Therapeutic options for psoriasis: Review and update

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ABSTRACT

Psoriasis is a chronic skin condition that affects 2.6% of the population, or approximately 8 million people in the United States. Even though typical plaque-type psoriasis looks similar in different individuals, the way these individuals respond to various treatment modalities can be unpredictable. Moreover, even within the same person, it is not unusual for one lesion to respond to a treatment while another psoriatic plaque right next to it fails to respond. Therefore, it is important to have as many treatment options at one’s disposal as possible to best meet the needs of psoriasis patients. The treatment options available can be roughly divided into three groups, namely topical therapy, phototherapy and systemic medications. In addition, these treatment options can be used in various combinations to maximize the benefits and minimize the side effects. Also, for those who need long-term maintenance therapy, these treatment options can be rotated form one to another to minimize the risk of long-term, cumulative side effects from any one treatment option. The topical treatments which can actually reverse the basic pathology of psoriasis include topical steroids, coal tar, anthralin and calcipotriene/calcipotriol. Modes of phototherapy include ultraviolet light B phototherapy or PUVA phototherapy. PUVA phototherapy can be applied either systemically or topically. The systemic agents available to treat psoriasis in the United States include acitretin, cyclosporin, hydroxyurea, sulfasalazine, and 6-thioguanine. Among these, the first three agents are known to be the most effective systemic agents in use. Generally, topical treatment are tried first and phototherapy next. Systemic medication are often reserved as a last choice because of the increased risk of systemic side effects, both acute and long-term, cumulative. The new medications which have recently become available in the United States or which are expected to become available soon include Tazarotene gel, a topical modified vitamin A-type medication; Micronal, a less staining form of anthralin; Calcipotriene cream and scalp solution; Acitretin; and Neoral, a new formulation of cyclosporin with better and more reliable bioavailability. Lastly, despite the new medications which have become available over the years and the new research that is being conducted, the author’s experience has been that no treatment works faster with fewer side effects and higher probability of long-term remission than the traditional Goekkerman/Ingram regimen in which the patient is coated in black tar and anthralin all day, every day (Monday through Friday) for several weeks, in addition to receiving outpatient UVB phototherapy. Unfortunately, in the United States, due to “tightening health care resources,” this traditional Goekkerman therapy, which needs to be conducted in special centers, is slowly decreasing in availability. Therefore, in terms of actual patient care, it is not clear whether psoriasis therapy is going forward or backward in the United States.

Keywords: Psoriasis phototherapy.


Psoriasis affects at least 2.6% of the population in the United States, or roughly 8 million people. Even though different cases of plaque-type psoriasis clinically appear to be very similar, their responses to any given treatment modality vary tremendously. Therefore, it is important to move on to a more effective but possibly more involved or complicated treatment modality if simpler options are not effective, feasible or available. The various treatment modalities are generally classified into three categories: topical therapy, phototherapy, and systemic medications. If the use of any one of these as a monotherapy is not adequately effective or poses excessive concern for long-term, cumulative side effects, a combination or rotational therapy may be utilized to maximize the benefit and minimize the
side effects.

**Topical therapy.** There are four main topical therapies that are used to try to reverse the basic pathophysiology of psoriasis. They are topical steroids, tar, anthralin and calcipotriol (calcipotriene in the U.S.). Even though other topical agents such as moisturizers, salicylic acid, or lactic acid can be employed to facilitate other treatment modalities, these do not have the capacity to reverse the basic pathophysiology of psoriasis and they are therefore considered as adjunct topical therapeutics.

**Topical steroids.** Psoriasis tends not to respond as well to topical steroids as eczema does. Consequently, it is not unusual that topical steroids of superpotent strength need to be utilized for adequate improvement of indurated psoriatic lesions. Even though high-strength topical steroids work most rapidly to clear the symptoms and signs of psoriasis, they are not as ideal for long-term control of psoriasis due to the risks of side effects, such as skin atrophy, adrenal suppression, and the development of tachyphylaxis. Also, the long-term use of a topical steroid on the face may result in the development of glaucoma or cataracts. Therefore, topical steroids are most useful for “quick fixes,” but they have their drawbacks when used long-term.

