Treatment of Vitiligo, "making it simple"!

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Doctors have noticed some patients seem to have difficulty in understanding why so many treatments are available for diseases in general, and vitiligo in particular. The main objective of this article is to describe and clarify for patients, families, friends, and the general public the basis of, and options for, vitiligo treatment. This material will be presented as simply as possible while maintaining the most current and reliable medical and scientific information. In an uncomplicated way, "*Treatment of Vitiligo, making it simple!*" is presented for all to understand. I have chosen the question/answer approach to present each topic concerning vitiligo treatment. Why? Because most people initially confronted with the subject of vitiligo are filled with questions about this relatively unknown and undiscussed disease. You can expect to have your DOUBTS or QUESTIONS about vitiligo treatment ANSWERED here. You can then comfortably search the National Vitiligo Foundation (NVF) web site for more detailed answers to your questions and interests.

Why there are so many drugs and treatments for vitiligo therapy?

The main answer to this question is that everyone is not the same. People have many general characteristics in common, however many important differences do exist between us. It appears that vitiligo is a chronic disease that may have a different medical origin or a different development in each person. Therefore, vitiligo may not be a single or simple disease in the human population. For each individual with vitiligo, the disease may have its own unique characteristics. As such, a specific design for a therapeutic approach needs to be applied to each patient affected by vitiligo. As a complex disease, the treatments have to be applicable to each single patient.

While prescribed medications can be an effective way to treat vitiligo lesions, each patient can react differently to the various medications, and not all treatments will work for all patients. Once an effective treatment is found, there is a chance that it may not remain effective for that patient as time goes on. Therapy will require a kind of experimentation to see which treatment works best for that individual.

What kind of treatment can the patient expect?

Again, this is specific to each individual patient depending on the symptoms and stage of the disease. Through their dermatologist, patients can be made familiar with the many different treatment options available. The patient should discuss these treatments with the physician to jointly determine what option would be the best.

Why do doctors ask so many questions before prescribing a treatment for vitiligo?

This is because each patient with vitiligo has a unique or specific situation among the many possibilities that characterize this complex disease. Clearly identifying the patient's specific situation is essential for the dermatologist. Heredity (the genetic background of the individual) may be one important factor because there's an increased incidence of vitiligo in some families. Another important factor is what may have caused the onset of vitiligo. Some people have reported that a single event such as a sunburn or emotional distress may have triggered their condition. Moreover, the dermatologist needs to know if previous treatments were used on the patient by himself or herself or by other doctors. If so, the dermatologist would be interested in obtaining information about any successes or failures from each treatment that the patient had experienced. Failure or partial success of previous treatments helps the dermatologist decide what other treatments might be more suitable for treating the current disease state.

What causes the skin to change color in vitiligo and how is this related to treatment?

The change in skin color is caused by a loss of pigment called melanin. Melanin determines your skin, hair, and eye color, and is produced in cells called melanocytes. Melanocytes produce the melanin and transfer this pigment into the major cells of the skin, called keratinocytes. If the melanocytes are lost, as in vitiligo, melanin is not made and the skin becomes lighter or completely white. Because melanocytes generally do not divide to create new melanocytes that could replace those that are lost, the white areas of the skin remain.

What is the goal in treatments for vitiligo?

The primarily goal in treating vitiligo is to stop it from spreading and then to stimulate the melanocytes to move from pigmented areas of skin, or from pigmented hair follicles, to those areas where melanocytes were lost. There are several possible ways to accomplish these goals.

What is the sequence of treatments for vitiligo?

While there is a generalized sequence for the treatment of vitiligo, multiple variations on this sequence can occur. The initial basis of any vitiligo treatment is to slow or stop the melanocyte destruction that is causing the lesions (white areas) to grow or new lesions to appear. Some of these treatments to stop the spread of vitiligo may also stimulate melanocytes to divide and reverse the vitiligo. This is called repigmentation therapy. After control of vitiligo progression has been obtained,

other treatments can be initiated to promote repigmentation separately. For example, some treatments transfer melanocytes from a normal pigmented area of the patient's body to the white areas. However, if the disease is not responsive to any of the various treatments and the extent of the body surface that is covered with vitiligo is greater than 50%, the doctor may propose depigmentation therapy. The objective of this treatment is to remove the remaining skin pigmentation and create an even color in the patient's skin.

