conservatively specified that continuous use of this agent should not exceed one year; although international guidelines allow continuous use for up to two years. After one year of therapy, dermatologists are expected to take patients off cyclosporine for at least several months before starting another one-year course. If necessary, cyclosporine may be used "off-label" for more than one year continuously at a lower dose by combining it with another systemic agent, like acitretin, thus maximizing safety.

Many dermatologists in the United States, however have not yet gained enough experience with this agent to feel comfortable using cyclosporine for even one year. Therefore, using this agent in sequential therapy, as described below, may minimize the length of time cyclosporine must be used while still reaping the benefit of this agent. Cyclosporine may also be used in rotational therapy to minimize the risk of nephrotoxicity or hypertension in patients. A simple rotational scheme would be to alternate between cyclosporine and methotrexate, using both at their highest dermatologic dosages for months at a time. Because both of these agents have short half-lives, patients may be abruptly switched from cyclosporine to methotrexate after a one-week "wash-out" period. This transition may be made with little concern for a rapid psoriasis flare since abrupt discontinuation of either cyclosporine or methotrexate generally does not result in a severe psoriasis flare within one week.

Sequential Therapy

Because a wide variety of agents are available for the treatment of psoriasis today, a new therapeutic paradigm has been introduced recently to take advantage of the different strengths of these agents, while at the same time minimizing their side effects.[25,26] Sequential therapy entails using different therapeutic agents in a deliberate sequence to maximize the speed of improvement initially and to minimize toxicity in the long run. This paradigm is comprised of three steps. Step 1 is the clearing phase. Step 2 is the transition phase. And Step 3 is the maintenance phase. The clearing phase usually requires relatively potent and faster-acting agents to calm a flare of psoriasis. Because the agents used for the clearing phase are not necessarily the most ideal for long-term control of psoriasis, a switch to agents more suited for maintenance therapy should be made. Rather than making this change abruptly from the clearing phase (Step 1) to the maintenance phase (Step 3), the transition phase (Step 2) is recommended to minimize the risk of psoriasis recurrence while introducing the maintenance agents.

With the myriad of agents available for treating psoriasis, there are innumerable possible sequential therapies available. Examples of both a topical sequential therapy and a systemic sequential therapy follow.

Topical sequential therapy

The most commonly practiced topical sequential therapy for psoriasis consists of using halobetasol propionate and calcipotriol as follows. The clearing phase (Step 1) entails using calcipotriol ointment once per day in the morning with halobetasol propionate ointment once per day in the evening for approximately one month. The transition phase (Step 2) is then begun: calcipotriol is applied twice per day only on weekdays and halobetasol is applied twice per day only on weekends. After a month in the transition phase, calcipotriol, a safer long-term maintainence agent, is continued at twice-per-day application daily in the maintenance phase (Step 3) and halobetasol is discontinued. Eventually, as the psoriatic lesions resolve, the use of calcipotriol may be tapered from twice-per-day to once-per-day application and then may be discontinued when the lesions are no longer visible.

The topical sequential therapy described above is the only sequential scheme thus far where each step is validated by a randomized clinical trial. The regimen for the clearing phase has been documented by a randomized, double-blind, multi-centered trial to be the most rapid and effective topical regimen for treating psoriasis.[4] The transition phase is supported by a subsequent double-blind, randomized study conducted by Lebwohl *et al.*[27] Patients using calcipotriol ointment twice per day on weekdays and halobetasol propionate ointment twice per day on weekends, known as "pulse therapy," stayed in remission at nearly twice the rate of patients using the vehicle of the calcipotriol ointment twice per day on weekdays (i.e. no calcipotriol on the weekdays) and halobetasol propionate ointment twice per day on weekends. Besides improved remission rates, the use of the transition phase (Step 2) is valuable in minimizing the recurrence of psoriasis and also steroid rebound effects. Pulse therapy is, in essence, a steroid taper when used as Step 2 in sequential therapy.

Recently, a study found that calcipotriol and halobetasol propionate ointments are compatible and do not inactivate each other for up to fifty hours.[28] Given this fact and the fact that both calcipotriol and halobetasol propionate are more efficacious when used twice-per-day rather than once-per-day, a theoretically opitmal regimen for Step 1 would consist of using both calcipotriol and halobetasol propionate twice per day. Practically, one would mix equal amounts of each agent in the palm of the hand just prior to application. To maximize compliance, the cream formulations of both agents, which are currently available, may be prescribed for morning application; and the ointment formulations