**Coal tar.** Since Dr. Goeckerman developed the famous combination treatment with coal tar and UVB therapy, Goeckerman therapy has been employed throughout the United States for greater than half a century. The commercially available tars, which are more elegant, are usually not as effective as the original black tar used in Goeckerman therapy as conducted in the hospital or in psoriasis day treatment center. Consequently, outpatient tar is most useful when such treatment is combined with outpatient UVB phototherapy. By themselves, brown tar preparations tend to be of equivocal value in most patients.

**Anthralin.** Anthralin can be compounded up to 10% in strength. Except for the possibility of skin irritation, anthralin is very safe, but its major drawback is that it stains clothing, furniture and sinks, as well as patients' skin. For this reason, anthralin is not very popular in the United States.

**Calcipotriol (calcipotriene).** Calcipotriene ointment (Dovonex) is the first non-messy, non-smelly alternative to topical steroids which can be used long-term as a maintenance agent. For initial usage as an induction agent to clear psoriasis, calcipotriol may work faster than the high-strength topical steroid floucinonide ointment. However, this only happens if calcipotriol ointment is applied faithfully twice per day rather than once per day. Because of many patients' reluctance to use an ointment, in the morning, and because calcipotriol was demonstrated to be synergistic in its therapeutic efficacy when used along with superpotent topical steroid halobetasol, an alternative regimen which can give maximal speed of improvement involves the application of superpotent topical steroid once per day and calcipotriene ointment once per day. They are not applied at the same time due to the concern that calcipotriene ointment may be inactivated by other preparations. After several weeks, this regimen is switched over to pulse therapy, where calcipotriene ointment is used twice per day on weekdays and a superpotent topical steroid is only used twice per day on weekends. Eventually, once the psoriasis is almost invisible, the regimen is once again changed to using only calcipotriene ointment twice per day for long-term maintenance.

**Phototherapy UVB phototherapy.** The main types of phototherapy available to treat psoriasis are UVB and PUVA. UVB phototherapy is simpler to perform than PUVA phototherapy; long-term, it is also safer for the skin. However, UVB therapy is usually not as efficacious as PUVA therapy. To maximize its benefit, it is important to avoid under-treatment. If no improvement is seen, the intensity of UVB irradiation needs to be gradually increased up to the minimal erythema dose. Also, to optimize the therapeutic benefit of UVB phototherapy, more intense exposure may be needed for the lesions on the lower extremities. This is because the minimal erythema dose of the lower extremities tends to be much higher than that of the trunk for most patients. UVB phototherapy can be further optimized by the concurrent use of adjunct therapies such as coal tar, anthralin or low-dose etretinate or acitretin.

**PUVA phototherapy.** PUVA phototherapy can be conducted systemically or topically. Topical application of PUVA phototherapy avoids the side effects associated with systemic use such as nausea, dizziness or headaches. There are three types of topical PUVA, namely “paint,” soak,” and “bath” topical applied to the skin 30 minutes prior to the application of ultraviolet light A Topical “paint” PUVA therapy is most powerful, but also carries the greatest risk of inducing a burn on the patient. Therefore, the adjustment of UVA dosage is much more conservative than with other forms of PUVA therapy and patients need to be very closely monitored for both benefits and side effects. It is also critical to avoid extraneous sunlight exposure at all times while undergoing topical “paint” PUVA.

Topical "soak" PUVA therapy utilizes a psoralen concentration that is much more dilute. This form of treatment is convenient when treating patients with localized psoriasis where the lesions are too scattered to make individual “painting” of the lesions feasible.

In “bath” PUVA therapy, the patient immerses himself in a bathtub containing psoralen. This form of treatment is most appropriate for patients with generalized psoriasis.