What are the main things responsible for causing vitiligo?

Doctors and scientists have several theories as to what causes vitiligo. The basic mechanisms currently proposed are: 1) the melanocytes (pigment cells) are destroyed by other cells from the immune system (system of defense) of the individual, 2) the melanocytes are destroyed by internal biochemical reactions that occur while the melanocytes are making pigment, which results in the death of the cells, and 3) the nerves in the skin produce signals that destroy the melanocytes. In all cases, one or more of these mechanisms may act together to produce vitiligo. Some of the available medical treatments attempt to stop each of these mechanisms. Other treatments try to stimulate the division and movement of existing melanocytes into depigmented areas.

How is the skin affected by vitiligo different from the normal skin and how this is related to treatment?

The skin affected by vitiligo no longer has natural protection from sun. The melanin produced by the melanocytes protects the skin from damage caused by sunlight. White areas, which do not have any melanin, are therefore more easily sunburned, and people with vitiligo have a possible increased risk for skin cancer and skin aging. Patients with vitiligo should wear a sunscreen with a SPF (solar protection factor) of at least 30 on all white areas not covered by clothing. Also, to avoid burns, they should avoid the sun when it is most intense.

How many classes of treatments exist for vitiligo?

Treatments are focused on two main issues: combating the origin of the vitiligo, and stimulating the melanocytes to repopulate the vitiligo lesions. One treatment class tries to stop the immune cells that are attacking the melanocyte and are causing progression of lesions. This treatment may also provide time for new melanocytes to multiply and replenish missing ones. In this class, corticosteroids and ultraviolet light are used separately or together. In another treatment class, drugs are used to stop the production or imbalance of internal chemicals (biochemicals) that cause melanocyte death. Corticoids are the main drug in this group. Some treatments are used to stop the release of chemical signals (neurotransmitters) that cause melanocyte death. In this case, corticosteroids are also considered the main treatment. In addition, there are treatments that stimulate melanocyte multiplication. In this group, ultraviolet light and microsurgery procedures are used. Finally, there are treatments with the objective of reducing the color differences between the lesions and normal skin. In this last approach, chemical substances and lasers are used to destroy melanocytes and produce an even-colored complexion throughout the body. In some cases, the temporary or definitive use of

camouflage or make-up is desired. Finally, in cases where emotional stress occurs, psychological support is included in the therapy.

How do doctors select the treatment for a patient among so many options?

The basis of Hippocratic medicine (named after Hippocrates of Cos, the father of medicine) rejects superstitions, legends and beliefs that credit supernatural or divine forces with causing illness. Hippocratic medicine is concerned with patient care and prognosis. The modern physician focuses on specific diagnosis and specialized treatment for the disease origin. Treatment for vitiligo aims to stabilize the depigmenting process and to achieve repigmentation in the lesions. Each year, many articles are published about the effectiveness and safety of different repigmentation therapies. Because of the increasing clinical knowledge and literature, it is essential to create strategies that may facilitate therapeutic decision making.

There is a growing interest in the use of clinical guidelines for the practice of medicine. Guidelines contain systematically developed statements that assist the clinician in choosing the most appropriate therapy for a specific condition. Guidelines are regarded as tools to reduce inappropriate care, control geographic variations in practice patterns, and make the use of health care resources more effective. Doctors prescribe treatment based on the characteristics of each patient, such as possible cause, development, extension, patient's age, and disease pattern prognosis, among others. The idea is to maximize the treatment effect with low or no undesirable side effects.

When should a doctor initiate vitiligo treatment?

Treatment should begin as early as possible. Vitiligo can be an emotionally distressing and physically disfiguring disease, especially in dark-skinned individuals and in children, and when it is present on exposed areas such as the face or hands.

Why do some doctors not prescribe any treatment?

Sometimes the best treatment for vitiligo is NO TREATMENT. This approach may be used for fair-skinned individuals with few lesions. Sunscreen is still recommended in these cases. Avoiding tanning of normal skin can make areas of vitiligo almost unnoticeable in light skinned individuals.

