent taurine and as permeabilizer for oral and mucosal delivery of drugs are examined. It's highlighted how the low molecular weight chitosans (LMCS) are, for example, very effective in lowering pH in dental plaque; how the chitosan-ascorbate used in form of dusting powder seems able to reduce local hemorrhage in the oral cavity; how a chitosan-poly (acrylic acid) hydrogel seems to reduce or obliterate microchannels in human teeth; how some water soluble modified chitosans applied to a wound may exert hemostatic or/and bactericidal/bacteriostatic and candidacidal action.

As matter of fact, chitosan gel delivery vehicles have ideal placement characteristics for oral muco-

sal delivery. It can be considered a polysaccharide that structurally mimics extracellular glycoprotein carbohydrates, demonstrating similar properties.
In conclusion chitin/chitosan represents an exciting biomaterial that has a number of interesting pharmaceutical and cosmetic applications.
Many are the uses already studied and many are to be examined ex novo.
These book gives many original imputs and will be invaluable to all the problems connected with our health. It could also be a fundamental reference for dermatologists, plastic surgeons but also for all the students in medicine and chemistry and marketing experts who will find many ideas for application and/or development of innovative products.

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TREATMENT OF VITILIGO

By Marcellus Davy Njoo
2000, 223 pg. Softcover
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This thesis of M.D. Njoo edited by the Department of Dermatology of the University of Amsterdam, reviews in a critical way the modern clinical manifestations and the more updated therapies used for the treatment of vitiligo. In this interesting book are reported for the first time the guidelines for the treatment of vitiligo too often considered by the majority of the medical doctors not a disease but a trivial cosmetic disorder.
It would be of help for the physician in daily decision making for patients with vitiligo. There are reported all the newly obtained chemical and experimental data. After having introduced the topic of vitiligo in chapter 1, in chapter 2 the current concepts regarding the pathogenesis of vitiligo are reviewed and historical aspect epidemiology, clinical picture, differential aspects, of this pigmentary disorder are discussed. Vitiligo, which equally affects individual of all ethnic origins and shows no special predilection for either sex, may cause serious psychosocial problems for those afflicted. Therefore the medical doctor should not undervalue this pathology.
The therapies commonly used are:

A) Non surgical repigmentation therapies

a) Personal plus UV-A which can be used either topically (topical PUVA) for patients with "localized" vitiligo or orally (oral PUVA) for patients with generalized vitiligo;
b) Narrowband UV-B that requires no oral drugs and shorter treatment times;
c) Broadband UV-B whose mechanism of action is unknown;
d) Phenylalanine plus UV-A where short-term side effects reported are erythema, pruritus, xerosis cutis and mild nausea after oral ingestion of the drugs;
e) Khellin plus UV-A that has a low genotoxic potential but seems to cause pruritus and xerosis cutis;
f) Corticosteroids given intralesional or orally, to those patients with rapid progressive disease. Local and temporary side effects include dermatitis perioralis, contact dermatitis, rosacea-like or acneicform eruptions, pruritus and other local manifestation :

B) Autologous transplantation method such as a minigrafting

(a) the split-thickness skin grafting;
(b) grafting of epidermal blisters;
(c) grafting of cultured autologous melanocytes;
(d) grafting of non-cultured melanocytes;
(e) grafting of non-cultured melanocyte suspension.

C) Depigmentation therapy

By bleaching agents, such as monobenzylether of hydroquinone (MBEH) or monomethylether of

hydroquinone (4-methoxyphenol) or by laser therapy by a Q-switched ruby laser apparatus (QSR)

D) Adjunctive "therapies"

Sun protection by use of brand-spectrum sunscreens, camouflage tattooing, micropigmentation and psychological counseling.

E) Novel therapeutic approaches

The latest therapeutic approaches are:
* fluticasone propionate plus UV-A therapy (10J/cm2);
* focused microphototherapy which uses UV-B light with a spectrum of 280-315 nm that requires an expensive equipment and trained personal and will therefore not be available for many patients around the world;
* pseudocatalase plus UV-B therapy based on a low molecular weight manganese complex (MW 328);
* systemic antioxidant therapy using the oral administration of antioxidant compounds, such as ubiquinone, vitamin-E, selenium and methionine;
* treatment with suplatast tosilale (IPD) an anti-allergic drug used for the treatment of atopic disorders;
* melagenine and infrared and /or UV radiation.

The latter therapy from Cuba is based on the use of melagenine, hydroalcholic extract of the human placenta poorly controlled. There is not much known about the biochemistry, biologic activity and pharmacology of this drug.
All these new vitiligo therapies should be interpreted with caution also because the studies were uncontrolled and/or had included only a few patients. More studies are therefore needed to establish the long-term effectiveness and safety.
In chapter 3, literature and clinical studies are presented in 7 different subchapters. Chapter 3.1 describes the results of a written survey concerning the management of vitiligo that was sent to all practing dermatologists in The Netherlands. What is interesting to underline is that most dermatologists do not offer active treatment in patients with vitiligo, because the estimated effectiveness of repigmentation therapies is low. In case of therapy its choice should depend on the clinical presentation of the disease, patient's motivation, psychological impact of the disease, and the risk to benefit ratio prolonged therapy.
Chapter 3.2, 3.3 and 3.4 describe the several steps that are involved in the making of evidence-based guidelines for the treatment of vitiligo.
The obtained results indicate that class 3 corticosteroids and UV-B therapy are the most effective and safe therapies for localized and for generalized vitiligo, respectively. Moreover no definite conclusion can be drawn about the effectiveness of culturing techniques, because only a small number of patients have been studied. The choice of method also depends on certain disease characteristics and the availability of specialized personnel and equipment.
Therefore clinical guidelines are to be considered not static and should regularly be updated to take into account changes in medical knowledge and practice and particularly the results of randomized trials and meta-analysi.
Chapter 3.5 contains a report on the association of the Koebner phenomenon with disease activity