**Systemic therapies.** The systemic agents used in
the United States include methotrexate, etretinate, cyclosporin, hydroxyurea, sulfasalazine, and 6-thioguanine. Systemic medications can be very effective and very convenient. However, they pose a greater risk of serious systemic side effects than topical therapies or phototherapy do. This statement applies both to the acute side effects and the possible cumulative side effects. The systemic agents that are more frequently used and thought to be more effective in the United States are methotrexate, etretinate, and cyclosporin. However, all of these agents have the possibility of cumulative, long-term side effects, even if the patient does not experience any acute side effects. For methotrexate, the cumulative side effects include liver toxicity. For etretinate, there are changes in the skeletal system. For cyclosporin, the long-term side effects are manifested by the gradual decrease in renal function. Acitretin is now available in the United States.

**Combination therapy.** In order to maximize the therapeutic benefit and minimize the side effects, many of the above agents are used in combination. In fact, for the treatment of psoriasis, combination therapy appears to be the rule rather than the exception for those with moderate to severe disease. Certain combinations are known to be synergistic. For example, calcipotriol ointment used once per day along with superpotent topical steroids appears to work better than either one. The combination of etretinate with UVB or PUVA phototherapy consistently outperform the use of etretinate in a higher dose as a monotherapy or the use of UVB or PUVA phototherapy alone. Care must be exercised in choosing the right combination and also the right method of executing the combination to avoid adverse effects. For example, if methotrexate and phototherapy are combined, it is important to instruct the patient not to receive phototherapy for at least 48 hours after taking methotrexate to avoid the possibility of methotrexate-induced photosensitivity resulting in a phototoxic reaction. Also, when low-dose etretinate is added to a patient who has been undergoing phototherapy where the irradiation with ultraviolet light is already maximized, it is also prudent to decrease the dose of UVB or UVA (for PUVA) to avoid so-called “delayed etretinate burn”, which may happen at the same dose of light that the patient has previously tolerated well. There are many many other combinations that are possible. As long as the combinations are used with care, the art of combination therapy in psoriasis can be of great help, especially in the management of recalcitrant cases.

**Rotational therapy.** Since psoriasis is a chronic disease that can last one’s lifetime and many of the major treatment modalities have their own special profiles of long-term, cumulative side effects, it is common practice in the United States to rotate patients from one treatment modality to another every one to two years, even if the former treatment modality has been working well. For example, even if methotrexate therapy is working beautifully for a particular patient with no apparent side effects, because of the possibility of increased risk of developing cirrhosis of the liver with cumulative, lifetime exposure to the medication, it may be advisable to switch to some other treatment modality after one to two years’ continuous use of methotrexate. The major choices for rotational therapy are UVB phototherapy with tar and/or anthralin, systemic or topical PUVA therapy, etretinate, methotrexate, cyclosporin and other systemic agents.

**Psoriasis day treatment program.** The psoriasis day treatment program is an intensive regimen designed to treat patients with severe, generalized and recalcitrant psoriasis with as little reliance on steroids or systemic medications as possible. The aim is to clear psoriasis with minimal risk of either acute or cumulative systemic side effects. More and more, these types of programs are conducted in specialized psoriasis day treatment facilities in the United states rather than in the hospital, due to the fact that hospitalization in the U.S. is very expensive. Traditionally, day treatment programs either conducted Goeckerman therapy, the combination of UVB phototherapy with coal tar, or Ingram therapy, the combination of UVB phototherapy and anthralin. However, due to increased pressure from managed care insurance to make even the most difficult to treat patients recover as quickly as possible, the tendency now is to abandon ideology and try to use both tar and anthralin together.