What happens if vitiligo lesions are left untreated?

The course of vitiligo without treatment is unpredictable. The white lesions may progress slowly or rapidly or not at all. Many patients live a normal life with vitiligo on their body.

Is there any treatment that cures vitiligo?

Unfortunately, at present, there is no known cure for vitiligo, but scientists are working hard to develop one.

Bear in mind that the definition of cure may be different for different individuals. For some patients, curing the disease will mean maintaining it under control. For others, curing the disease will mean the complete recovery of all depigmented areas.

It is worth mentioning that a patient may have stabilization, reduction, or even disappearance of affected areas without any treatment at all. There are reports in the medical literature of patients who spontaneously achieve a sustained remission from the disease.

Why do doctors not use the most potent medication available?

Doctors prescribe a treatment based on the characteristics of the patient's vitiligo, such as possible cause, development, extension, patient's age, disease pattern prognosis, and other items. The goal is to maximize the effect of the therapy with low or no undesirable side effects. This is often not achieved by using the most potent medications available. The patient needs to realize that repigmentation is a slow process and depends upon the patient's unique circumstances and compliance with treatment. Patience and dedication is required. All suggested treatments are based on the best available scientific evidence and validation of the treatment.

When do doctors prescribe a corticosteroid?

A number of decisions must be made before a topical steroid is prescribed. Considerations include the stage of the disease being treated, anatomic site, patient age, cost, frequency of application, side effects, number of refills, and the specific medication. Because of their extensive used and because a wealth of scientific information exists about them, corticosteroids are often considered the first line of therapy in vitiligo treatment. Corticosteroids may be used topically (applied to the skin surface) or systemically (ingested or injected into the body). Topical use is usually indicated for localized lesions, small lesions, and few affected areas of the body. Systemic use is usually indicated for numerous lesions, relatively large lesions, and lesions covering many sites on the body.

Are all topical corticosteroids the same?

No, they are not the same. After the decision is made to use either topical or systemic corticosteroid therapy, the next step is to decide on the potency of the corticosteroid. Low potency steroids are used for facial lesions, small lesions, or with children. More potent corticosteroids are used for lesions on the body, excluding the groin, genital area, or under the arm. High potency corticosteroids should be used for only a short period of time.

How is the potency of topical steroid medications determined?

The vasoconstrictor (shrinking of blood vessel) assay is the standard for determining the anti-inflammatory properties of topical steroid medications. Although this assay measures only one biological function of the drug, it is known that the amount of vasoconstriction correlates with the potency (and clinical effectiveness) of the steroid.

Are topical corticosteroids medications effective?

Based on a review of numerous clinical trials, topical steroids are associated with some repigmentation and may be effective in returning pigment to small areas of skin affected by vitiligo. They can be used along with other treatments to create an effective regimen. Evidence suggests that topical steroids such as clobetasol propionate are more effective than topical psoralen (discussed more below).

What are the side-effects of using topical corticosteroids?

The prolonged use of topical corticosteroids, especially potent corticosteroids, can cause thinning of the skin (mild skin atrophy where the skin becomes very thin and relatively easy to rip or bleed), stretch marks, telangiectasia (permanent dilation of pre-existing small blood vessels that create red lesions), hypertrichosis (excessive growth of hair), and acneform papules (resembling acne lesions). All corticosteroids should be used under your dermatologist's care.

Can topical corticosteroids be used with other treatments for vitiligo?

Yes, topical corticosteroids can be used along with other treatments. For example, a combination of topical fluticasone propionate plus ultraviolet A (UVA) light has been associated with higher rates of complete repigmentation than either therapy alone. Topical steroids may also be associated with higher repigmentation rate in patients taking levamisole (an immunomodulator used as an adjunct treatment).

Is the topical treatment of vitiligo in children effective?

Aggressive treatment is generally not used in children. Sunscreen and cover-up measures are usually the best treatment. Topical corticosteroids can be used but must be monitored. Children under the age of 12 should use lower potency preparations such as fluticasone propionate cream or desonide 0.05% cream once a day for four months. When higher potency preparations are used to treat vitiligo in children, there is a substantial risk of systemic absorption into the child's body. This can cause other undesirable side effects.

