TruGen3

Case Study:
High Risk Skin Cancer Patient

Detection, prevention, and essential skin care vitamins discussion

Tru Derma Health

TRUGEN TRU DERMA HEALTH, JUSTIN VUJEVICH, M.D.

THE HIGH RISK SKIN CANCER PATIENT

As a case example, Robert is a 65 year-old retired engineer who presented to his dermatologist with a non-healing, growing bump on his left cheek. A full-body skin exam revealed many brown spots and a few pink scaly areas on the sun-exposed areas of his skin. As a youth, Robert grew up on a farm during a time when sunscreen was not utilized and frequently worked outside with his father maintaining the land. As an adult, Robert spends many weekends on the golf course and enjoys fishing with his grandchildren.

A biopsy of the non-healing growth on the cheek revealed a basal cell carcinoma, the most common type of cancer in the U.S. In Robert's case, his fair Irish skin and history of previous skin cancer makes Robert a high-risk candidate for skin cancer. While this tumor can be treated by surgical removal, Robert asked his dermatologist if there was anything else he could do to help reduce his risk for developing an additional skin cancer?

SKIN CANCER, DETECTION, `AND PREVENTION

Skin cancer will affect 1 in five Americans during their lifetime. Skin cancers are generally classified as non melanoma skin cancers (basal cell carcinomas and squamous cell carcinomas) and melanoma skin cancer. Non-melanoma skin cancers arise within the top part of your skin, and clinically appear as red, scaly persisting growths or non-healing wounds. They are typically found on sun-exposed areas of the body. Melanoma, the deadliest form of skin cancer, may appear anywhere on the body and can develop from an existing mole.

While genetic factors (fair skin, hair and eye color, number of moles on skin, family history of skin cancer) contribute to our risk of developing skin cancer, exposure to ultraviolet light from the sun and indoor tanning devices is the most common risk factor for the development of all forms of skin cancer. Ultraviolet light consists of two types of harmful rays, ultraviolet A (UVA) and ultraviolet B (UVB) rays. UVA exposure leads to premature aging of the skin, causing wrinkles and age spots. In addition, UVA rays can also indirectly promote skin cancers through the formation of harmful free radical compounds. UVB exposure leads to sunburns and direct DNA damage of skin keratinocytes, leading to skin cancer.

Sun protection measures include limiting outdoor activities between the hours of 10am and 3pm, wearing protective clothing and broad-brim hat, avoiding tanning salons, and daily application of a broad-spectrum sunscreen that offers protection from UVA and UVB rays and has a Sun Protection Factor (SPF) of 15 or greater.

RATIONALE FOR TRU DERMA HEALTH

While skin precaution measures and regular use of sunscreen help in the prevention of skin cancer, patients frequently ask if there is anything else they can do in terms of skin cancer prevention? As a board-certified dermatologist and Mohs surgeon specializing in the diagnosis and surgical treatment of skin cancers, Dr. Justin Vujevich is frequently asked this question. Until recently, there were no placebo controlled studies demonstrating a benefit of affordable, over-the-counter ingredients that helped reduce the incidence of non-melanoma skin cancer, especially among patients with high risk. High risk patients include those whom have had multiple skin cancers, have a strong family history of skin cancer, have had extensive outdoor or indoor ultraviolet exposure, or whom are immunosupressed secondary to disease, immune-suppressing medications or post-

