PIGMENTARY DISORDERS

Dr. Charlene DeHaven M.D.
Clinical Director, INNOVATIVE SKINCARE®

MELANIN AND PIGMENTARY DISORDERS
Abnormalities in pigmentation are common and frequently produce considerable stress in the patient, since they affect appearance. Some of these concerns are purely cosmetic, and other pigmented changes, as with lupus, can signal serious underlying disease. Pigmentary disorders all relate to either increases or decreases in the amount of the skin pigment melanin in a particular area of skin in comparison with the surrounding area. Disorders resulting from excess melanin are more common and are known as hyperpigmentary or hypermelanotic conditions. Those with too little melanin or loss of melanin are termed hypopigmentary or hypomelanotic. Healthcare practitioners are consulted far more commonly for hyperpigmentary disorders than decreases in pigment. In fact, for women of color, hyperpigmentation is the most common reason for dermatologic consultation.

PIGMENTATION PROCESS OF SKIN
The visual appearance of pigment in the skin requires multiple steps. It begins with the melanocyte, the pigment-producing cell located in the basal layer of the epidermis. Melanocytes begin their production of melanin when stimulated by external forces such as sunlight or skin injury, both of which are associated with free radical damage and inflammation. Melanin is produced by a complex, multistage chemical process requiring the enzyme tyrosinase for its most critical step. This pigment is then stored within the melanocyte in small packets called melanosomes. The most prevalent cell in the epidermis, the keratinocyte, then accepts the transfer of melanin pigment from the melanocyte through small projections called dendrites. Only when the melanin is incorporated into the keratinocyte does it become visible. As keratinocytes migrate upward in their normal movement through the epidermis, melanin moves with them, becoming more visible. In the outermost stratum corneum, keratinocytes become very flattened and pigment appears visually more prominent.

In Caucasians, pigment packets are bound to the keratinocyte cell membrane and are of smaller size. In people of color, melanin is dispersed throughout the cytoplasm (cell body) of the keratinocyte and are also larger. Asians and red-haired persons have slightly different chemical types of melanin.

The amount of visible pigment may be altered by influencing any of the steps in the pigmentation of skin. In fact, more efficient products and treatments address multiple steps in the pigmentation process in order to potentiate each other. It is important to realize that the most potent stimulus for melanin production is skin’s exposure to sunlight. For any hyperpigmentation treatment to be effective, use of a sunscreen and avoidance of solar stimulus is mandatory and must be part of the treatment regime.

POSTINFLAMMATORY HYPERPIGMENTATION
Melanin production also is part of the skin’s response to injury. This response is more vigorous and therefore more noticeable in persons of color. Inflammatory mediators called cytokines signal the melanocyte to increase melanin production. The inflammatory response seen with sunburn serves as a potent trigger, as well as injury from other sources such as surgical procedures, the inflammation of acne or rosacea, and other conditions. Postinflammatory hyperpigmentation is less common in fair-skinned individuals and also easier to treat than in those with more intrinsic melanin.

LENTIGINES
Lentigines (liver spots) are flat, irregularly shaped, hyperpigmented areas of varying size found on
sun-exposed areas. These develop when the skin lipid lipofuscin is oxidized and turns brown. Lentigines are extremely common, and their incidence increases with sun exposure. Ninety percent of lighter-skinned individuals develop lentigines by the age of sixty.

**MELASMA**
Melasma is a very common hyperpigmentary disorder that affects sun-exposed areas in women, most typically in a butterfly pattern over the nose and face but also on other facial areas. Sun exposure, especially tanning, exacerbates the problem. The hyperpigmented areas occur on the cheeks, central face, forehead, upper lip, and chin. Melasma can occur in men, but males compose only 10% of cases. It is usually related to hormone excess, as in pregnancy (when it may be termed the "mask of pregnancy"); oral contraceptive pill use; and endocrine disorders. It may be associated with some cosmetics, some medications (dilantin, oral contraceptives), and severe liver disease. In women taking oral contraceptives, about 30% develop melasma. Postmenopausal women on estrogens do not usually develop melasma. It is treated with skin lightening agents, camouflage makeup, strict avoidance of tanning, and the stopping of any potential causative medicines.

**VITILIGO**
This disease causes loss of pigment by destroying melanocytes via an autoimmune mechanism. As with other processes of immune origin, genetics plays a role, and 30% of people with vitiligo have an affected family member somewhere in their family tree. Affected families have an increased incidence of graying of the hair. All races are affected, but it is more noticeable in darker complexions.

Men and women are affected equally. One to two million Americans have vitiligo, and it is found in 1–2% of the world’s population. The most common age of onset is in the first 2 decades of life. Sometimes spontaneous remission occurs and repigmentation is seen. The most common areas affected are the face, back of the hand, wrists, armpits, central abdomen, and genitalia. Childhood vitiligo is seen in children under 12 years and is different from the other type in that depigmentation frequently occurs in long segments.