How effective is the corticosteroid treatment of vitiligo in adults?

Adults and patients over the age of 12 should be treated with mid-potency topical corticosteroids such as fluticasone propionate ointment or mometasone cream once a day for four to six months. If repigmentation occurs, treatment should be continued until no further response is noted. Patients should be followed every four weeks during therapy to monitor for signs of steroid-induced skin side effects (described above).

Can oral corticosteroids be used for vitiligo?

Oral corticosteroids have been successfully used in patients with progressive disease. Systemic corticosteroids have been claimed to rapidly arrest spreading vitiligo and induce repigmentation.

However, given the significant potential for serious side effects, their use remains controversial. They are typically reserved for severe cases. Referral to a dermatologist is warranted for such patients.

Is there any other topical treatment for vitiligo?

Physicians have welcomed the introduction of a new, non-steroidal group of topical immunomodulators (materials that regulate activity of the immune system). Pimecrolimus (Elidel®) and tacrolimus (Protopic®) are being used topically for vitiligo treatment.

How do these topical immunomodulators control vitiligo?

They reduce or stop the effectiveness of the skin immune system. Consequently, these drugs stop the immune system from causing melanocyte destruction.

If these immunomodulator drugs can reduce my local immune system, what is their advantage when compared to corticosteroids?

Tacrolimus and pimecrolimus work in a different way than corticosteroids to affect the immune system and hence have a different effect on skin. While tacrolimus seems to be almost as effective as clobetasol (a high potency corticosteroid) in improving repigmentation, it has a lower incidence of skin atrophy (discussed above for corticosteroids). Pimecrolimus has not yet been shown to improve repigmentation, but further studies are necessary.

Can these topical immunomodulators be used to replace corticosteroids?

Topical forms of corticosteroids and these newer immunomodulators can be used to control acute development of vitiligo. Topical corticosteroids are usually the first choice. However, when long courses of topical corticosteroid are necessary to control the disease, other topical immunomodulators such as tacrolimus should be used. Tacrolimus can be considered for first use in areas such the face, neck, around the eyes, under the arm, groin, and genitals (places were the use of high potency corticosteroids or prolonged corticosteroid treatment poses greater risks).

What are the side-effects of these newer topical immunomodulators?

Tacrolimus and pimecrolimus can cause a stinging and burning sensation in the skin. However, a major side effect is that they might not be selective for reducing the local immune system that causes vitiligo. The FDA issued a public health advisory that tacrolimus and pimecrolimus may have some cancer risk based on animal studies using higher doses of the compounds and a few human case reports. That said, definitive human studies may take 10 years or more to determine if a real cancer risk is associated with these drugs.

If topical immunomodulators stop the disease, how is melanocyte growth stimulated?

Phototherapy is used to stimulate melanocyte division. Phototherapy refers to the use of ultraviolet (UV) light with a wavelength of 290-320 nm to treat cutaneous disease. This approach uses either a device that emits UV light or natural (solar) light. The process is similar to tanning, where the sun's UV light stimulates melanocytes to increase melanin production, resulting in darker skin. Unlike tanning, however, phototherapy allows precisely controlled exposure to UV and can be limited to certain areas of the body.

When do doctors prescribe phototherapy?

Phototherapy is often used when topical treatments have not been effective or it can be used in combination with topical medications.

Is phototherapy a single type of therapy?

There are three basic types of phototherapy available: UVA, UVB, and Excimer laser. All are based on the emission of UV light (which stimulates melanocytes).

UVA and UVB: What is the difference?

UVA has a longer wavelength than UVB. UVA is used in commercial tanning salons. For treating vitiligo, however, UVA is relatively ineffective unless the patient is also treated with a photosensitizing medication such as psoralen. The combination of psoralen and UVA light is known as PUVA (**P**soralen and **UVA** light). Physicians now more commonly use UVB because it has been proven to be an effective type of phototherapy and does not need psoralen.

