Nutrition for Healthy Skin

Strategies for Clinical and Cosmetic Practice
Nutrition for Healthy Skin
The intimate relationship between dermal demand of nutrients and adequate supply from the blood circulation seems to have been understudied. In fact, the title of this book can be read in two ways; balanced nutrition is necessary for maintaining healthy skin, and there are nutritive aspects to restore healthy conditions after a disease state has developed. Skin care has an important metabolic and nutritive component. Maintenance and restoration are integral processes in skin health.

It is satisfying to see that the two editors, Professors Jean Krutmann from Düsseldorf, Germany, and Phillippe Humbert from Besancon, France, have been able to compile the pertinent aspects by attracting contributions from the world leaders in this subject area. Three major sections make up the treatise: Nutrition and Skin, and its scientific basis; Functional Food, addressing botanicals and other micronutrients as well as probiotics and; thirdly, Aspects of Clinical Dermatology, culminating in the topic of beauty from inside.

The need for scientifically sound information on this subject area is particularly urgent, since the general public is being supplied with suggestions from the news media and, increasingly, from the Internet with material which is not always based on sufficient scientific evidence. The present treatise will also be good for delineating the problems and limitations in current knowledge. The authors, the editors, and the publisher can be congratulated to a timely opus!

Duesseldorf, Germany

Helmut Sies
The relationship between nutrition and skin has become a “hot” topic that is exciting researchers and clinicians worldwide. New insights into the effects of orally applied, biologically active molecules on skin functions have stimulated a continuously growing interest in the development of nutritional supplements and, most importantly, functional food products to benefit human skin. This monograph attempts to provide an up-to-date overview regarding all aspects of nutrition and skin. It includes in-depth, critical discussions of the molecular basis as well as current concepts propagated for nutrition-based cosmetic, preventive, and therapeutic dermatological strategies. The explosion of knowledge in this field over even the last few years is remarkable with consequences for practicing dermatologists, patients, cosmetic and nutritional industry, and consumers in general. To capture the depth and breadth of this learning, we have recruited leading experts from multiple subdisciplines. All authors are internationally recognized, and we are very grateful for their excellent contributions. We hope that this book will serve you as a state-of-the-art reference and will further stimulate your interest in this fascinating area.

Duesseldorf, Germany  
Jean Krutmann
Besançon, France  
Philippe Humbert
March 2010
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Nutrition and Skin: The Scientific Basis
Core Messages

- Abnormal nutrition causes cutaneous changes that are either due to insufficient food supply; i.e., inadequate intake of nutrients, vitamins, and minerals, or to excess calory intake.
- In countries with inadequate food supply, protein-energy malnutrition (marasmus, kwashiorkor) is common and children ≤ 5 years are at highest risk. In 2001, approximately 50% of childhood deaths were indirectly or directly attributable to inadequate nutrition.
- In countries with adequate food supply, the most common nutritional abnormalities are obesity due to excess food consumption, and malnutrition due to psychological (anorexia nervosa, bulimia) or medical conditions (metabolic disease, chronic illness, hospitalization), affecting both children and adults.
- Skin changes provide important clues for lack or overabundance of individual nutritional components and can help clinicians to correctly detect, diagnose, and consequently treat nutritional disease, which can be confirmed by laboratory testing.

While the importance of individual components for normal function of the skin is undisputed, there are many compensatory mechanisms in place. Nutritional disease is rarely the result of the deficiency of a single nutrient.

While substitution of deficient nutritional components usually results in rapid resolution of symptoms, toxic effects of overload have become more common with the increasing popularity of dietary supplementation. This is particularly common with lipophilic vitamins (A, D, E, and K) because they accumulate in the tissue.

