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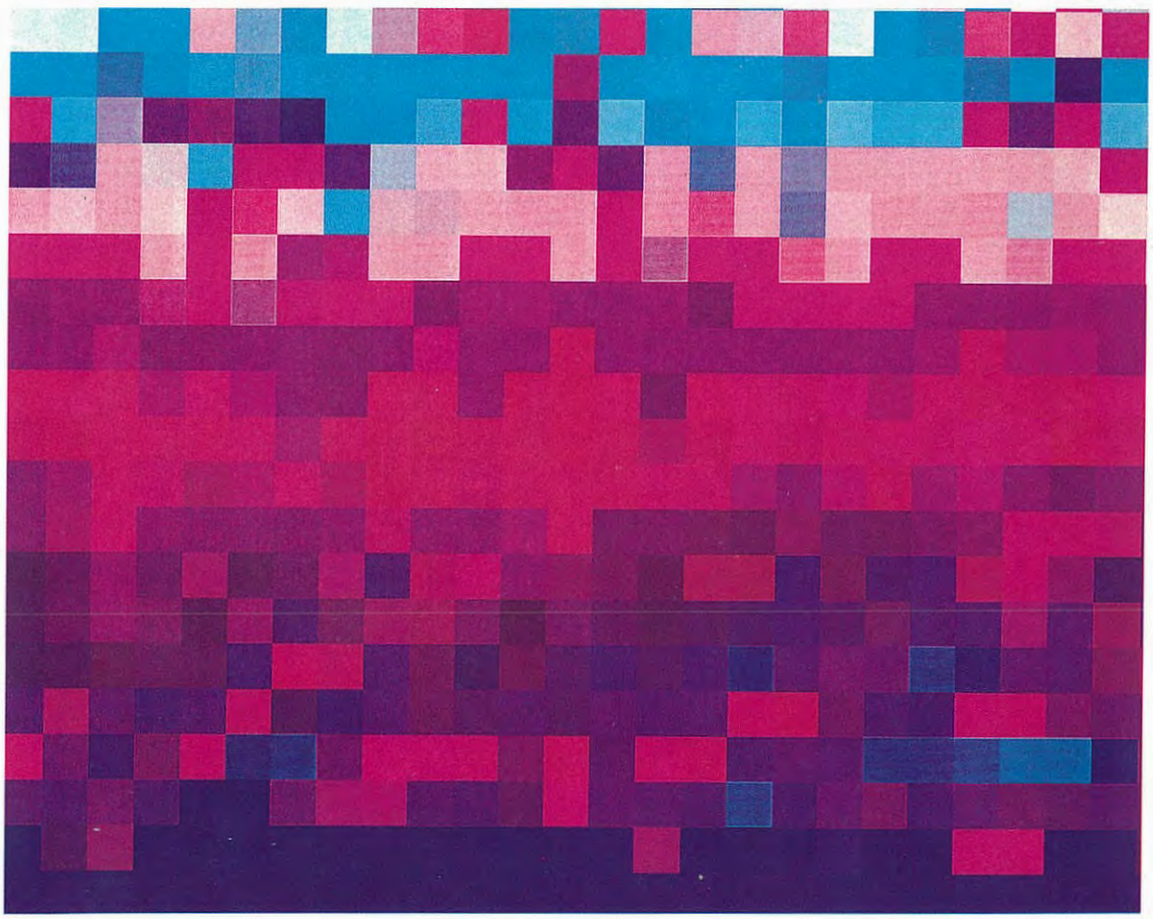

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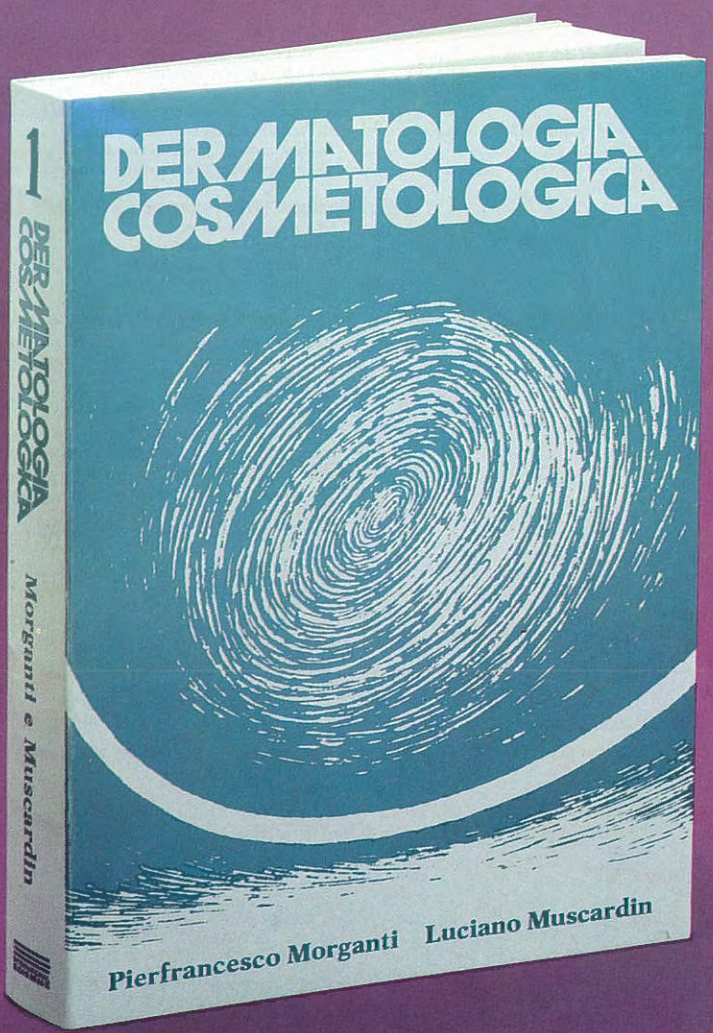

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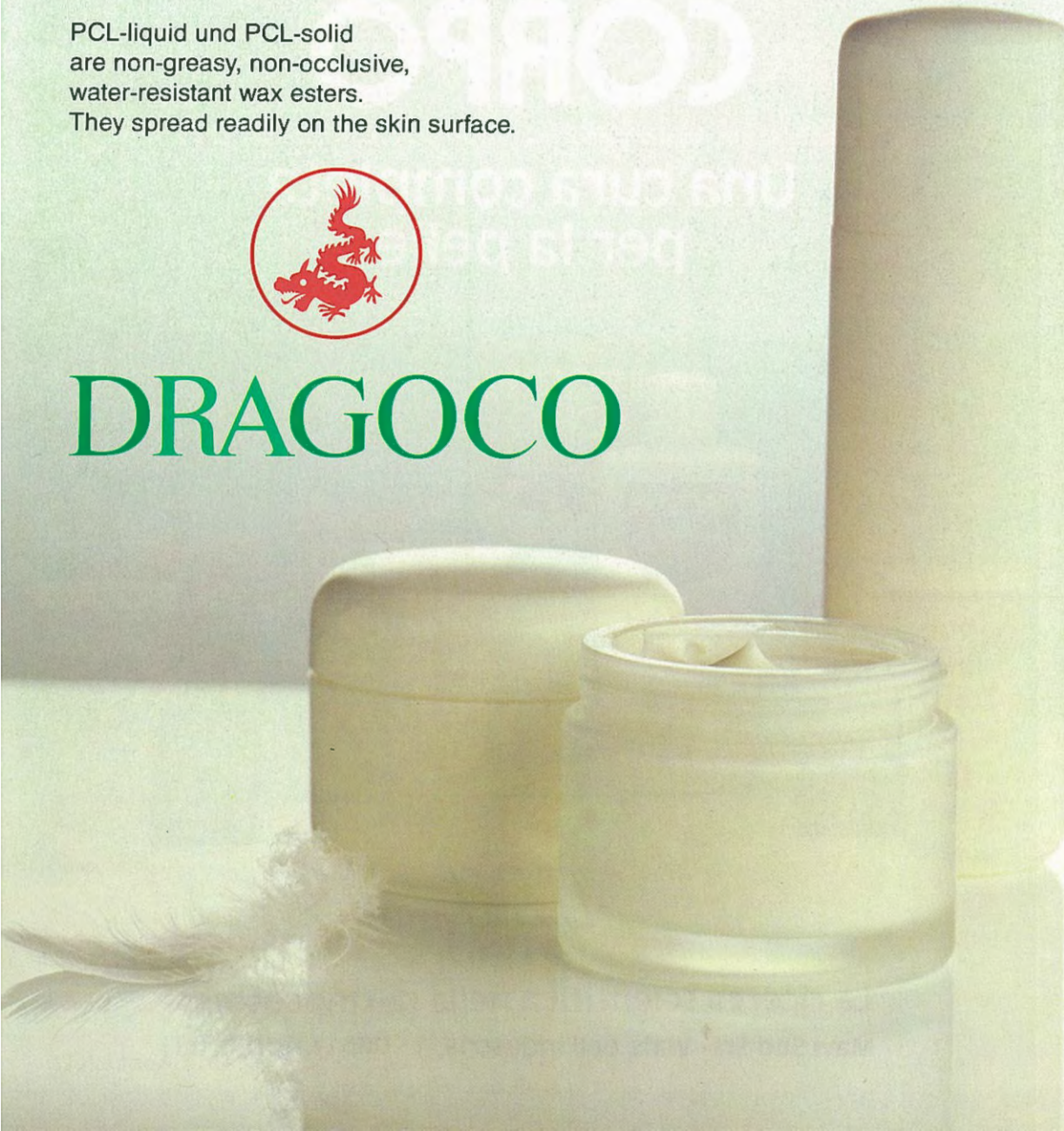

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1st International Meeting on Cosmetic Dermatology, Rome, Italy, March 7-9, 1985

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The proceedings contained in this volume provide comprehensive view of the different aspects of the skin aging with its cosmetological implications.

