Series Editor: Camila K. Janniger, MD

# Update on Pediatric Psoriasis, Part 2: Therapeutic Management

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*Pediatric psoriasis is an autoimmune diathesis with a complex immunologic basis. It is associated with extensive psychological morbidity and should be treated rapidly and effectively to limit psychologic effects on children. The most common trigger in childhood is upper respiratory tract infection. Once disease has occurred, treatment is based on severity and presence of joint involvement. Topical therapies include corticosteroids and calcipotriene. UV light, systemic retinoids, and cyclosporine remit cutaneous psoriatic lesions. Methotrexate sodium and etanercept benefit both skin and joint manifestations of psoriasis. Concern for psychological symptoms and psychological growth is needed in treating pediatric patients with psoriasis vulgaris.*

*Cutis.* 2010;86:172-176.

Psoriasis vulgaris of childhood is a complex immunologic disease.[1] Many new therapies have become available for the treatment of pediatric psoriasis in the last 10 years.[1,2] Topical therapy remains the first-line treatment of skin-limited disease in children. These agents can be used with a host of oral antibiotics, when indicated.[2] In more severe cases and for chronic illness, systemic therapy and phototherapy are added to help induce improvement and ideally remission. Regardless of the extent of body surface involvement, psoriasis can have negative psychologic and quality-of-life (QOL) effects. Systemic therapies or phototherapy should be considered if lesions are refractory to topical therapies, if the disease involves a substantial body surface area (BSA), or if the patient shows evidence of psoriatic arthritis or reduced QOL.[3] A treatment algorithm for pediatric psoriasis is shown in the Figure.

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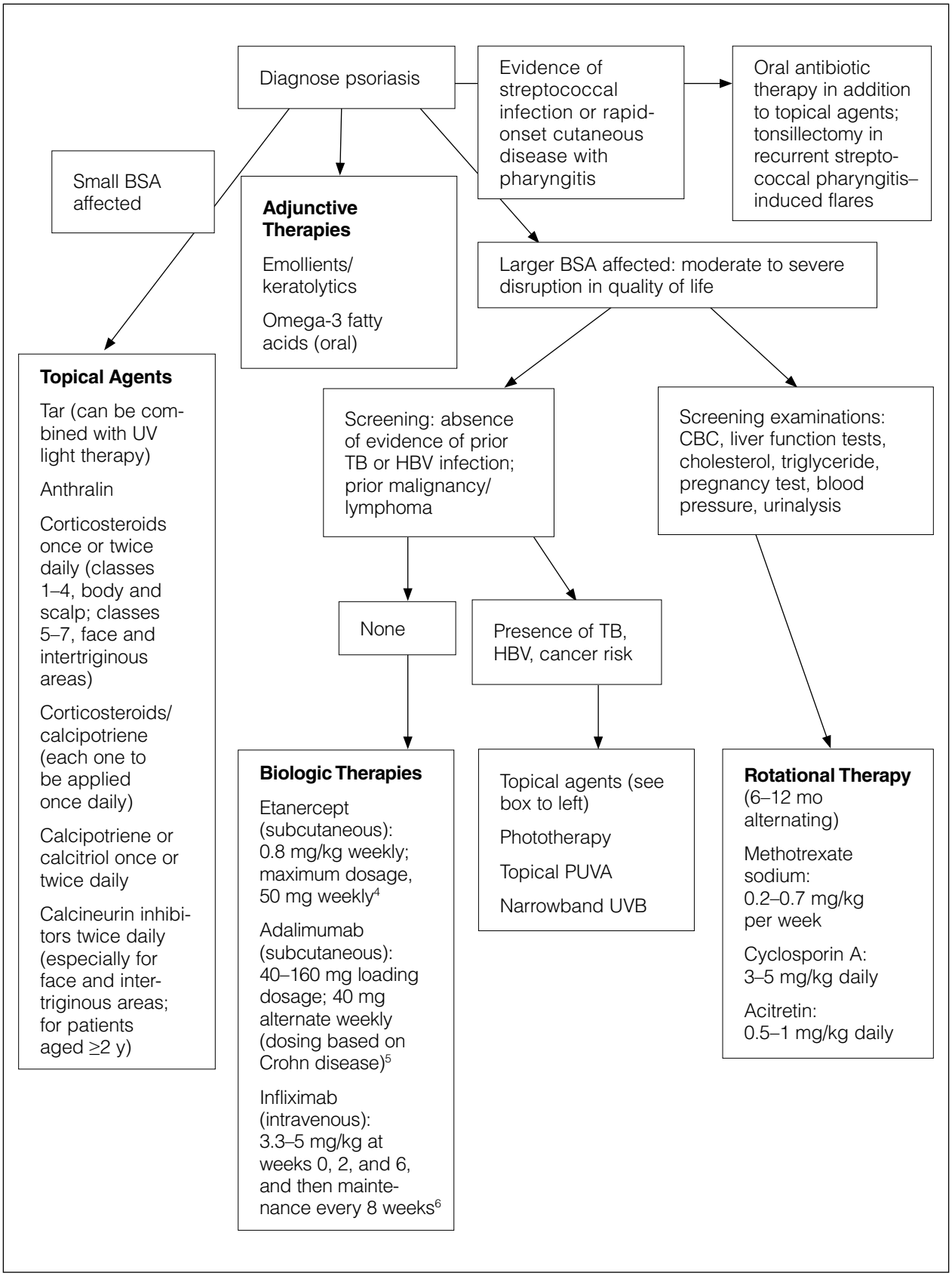
## Topical Therapy