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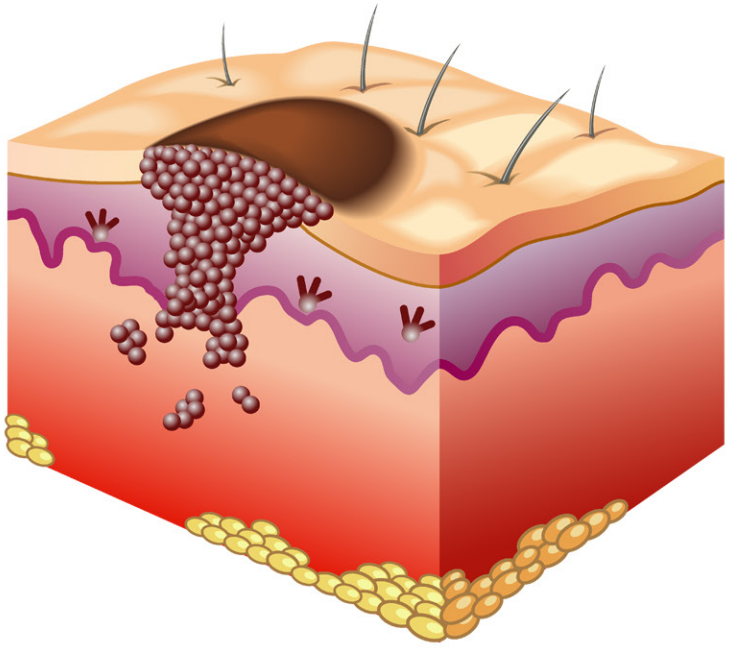

organ transplantation. Searching the marketplace, Dr. Vujevich would find one vitamin that may reduce the incidence of non-melanoma skin cancer (niacinamide), or one vitamin that serves as an antioxidant to help thwart skin aging (selenium, vitamin C) or another that promotes hair and nail re-growth (biotin), but there was not one vitamin that combined all of these clinically studied ingredients into one complete over-the counter product.

TruGen's Tru Derma Health is the first supplement that combines the essential skin health vitamins into one product. The discussion below illustrates the ingredients chosen based on clinically based studies, including the rationale on why certain dosages were chosen.

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NIACINAMIDE

Niacinamide is the physiologically active, water soluble amide form of niacin (vitamin B3). Niacinamide serves as a precursor to niacinamide adenine dinucleotide (NAD) and niacinamide adenine dinucleotide phosphate (NADP). NAD and NADP are very important for cellular energy production and act as coenzymes for biochemical reactions in the body. Niacin and niacinamide are not synthesized in the human body and are found in meats, daily produces, vegetables, coffee and tea. The USDA recommended intake for niacinamide is approximately 16-18mg/day.

Niacinamide has a history in dermatology of treating several inflammatory disorders, including autoimmune bullous diseases (5), acne and rosacea (6), and atopic dermatitis. Although the exact mechanism of action of niacinamide as an anti-inflammatory agent is unknown, it is thought to inhibit mast cell histamine release and the release of other inflammatory mediators.

Niacinamide has also been shown to demonstrate a chemo preventative role in precancerous and skin cancer tumors. Niacinamide also appears be effective in preventing and treating precancerous growths called actinic keratoses, which may progress to squamous cell carcinomas. In a phase II double-blinded controlled trial, 34 patients were randomized to receive oral niacinamide 500mg or placebo orally twice a day for four months (4). A 35% reduction in actinic keratoses was demonstrated in the niacinamide treated group compared to placebo group. Another randomized, placebo-controlled study of 38 transplant patients treated with niacinamide 500mg orally once daily for 6 months versus placebo demonstrated a significant decrease in number and size of actinic keratoses compared with the placebo group. In addition, none of the existing actinic keratoses developed into squamous cell carcinomas in the niacinamide treated group, while 7 new SCCs developed within the placebo group.

Niacinamide has clinical evidence of preventing skin cancers in high risk immunocompetent patients. A one-year, double–blinded, randomized, placebo controlled-phase III clinical trial of 386 patients demonstrated a 23% reduction in new non-melanoma skin cancers in skin cancer patients whom took 500mg of niacinamide twice a day (1). Actinic keratoses were also reduced in the niacinamide-treated group.

The mechanism of action of niacinamide in chemo prevention appears to be the enhancement of repair of ultraviolet radiation-induced DNA damage (7).