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Original Laboratory Studies

J. Appl. Cosmetol. 8, 65-76 (July - September 1990)

THE VAGINAL MUCOSA AND PERSONAL HYGIENE

R. Forleo, F. Mastroianni
Ospedale Fatebenefratelli - Isola Tiberina - P.zza Fatebenefratelli, 2 - 00186 Roma (Italy)

Received: *June 25, 1988. Presented at the "1° Corso Europeo di Dermatologia Cosmetologica". June 25-26, 1988. Roma (Italy)*

Key Words: *Vaginal Mucosa; Vaginal Ecosystem; Vagina pH; Vaginal Cleansing; Personal Detergents; Vulvar Cosmetic Treatment.*

Synopsis

The vagina is a peculiar organ of the woman's body: it is virtually an exposed cavity which undergoes substantial changes over the years and during the menstrual cycle in relation to hormonal stimulation; it thus has highly variable defences against external agents. In adult women the hair on the mont of Venus and the labia majora are a first protection barrier.
A very important feature in maintaining the physiological "ecology" of the vagina is a pH which also undergoes substantial changes troughout the menstrual cycle and over the years. pH is very low at ovulation and increases during the luteal phase.
The vaginal ecosystem can be heavily influenced by hormonal changes and is made up of many microorganism living together in perfect harmony. Amongst them, Doederlein's bacillus pays a major role, turning glycogen into lactic acid and determining vaginal pH.
The use of personal detergence characterizes Mediterranean countries and has no pendant in Anglo-Saxon countries, where the bath replaces the bidet.
Such trend has increased during the last 5 years, indicating greater bodily care and awareness.
The perfect personal care detergent must:
- be gentle
- be as close to physiologic pH (3.8-4.2) as possible
- have a lenient effect on mucosae
- have no selective disinfecting effect
- not dry the cutis
- attenuate unpleasant smells naturally
- be packaged practically and hygienically

so as to remove pabulum, which may favour the development of pathogenic germs, and also keep the vaginal mucosa trophism (especially when it is physiologically insufficient), which may involve the development of Doederlein's bacillus and also favour tissural metabolism.
Furthermore it is important that sexual intercourse is made easier if the vagina is dry. This means that personal detergents are necessary for women to keep such an important organ as the vagina healthy without making use of hormones (which are easily absorbed by the mucosa and may give rise to systemic effects) or of antimycotic or antibacterial substances (their abuse may cause diminished local resistance to phlogosis, resulting in a real immunodepression of the organ).

Riassunto

La vagina è un organo peculiare nel corpo femminile: è una cavità virtuale che comunica con l'esterno e che subisce notevoli modificazioni nelle diverse età e nelle varie fasi del ciclo a seconda degli stimoli ormonali cui è soggetta; conseguentemente le sue difese dagli agenti esterni sono estremamente variabili. Nella donna adulta una prima barriera di protezione è costituita dagli stessi peli che ricoprono il monte di Venere e le grandi labbra.
Un fattore estremamente importante per il mantenimento della fisiologia "ecologica" vaginale è rappresentato dal pH che subisce anch'esso notevoli modificazioni nelle diverse età e nelle varie fasi del ciclo: molto basso al momento dell'ovulazione, sale in fase luteinica.
Dell'ecoambiente vaginale, tanto sensibile alle variazioni ormonali, fanno parte diversi microorganismi che convivono generalmente in perfetto equilibrio. Tra di questi un ruolo di "primo attore" è svolto dal Bacillo di Doederlein, che con il suo metabolismo determina la trasformazione del glicogeno in acido lattico stabilendo così il grado di acidità del pH vaginale.
L'impiego di prodotti per l'igiene intima è un fenomeno caratteristico dei paesi mediterranei che non trova riscontro nei paesi anglosassoni dove l'uso del "bidet" è sostituito dalla doccia integrale. Tale fenomeno è andato ad aumentare nel corso degli ultimi 5 anni, sintomo di una maggiore attenzione e di una maggiore consapevolezza del proprio corpo.
Il detergente ideale per l'igiene intima deve:
- essere delicato
- avere un pH vicino ai valori fisiologici (3,8-4,2)
- possedere azione lenitiva sulle mucose
- essere privo di azione disinfettante selettiva
- non provocare secchezza della cute
- attenuare in maniera naturale gli odori sgradevoli
- avere una confezione pratica ed igienica

in modo da rimuovere il pabulum favorevole allo sviluppo dei germi patogeni mantenendo - specialmente nei casi in cui non sia fisiologicamente sufficiente - un trofismo della mucosa vaginale che comporti lo sviluppo del Doederlein e favorisca il metabolismo tissutale.
E' importante inoltre che venga facilitato il rapporto sessuale là ove esistono situazioni di secchezza vaginale. Si devono cioè trovare prodotti intimi per la donna che mantengano vitale questo importante organo che è la vagina, senza ricorrere né ad ormoni - che vengono facilmente assorbiti dalla mucosa e possono dare effetti sistemici - né a sostanze antimicotiche o antibatteriche il cui abuso produce una diminuzione della resistenza locale della flogosi, una vera e propria immunodepressione d'organo.

The vagina is a peculiar organ of the woman's body: it is virtually an exposed cavity which undergoes substantial changes over the years and during the menstrual cycle in relation to hormonal stimulation; it thus has highly variable defences against external agents (1,12,14,17).

In adult women the hair of the mount of Venus and the labia majora are a first protection barrier. In young women, the labia majora are thick and resistant thus providing a further mechanical barrier which elderly women lack. After the menopause the labia majora become thinner, while the hair dicreases and the rima pudendi remains disclosed. The local administration of a 2% minoxidil solution seems to be ineffective in preventing the substantial reduction pubic hair which occurs in elderly women, as the authors themselves have observed.

Even the labia minora protect the vagina. They are skin folds which are rich in dense and highly vascularized connective tissue having erectile properties. The labia minora have no hair follicles but are rich in oil glands which secrete a cheesy substance, with a peculiar and intense smell, on the vaginal vestibule, in the interlabial groove and below the clitoris cap. This mixes with secretions from the oil and sweat glands of the labia majora, with debris of soaked hair and stratum corneum, secretions from the major (Bartolino's) and minor (Skene's) glands of the vastibule, and with paraurethral secretions. Obviously such substances, rich in fats, sugars and proteins, may be an excellent medium for the development of several microorganisms (16,21,23,27) when proper personal care is lacking. Yet they also give rise to aesthetic and psychological problems connected with a feeling of "disorder".

A passage by the greatest surgeon of the XVI century, Ambroise Paré, describing the vagina and its sexual function, is both interesting and humorous. He wrote:

"there is a certain serous moisture, similar to sperm but more liquid and less dense, which causes a sharp and exciting pungency odour like a light itch tickling, that stimulates the parts to perform their action, giving desire and pleasure, which builds up a great amount of hot spirits that long for release. On the other hand, this moisture - besides giving the desire for coupling, and a great pleasure - becomes very wet and soaks the urinary canal against their pungency odour. Could anyone reflecting on a woman's natural canal and the filth passing through, the adjacent anus and bladder, be eager for coupling?".

When parted, the labia minora reveal the vaginal vestibule where the hymen is located. The hymen is a highly vascularized membrane of variable shape and thickness: it can be lunate, annular, septate, cribriform, and rarely imperforate, which can create serious problems during puberty. Obviously, even the hymen performs a protective function. Into the vestibule open canals of Skene's and Bartolino's glands. These secretions contribute to the humidity of the cunnus but, in spite of belief to the contrary, they are not useful to sexual life. Lubrication during coitus depends on perivaginal plexus transudation which is proportional to intensity of sexual stimulation and is related to stage of the menstrual cycle and to the patient's age; in elderly women the mucosa is atrophic and fragile and lubrication is scarce (10,26).