Topical therapy for pediatric psoriasis starts with exfoliants including urea, salicylic acid, and α-hydroxy acids, all of which remove superficial hyperkeratosis, allowing secondary penetration of medications. Coal tar is beneficial, especially when combined with UV light in the Goeckerman treatment. Caution in usage is advised due to reported genomic alterations, including chromosomal aberrations in peripheral blood lymphocytes.[7] There are no topical therapies that are specifically approved by the US Food and Drug Administration (FDA) for the treatment of psoriasis in young children; however, the English-language literature includes many reports of successful improvement in pediatric psoriasis with off-label usage of topical agents.[2,8-12] Formulations and strengths should be determined based on patient age, psoriasis global severity scores such as the psoriasis area and severity index (PASI), and impairment of QOL.

Anthralin cream 1%, or dithranol, can be used for localized areas of psoriasis. Side effects include staining of hair and clothing as well as irritation. A head-to-head study of dithranol and calcipotriol applied topically showed that these agents may have similar efficacy.[8,9] Choice of topical corticosteroids for pediatric psoriasis is similar to therapy for lichenified atopic dermatitis. The head, neck, and intertriginous areas are treated with weaker agents (classes 5–7), while the scalp and extremities generally are treated with mid-potency topical corticosteroids (classes 2–4).[13] Class 1 corticosteroid agents work rapidly in flattening psoriatic lesions but are likely to cause atrophy of the skin, striae, and hypothalamic-pituitary-adrenal




Treatment algorithm for pediatric psoriasis. BSA indicates body surface area; TB, tuberculosis; HBV, hepatitis B virus; CBC, complete blood cell count; PUVA, psoralen plus UVA.

axis suppression with extended usage. One class 1 agent, clobetasol propionate emulsion aerosol foam 0.05%, has been approved for steroid-responsive diseases in children 12 years and older for up to 2 weeks.[10] Halobetasol also has been tested in pediatric psoriasis (it is not approved in children).[14] These agents are reserved for short therapy (<2 weeks) of thick stubborn lesions. Clobetasol and halobetasol can be quite effective for usage in psoriatic lesions in adolescents but run a risk for atrophy due to class 1 corticosteroid status.[8,10,14] All topical corticosteroids, including products from classes 2 to 7, run a risk for local atrophy and systemic absorption; systemic absorption is more likely when used on larger BSAs. Vitamin D analogues, calcipotriene[11] and calcitriol,[9] can thin and clear psoriatic lesions in children. These agents may cause cutaneous erythema or local irritation. Systemic absorption is thought to potentially cause symptoms of hypervitaminosis D, including alterations in calcium levels; however, the risk is small for limited BSA application. Topical calcineurin inhibitors (ie, tacrolimus ointment 0.03%,[15] pimecrolimus cream 1%[16]) applied twice daily also can be beneficial for pediatric psoriasis. As these agents do not carry a risk for atrophy, they can be applied to areas of skin at high risk for atrophy, including the face, neck, axillae, groin, and inner thighs. Usage is off label for pediatric psoriasis. Treatment of atopic dermatitis with calcineurin inhibitors is not recommended by the FDA for children younger than 2 years. Topical calcineurin inhibitors bear a black-box warning regarding theoretical skin cancer and lymphoma risks, and combination with UV light is routinely avoided.