and therapeutic responsiveness in 61 adults with vitiligo vulgaris. To date, there are no clinical markers available to assess disease activity. At this purpose a novel scoring system, the "vitiligo disease activity (VIDA) score", is proposed as a semiquantitative measure of disease activity.
Many investigators consider the treatment of vitiligo in children to be a separate issue. Chapter 3.6 describes the results of an open prospective clinical stndy on the effectiveness, safety and the impact on the quality of life of narrowband UV-B phototherapy in 51 children with generalized vitiligo
This novel therapy can represent a first choice and safe treatment modality for children having generalized vitiligo, especially for those cases with associated psychosocial problems.
In case of vitiligo universalis, treatments are directed to obtain a uniform depigmentation by the use of monobenzylether of hydroquinone (MBEH).
Because of the adverse effects reported with this drug, the use of MBEH has been restricted in the Netherlands.
In chapter 3.7, the long-term effectiveness and safety of topical 4-methoxyphenol (4-MP) cream and or Q-switched ruby (QSR) laser are evaluated in 16 patients with vitiligo universalis, obtaining interesting results.
Moreover a randomized controlled trial is needed to confirm these findings, according to author's view.
In chapter 4 reported conclusions and recommendations are made for future clinical trials necessary for better define the more efficacious and safe therapies.
This interesting book, thanks to the exhaustiveness of the therapies reported represents an indispensable tool for all those dermatologists who want to investigate and face with scrupulosity all the clinical problems connected with vitiligo and to its therapeutic resolutions.
It represents also a useful basic study tool for who want to start other innovative therapies in the attempt to find a solution to this pathology, and its still present shadows.

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PIGMENTARY DISORDERS

By Wiete Westerhof
1999, 101 pg. Softcover
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This small book describes the different treatments developed in the Netherlands Institute for Pigmentary Disorders directed by Prof. Wiete Westerhof between 1994 and 1999.
In a world where people affected by pigmentary disorders are said their "it is only a cosmetic problem and therefore, you have to live with it" it's necessary to inform patients on the different possible therapies and on the ongoing progress in the field. If from one side the fact vitiligo and hyperpigmentation are not scaring because they are not transmissible, it's true also that from an aesthetic point of view they can disfigure and psychologically depress the affected people. Even if some patients did not react at all, the combination treatment in vitiligo of fluticasone propionate (FP) and ultraviolet -A (UV-A) (10j/cm2) seems to be much more effective and safe in the long-term in reaching complete re-pigmentation that each separate treatment. This is the conclusion of the experimental work described in the first chapter.
In the second chapter it's compared the efficacy and safety of 2 treatment modalities, topical psoralen plus UV-A (PUVA) with a substituted psoralen and 311-nm UV-B irradiation, in-patients with vitiligo.
For PUVA therapy it was used a gel based on an unsubstituted psoralen (0.05% in 10% carbomer 934P) which seems to be skin absorbed. The second study group was treated by UV-B lamps (Phylips TL 100W/01) with a spectrum of 310-315 nm and a maximum wavelength of 311 nm. The treatment was applied twice weekly. In comparing the two different treatments, UV-B therapy was more effective and had fewer adverse effects.
The third chapter describes the use of the mingrafting test on 19 patients.
This methodology seems to be more efficacious towards people vitiligo vulgaris affected than in localized vitiligo.
The use of this split-thickness skin grafting in combination with minigrafting in piebaldism is the topic of chapter four. According to the results reported the contemporaneous use of dermoabrasion and split skin grafting followed by minigrafting should be considered as the first choice of therapy in piebaldism.
From chapter fifth to tenth hyperpigmentation is discussed. In chapter five is reported a study using 20% of 4-methoxyphenol (4-MP), which it's supposed to be possibly used as a depigmenting agent in vitiligo universalis.
If compared to the use of monobenzylether of hydroquinone (MBEH) 4-MP proved to be less irritating and very useful if used in combination therapy with the Q-switched ruby laser.
Ruby laser can be effective fast and safe method for removing cosmetically disturbing reminants of normal pigmentation in the vitiligo patients with a positive Koebner phenomenon.
These are the conclusion reported in chapter six.
Positive results using Q-switched ruby laser are reported also in the lentigo treatment (chapter 7) and in acquired melanocytic nervi (chap. 8).
Few are the side effects.

The last chapter finally reports the results on the use of N-acetylcysteine (NAL) in the treatment of melasma. NAC seems to be more active than hydroquinone as bleaching agent.
This small book is surely a useful mean to have at disposal the latest therapies used in the treatment of the pigmentary disorders. It's helpful for the dermatologist and for who wants to know the problems linked to the alteration of the skin pigmentation, both from a clinical and study point of view.

P. MORGANTI
Editor-in-Chief

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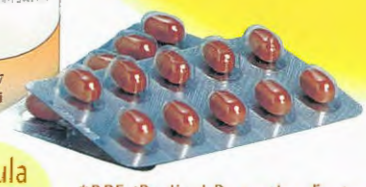

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