Further in, the vagina becomes wider, forming the fornices with the uterine cervix. The rear fornix is wider and is where vaginale and cervical secretions, microorganism and flaking cells accumulate. In the rear fornix the material for vaginal smears is taken.

In addition to macroscopic anatomy the vaginal histology in different stages of the cycle and the woman's life must be taken into account. In fact, a greater or lower sensitivity to external agents in strictly related to the condition of vaginal epithelium and thus to the hormonal situation (11,19,20,24,25).

The vaginal mucosa is polyptychial, rich in glicogen and the surface cells contain keratohyalin granules. In the follicular stage, just before ovulation, higb levels of estrogens are responsible for thickening of the mucosa and a substantial glycogen content. Soon after ovulation, this gathers in granules, which are released externally by shedding of surface cells. During the luteal stage the epithelium appears thin and has a low glycogen content. Obviously everything is related to procreation finalism linked to the different cycle stages.

A very important feature in maintaining physiological "ecology" of the vagina is pH which also undergoes substantial changes throughout the menstrual cycle and over the years. pH is very low at ovulation and increases during the luteal phase.

Changes in the vaginal epithelium during the menstrual cycle can be followed in vaginal smears made in the different phases. In the beginning of proliferative stage, that is soon after menstruation, cells are scarce and basophilic. In the late proliferative stage, influenced by the high estrogen level, shedded cells are keratinized, acidophilic and flat or curved according to the degree of shedding. In the initial secretory stage, due to progestational hormone production, surface cells increase in number looking wide, with curved edges and basoplasm, and some polymorphonuclear cells and Doederlein's bacilli appear. Finally, in the late secretory stage some days before menstruation, collections of curved-edge basophilic cells can be noticed, shedding is at its maximum and free nuclei, Doederlein's bacilli, cytoplasmic fragments, mucus and polymorphonuclear cells can be detected in the smear.

Babies have excellent defences against external agents. They have anatomic defences, such as hymen and cunnus turgor and the polyptychial vaginal epithelium, as well as biological defences, like the acid pH, the shedding of the vagina epithelium, and the secretions of the cervical glands stimulated by the high maternal-placental estriolemia (1).

After few weeks of life, to improve hepatic glycuronide conjugation, estriolemia and therefore the defences against external agents decrease (1). The mucosa appears thin and atrophic and will remain like that throughout childhood. The vaginal pH increases due to a glycogen lack and the absence of Doederlein's bacillus. Cervical secretions is scarce and thus also vaginal cleansing. The protective effect due to turgor of the labia majora, labia minora and hymen decreases and the absence of pubic hair is a further lack of mechanical protection. The external genitalia are therefore more exposed to irritant and allergenic agents and to infection by microorganisms (1).

During pregnancy, as a consequence of the high levels of estregens and progestational hormones, the mucosa grows to its peak, forming a thick layer of keratinized surface cells.

In late pregnancy, the increase of progestational hormones leads to the formation of smaller cells with curved edges called "navicular cells".

During confinement, due to the sudden fall in hormone levels, the vaginal epithelium flattens and basal cells prevail in the smear.

After the menopause, the vaginal mucosa looks very thin, pale and bleeds easily. The vagina is no longer acidic and infections become more frequent. Vaginal smears are atrophic and made up almost entirely of basal cells. Polymorphs con also be seen. The rate of anaerobic glycolysis decreases substantially. Glucose 6-phosphate decreases by 35%, fructose 6-phosphate by 76%, pyruvate by 39%, lactate by 40% and ATP by 12%.

In women undergoing estriol treatment, pyruvate, lactate and ATP increase while ADP decrease (12).

The vaginal ecosystem can be heavily influenced by hormonal changes and is made up of many microorganism living together in perfect harmony. Amongst them, Doederlein's bacillus

plays a major role, turning glycogen into lactic acid and determining vaginal pH, physiologically ranging between 3.8 and 4.2, thus stopping microorganism developing in an alkaline environment (6,3,4).

Upsets of this balance can cause vaginitis. Microbiological or infectious alterations of the vaginal ecosystem may be due to pathogenic microorganism such as trichomonas vaginalis, hemophilus vaginalis, candida albicans, clamydia trachomatis or to common forms like colon bacilli, aerobic streptococci, anaerobic cocci developing beyond control (27,5,4,23).

Traumatic and irritating causes are also to be taken into account. Such causes can be identified with wearing clinging or synthetic clothes (tights), the improper use of diaphragm, irrigators, the use of spray deodorants and alkaline soaps, and an incorrect care of the external genitalia after defecation. Local irritation ensuing from such practices creates an ideal medium for microorganisms to develop.

Poor physiological protection of the vaginal mucosa (1) during the menopause and in childhood may lead to vaginitis. Abundant unmetabolized glycogen may predispose to fungal infections, and diabetes is another biological cause of vaginitis. Pregnancy and other conditions in which the natural defences are reduced, increased mucosal congestion, can be included in this category.

Antibiotic therapy can cause vaginal imbalance and encourage growth of fungi. Sexual intercourse can be a contagion. Poor personal hygiene especially after menstruation, parasitic infestations (phtheiriasis, scabies), fig warts and herpes genitalis can cause vaginitis. Oral contraceptives, on the contrary, do not seem to be responsible for candida, despite the common belief.

The symptoms of vaginitis depend on the responsible agent, with various discharges and irritation. Local aspects can be worsened by unrest and nervousness causing deep prostration in the most serious and recurrente forms. According to seriousness of the infection and the responsible agent, treatment is by antibiotics or antimycotics by oral and/or topical administration.

pH is a major factor influencing the susceptibility of the vagina to the development of microorganisms. Usually, its value ranges from 3.5 to 4.2 rising to 4.5-4.9 during menstruation. Sometimes during pregnancy, it tends to dicrease further, while during menopause it increases by 1 or 2 digits.

Vaginal acidity is due to lactic acid production by lactobacillus in balance with fungi or other pathogens that proliferate in alkaline environments. In fact, there is a correlation between pathogenic fungi or bacteria and vaginal alkalinity. Vaginal secretions may reach a pH as high as 8.5. In candida infections pH remains in general within normal range, whereas in trichomonas and hemophilus infections it may reach 5.0-5.5. Normalization of the pH can be a way to make the environment as inhospitable as possible to these microorganisms.

In vaginitis, leukorrhea is to be distinguished from the normal odourless white secretions whose pH is around 4 that are physiological in all fertile women. Such secretions are made up of gland secretions, epithelial cells, vaginal serous extravasation and of the metabolic material of the microorganisms forming the normal vaginal saprophyte flora.

Sometimes such secretions are interpreted as due to lack of personal care or as inflammation requiring the over use of disinfectants leading to alterations in the physiological pattern. It is worth recalling that sometimes such secretions can smell unpleasantly, probably because of ammoniacal superfermentation.

The menstrual cycle, even though it is physiological catastrophe for the reproductive tract, does not cause substantial alterations in the overall pattern as tissue repair occurs in few days: cells are replaced, debris disappears and everything

turns back to normality.
Genuine leukorrheas caused by bacterial, fungal or protozoan infections are white, yellow or dark green, often smell unpleasant, and provoke itching and irritation. Candida albicans and Trichomonas vaginalis are the germs most commonly involved. Recently, a microscopic bacterium, Clamydia trachomatis is increasingly implicated when adapted to obligatory cell parasitosis, as responsible for recurrent subacute vulvar vaginitis and salpingitis with sterility, a possible outcome.

Irritating layers

All skin affections can be located on the female external genitalia, yet the most common are irritating vulvitis immediately followed by contact allergical vulvitis.
The possible factors which can lead to an irritating vulvitis have already been mentioned. They are: deodorants, disinfectants, spermicides, clinging or synthetic clothes, unsuitable soaps or detergents, the abuse of therapeutic agents (antibiotics), debilitating affections (diabetes), nutritional deficiencies and so on.
When in contact with an irritated mucosa, sweat acts as a worsening agent, sometimes causing serious itching that can end up in impetigo.
Obviously, in irritative status, the overall physiological balance is altered, personal care is neglected or reaches paroxysm and could be a worsening agents if performed using unpropoer means.

Personal odours

The distinctive personal odours originate from many different sources in the pubic and perineal areas.
In addition to normal aprocrine secretion, the odours of smegma are to be taken into account. Smegma arises from the oil gland secretions of the labia minora, the major vestibular lips, the small and strewn minor vestibular and paraurethral lips, and concentrates in the vaginal vestibule.
In the perineal region, the cutis of the anal orifice is rich of oil and sweat glands. Sweat glands are partly made up of circumanal glands whose secretion has a peculiar odour.
Further, exacerbating agents are soaked debris of hair and stratum corneum which collects in the inguinal wrinkles and the secretions of the oil glands long hair follicles. After puberty, these glands extend over the pubis down the labia majora and almost up to the abdomen.
The perineal and genital skin area as well as the remaining portion of skin surface are affected by the olfactory differences connected to genotypes, environment and nutrition, and by the considerable changes occurring during female adolescence especially in external genitalia.
In elderly women the vaginal mucosa is atrophic, and more liable to be attacked by external agents. Often different urinary disorders coexist (4,9,13,2,15,7,11,8,22,18).
In girls lubricating secretions are scarce, since there is apocrine perspiration in the pubic area until puberty (1).
During the fertile period, considerable changes occur in respect to both maximum secretion and transitory physiological conditions due to sexual activity or to small gynaecological disorders.
In this period many common female situations can be noticed.
Often in women using contraceptive pills mucosal secretions increase and in the genital area a stronger smell can be perceived that can become even stronger in time.
The peculiar smells of menstruation, even more violent in pathological states, are a real physic trauma for many women.