## Phototherapy

Phototherapy is a safe and effective treatment option for children old enough to stand still in a phototherapy booth, particularly in teenagers with extensive disease. A variety of forms of phototherapy can be used to treat pediatric psoriasis, including narrowband UVB, psoralen plus UVA, and broadband UVB. Delivery systems include hand/foot units, generalized phototherapy booths, and excimer laser systems. Topical psoralens are preferable to oral psoralens because of the difficulty wearing protective eyewear for 24 hours after oral psoralens. Psoralen plus UVA has been associated with long-term carcinogenicity in adult patients with psoriasis; therefore, narrowband UVB is likely safer in children.[17-19] Treatment is performed twice weekly accompanied by protective eyewear and generally requires a few months for clearance and maintenance therapy to prevent future flare-ups. Ocular screening and periodic reevaluation are required for oral psoralen plus UVA therapy.

## Systemic Agents

Indications for systemic agent usage in pediatric psoriasis include severe psoriasis (ie, extensive BSA, intractable symptoms), disabling psychological ramifications, and psoriatic arthritis. All systemic agents available for pediatric psoriasis have side effects. Consequently, cyclic usage of 6-month courses of agents is advisable. Longer usage periods have been observed to be safe in rheumatoid arthritis patients using etanercept; however, usage beyond 1 year has not been well-assessed in patients with pediatric psoriasis. Of the systemic therapies, oral antibiotics have the best safety profile in early disease due to their superior side-effect profile.[2,20-22]

*Oral Antibiotics*—Oral antibiotics have been described to be useful in pediatric psoriasis.[20-22] Benefits are best noted in the setting of rapid-onset cutaneous disease associated with positive oral pharyngeal cultures, presence of perianal streptococcal disease, pustular psoriasis,[20] or in psoriasis guttata of childhood. Usage of oral antibiotics has demonstrated mixed results.[22] The best reported results with oral antibiotic usage were noted in adult patients placed on cyclic usage of azithromycin 500 mg for 4 days out of every 2 weeks for 48 weeks.[23] Tonsillectomy may be performed in the setting of recurrent streptococcal pharyngitis–induced psoriatic flares.[21]

*Methotrexate Sodium*—Systemic therapies are most effective in improving QOL for children with chronic and severe psoriasis. Methotrexate sodium is the original therapy available for extensive psoriasis. Collin et al[24] and Kaur et al[25] have reviewed case series of children treated with methotrexate sodium for psoriasis. The treatment regimens described are methotrexate sodium dosed at 0.2 to 0.7 mg/kg per week, with frequent achievement of PASI 75 (>75% improvement). Although monitoring complete blood cell counts and liver function tests are required, liver function alteration rarely is observed.[24-26] Risk factors include obesity and fatty liver changes. Unlike cyclosporine, methotrexate sodium can clear psoriatic arthritis as well as skin disease.[26] Therapy is started with a small dosage followed by escalating dosages while sequentially monitoring laboratory test results.[24] Folic acid supplementation protects against pancytopenia, microcytic anemia, and liver enzyme alterations.[27]

*Cyclosporin A*—Cyclosporin A is a systemic immunosuppressant originally developed to prevent allograft rejection. In dosages of 3 to 5 mg/kg daily, cyclosporine has been shown to reduce skin-limited pediatric psoriasis. Side effects include altered renal function including high blood pressure and increased serum urea nitrogen and creatinine levels. Close monitoring including serum urea nitrogen and creatinine levels as well as blood pressure is required. Although there have been reported risks for malignancy and lymphoproliferative

diseases due to immunosuppression, short courses and dosages that are lower than those used in transplant recipients minimize this risk.[26,28]

*Retinoids*—Oral acitretin 0.5 to 1 mg/kg daily has been used for disorders of cornification and psoriasis. Oral contraceptives for a month before initiation of therapy, during therapy, and for 3 years after therapy are required. Short-term side effects require monitoring for elevations of liver enzymes and lipids or alterations in complete blood cell counts. Cyclic brief (6–12 months) usage limits risk for bony abnormalities.[26] Oral retinoid usage for prolonged periods (at least 2.5 years), particularly at high dosages for weight, reportedly has been associated with premature epiphyseal closure. Other bony defects that can be induced by retinoids include osteoporosis and hyperostosis. Consequently, short courses (6–12 months) are advisable. More prolonged courses require periodic skeletal surveys.[29]