Treating vitiligo in a tanning salon can be risky since attendants are not medically trained and the potency of the light equipment can vary greatly. Evidence is mounting that overuse of UVA plays a role in initiating some skin cancers.

Is PUVA a form of repigmentation therapy?

Yes, it is. Psoralen itself has no therapeutic benefit. It is a plant extract. Psoralen drugs increase the energy from UVA light. Taken in pill form or applied topically to the skin, psoralen interacts with UVA and amplifies its effect. It is like adding a chemical magnifying lens to the light beam. Psoralen makes the skin more sensitive to UVA light, which then penetrates deeper into the skin.

How is PUVA used?

When vitiligo is limited to few small areas, psoralen can be topically applied to vitiligo areas before UVA treatment. However, psoralen is usually given in pill form. PUVA treatments take place in a doctor's office. A physician knows exactly how much time should elapse between the patient taking the pill or applying psoralen topically and exposing the lesions to UVA light. PUVA can be combined with

other therapies. PUVA therapy in combination with epidermal grafting can be used for areas of vitiligo that are unresponsive to PUVA therapy alone.

PUVA treatments are usually given two to three times a week. Initially, exposure to UVA may be very short depending on the patient's skin type and the kind of UVA device. Exposure time will gradually increase with continued therapy. Satisfactory repigmentation generally requires 1-3 years of treatment.

Why is timing critical to PUVA success?

Timing is critical to the success of the treatment because, for the UVA light exposure to work, it must be administered at the time when psoralen is at a maximal level in the skin.

How effective is PUVA?

Topical or systemic PUVA therapies are well established treatments for non-segmental vitiligo. Treatment with PUVA has more than a 50% chance of returning color on the face, trunk, upper arms and upper legs. Hands and feet respond very poorly.

How does PUVA induce repigmentation?

PUVA causes a systemic and local suppression of the immune system, which stops melanocyte destruction and progression of vitiligo lesions. PUVA also stimulates the division of melanocytes, which leads to their repopulation in lesions. In addition, PUVA causes stimulation of melanin production by the melanocytes.

Does the patient need medical supervision for PUVA?

PUVA must be given under close supervision by the patient's dermatologist. Oral PUVA has side effects that need medical attention to reduce their occurrence. PUVA may induce a sunburn-type reaction, which may include nausea, itching and redness of the skin. Ingesting food when taking oral psoralen may prevent nausea. Other less frequent side effects that may be related to psoralen include depression, dizziness, insomnia, headache, nervousness, rashes and legs cramps.

When used long-term, freckling of the skin may result and there is an increased risk of skin cancer. Because psoralen also makes the eyes more sensitive to light, UVA blocking eyeglasses must be worn during daylight time to prevent the increased risk of cataracts. PUVA is usually not recommended until after age 12, in pregnant or breast feeding women, or individuals with certain medical conditions. The risk and benefits of this treatment must be carefully weighed.

Do similar side-effects happen with topical PUVA?

Topical PUVA reduces the short-term side effects that are associated with oral PUVA. However, topical PUVA poses a higher risk of a person's skin burning and it is more labor intensive. It is an alternative for individuals who do not tolerate oral psoralen ingestion.

How is topical PUVA used?

Topical PUVA is referred to as “paint”, “soak” and “bath” PUVA, reflecting the different ways it can be applied. The UVA light should be administered within 15 minutes after the psoralen is applied to the skin.

Is UVB another way of avoiding psoralen intolerance?

With UVB phototherapy there is no need for psoralen. The patient’s skin is exposed to UVB light generated from a special lamp or laser. UVB is considered when topical treatments have not been effective. It may be used alone or in combination with topical treatments such as corticosteroids, antralin or coal tar.

How is UVB used?

There is both broadband UVB and narrowband UVB. Narrowband UVB emits a more specific range of wavelengths and is more effective with fewer side effects. This is a form of phototherapy that requires the skin to be treated two to three days a week. UVB requires a significant time commitment and devotion.

Is UVB effective?