In this period susceptibility to pathogenic microbes (changes of physiological pH) and the reproduction of autochthonous microbes increase, with odorous consequences.

Generative tract and personal care

The use of personal detergence characterizes Mediterranean countries and has no pendant in Anglo-Saxon countries, where the bath replace the bidet.
Such trend has increased during the last 5 years, indicating greater bodily care and awareness.

Personal care

The first rule to be followed in correct care of the genitalia is frequent washing. Cleansing should be done very methodically during the day, even after urination, and drastic practices which may alter the vaginal saprophyte flora must be avoided.
Women should clean themselves properly, working in the right direction, e.g. always from cunnus to anus and never vice versa; in case germs hosted by anus (such as Escherichia coli) could penetrate the vagina. In the intestine such germs are innocuous, but in the urinary tract they may cause several disorders, such as smarting, tenderness, aches or, in the worst cases, kidney disease. For proper cleansing of the genitalia a detergent is necessary which keeps the environment at standard acid values, maintaining or restoring physiological pH values.
Before menstruation, hormonal variations cause an imbalance, resulting in changes in vaginal mucosa and increased vulnerability (pH).
During the menstrual cycle infections are more likely to increase, due to detachment of the mucosa and continuous laceration; the dilated cervical canal may also favour microbial penetration. During menstruation mucosal congestion may also make irritation more likely.
As previously said, during childhood, pregnancy and old age hormonal activity leads to a decrease in local defences and this must be offset by proper care.

Personal detergents

Personal detergents are products based on rinsing. They fall within liquid tensiolytes, e.g. mixtures of surface-active substances with specific wetting, frothing and cleansing properties.
Detergents have a high capacity to lower surface tension; they concentrate on the mucosa surface, where they solubilize, emulsify and detach waste substances which may be adherent, making their removal easier. Their molecules are relatively big, and are made up of lipophilic and hydrophilic components. With a heterogeneous system surface-active agents push hydrophilic group towards water and the lipophilic group towards the other medium. In practice this property is used to obtain wetting, emulsioning, frothing or cleansing effect under special circumstances and as needed.
It is known that the cutis is physiologically covered by a layer of fats, gases and aqueous solutes; furthermore this layer, especially in its lipidic part, is very important for skin impermeability and its integrity. Not only do detergents remove possible soiling materials, they also emulsify and detach the lipidic phase of the epicutaneous layer, depriving the cutis of its impermeable and protective layer. Amongst detergents, nonionic (surface-active or nonionic emulsifyng) detergents are definitely preferable both in cosmetology and dermatology. In the first case they are used for the preparation of cleansing creams and milks for face and hand care, face and eye make-up etc. In the second case - when combined with medicines - they

enhance their activity by increasing dispersion and consequently the contact areas and the penetrating potential. On the other hand they have a direct effect on the cutis by modifyng the electrical potential of the horny layer, thus favouring the imbibition of superficial layers which facilitate absorption through fat glands. When carryng medicines these may penetrate even deeper, thus extending and completing their action. Differing from ionic detergents, nonionic ones are in general negligibly toxic, and they are well tolerated locally, with no injury and unwanted reactions.

There are different chemical types of surface-active agents:

- cationic surfactants
- anionic sufactants
- amphoteric surfactants
- nonionic surfactants.

1) Cationic surfactants (or active cations), with the hydrophil terminal positively charged. They are not suitable for cleansing, since they are repelled by filth, which is normally positively charged.

2) Anionic surfactants (or active anionics), with the hydrophil terminal negatively charged, are amongst the most powerful and effective detergents; they include soaps and modified soaps. Soaps are salts of weak acids and thus tend to hydrolyze, releasing alkalis and producing a basic pH. Therefore they are not recommended for preparation of personal detergents since they may cause pH imbalance which, even if temporary, may affect the standard bacterial flora by weakening its defensive effects.

On the other hand, newly-conceived anionic surfactants, such as for example collagenic by-products or starch soaps, are stable with an acid pH; thanks to the polypeptide chain they cleanse softly without causing irritation.

Furthermore, the advantage of such surfactants consists in the protein groups contained, in their molecules, which show considerable affinity with skin, whose surface is mainly protein.

3) Amphoteric surfactants (or anion-and cation-active) are molecules containing both positive and negative charges: this is why they are more keen to cutis and have a weakened cleansing effect. They are considered to be the most suitable surfactants for personal cleansing.

4) Nonionic surfactants (with no active ions) have hydroxylated-chain hydrophil terminals; their properties enhance cleansing performance. Sometimes they may also enhance the dermal features of the principal surfactant and make it better tolerated by the skin.

Other substances which may be included in the composition of personal detergents are those with disinfecting soothing, refreshing and deodorizing effects.

Very recently, pH-sensitive dye-indicators have been introduced. It seems possible that by making use of such indicators, cosmetic or therapeutic compounds can be made sensitive to the presence of pathogenic conditions of cutis and mucosa either before, during or after pharmacological local and general treatment.

In fact, such dyes could, for istance, be contained in a standard cosmetic detergent for external use only, and existing diseases or the therapeutic effectiveness of a medicine could be checked by verifying colour changes in the cleansing water.

Deodorizing substances

Personal detergents may contain limited doses of antimicrobials.

Compounds listed in the document VI of the EEC directive may be employed; such compounds are designed to act primarily as preservatives, some of which are also authorized as skin deodorants.

The most suitable are some formaldehyde, liberating agents, quaternary salts (particularly chlorhexidine) and polyphenol (usnic acid type).

On the other hand, halogenated diphenols are advised against by the manufacturing houses themselves (hexachlorophene, trichlorhydroxydiphenylether, halogenated compounds etc.).
The present trend is to reduce the use of antimicrobials to the lowest limit and to act odour by other methods: enzymatic diverters (triethylcitrate), smell-absorbers (ricinoleate zinc) and perfumed compounds with both deodorizing and bacteriostatic effect.

Refreshing substances

Sometimes essential oils are fragrant chemical bodies characterized by a particular chilling or refreshing effect are used instead of the perfumed compound: peppermint oil and menthol, eucalyptus and eucalyptol, thyme-oil and thymol etc.
The use of these mixtures is very appreciated in hot months. Their dosage is usually quite high (2%-3%), and this may cause irritation, especially if the detergent is applied directly on the vulvar area instead of being previously diluted with water.

Anti-reddening substances

However short the contact, substances with good decongestant effect may be used.
Saponins of butcher's broom, horse-chestnut and marigold, camomile flavonoids and mallow mucilages seem to be the most suitable ones.
Sometimes astringent substances both organic (hamamelis or retania tannins) and inorganic (aluminium salts) are employed. The use of extracts rich in flavonoids and essential oils is fairly widespread among herbalists; such extracts seem to have bacteriostatic, deodorizing and soothing effects.
Personal detergents are rarely solid or powered.
There are generally three types of detergents:
A) limpid very fluid
B) limpid semifluid (or gel)
C) opaque semifluid (or cream).
A standard bottle or pipe or - for more moderate quantities - a pumpe bottle may be used for applications. Personal detergents containing peppermint oil and eucalyptol in high doses are usually in a very fluid form. To solubilize such substances lauryl sulphate is not sufficient, and it is necessary to add both heteroglycols and specific solubilizers (e.g. ethoxylated ricinus-oil or ethoxylated alcohols). As a result of adding such solvents the system is made fluid.
Mixtures of alkylsulphates and betaines or betaines and amphoteric imidazolines - which in combination may make make-systems more viscous or even gel - are less fluid.
Personal detergents may be made opaque until they have a milky-creamy appearance - sometimes with pearly reflections - by addition of fatty substances which are insoluble in surfactants, for example, ethyleneglycol stearate, glyceryl stearate and similar materials.
Viscosity, limpid and opaque appearance, pH, possible colour, fragrance and frothing characterize and distinguish different personal detergents.
Functional components as listed above may also be added in these structures.
In such detergents optimum pH values usually range between 4 and 5 and are never above neutrality (pH 7).
Finally, the perfect personal care detergent must:
- be gentle
- be as close to physiologic pH (3.8-4.2) as possible
- have a lenient effect on mucosae
- have no selective disinfecting effect
- not dry the cutis
- attenuate unpleasant smells naturally
- be packaged practically and hygienically
so as to remove pabulum, which may favour the

development of pathogenic germs, and also keep the vaginal mucosa trophism (especially when it is physiologically insufficient), which may involve the development of Doederlein's bacillus and also favour tissural metabolism.
Furthermore it is important that sexual intercourse is made easier if the vagina is dry.
This means that personal detergents are necessary for women to keep such an important organ as the vagina healthy without making use of hormones (which are easily absorbed by the mucosa and may give rise to systemic effects) or of antimycotic or antibacterial substances (their abuse may cause diminished local resistance to phlogosis, resulting in a real immunodepression of the organ).
Potential allergens contained in the products must be equally avoided, since it has been ascertained that many of the so called "recidivous vaginal phlogoses" are caused by allergic reactivity to medicines.
Vaginal and, even more, vulvar cosmetic treatment seems to be a completely new area to be investigated, on which there are no precise scientific references; one reason may be the lack of cooperation on this delicate subject between dermatologists and gynaecologists.
The initiative taken in this congress to put together knowledge from different disciplines within the vast cosmetologic tradition may be very helpful in solving the numerous problems of this large branch of medicine.