Treatment is difficult. Some treatments include PUVA (psoralen plus ultraviolet A light exposure), topical steroids, and surgical treatments of various grafting or micrografting types. Stem-cell therapy may have potential for the future.

**TINEA VERSICOLOR**
Tinea versicolor is also called pityriasis versicolor and is a superficial infection of the stratum corneum caused by the yeast Malassezia furfur. It is found throughout the world and in all races, although it favors tropical climates. It also tends to be more severe in the tropics. The small, circular, hypopigmented lesions are most commonly found on the torso and may be very numerous. Affected areas do not tan well and become more noticeable in the summer or with tanning. Eradication of the infection is difficult, and recurrence rates within 2 years are 60–80%. Topical antifungal medicine is used to treat the infection.

**ACANTHOSIS NIGRICANS**
This is a disorder of increased pigment. A velvety hyperpigmentation occurs in large patches that are found, in descending order of frequency, in the axillae (armpits), neck, groin, breast folds, inner elbows, back of the knees, and mouth area. Interestingly, the patient usually refers to the appearance of the initial lesion as a "dirty area," although it is certainly not dirty. Skin thickening occurs as the disease advances. There is an association with obesity, and the disease worsens as the patient gains weight. Acanthosis nigricans occurs in 13% of African Americans, 6% of Latin Americans, and about 1% of Caucasians.

There is a variant of acanthosis nigricans with onset in adulthood that is associated with internal malignancies. The rapid onset of this disorder or large, generalized lesions should prompt the physician to search for underlying malignancy.
Treatment is weight loss if the cause is obesity. In all other types, treatment is extremely difficult, although various topical therapies (topical retinoids, topical corticosteroids) have been tried.

**CAFÉ AU LAIT MACULES (CALMS)**
CALMS affect larger areas of skin and are brownish (café au lait or coffee with cream) in color. They have irregular margins and may be from 0.2 to 20 cm in diameter. They have an association with a potentially serious genetic disease, neurofibromatosis.

**OTHER MEDICAL DISORDERS**
A number of other medical conditions may be associated with pigmented changes. These may include lupus, Addison’s disease, Cushing’s syndrome, thyroid disease, neurofibromatosis, and others. A physician should be consulted for accurate diagnosis and appropriate advice.

**TREATMENT**
Consultation is sought most commonly for treatment of postinflammatory hyperpigmentation, melasma, and lentigines. Treatments can involve topical agents and/or procedures. Lighter Fitzpatrick skin types generally have more favorable response to treatment, since they are less likely to develop hyperpigmentation from the treatment efforts themselves. Hyperpigmentation in response to treatment, sometimes called reactive hyperpigmentation, is a type of postinflammatory hyperpigmentation related to applying potentially irritating substances or treatments to the skin with induction of the melanocyte.

A magnifying lamp, or Wood’s UV lamp, may be used to determine if only the epidermis is involved or if hyperpigmented areas may extend into the dermis. Dermal hyperpigmentation occurs with melanoma, a very aggressive skin cancer. Any new or unusual areas of hyperpigmentation should be promptly evaluated by a physician for possible melanoma. There are 5 warning signs of melanoma, designated as ABCDE: A = asymmetry; B = irregular border; C = variable color with dark areas; D = diameter greater than 6 mm; and E = evolution, referring to changing appearance with time. Early detection of melanoma is key to successful treatment. All races are at risk for melanoma.

As mentioned previously, treatments targeting multiple steps in the pigmentation process are more likely to be effective than those affecting one step alone. A number of topical products inhibit tyrosinase, thereby decreasing melanin production within the melanocyte. Many topicals, some of botanical origin, can play a role in treatment. These include kojic acid, arbutin, niacinamide, azelaic acid, alphahydroxy acids and other resurfacing agents, soy, licorice, vitamin C, and more. Hydroquinone has been used, but it is cytotoxic (cell-killing) to the melanocyte and thus can induce more inflammatory pigmentation. If used, hydroquinone should be carefully managed by a physician and applied for limited periods of time only.

Procedural treatments can be ablative or non-ablative. Inflammation can occur with procedures, and this risk should be addressed by the treatment professional. Ablative treatments include ablative lasers and deep chemical peels. Non-ablative treatments may include intense pulsed light (IPL), microdermabrasion, lighter chemical peels, and lasers. Topical and procedural treatments may be combined.

Prevention of further hyperpigmentation is key in any treatment regime. This includes sun avoidance and aggressive sun protection with use of an effective sunscreen. Inflammation in response to potential treatments must also be kept to a minimum.

**PRODUCT RECOMMENDATIONS**
iS CLINICAL® products that help treat pigmentary disorders include WHITE LIGHTENING™ COMPLEX, WHITE LIGHTENING™ SERUM, SUPER SERUM™ ADVANCE®, PRO-HEAL® SERUM ADVANCE®, C EYE SERUM ADVANCE®, YOUTH COMPLEX®, and ACTIVE SERUM™.

iS products that help treat pigmentary disorders include EXTREME PROTECT SPF 30, ECLIPSE SPF 50+, EXFOLIATING ENZYME TREATMENT,