1.1 Nutritional Deficiencies

1.1.1 Marasmus and Kwashiorkor

Nutritional deficiencies can be exogenous or endogenous. The primary exogenous reason is insufficient intake of nutrients. Endogenous etiologies include intestinal or metabolic disease that interferes with the absorption and delivery of nutrients to the cellular machinery (e.g., intestinal malabsorption, gastrointestinal and metabolic disease, infections, cancer) (Table 1.1). With prolonged nutritional deficiencies, energy storage is exhausted and energy supply lags behind. Because of their increased nutritional needs during the growth phase, children ≤ 5-years old are particularly susceptible to the developmental and physiologic consequences of poor nutrition.
Marasmus is due to insufficient (although balanced) nutritional quantities. Marasmus is not only due to decreased overall caloric supply, but also results from a deficit in essential nutritional components (e.g., vitamins, essential amino acids, minerals). Therefore, the cutaneous changes of marasmus are multifold. Aside from a decrease in the subcutaneous fat, the dermal and epidermal layers are thinned which gives the skin an aged appearance. In addition, there is dryness of the skin, sometimes to the degree of ichthyosis-like scaling. Vitamin A and C deficiency result in follicular hyperkeratosis (see below, Table 1.2). Because of anemia and vasoconstriction, the skin color is pale, while in sun-exposed areas there is spotty hyperpigmentation. The hair is dry, loses color (“premature graying”), and hair loss (telogen effluvium) is common. The growth of the nails is delayed, and the nail plates may show longitudinal ridging. Marasmus is corrected by carefully restoring protein-calorie intake and by supplementation of vitamins, essential fatty acids, and zinc according to their respective blood levels.

Kwashiorkor occurs if normal carbohydrate consumption is coupled with insufficient protein intake; i.e., chronic malabsorption such as in cystic fibrosis. It is most common in infants in third world countries as soon as their mothers discontinue breast feeding. Kwashiorkor can also occur in children receiving a calorie-rich diet that is poor in proteins of animal origin [4]. These children show the cutaneous changes of marasmus (see above), and in addition develop diffuse edema due to hypoalbuminemia, and increased vulnerability of the skin (e.g., to mechanical trauma), which results in erosions and blisters in areas of friction. A further characteristic of kwashiorkor is a reddish-brown scaly dermatitis (“flaky paint”), and dusky erythematous plaques with a waxy appearance in pressure-exposed areas (diaper area, over bony prominences) with a thickened, pigmented stratum corneum on histology. Depigmentation of the skin can be observed (predominantly in the perioral area and on the lower legs). Moreover, depigmentation of the hair to a reddish color is often observed. Correction of kwashiorkor must be undertaken carefully; electrolyte imbalances need to be taken into account, combined with supplementation of vitamins, essential fatty acids, and zinc as above.

In both marasmus and kwashiorkor, individual hair shafts show pigmented areas alternating with depigmented areas (“signe de la bandera” or “flag sign”), reflecting intermittent periods of food availability. In fact, because of overlapping features, a clear distinction between marasmus and kwashiorkor can not always be made with certainty. In these cases, the term protein-calorie malnutrition is used instead. Generally, chronic nutritional deficiencies increase the susceptibility to opportunistic infections by causing a secondary immune deficiency. Particularly problematic are mixed infections of the skin with fusiform bacteria and spirochetae (e.g., bacterium fusiforme, spirochäta refringens) causing necrotizing ulcerative gingivitis, noma, or cancrum oris which can be life-threatening. In adults, similar treatment-recalcitrant ulcerations occur on the lower legs following insect bites.

Most commonly, malnutrition is due to inadequate food availability, but it is also seen in individuals with medical conditions, particularly in hospitalized patients, which often can simply be ascribed to poor logistics (neglect of nutritional needs in patients waiting for a complex diagnostic workup). Other reasons are individuals voluntarily subjecting themselves to unusual diets and individuals with excessive alcohol consumption [3]. Anorexia nervosa and bulimia are psychiatric disturbances that lead to physical disturbances. Cutaneous changes associated with these disorders are manifold including dry skin, pruritus, patchy hyperpigmentation, freckles, lanugo hair, brittle terminal hair and nails, and paronychia. Russell’s sign refers