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THE HUMAN HAIR GROWTH CYCLE

W. Montagna
Oregon Regional Primate Research Center, 505 N.W. 185th Avenue - Beaverton OR 97006 U.S.A.

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Synopsis

Four post pinkus events changed the course of dermatology:
1-the publication, in 1926, of Dry's article he described the growth cycles of the haircoat of mice, coining the dreadful terms anagen, catagen and telogen.
2-The publication of Butcher's article in 1934 indicates the intensity with which biologists of yore studied hair.
3-The publication, in 1951 by N.Y. Academy of Science of the proceedings of a conference on "Growth Replacement and Types of hair", organized by J.B. Hamilton
4-it was not until 1954, when Chase's review article, "Growth of the Hair", on the hair growth cycles of the mouse, that hair research really caught on.
This last event, was, for all practical purposes, the dawn of modern hair reasearch in the United States and everywhere else in the world. Soon after that event, the number of publications dealing with hair growth became very numerous.
It is amusing that the same questions that were asked by the pioneers remain unanswered: what initiates anagen, and, what terminates it?

Riassunto

Quattro fondamentali eventi hanno cambiato il corso della conoscenza dermatologica sul "ciclo" di crescita del pelo.
1-La pubblicazione nel 1926 dell'articolo di Dry che descrisse tale ciclo coniando i termini anagen, catagen e telogen.
2-La pubblicazione dell'articolo di Butcher nel 1934 che confermava l'importanza di questo ciclo.
3-La pubblicazione nel 1951 da parte della N.Y. Academy of Science di una conferenza di J.B. Hamilton sul tema della "caduta patologica dei capelli".
4-La pubblicazione dell'articolo di Chase "sulla crescita del pelo" che rappresenta il vero inizio USA di tutti gli studi sperimentali sui capelli.
Molti sono i lavori pubblicati a tutt'oggi sul ciclo del capello. Ciò che lascia perplessi è che ancora oggi non è stata data una risposta sicura a questo interrogativo.
Quale fenomeno permette l'inizio della fase anagen del pelo e quale fenomeno l'induce a regredire?

If nothing had been written on hair reasearch since Felix Pinkus (1927) wrote his article on skin in Jadasson's Handbook, our knowledge would not be very far behind what it is today. Even if one's knowledge of German is limited, one should leaf through that monumental work. It contains almost everything that is important on what is known about the hair Growth Cycle. Pinkus was a visionary and his masterpiece in Jadasson's Handbook is perfection, like Beethoven's 9th symphony.

Now I will review the four post-Pinkus events that changed the course of dermatology: 1) the publication, in 1926, of Dry's article in which he described in painful details the growth cycles of the haircoat of mice, coining the dreadful terms anagen, catagen and telogen. The German terms Haarkeim- (hair germ stage), Haarzapfen- (hair-peg stage), Bulbuszapfen- (bulb-peg stage), and Scheidenhaartstadium (hair sheath stage) cover the same territory but are more cumbersome. Anagen: literally means the reproduction of a structure; catagen: the regression (distruction) of a structure; and telogen: can mean a mature structure or distant formation: cf. telecontrol or as in distant or remote control, telephone, distant sounding or voice. Dry did not explain his reasons for using these barbarous terms. The identification and the naming of these phases was one of the most important contributions to modern cutaneous biology. 2) The second event, the publication of Butcher's article in 1934, indicates the intensity with which biologists of yore studied hair. Even though Butcher published his observation on the hair growth in rats, eight years after Dry's publication, he either ignored or deliberately avoided citing Dry. In the introduction of his paper Butcher stated that "The quiescent condition and the growth stage together, constitute a cycle". 3) The third historical event is, perhaps the most significant: the publication in 1951 by the N.Y. Academy of Science of the proceedings of a conference on "Growth Replacement and Types of Hair", organized by James B. Hamilton, whose article "Patterned Loss of hair in Man: Types and Incidence", became the keystone of all subsequent articles on baldness. And yet, 4) it was not until 1954, when Chase's review article, "Growth of the Hair", another very dull contribution on the hair growth cycles of the mouse, that hair research really caught on. This last event, was, for all practical purposes, the dawn of modern hair research in the United States and everywhere else in the world. I wonder still about the importance of that article; perhaps both the academic and medical environments were ready for it. Chase resuscitated Dry's terminology but was more crisp than Dry and Chase also made some allusions to human hair growtb. The publication of his review, then, may be the most important event in modern dermatology since it caught its imagination as well as that of experimental biologists. Soon after that event, the number of publications dealing with hair growth became very numerous. Chase's publication was the turning point of dermatology which emerged as a really exciting medical speciality. Every conceivable new discipline was eventually applied to better explain the phenomenon of the growth cycle. And yet, it is amusing that the same questions that were asked by the pioneers remain unanswered: what initiates anagen, and, what terminates it?

It is regrettable that reasearch on hair growth, with singular exceptions, has been poor. Perhaps, behind this shoddiness is the lure of the rewards that would came from the cosmetic industry which is forever looking for panacea drugs that might restore the "crowning" glory of bald people; I suspect that they believe to have found such a drug.

Have we made any progress in understanding the mysterious ways of the hair growth cycles? In the skin of mammals which are born naked, (most rodents, logomorphs, and a few others) hair neogenesis occurs largely postnatally. This may be one of the reasons why so many biolo-

gists have studied the growth of the hair coat of mice and rats. In other mammals, such as the primates, including man, hair growth is already well estabilished at birth. The postnatal continuation of hair growth cycles are a reflection of the phenomenon that began in utero. All development proceeds cephalocaudally, and it follows that hair is formed first on the head, and hair growth cycles are established first there. In human fetal scalps, and in newborn infants, three or more cycles may already have occurred. The mechanism that triggers catagen, then, is phylogenetically and ontogenetically ancient. The human fetal scalp of 7 months or older contains numerous club hairs, quiescent follicles, as well as hair follicles in early anagen. In rhesus monkeys, which have a gestation period of roughly 150 days, hair differentiation begins (on the head) at about 54 days; many telogen follicles can be found at 100 days or earlier (Bell, 1969, 1973). Why hair follicles stop producing a hair after a period of growth is still unknown. Uno et al. (1985), however, seems to have the answer. These authors dismiss the issue by saying: "Individual hair follicles cannot, however, produce shafts indefinitely." It is a calamity that the only people in the world who have the answer, don't tell us why follicles cannot "produce shafts indefinitely." We don't really know why and how follicles grow and rest.

Antagen is a truly miraculous event. Every hair follicle in anagen is a microcosm where growth and differentiation, similar to what had occurred in utero when the follicles were first formed and repeated in almost every detail during our entire life. And, here is something that is not usually appreciated: every individual hair formed is a structurally unique entity. Its structure can be very different from segment to segment, as are subsequent hairs formed by the "same" follicle. I emphasize here that consecutive hair generations are not formed by the same follicle since the reproducing part of every follicle is destroyed during each phase of catagen and each hair is produced by a new and different follicle. The only things that all succeeding hair generations have in common is that they come from a common stock, the cells of the outer root sheath, and that they emerge from an established pilary canal and orifice.