In these program, patients generally show up early in the morning and receive whole-body UVB phototherapy. This may be followed by applications of more intense UVB irradiation using specialized machines that give out much stronger UVB radiation than regular UVB boxes. Metal halide phototherapy units such as hot quartz lamps and Dermalight panels are designed to treat localized psoriatic plaques that are resistant to regular UVB box phototherapy. With these machines, very intense UVB radiation can be conveniently focused to localized, recalcitrant areas such as the shins. Following this customized exposure to ultraviolet light B, where different intensities of irradiation are given to different anatomical areas, the entire body is coated with crude coal tar (“black tar”) up to concentrations of 10% with 10% salicylic acid (or lactic acid) in petrolatum. This tar preparation is applied thickly and left on for the entire day. Sometime before or after the application of the black tar, compounded anthralin in concentrations up to 10%, which is also usually compounded with salicylic acid, is applied to the resistant area. If anthralin is well-tolerated, it can be left on for the entire day along with the coal tar. If
the anthralin is not as well tolerated, it is used as a short-contact therapy -- that is, the anthralin is left on the skin for 30 minutes to one hour. For all of the topical agents such as tar, anthralin, salicylic acid or lactic acid, a lower concentration is tried first before progressing to a higher concentration. In the late afternoon, both crude coal tar and anthralin are washed off and replaced with 20% LCD in Aquaphor ointment, a more elegant but less effective "brown tar" preparation (as opposed to the "black tar"). The patient is encouraged to reapply the brown tar at bedtime.

The daily treatment regimen as described so far is thought to be extremely safe; therefore, it is frequently the treatment of choice for children, pregnant women, or elderly patients with multiple other medical problems along with their severe, generalized psoriasis. For patients who have truly recalcitrant cases of psoriasis where a medical contraindication does not exist, the aforementioned regimen can be further intensified by the use of topical PUVA therapy at the end of the day, after the tar is washed off. It is critical that topical PUVA therapy be conducted after the UVB radiation and not before in order to avoid overdosing the patient on ultraviolet light A, since some UVB boxes, and practically all metal halide units, give out UVA as well as UVB. In some rare patients, a "smarting response" characterized by peculiar discomfort on the skin, which is not quite the same as a burn, may be experienced when Goeckerman/Ingram therapy and PUVA therapy are conducted simultaneously. If such a reaction occurs, the combination of Goeckerman/Ingram therapy with PUVA therapy may not be possible. Lastly, if the patient still remains recalcitrant and only partially improved, systemic agents such as low-dose etretinate can be introduced along with the rest of the therapy to maximize the therapeutic benefit.

There are special cases where this type of therapeutic regimen may have to be postponed. Until the intensity of the inflammation of psoriasis is brought under control. More specifically, erythrodermic patients may react badly to even a gentle phototherapy. Therefore, if the patient is erythrodermic or nearly erythrodermic, their skin is cooled with triamcinolone ointment, with or without the use of a space suit, before Goeckerman or Ingram therapy is initiated. If the patient presents with pustular psoriasis, Goeckerman therapy may be contraindicated since it may make pustulation worse. However, for regular generalized, plaque-type psoriasis, according to the author's experience, the combined Goeckerman/Ingram regimen seems to work faster than phototherapy or any topical or systemic therapy available. The basic day treatment regimen is also safer than any systemic treatment known. Lastly, if patients are able to continue with this type of regimen until the psoriasis completely clears, it is not unusual to find that they go into long-term remissions of one year or longer. This is in contrast to many other treatment modalities such as the use of methotrexate, cyclosporin, etc., where recurrence can be expected relatively quickly if the treatment modality is discontinued. It should be noted that this type of result is only possible if Goeckerman/Ingram regimen is conducted appropriately -- which means that these topical agents need to be applied thickly and left on all day, every day. Due to the unsightly appearance of properly conducted day treatment regimen, nurses and other staff need to be properly educated so that they do not unknowingly sabotage the treatment by changing the pajamas too often just because the patient looks "dirty."

New medications for psoriasis in the United States. There are 5 new medications which have just recently become available in the United States or are expected to become available within the next year. These are tazarotene gel, micanol cream, Devonex cream and scalp solution, acitretin, and neoral.