## Biologic Therapies

The injectable drugs etanercept (subcutaneous), adalimumab (subcutaneous), and infliximab (intravenous) can be used in pediatric psoriasis but are not FDA approved for this indication. Tumor necrosis factor α–inhibitor therapies have been used for more than a decade for pediatric autoimmune diseases including rheumatoid arthritis,[30] tumor necrosis factor receptor 1–associated periodic syndrome without fever,[31] juvenile idiopathic arthritis,[32] and Crohn disease.[5] Juvenile rheumatoid arthritis patients have the longest usage history with tumor necrosis factor α inhibitors, with up to 8 years of published safety and efficacy data. In a small case series, long-term usage did not seem to increase side effects for children with rheumatoid arthritis.[33] An American College of Rheumatology pediatric score reduction of 70% was achieved by all 11 children treated for 8 years and 61% (28/46) of all children treated long term, with no reported cases of tuberculosis, opportunistic infections, malignancies, lymphomas, lupus, demyelinating disorders, or death.[30] Long-term improvements on bony disease in arthritis of childhood have been demonstrated with etanercept.[33]

Anecdotal data have described efficacy of etanercept for pediatric psoriasis.[34] Paller et al[4] described the results of a phase 2 clinical trial of etanercept in 211 pediatric psoriasis patients aged 4 to 17 years. The study consisted of a 12-week double-blind treatment phase with a 24-week open-label phase. The 12-week data demonstrated a statistically higher PASI 75 and PASI 90 (75% and 90% clearance, respectively) for etanercept-treated children versus placebo. Psoriasis area and severity index 75 was noted in 57% of etanercept-treated pediatric psoriasis patients versus 11% of placebo-treated participants ($P<.001$) but was lost in 26 of 69 children assigned to placebo on weeks 36 to 48. Four serious adverse events including 3 serious infections (gastroenteritis requiring hospitalization and basilar pneumonia) and an ovarian cyst occurred in participants treated with open-label etanercept; all resolved without sequelae. No deaths, episodes of demyelination, reactivation of hepatitis or tuberculosis, or malignancies occurred. Three patients had transient elevations of hemoglobin levels.[4] Two reports of infliximab clearing pediatric psoriasis have appeared in the literature; treatment with oral methotrexate sodium and mycophenolate mofetil had failed in one case and treatment with etanercept failed in another case.[6]

## Natural Supplements

Guardians of children with psoriasis often ask the question "What dietary changes or natural supplements can I give my child to improve his/her skin disease?"[2] Although natural supplements or dietary alterations are not curative of psoriasis, disease severity may be reduced with usage of supplements. Fish oil, which contains omega-3 fatty acids, and omega-3 fatty acid supplements often are taken for psoriasis. Inuit populations that eat a diet rich in omega-3 fatty acids/fatty fish have a lower incidence of psoriasis, supporting usage in patients with psoriasis. Both oral and intravenous supplementation have been described for omega-3 fatty acids and the less effective omega-6 fatty acids.[35] These agents may work through alterations in production of arachidonic and docosapentaenoic acids.[36] Eating 4 to 6 meals of fish per week can mimic supplementation in reduction of psoriasis.[37] One anecdotal report has been published demonstrating that indigo naturalis, a traditional Chinese medicine, helps to clear pediatric psoriasis with 8 weeks' usage.[38]

## Conclusion

Recent advances in therapeutics for psoriasis have been applied to the pediatric psoriasis population with good results in disease reduction and consequent improvements in QOL. Further data on long-term usage of systemic agents and biologic therapies in children with psoriasis remain to be published.