One might suppose that years of fierce reasearch on human hair growth by morphologists, whether they used the light or the electron microscope, would have resulted in the unveiling of every conceivable detail in the anatomy of a growing follicle. And yet, it was not until recently that certain thing have come to light. For istance, the Arao body, discovered in 1969 by Arao and Perkins, continues to be ignored by nearly everybody. Also, no one takes cognizance of the fact that the dermal papilla is not just a candle wick flame-shaped structure. In sections of human hair follicles made exactly through the center of the bulb, the papilla is drawn out into very thin tracks for some distance into the prekeratogenous zone, as in the follicles of rodents and swine. I wonder what the specific tinctorial peculiarities of the dermal papilla in anagen follicles mean: a brilliant metachromatic staining with toluidine blue, PAS-positivity, deep azurophily when treated with the Giemsa stain, and materials that stain with colloidal iron techniques. The identity of the substances responsible for these tinctorial attributes does not enlighten us about how the follicle produce a hair. A final point is that anagen, as Uno et al. (1985) have shown, is not the explosive phenomenon it apprears to be in healthy rodents (Chase and Eaton, 1954) but can sometimes lag for years in its early stages. For example, in my own long forgotten paper (Montagna, 1959), I observed that the hair follicles in children's axillae remain in a form of arrested anagen until early puberty.

Furthermore, what makes the well-oiled machinery of anagen stop is a mystery that has yet to be solved. Catagen, which is often mistaken for a calamitous event when things go to dust, is a-

ctually an orderly and process during which the follicles form a club and proceed to largely discard the cells of the bulb, and select only a few cells mostly from the outer root sheath to form a new hair follicle anlage, and prepare for the next growth cycle which could come soon or much later.

Most dermatologists know the stage telogen because Kligman (1959) made many acute observation on human hair growth and because he coined the clever term 'telogen effluvium" (Kligman, 1961). Telogen is like a time bomb, ready to explode. No one has yet discovered what sets it off.

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THE EFFECT OF GELATIN-GLYCINE ON SKIN HYDRATION.

(1) Morganti P., (2) James B. and (3) Randazzo S.D.
(1) President /Director Research & Development, Mavi sud s.r.l. - Aprilia (LT) Italy
(2) Program Director International Society of Cosmetic Dermatology - James Clinic - Perrysburgh (Ohio) USA
(3) Professor of Experimental Dermatology University of Catania (Italy).

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Key words: *Stratum Corneum Flexibility; Skin Chapping; NMF; PCA; Gelatin-Glycine; Oral Cosmesis; 3C System; Skin Hydration; Skin Hydration Measurements.*

Synopsis

The water content of stratum corneum is of great importance in maintaining the skin flexibility. Skin chapping, cracking and scaling I thought to be the result of a low water content in the SC. The SC either loses or absorbs water from its envinronment depending upon certain of its own internal material, the normal moisturizing factors (NMF), the temperature and the relative humidity of the atmosphere.
Our previously obtained data indicates that the levels of Pyrrolidone Carboxylic Acid (PCA) in the SC may be directly affected by oral administration of gelatin-glycine.
The results presented here confirm our previous investigation. The oral administration of gelatin-glycine seems to exert an interesting moisturizing action, influenzing the extensibility (Tab. 1,5), the water content (Tab. 2,4) and the level of PCA of SC both in guinea-pigs and in human skin.
On the basis of this study, treatment by oral gelatin-glycine would seem to be useful complement to cosmetic use for dry and aged skin.

Riassunto

L'acqua presente a livello dello strato corneo è fondamentale per mantenere la cute morbida ed idratata.
La perdita anche di una piccola quantità di tale acqua si traduce subito in secchezza della pelle con comparsa anche di fessurazioni. Lo strato corneo perde o assorbe acqua dall'ambiente anche in dipendenza della quantità di NMF presente tra le tegole cheratiniche.
I risultati ottenuti con questo studio confermano i nostri precedenti dati. La somministrazione anche della gelatina Gelatina-Glicina sembra esercitare un'interessante attività idratante a livello cutaneo influenzando l'elasticità, il contenuto di acqua e il livello di PCA dello strato corneo sia negli animali che nell'uomo. Sulla base di questo studio sembra possa affermarsi che la somministrazione orale di gelatina-glicina può essere considerata un utile complemento all'uso dei cosmetici per la pelle secca ed invecchiata.

Introduction

A dry, inflexible, cornified epithelium results from an excessive loss of water. The water content of stratum corneum (SC) is of great importance in maintaining the skin flexibility (1). Skin chapping, cracking and scaling is thought to be the result of a low water content in the SC. The SC either loses or absorbs water from its envinronment depending upon certain of its own internal material (2), the normal moisturizing factors (NMF), the temperature and the relative humidity of the atmosphere (3,4).
Our previously obtained data indicates that the levels of Pyrrolidone Carboxylic Acid (PCA) (one of the most effective naturally occurring humectants in NMF) in the SC may be directly affected by oral administration of gelatin-glycine (5,6).
The objective of this study was to determine the influence of tbe gelatin-glycine on the biomechanical properties of normal SC and attempt to relate these to the amount of waters and PCA recorded.

Methods

The studies, in guinea-pigs and in women, were carried out using pills (QM)* containing each one Gelatin-glycine (Gelatin 150 mg - Glycine 75 mg) together with some vitamins (Vit B6, 0,2 mg; Vit. C, 5 mg; and minerals, Mn++0,25 mg; Cu++0,3 mg; Fe++1,5 mg and Ca++20 mg. As a control, pills were used containing gelatin and starch only.

Evaluation in guinea-pigs

60 male albino guinea-pigs were employed of the average weight of 400 g±20. 10 guinea-pigs were kept on a gelatin-glycine diet for 90 days, while the remaining 10 served as control.
The diet was administered weekly in the cage and in accurately weight quantity so that the guinea-pigs, kept in single cages, would ingest together with the feed 105 mg per kg a week of gelatin-glycine mixture (Product QM).

Water content and extensibility of stratum corneum in guinea-pigs

The SC for the experiments was obtained (61st day) from the hind footpads of the two groups of guinea-pigs. The whole footpads were incubated for 18hr at 37°C in a solution containing 2M urea, 0,5% trypsin and 0,1M tris buffer, pH 7,4 (3). The rectangular (0,6x1,5 cm) separated corneum pieces (two for each animal) were equilibrated in atmospheres of controlled humidity prior to measuring extensibility and water content (RH 81%).

* *trade name QUICK MOIST*

Measurement of extensibility

The extensibility of the strips of SC measured on an Instron Tester (3).
At the start of the experiment the jaws were O,5 cm apart and the corneum strip (1,5 cmx0,6 cm) was stretched to a lenghth of 0,75 cm at a costant rate of extension of 0,5 per min. The force required for this extension was measured with a tension cell and automatically recorded.
RH was 81% at 22°C. The extensibility is expressed as the percentage extension per 100 g load.
The obtained values are shown in Fig. 1.

