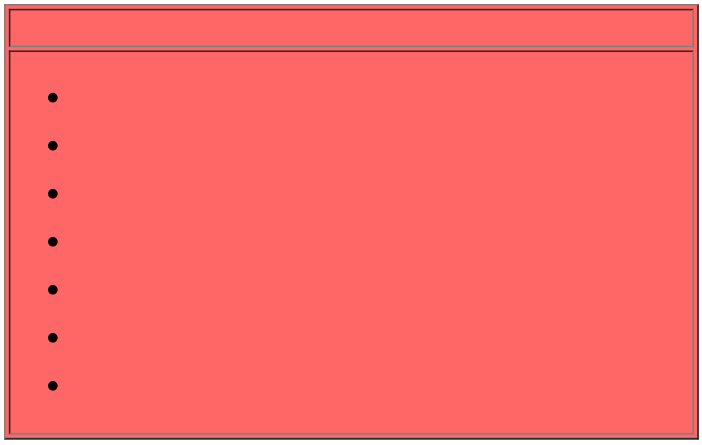

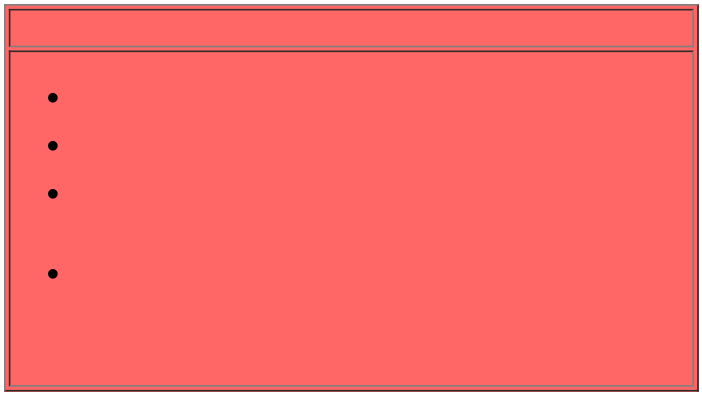

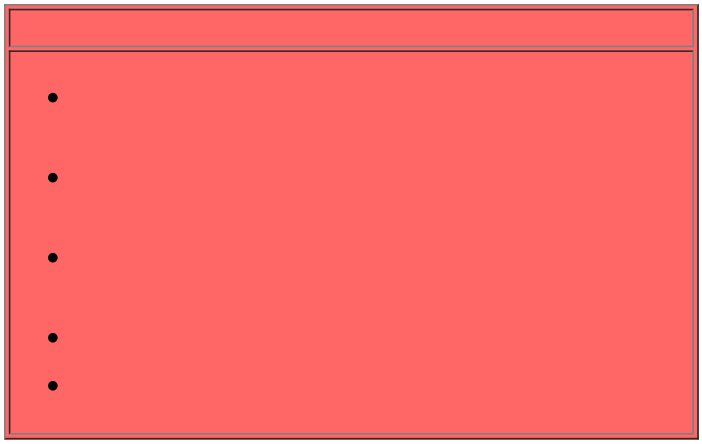

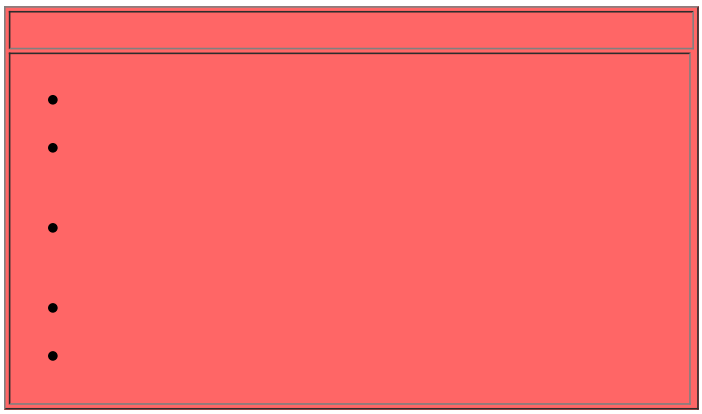

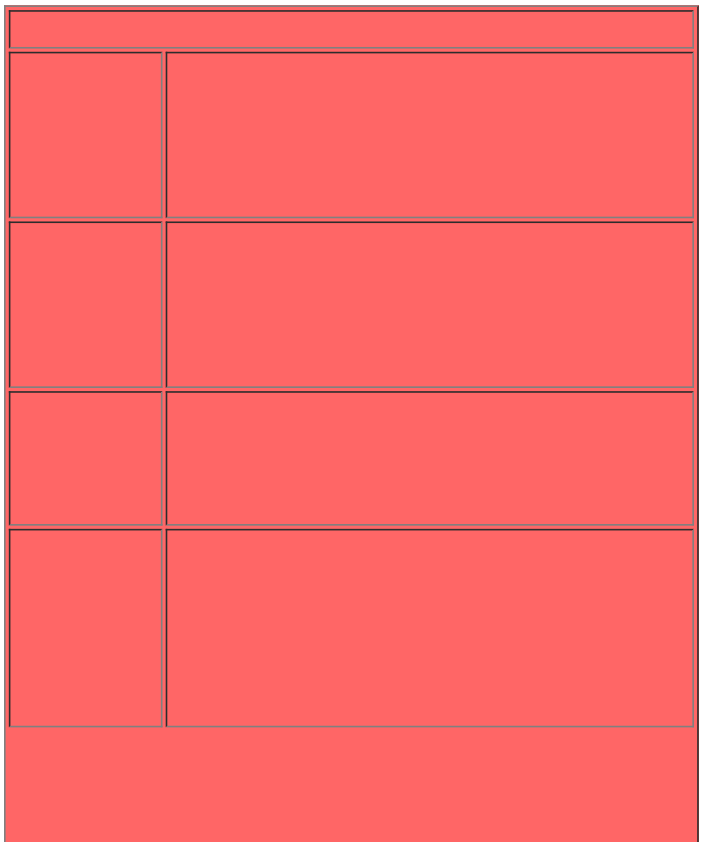

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Table 8: Methotrexate

- Effective, but potential for life-threatening side effects
- Use of the NPF brochure on methotrexate helps educate patients about potential risks and can help physicians easily document that they have provided information on the risks of treatment
- Start with 5 mg test dose, increase in 5 mg/wk intervals until clinical response or maximal dose of 20-25 mg/week is achieved (reduce the initial and incremental doses to 2.5 mg in the elderly or others with suspected renal impairment
- Check complete blood count and liver function tests one week after initial dose and after each increase in dose
- Trimethoprim-sulfmethaxazole also affects folic acid and should not be taken during methotrexate therapy. Non-steroidal anti-inflammatories can reduce renal function; increased monitoring for methotrexate toxicity is indicated when these agents are started during methotrexate therapy
- Be prepared to use folinic acid (not folic acid!) if needed to treat acute toxicity
- To reduce nausea, a divided dose may be taken one day a week. Folic acid (1-5 mg/day) may also be helpful.
- The cost of oral therapy may be reduced by use of the intravenous solution in place of the pill formulation

Laboratory studies should be repeated one week after every increase in dose of the medication. After a stable dose is reached, the frequency of the laboratory testing may be reduced. There are published recommendations for continued repeat blood tests every 4 to 6 weeks, although such frequent testing is probably not necessary in patients on stable doses of methotrexate. A number of factors may increase methotrexate blood levels including concomitant administration of another inhibitor of folate metabolism (the commonly used antibiotic trimethoprim-sulfamethoxazole [Septra, Bactrim] and reduction of renal clearance (which may occur with nonsteroidal anti-inflammatories).[43] It is essential that patients be aware of these potential interactions; however it is not clear that the frequency of laboratory testing alone will prevent these events. Folinic acid (Leucovorin) may be given if acute hematologic toxicity occurs; it should be instituted as early as possible. Folic acid is not a replacement for folinic acid in this situation.

In a review of the literature most physicians did not document the history/physical exam findings on which they based giving methotrexate, nor did they carefully document informing their patients of the risks of this treatment.[44] Very helpful in this regard is the NPF brochure on methotrexate. Written in language for the lay person and reviewed by dermatologists, the brochure provides patients the necessary information on the risks of treatment. It is good medicine both to provide this information and to document that it was provided.