Tazarotene gel is a modified vitamin A molecule that is being developed by Allergan Pharmaceuticals. In several multi-center, double-blind trials, tazarotene was found to be safe and effective for the treatment of psoriasis. Because it is a modified vitamin A molecule and not a topical steroid, tazarotene is expected to be free of topical steroid side effects. However, just like any other retinoids, tazarotene probably has the potential for irritating the skin with much more frequency than topical steroids, calcipotriene, tar or anthralin at commercially available strengths. On the other hand, just like other retinoids such as etretinate, the author's experience has been that tazarotene has been especially effective in reducing the induration of very thick, scaly plaques of psoriasis on more resistant areas such as the elbows, knees, and shins. It also works well with once-per-day application. Tazarotene gel greatly enhance UVB phototherapy but, whether it enhance PUVA phototherapy remains to be proven.

Micanol is a new formulation of anthralin that is coated with a special lipid to reduce its staining quality. This lipid coating breaks down only when in contact with body temperature. Therefore, if Micanol is inadvertently applied to the clothing, sinks or furniture, the risk of staining is greatly reduced. In clinical testing, Micanol appeared to be just as effective as regular anthralin with a greatly reduced frequency of staining episodes. Calcipotriene cream and scalp solution are expected to become available in the United States soon. Calcipotriene cream is not as effective as the ointment, but it is more elegant. Therefore, the optimal usage probably involves morning application of the cream and night time application of the
Therapeutic options for psoriasis ... Koo

ointment.

Acitretin is an acid metabolite of etretinate which is eliminated from the body much more quickly than etretinate. This medication is available in practically all developed countries except the United States. The long-awaited introduction of acitretin may make it possible for women of reproductive age to be treated with a systemic retinoid, which is more specific for psoriasis than acitretinoin (Accutane). In low doses, acitretin is known to enhance the therapeutic effects of both UVB and PUVA phototherapy, just like etretinate.

Neoral is a new formulation of cyclosporin. The old formulation of cyclosporin is called Sandimmune in the U.S. Even though cyclosporin is known to be very effective in the treatment of psoriasis, Sandimmune, the old formulation, is known to have a certain unpredictability in its bioavailability. This is because the absorption of Sandimmune is dependent upon the medication being "digested" in the small intestine by mixing with bile, pancreatic juice, lipids in the lumen, etc. before the medication can be efficiently absorbed. Neoral is "pre-digested." Therefore, the absorption of Neoral is not dependent upon the availability of bile, pancreatic enzymes or a particular food content in the lumen of the small intestine. Consequently, Neoral is much more dependably absorbed, both because there is less chance of having a patient being a "poor absorber" and because there is significantly less variability in absorption for any particular individual as measured over time. Consequently, in a head to head comparison between Neoral and Sandimmune in the treatment of psoriasis which was conducted both in Europe and the United States, as a group patients who were treated with Neoral were shown to respond faster and at a lower average dosage than patients who were treated with Sandimmune. There were no significant increases in side effects among patients who were treated with Neoral as compared to those who were treated with Sandimmune.

Conclusion. Because it is nearly impossible to predict which treatment modality a particular patient with recalcitrant psoriasis responds to, it is important to keep an open mind and have as many treatment options available as possible. If a treatment option is not adequately effective or is not tolerated as a monotherapy, the possibility of a combination therapy should be pursued for more efficacy and fewer side effects. Even if a particular treatment modality turns out to work well, it is important to consider rotating to another treatment modality in one to two years to minimize the risk of long-term, cumulative side effects. Even though there is a good deal of new research being conducted to find new systemic agents for psoriasis, most of which are immunologically based in a proposed mechanism of action, the author has yet to find a treatment modality that works faster, more safely, or with better probability for long-term remission than the traditional, properly-conducted Goeckerman/Ingram therapy.

References