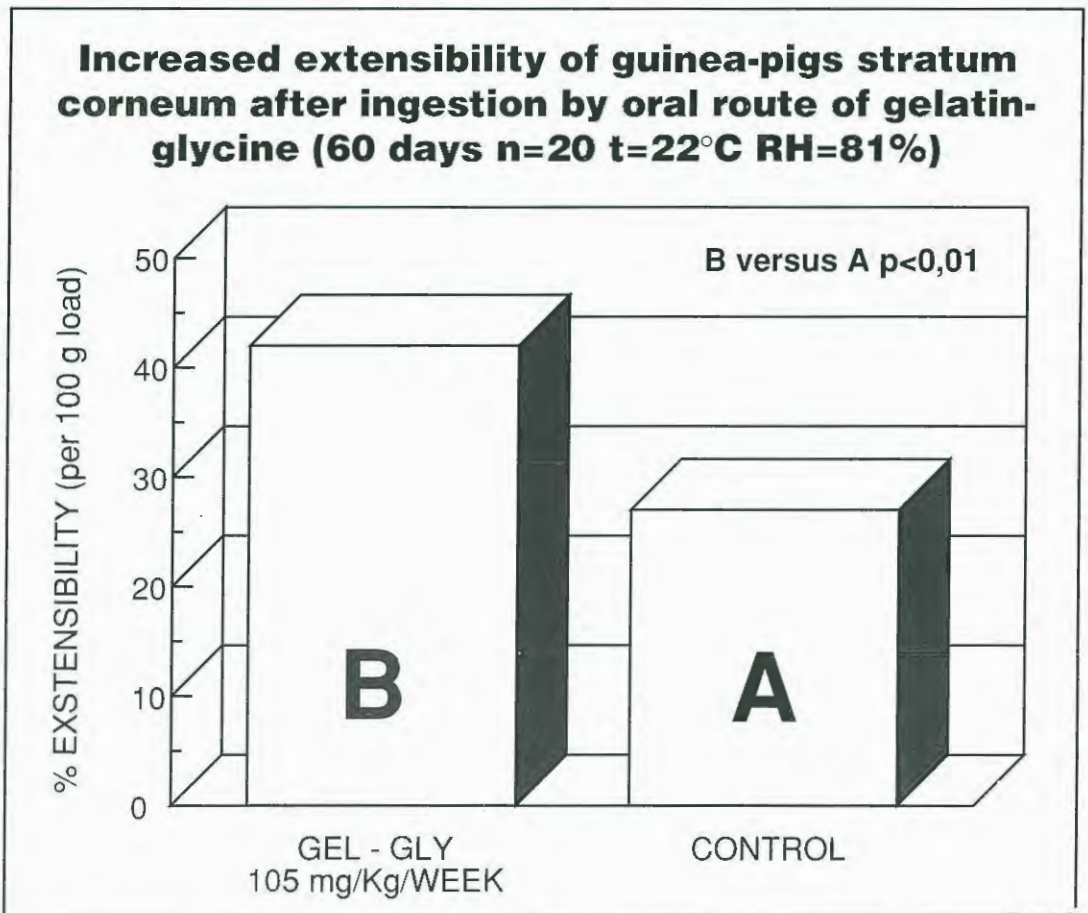

Figure 1

Measurement of water content

The water content of SC (pieces of 20-40 mg) was measured by equilibrating in an atmosphere of costant relative humidity (RH 81%) weighting, and comparing this with the dry weight following the method of Middleton. The SC was suspended on hooks over saturated potassium bromide solution at 81% RH in small crew-capped bottles. After 6 days equilibration SC was weighted to obtain a wet weight.
After a further 6 days equilibration over a mixture of molecular sieve and self-indicating silica gel a dry weight was obtained. From the wet and dry weights the water content was calculated, expressed as mg water content per 100 mg dry corneum. The obtained values are shown in Fig. 2.

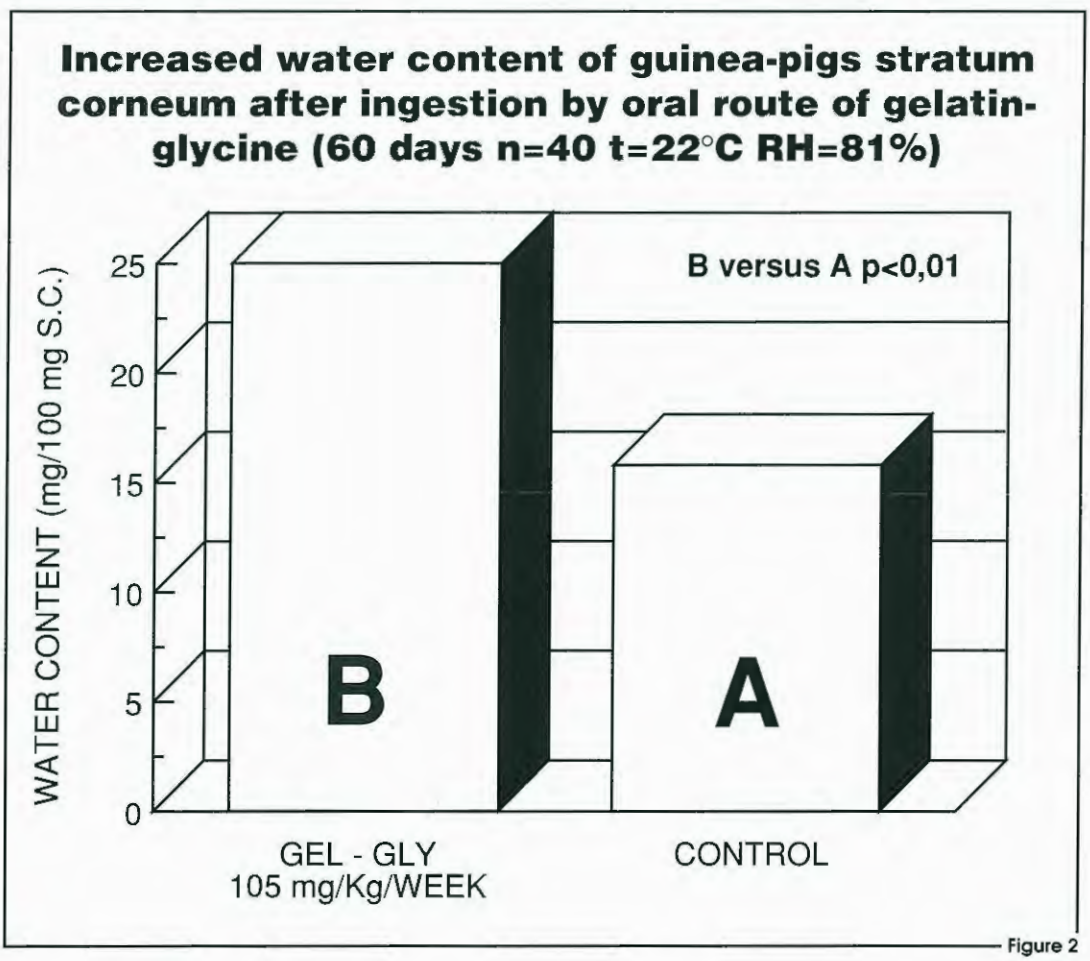

Figure 2

PCA content of stratum corneum in guinea-pigs

Layers of stratum corneum (0,6x1,5 cm) from the hind of footpads of the two groups of guinea-pigs were extracted in 5,0 ml of 2,0 M HCl solution at 4°C for 3 days, then the extract was filtered through a 0,45 μ millipore filter.
Pyrrolidone Carboxylic Acid (PCA) contents recorded with an autoanalyzer were determined by analysing samples after heating the extract at 100°C for 2h. The obtained results are shown in Fig. 3.

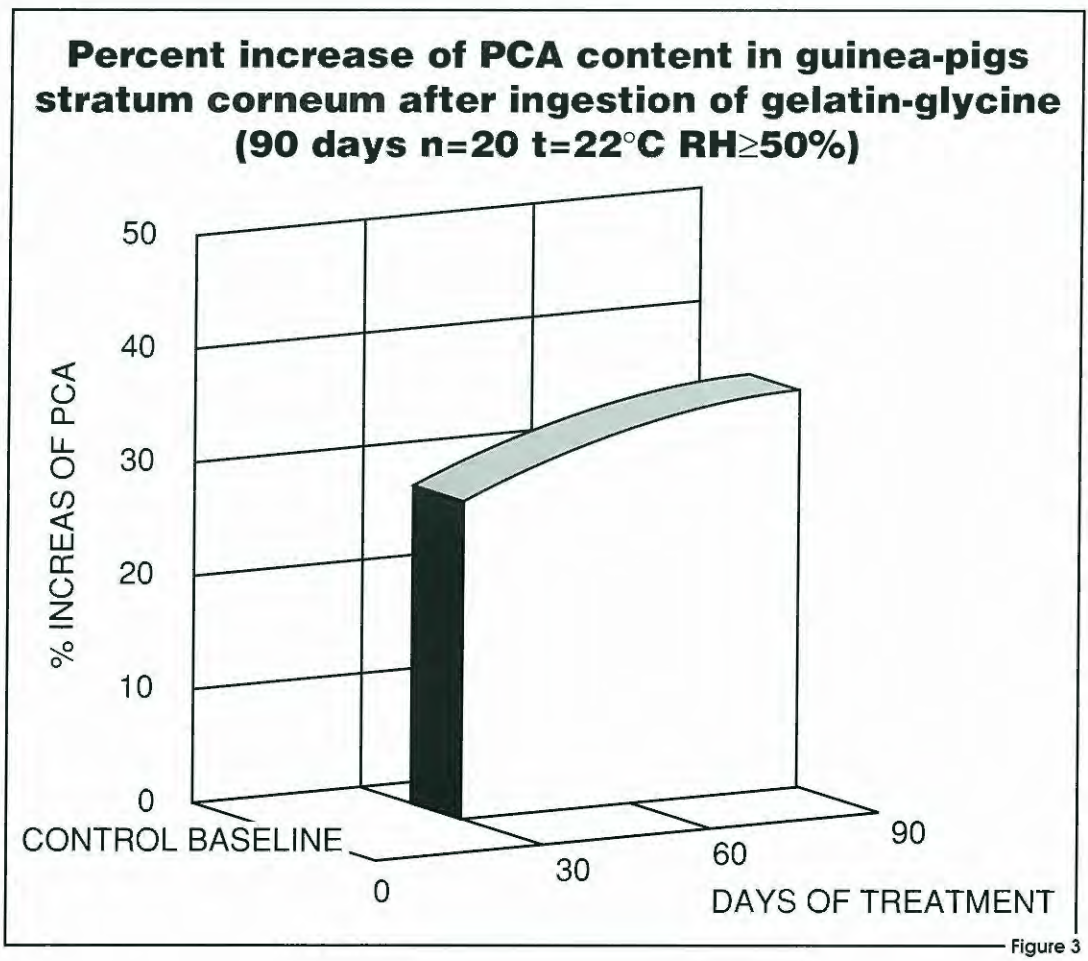

Figure 3

Evaluation in women

Fifthy healthy women volunteers, between 42 and 55 years of age, all with persistant dry skin, were divided into 2 groups of 25 individuals. Each group was randonly given pills sufficient for three months of treatment (4 pills a day). The two groups were:

A- Gelatin and starch (control)

B- Gelatin-Glycine. The pills were administered orally (4 a day) for 120 consecutive days from January to April 1990.