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**Table 1.1** Causes of nutritional deficiency

<table>
<thead>
<tr>
<th>Exogenous (inadequate food intake)</th>
<th>Endogenous (inadequate food absorption/metabolization)</th>
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</thead>
<tbody>
<tr>
<td>Poverty</td>
<td>Intestinal malabsorption</td>
</tr>
<tr>
<td>Old age</td>
<td>Gastrointestinal disease</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>Metabolic disease</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Chronic systemic disease</td>
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<tr>
<td>Diets (e.g., “fad diets,” “allergy diets”)</td>
<td>Cancer</td>
</tr>
<tr>
<td>Child neglect</td>
<td>Recurrent infections</td>
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<td></td>
<td>AIDS (inadequate intake, e.g., due to candida esophagitis)</td>
</tr>
</tbody>
</table>

**Table 1.2** Differential diagnosis of hyperkeratotic papules on the extremities due to nutritional deficiency

- Vitamin A deficiency (phrynoderma)
- Vitamin C deficiency
- Essential fatty acid deficiency

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to callus formation on the hand used to elicit vomiting, which is another diagnostic clue. Early recognition is desirable, because the mortality is much lower with early intervention.

**1.1.2 Essential Fatty Acid Deficiency**

Malnutrition is a common cause of essential fatty acid (e.g., linoleic, linolenic, and arachidonic acid) deficiency. Patients present with diffuse eczematous skin changes that can be pruritic and preferentially affect the periorificial areas. With long-standing essential fatty acid deficiency, there can also be depigmentation and alopecia (telogen effluvium). In children, there is growth failure. Essential fatty acid deficiency is associated with impaired wound healing, capillary fragility, abnormal liver, and kidney function, and neurologic damage. The differential diagnosis includes zinc deficiency (see below), and necrolytic migratory erythema. Plasma levels of linoleic, linolenic, and arachidonic acids are decreased. In contrast, palmitoleic and oleic acids are increased, and there is abnormal presence of 5,8,11-icosatrienoic acid in plasma. Therapeutic fatty acid supplementation is effective.

**1.1.3 Vitamin Deficiencies**

Vitamins are cofactors in metabolism; nutritional vitamin deficiency results in metabolic disturbances. In Western societies, this is mostly due to impaired intestinal absorption (e.g., in inflammatory bowel disease, inherited metabolic disease, parenteral nutrition, following surgery), or due to alcoholism. Because the deficiency usually involves multiple vitamins, it is often difficult to determine the relative role of individual vitamins [1].

**Vitamin A** deficiency causes ichthyosis-like skin changes with generalized fine scaling and a thickening of the outermost skin layer, the stratum corneum (“phryonoderm”), which is particularly pronounced in the follicular openings, causing follicular hyperkeratosis [2]. This is often associated with effluvium and fragility of the hair. One of the earliest signs of vitamin A deficiency, however, is impaired night vision and the inability to see in bright light. Metaplasia of the conjunctival epithelium in vitamin A deficiency has been called keratoconjunctivitis sicca (Bitot macules), which can progress to keratomalacia, permanent scarring and blindness. Finally, vitamin A deficiency is associated with an increased incidence of epidermal neoplasias (anticarcinogenic activity of vitamin A). The differential diagnosis of vitamin A deficiency includes lichen pilaris, ichthyosis vulgaris, Darier disease, and other vitamin deficiencies (see biotin, vitamin C deficiency below). Extracutaneous manifestations include growth failure and mental retardation. For diagnosis plasma retinol levels are measured. Vitamin A supplementation resolves ophthalmologic symptoms within days and cutaneous changes within weeks.

**Vitamin B1 (thiamin)** is involved in carbohydrate metabolism, and B1 deficiency is known as beriberi. It is seen with gastrointestinal disease, a diet restricted to polished rice, alcoholism, pregnancy, lactation, and diabetes mellitus. Muco-cutaneous changes include edema and glossitis with glossodynia. Predominant are neurologic symptoms including peripheral neuropathy, confabulation (Korsakoff’s syndrome), and encephalopathy (Wernicke). Low urinary aneurin excretion is used as a diagnostic test. Supplementation is effective.