BOTIN

Biotin, also known as vitamin H and coenzyme R, is another water-soluble vitamin B member that is derived from our diet. Although not technically a vitamin, biotin is a cofactor that is important to several enzymes involved in carbohydrate metabolism, fatty-acid synthesis and protein formation.

Biotin deficiency in the skin has been associated with seborrheic dermatitis, an inflammatory condition of the scalp, face and chest, candida infection and alopecia or hair loss. Oral supplementation of biotin to infants with scalp alopecia due to biotinidase deficiency resulted in full hair regrowth after supplementation (8). In addition, children deficient in biotinidase whom are given oral biotin supplementation improve their inflammatory skin disorders (9).

VITAMIN D

Vitamin D is a fat-soluble vitamin found in fortified foods (milk, orange juice), fish and vegetables and produced in our skin in association with UVB exposure. In the skin, 7-dehydrocholesterol is converted by UVB exposure into previtamin D3 and subsequently vitamin D3. Vitamin D3 enters our body's circulation and is metabolized by the liver and kidney into its biologically active form. While social norms and other industry encourage sun tanning or indoor tanning as a source for vitamin D, the U.S. Department of Health and Human Services and the World Health Organization's International Agency of Research on Cancer panel have declared UV radiation from the sun and artificial sources to be a known cancer-causing substrate. Therefore, a healthier alternative for our bodies to get vitamin D is from a healthy diet and/or vitamin D Supplements.

Vitamin D was included in the TruGen supplement for high risk skin cancer patients whom need to avoid unnecessary sun exposure as

their source for vitamin D synthesis. Furthermore, many epidemiological studies have shown an association between low serum vitamin D levels and poor bone health, therefore, supporting adequate blood levels (11). Based on currently available scientific evidence, the National Academy of Sciences Institute of Medicine Recommended Dietary Allowance (RDA) for Vitamin D intake is between 400-800IU a day (10).

SELENIUM

Selenium is a natural element found in the human body. It is found in foods such as cereals, meat, fish and dairy products. Selenium is important in thyroid function and is the vital antioxidant required to form glutathione peroxidase, one of our most important natural antioxidant defenses. The selenium-glutathione peroxidase pathway removes superoxide free radicals and is thought to inhibit carcinogenesis and slow skin aging.

Selenium is thought to have antioxidant, anti-inflammatory and anti-carcinogenic effects on the body, including the skin. Selenium helps prevent the production of inflammatory cytokines that increase the number of damaged skin cells, particularly after ultraviolet exposure. In fact, one multi-center trial concluded that selenium 200mgper day reduced incidence of lung, colorectal and prostate cancers (12). In addition, animal and human studies have found that oral selenium demonstrated protection against ultraviolet-induced damage to skin cells (13, 14).

VITAMIN C

Vitamin C, or L-ascorbic acid, is a water-soluble molecule present in fruits and vegetables that is not synthesized in our bodies. In the skin vitamin C is a powerful inhibitor of the generation of reactive oxygen species, particularly after ultraviolet light exposure (15).

Vitamin C is also an important co-factor for enzymes in the synthesis of collagen and in particular, wound healing. Patients with low vitamin C levels have increased skin fragility. One study treated 20 patients with pressure ulcers with ascorbic acid 500 mg versus placebo and found that patients with supplemental vitamin C had a reduced pressure sore area compared with controls (16).

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ZINC

Zinc is an essential trace element found in high-protein meats, fish, dairy products and vegetables. Our body absorbs only 20% of the zinc in our diets so patients whom have gastrointestinal maladies may have low zinc levels. Low zinc levels can lead to hair loss and poor wound healing.

Zinc plays an important role in the skin, acting in catalytic, structural and regulatory roles (18). Zinc has antioxidant properties and is involved in the destruction of free oxygen radicals in the body produced post-ultraviolet exposure (17). In addition, zinc promotes the healing of skin wounds.

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