Liver biopsies are done to monitor for chronic hepatotoxicity that may not be revealed by blood tests. Pretreatment liver biopsy is probably unnecessary in patients without a history suggestive of preexisting hepatotoxicity.[42] If a baseline liver biopsy is to be done, it may be best to wait until it is clear that the patient will tolerate the drug (some do not due to severe nausea), that the drug is effective in controlling the patient's psoriasis (sometimes it is not), and that the drug will be needed long-term. Repeat liver biopsies may be done after approximately every 1.5 g cumulative dose. There is question whether liver biopsy needs to be done at all.[45] If in doubt, it may be wise to defer the decision to a gastroenterologist who specializes in liver disease and liver biopsy. There are certainly some scenarios in which the risk of liver biopsy is greater than the risk of chronic methotrexate hepatotoxicity. Intolerance to methotrexate due to nausea can be extremely severe and sometimes may be managed by switching to intramuscular methotrexate or by administration of folic acid 1-5 mg/day.[46]

The cost of methotrexate therapy may be reduced by switching from pills to oral administration of the intravenous solution in appropriate patients. The cost is approximately $100/100 mg of methotrexate pills versus $15/100 mg for the solution (50 mg methotrexate in 2cc vial). Accurate dosing is essential. Patients should consider purchasing insulin syringes when purchasing methotrexate and returning to the office for instructions on how much should be drawn up. The methotrexate solution can be put into a glass of water or flavored beverage and consumed.

Cyclosporine

Short-term use of methotrexate may be effective for some patients who have acute exacerbation of otherwise stable psoriasis

[47,48,49] Short-term use of cyclosporine allows very rapid control of psoriasis and is safer (though more expensive) than two tapers of oral corticosteroids. Administration of cyclosporine for as little as 5 days has been reported effective for the treatment of guttate psoriasis. Thus, cyclosporine may be best used in acute situations, followed by a switch to safer long-term treatments. Such an approach might include the initial use of cyclosporine to achieve rapid control followed by a transition to either acitretin or UVB phototherapy to maintain control.

Table 9: Cyclosporine
• Very useful for rapid, short-term control of psoriasis followed by transition to another treatment • Blood pressure and creatinine measurements should be assessed twice before initiating treatment to establish accurate baseline values • Elevation of blood pressure during cyclosporine therapy may be treated with antihypertensive medications • Reduction in cyclosporine dose is recommended if blood creatinine increases by 30% • Numerous potential drug interactions

Although cyclosporine is quite safe and effective in short-term use, it is associated with long-term toxicity including hypertension and decreased renal function [50,51] The prescribing dermatologist should be familiar with the 1998 consensus conference recommendations for monitoring cyclosporine therapy and delineates the numerous potential drug interactions [52] Among other interactions, increased renal toxicity may occur with nonsteroidal anti-inflamatories; increased cyclosporine levels may be seen with ketoconazole, cimetidine and macrolide antibiotics; and rhabdomyolysis may occur with HMG CoA reductase inhibitors.

Of all the oral agents for severe psoriasis, cyclosporine may be the safest for women who may become pregnant. Surprisingly, the FDA lists cyclosporine as a pregnancy category B drug.

Other Treatments
Other immune inhibitors modulators such as hydroxyurea may be used. The advantage of hydroxyurea is that it may be used in place of methotrexate in patients with cirrhosis. Monitoring for bone marrow toxicity is necessary.

Mycophenolate mofetil (CellCept) may be a helpful adjunctive immune modulator in psoriasis. The initial dose is 1 g by mouth twice daily. Doses of up to 3 to 4 g/day may be needed. Neutrophil counts should be followed closely, as severe neutropenia may occur in 2% of patients.

Summary

Psoriasis is a multifaceted disease and its treatment generally requires the expertise of dermatologists. The National Psoriasis Foundation is a tremendous resource for patient education and advocacy in psoriasis care. To plan for acute and long-term control of localized psoriasis, combinations of topical corticosteroids and either calcipotriene or tazarotene are the most effective approaches. For generalized disease, UVB treatment provides the safest means of achieving long-term control of disease. Acitretin is a very helpful adjunct for improving the efficacy of phototherapy. For patients with severe, refractory disease, methotrexate may be most effective, while cyclosporine may be most valuable for patients needing rapid, short-term improvement.

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