**Vitamin B2 (riboflavin)** can be due to a poor diet, but can also be caused by medications that impair its absorption (galactoflavin, phenothiazines, tricyclic antidepressants). Cutaneous changes that indicate vitamin B2 deficiency include seborrheic dermatitis-like scaling on the face (nasolabial folds), head, and genitocrural region. In addition, these patients present with cheilitis, perleche, pallor, and atrophy of the tongue.

<table>
<thead>
<tr>
<th>Vitamin Deficiency</th>
<th>Differential diagnosis of cheilitis due to nutritional deficiency</th>
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<tbody>
<tr>
<td>Zinc deficiency – genetic</td>
<td>Vitamin B2 deficiency*</td>
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<tr>
<td>Zinc deficiency – acquired</td>
<td>Vitamin B6 deficiency</td>
</tr>
<tr>
<td>Biotin deficiency</td>
<td>Vitamin B12 deficiency*</td>
</tr>
<tr>
<td>Folic Acid deficiency</td>
<td>Folic Acid deficiency</td>
</tr>
<tr>
<td>Iron deficiency*</td>
<td>Iron deficiency*</td>
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</table>

* in association with angular involvement (perleche)
Ophthalmologic involvement includes blepharitis, conjunctivitis, and corneal vascularization. Vitamin B2 is a cofactor of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), which are involved in many redox reactions. On blood testing, patients show a normochromic anemia. Decreased erythrocyte glutathione reductase activity confirms the diagnosis. The differential diagnosis includes seborrheic dermatitis and zinc deficiency. In mild cases, the recommended treatment is riboflavin 3–10mg daily per mouth, in refractory cases 2 mg daily via the intravenous route.

**Vitamin B3** (niacin) deficiency causes pellagra. Pellagra is characterized by a triad consisting of changes in skin, nervous system, and the gastrointestinal tract (“3D’s”: dermatitis, dementia, diarrhea). An early symptom is diarrhea. At later stages, patients report increased UV sensitivity (face, sun-exposed distal upper extremities) and sun-burn-like pruritic or burning erythematous macules, and occasionally blisters (Table 1.4). The facial rash at times resembles the butter fly rush of lupus erythematoses, but is always associated with other components of the triad. Quite characteristic is the sparing of the forehead as well as eczema of the neck and upper chest that can resemble a necklace (Casal’s necklace) (Fig. 1.1). Here the skin is erythematous to brown (or black), scaly. Sometimes there is an eczema craquele-like appearance with fissions and occasionally there are crusts. These lesions are common on the dorsal hands (Fig. 1.2), and can also be found on the feet and in the genitocrural region. Glossitis and stomatitis can also be present. Neurologic symptoms include peripheral polyneuropathy, encephalopathy, and depression. The differential diagnosis includes contact eczema, photo-induced dermatitis, and porphyria cutanea tarda. Pellagra is a clinical diagnosis, there are no laboratory markers. Niacin is a component of nicotinamide-adenine-dinucleotide (NAD) catalyzing redox reactions. A frequent setting for niacin deficiency is a niacin-deficient diet, which has occurred with the introduction of corn as a major food that only contains bound niacin that cannot be used by the human body. This is exemplified by endemic pellagra in geographic areas with predominant corn consumption, e.g., in South America. Aggravating factors include alcoholism, long-standing antibiotic therapy, isoniazid, 5-fluorouracil, inflammatory bowel disease, abnormalities of tryptophan metabolism (carcinoid), and Hartnup disease (see below). As with the other vitamin deficiencies, vitamin B3 supplementation will resolve the symptoms, but exogenous niacin can release histamine causing urticaria and worsening of preexistent asthma. Niacinamide is the preferred choice for supplementation, because it avoids these adverse effects.
Vitamin B6 (pyridoxine) deficiency is usually accompanied by other deficiencies and is associated with seborrheic dermatitis-like skin changes in periorificial distribution (eyes, nose, mouth) as well as cheilitis and glossitis. Pyridoxine is a cofactor of enzymes involved in amino acid metabolism (e.g., transaminases, synthetases, hydroxylases) and the metabolization of linoleic acid into arachidonic acid. Associations have been described with drugs such as isoniazid, penicillamine, hydralazine hydrochloride, oral contraceptives, phenelzine sulfate, cycloserine, and with uremia and liver cirrhosis. Diagnosis is made by measuring pyridoxine serum levels. Supplementation is effective.