In the 10 days before the treatment all subjects used no cosmetics except a cleansing lotion. Four weeks before, and continually during all the tratment period, drugs, diet foods and cosmetics were prohibited.

Evaluation of cutaneous hydration on human skin

The mean values for skin hydration were taken from each subject by carrying out four separate measurements in adjacent areas on the forehead. Measurements were taken three times per week (Monday, Wednesday and Friday) up to total of 48 measurements for each subject tested (120 days) between 8:30 and 10:30 a.m. under standardized conditions (RH≥50% t=22°C).

A computer-supported system called "3C" has been used to measure skin hydration. This Dermotest computerized system (3C system), based on the principle of costant dielectric measurements, records skin hydration values in direct readout (8). Results are shown in Fig. 4.

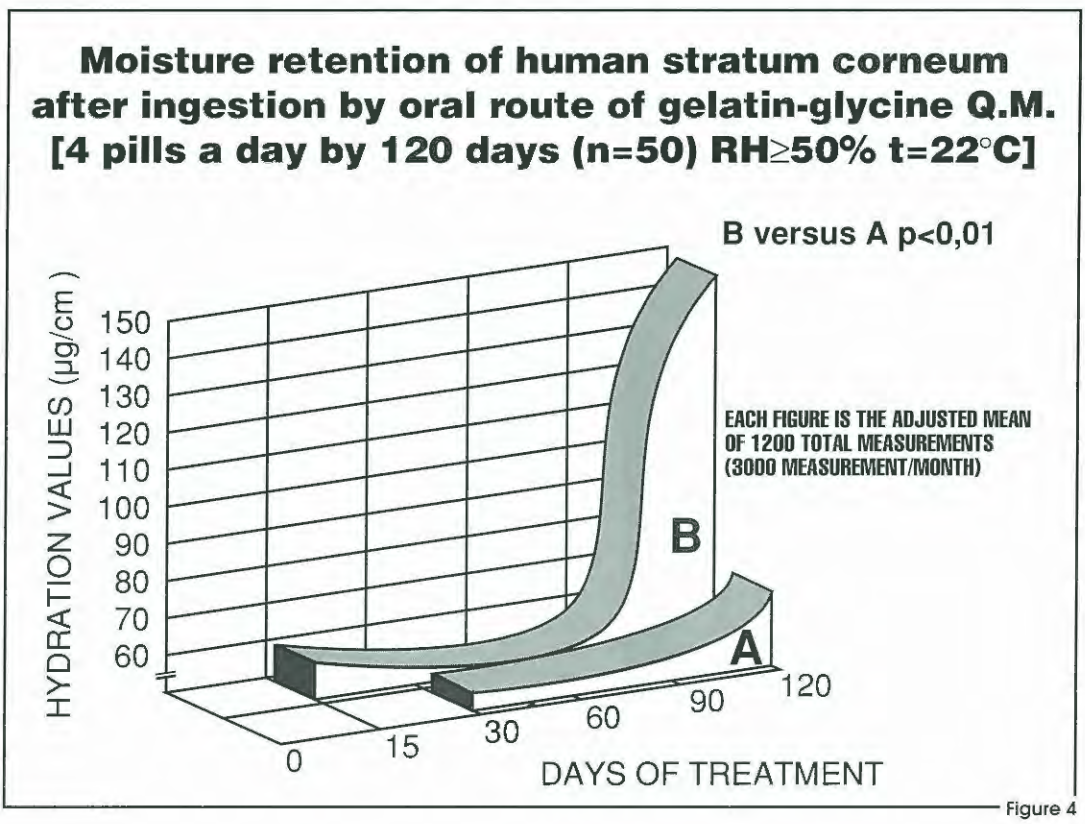

Figure 4

Extensibility of human SC

Isolated samples of human stratum corneum were obtained from the upper back of 20 subjects ranging in age from 42 to 55 years. These were 10 controls (from group A) and 10 treated (group B).
It was employed a modified version of the cantharidin blister procedure used by Kligman (7). Cantharidin was impregnated into 1 cm diameter disk of filter paper and placed under occlusive patches. The disk were removed after 4 hours and the SC extensibility was measured on the Instron Tester as described previously. The mean results are presented in Fig. 5.

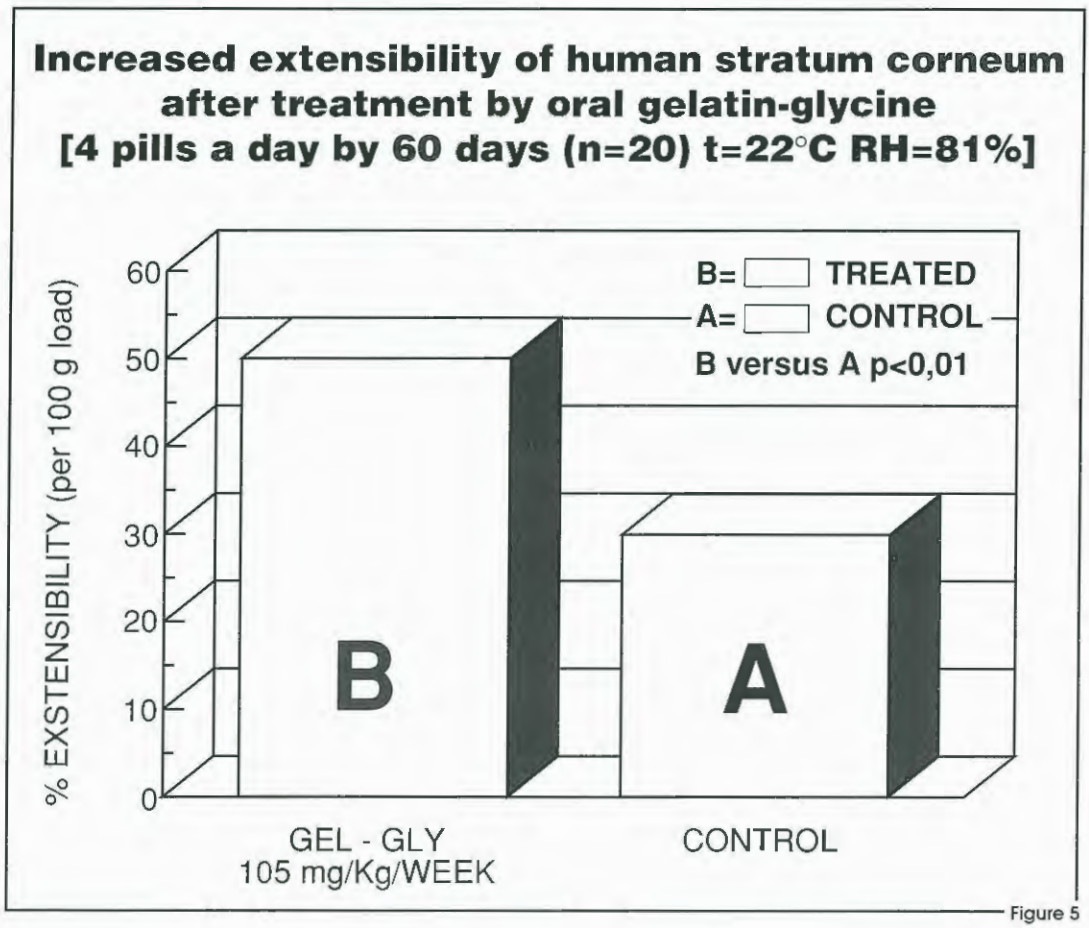

Figure 5

Conclusion

The results presented here confirm our previous investigation. The oral administration of Gelatin-Glycine seems to exert an interesting moisturizing action, influenzing the extensibility, (Tab 1,5), the water content (Tab 2,4) and the level of PCA of SC (3) both in guinea-pigs and in human skin.
The increased hydration related to a precise dosing of gelatin-glycine seems referable to an increased local production of PCA (Tab 3), probably connected also to a stimulation of new collagen and muco polysaccharides production. Moreover the better elasticity exibited by SC (Tab 1 and 5) is presumably due to a manifestation of the interaction of these macromolecules with the larger amount of absorbed water recorded (tab 2 and 4).
On the basis of this study, treatment by oral gelatin-glycine would seem to be usefull complement to cosmetic use for dry and aged skin.

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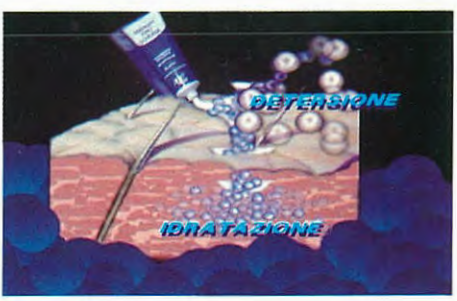

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