Analysis of scientific literature and a retrospective study demonstrated that oral PUVA, narrowband UVB and broadband UVB are statistically equivalent in terms of success rate. Because of the potential long-term side effects of PUVA and broadband UVB, narrowband UVB is becoming the first choice treatment for phototherapy. Narrowband UVB is considered the treatment of choice for patients with moderate to severe vitiligo or generalized vitiligo. It may be especially useful in treating children.

What are the side effects of UVB?

The skin may itch and become red due to exposure to UVB light. The long-term risks of UVB treatment are the same as the effects of chronic sun exposure: premature skin aging and skin cancer. The exact risk of developing skin cancers from long-term exposure to UVB is unknown.

What about the Excimer Laser? How is it different from UVB?

The excimer laser is a controlled beam of UVB light of 308 nm that can be focused directly on vitiligo-affected areas. Because only small areas of skin are treated, inflammation and melanocyte destruction are reduced. Excimer laser therapy requires fewer sessions, but is only practical for people with localized vitiligo.

When should the Excimer Laser be used?

The excimer laser is limited to use on small lesions spread across less than 20% of the body surface. It should not replace conventional phototherapy but rather should be considered as a complementary treatment option.

What are the side effects of the Excimer Laser?

Several prospective studies have shown that the excimer laser is quite effective and well tolerated in vitiligo. However, long-term follow-up is still lacking and optimal parameters for treatment have not been fully determined. The need for continued maintenance sessions is also still in question. Further prospective studies are necessary, including assessing the efficacy and safety of its use in combination therapies.

Are there any other systemic medications?

Methotrexate, azathyoprin, and cyclosporine are potent systemic medicines that have been prescribed in cases of severe vitiligo unresponsive to regular therapies. Because of the high risk, side-effects, difficulty of medical follow-up and cost, these drugs are rarely used to treat vitiligo.

What other appropriate therapies may be used for localized resistant vitiligo?

Surgical therapy is appropriate for localized vitiligo that is resistant to other medical intervention. This form of treatment is available only in specialized institutions and is useful for only a small group of vitiligo patients.

What surgical therapies are available?

There are several different surgical techniques. One method consists of transplanting skin from a pigmented area to a vitiligo lesion on the same patient. Both split-thickness skin or epidermal blister grafting have been associated with higher success rates than other transplant techniques. Transplantation using a suspension of skin cells may successfully repigment stable vitiligo. Also, high success rates can be achieved by transplantation of a cultured melanocyte suspension. Therapeutic wounding of lesions can stimulate melanocytes to migrate from pigmented hair follicles. Therapeutic wounding techniques include dermabrasion, laser ablation, cryosurgery (liquid nitrogen spraying), needling, and local application of phenol or trichloroacetic acid. Excision of depigmented areas and covering with a thin graft has also been described. Finally, introduction of artificial pigments, e.g. tattooing, gives excellent results in most patients with localized stable vitiligo.

Is it possible to manage vitiligo with "cosmetic camouflage"?

Disguising vitiligo with make-up, self tanning compounds or dyes is a safe, easy way to make vitiligo lesions less noticeable. Waterproof cosmetics that match almost all skin colors are available. None of these change the disease, but they can improve appearance and make the individual more comfortable.

What about depigmentation therapy?

For some patients with extensive involvement (vitiligo on more than 50% of the body surface, particularly on the face), the most practical treatment is to remove the remaining pigment from normal skin and make the whole body an even color. Depigmentation of normal skin should be used for

extensive vitiligo only. Topical agents for depigmentation include monobenzylether of hydroquinone 20% (Benoquin) and 4-methoxy-phenol. This therapy takes about a year to complete. Treatment is generally irreversible, however occasionally spots/areas of repigmentation may occur.

Are there any additional therapies?

Supportive psycho-social therapies are also important for patients with vitiligo. Patients find it very helpful to get counseling from a mental health professional who can talk about issues that are difficult to discuss with anyone else.

Where are we now and what's still needs to be done?

In the past two decades, research on vitiligo has increased greatly. A variety of technological advancements have permitted relatively rapid progress in knowledge and therapies. However, much more research is needed to improve our understanding of how to treat and prevent vitiligo. The National Vitiligo Foundation leads the way in enabling this research by funding investigators committed to curing this disease.