Lack of vitamin B12 (cyanocobalamin), because of decreased intrinsic factor, is known for causing pernicious anemia, but can rarely also be due to strict vegetarian diet. Aside from its hematologic consequences (megaloblastic anemia), occasionally vitamin B12 deficiency also is associated with atrophic glossitis, angular cheilitis, mucositis, and symmetric acral (dorsal fingers and toes) and flexural hyperpigmentation. Poliosis, vitiligo, and alopecia areata occur with increased frequency. The differential diagnosis for the hyperpigmentation includes Addison’s disease. Intramuscular supplementation is effective (1 mg per month), resolving symptoms within 2–12 weeks.

Folic acid deficiency has similar mucocutaneous changes to vitamin B12 deficiency including hyperpigmentation and glossitis, but cheilitis and mucosal erosions have also been described. Decreased serum folate is diagnostic; oral supplementation is effective.

Vitamin C deficiency is the cause of scurvy. In the past, this was common among sailors and other people without access to fresh fruits and vegetables for extended periods of time. Although vitamin C deficiency has become much less common today, it is still encountered in the setting of urban poverty where it preferentially affects the very young and the aged (exacerbated by general malnutrition, mental incapacity, alcoholism). It is also seen with fad diets. Cutaneous changes of vitamin C deficiency include follicular hyperkeratosis on the extensor surfaces of the extremities, which characteristically show perifollicular hemorrhage (Fig. 1.3). The propensity for hemorrhage is due to fragile blood vessels, which is particularly pronounced in newborns and infants that present with petechia (over mechanical pressure points) and intestinal as well as urinary tract bleeding. In children, subperiosteal hemorrhage with radiographic alterations and pseudoparalysis has been described. Adults with long-standing vitamin C deficiency report impaired wound healing, bleeding gums, gingivitis, gingival hypertrophy, and loss of teeth. General symptoms of scurvy include fatigue, muscle weakness, myalgia, arthralgia, diarrhea, and anemia. The onset is approximately 1–3 months after onset of insufficient vitamin C intake. Long-standing, severe vitamin C depletion can result in diffuse edema, oliguria, anemia, dyspnea, and neuropathy. Supplementation with vitamin C is usually successful, if the deficiency is recognized early enough. Left untreated, the condition can lead to death. Low vitamin C serum levels are diagnostic. The recommended dose for vitamin C supplementation in individuals with deficiency varies between 100–1,000 mg of ascorbic acid per day. Infants should be treated with 50 mg of ascorbic acid up to four times per day.

Vitamin D deficiency is not associated with cutaneous changes (it primarily causes bone disease; i.e., rickets in children and osteomalacia in adults). Vitamin D deficiency has also been associated with higher susceptibility to infections; i.e., tuberculosis.
Vitamin E deficiency is not associated with cutaneous changes (it primarily causes neurologic abnormalities).

Biotin (vitamin H) deficiency causes an exfoliative dermatitis on acral skin, cheilitis, and/or periorificial dermatitis. If occurring in newborns, the disease may present with erythroderma and alopecia. The most common extracutaneous feature is enteritis. Other extracutaneous findings include metabolic acidosis, developmental delay, hearing loss, parasthesias, seizures, and conjunctivitis. Biotin deficiency is associated with impaired cellular immunity, there is a predisposition for infections; i.e., candida dermatitis. Biotin is a cofactor of carboxylases (biotinidase, holocarboxylase). Decreased serum biotin levels can be acquired or genetic. The differential diagnosis includes essential fatty acid deficiency. Hyperamonemia and organic aciduria are used for screening; the definitive diagnosis is established by assaying carboxylase synthetase activity in fibroblasts. Supplementation is effective.

Vitamin K deficiency, in severe cases, can lead to hemorrhage of the skin and mucous membranes. Clinical hemorrhage together with a prolonged prothrombin time leads to the diagnosis. This is seen in newborns or in later life in individuals with malabsorption, cystic fibrosis, liver disease, and drugs (warfarin, salicylates, cephalosporins). Treatment consists of parenteral vitamin K (1 mg newborns, 2 mg children, 5–10 mg adults).

1.1.4 Trace Element Deficiencies

Zinc deficiency is known for the classic triad of dermatitis, alopecia, and diarrhea. However, only 20% of patients present with all three components of the triad at a given time. Zinc deficiency can be hereditary or acquired. Hereditary zinc deficiency (acrodermatitis enteropathica) is an autosomal recessive intestinal abnormality of zinc absorption due to a mutation in a zinc transport protein. Human milk contains a zinc transport protein that is much less abundant in cow’s milk. Therefore, infants typically develop cutaneous changes days to weeks after being switched to bottle feeding (cow milk). Following intestinal absorption, zinc is bound to albumin. Whereas 99% of body zinc is intracellular, zinc storage is poor (total body zinc 2–3 g) and depletion occurs rapidly; i.e., within a month (zinc deficiency =<70mg/dl). Patients initially present with a perioral erosive dermatitis and perleche that progresses to involve the entire face, scalp, acral sites, and the diaper area. This can be accompanied by ulcerations of the oral mucous membranes and glossitis. The periorificial distribution is helpful in making the diagnosis. Palmar erythema, sometimes with anular or collarette-like scaling, may be present. If the dermatitis is accompanied by alopecia (telegon effluvium) and/or photophobia, zinc deficiency needs to be considered. Conversely, telogen effluvium alone without accompanying skin changes cannot be ascribed to zinc deficiency. Other differential diagnoses of zinc deficiency include seborrheic dermatitis or other eczematous eruptions. At times, patients present with persistent cutaneous infections, e.g., candida dermatitis, paronychia, as well as with onychodystrophy, blepharitis, and conjunctivitis. There is an immunodeficiency, preferentially due to functional impairment of T cells. Before the advent of zinc supplementation, affected individuals, primarily newborns and infants, would die from infections. The predominant extracutaneous symptom is diarrhea with electrolyte imbalance of variable degree. Long-standing zinc deficiency also leads to delayed wound healing, growth retardation, anorexia, anemia, hypogonadism, and altered mental status. Individuals with zinc deficiency are frequently infertile. If they conceive, infants may show malformations.

The cutaneous changes of acquired zinc deficiency are similar, but usually milder than those of hereditary deficiency. Because of its relatively mild symptoms, acquired zinc deficiency may be underdiagnosed. It can develop relatively quickly with an unbalanced diet (exclusive high fiber content interferes with absorption), parenteral nutrition lacking sufficient zinc supplementation, malabsorption (including cystic fibrosis), or abnormal intestinal loss of zinc. Chronic diarrhea is a common cause and can lead to a vicious cycle where diarrhea compromises zinc absorption and zinc deficiency in turn causes diarrhea. Other disease associations include chronic renal failure, malignancy, drugs, alcoholism, HIV infection, and pregnancy (Table 1.5). Zinc is a critical component of many enzymes. An important consequence of zinc deficiency is poor incorporation of essential fatty acids into eicosanoids. Skin histology shows a “pallor” of the upper epidermis. In more pronounced cases, there may be vacuolar degeneration of the upper epidermis.