## REFERENCES


1. Silverberg NB. Update on pediatric psoriasis, part 1: clinical features and demographics. *Cutis*. 2010;86:118-124.
2. Silverberg NB. Pediatric psoriasis: an update. *Ther Clin Risk Manag*. 2009;5:849-856.
3. Beattie PE, Lewis-Jones MS. A comparative study of impairment of quality of life in children with skin disease and children with other chronic childhood diseases. *Br J Dermatol*. 2006;155:145-151.
4. Paller AS, Siegfried EC, Langley RG, et al; Etanercept Pediatric Psoriasis Study Group. Etanercept treatment for

children and adolescents with plaque psoriasis. *N Engl J Med*. 2008;358:241-251.
5. Colombel JF, Sandborn WJ, Rutgeerts P, et al. Comparison of two adalimumab treatment schedule strategies for moderate-to-severe Crohn's disease: results from the CHARM trial [published online ahead of print April 7, 2009]. *Am J Gastroenterol*. 2009;104:1170-1179.
6. Menter MA, Cush JM. Successful treatment of pediatric psoriasis with infliximab. *Pediatr Dermatol*. 2004;21:87-88.
7. Borska L, Andrys C, Krejsek J, et al. Genotoxic hazard and cellular stress in pediatric patients treated for psoriasis with the Goeckerman regimen. *Pediatr Dermatol*. 2009;26:23-27.
8. Farber EM, Nall L. Childhood psoriasis. *Cutis*. 1999;64: 309-314.
9. van de Kerkhof PC, van der Valk PG, Swinkels OQ, et al. A comparison of twice-daily calcipotriol ointment with once-daily short-contact dithranol cream therapy: a randomized controlled trial of supervised treatment of psoriasis vulgaris in a day-care setting. *Br J Dermatol*. 2006;155:800-807.
10. Kimball AB, Gold MH, Zib B, et al. Clobetasol propionate emulsion formulation foam phase III clinical study group. clobetasol propionate emulsion formulation foam 0.05%: review of phase II open-label and phase III randomized controlled trials in steroid-responsive dermatoses in adults and adolescents. *J Am Acad Dermatol*. 2008;59:448-454, 454e1.
11. Oranje AP, Marcoux D, Svensson A, et al. Topical calcipotriol in childhood psoriasis. *J Am Acad Dermatol*. 1997;36(2, pt 1):203-208.
12. Liao YH, Chiu HC, Tseng YS, et al. Comparison of cutaneous tolerance and efficacy of calcitriol 3 microg g(-1) ointment and tacrolimus 0.3 mg g(-1) ointment in chronic plaque psoriasis involving facial or genitofemoral areas: a double-blind, randomized controlled trial. *Br J Dermatol*. 2007;157:1005-1012.
13. Kiken DA, Silverberg NB. Atopic dermatitis in children, part 2: treatment options. *Cutis*. 2006;78:401-406.
14. Herz G, Blum G, Yawalkar S. Halobetasol propionate cream by day and halobetasol propionate ointment at night for the treatment of pediatric patients with chronic, localized plaque psoriasis and atopic dermatitis. *J Am Acad Dermatol*. 1991;25(6, pt 2):1166-1169.
15. Brune A, Miller DW, Lin P, et al. Tacrolimus ointment is effective for psoriasis on the face and intertriginous areas in pediatric patients. *Pediatr Dermatol*. 2007;24:76-80.
16. Hebert AA, Warken KA, Cherill R. Pimecrolimus cream 1%: a new development in nonsteroid topical treatment of inflammatory skin diseases. *Semin Cutan Med Surg*. 2001;20:260-267.
17. Jain VK, Aggarwal K, Jain K, et al. Narrow-band UV-B phototherapy in childhood psoriasis. *Int J Dermatol*. 2007;46:320-322.
18. Tay YK, Morelli JG, Weston WL. Experience with UVB phototherapy in children. *Pediatr Dermatol*. 1996;13: 406-409.
19. Pasić A, Ceović R, Lipozencić J, et al. Phototherapy in pediatric patients. *Pediatr Dermatol*. 2003;20:71-77.
20. Cassandra M, Conte E, Cortez B. Childhood pustular psoriasis elicited by the streptococcal antigen: a case report and review of the literature. *Pediatr Dermatol*. 2003;20:506-510.
21. Wilson JK, Al-Suwaidan SN, Krowchuk D, et al. Treatment of psoriasis in children: is there a role for antibiotic therapy and tonsillectomy? *Pediatr Dermatol*. 2003;20:11-15.
22. Dogan B, Karabudak O, Harmanyeri Y. Antistreptococcal treatment of guttate psoriasis: a controlled study. *Int J Dermatol*. 2008;47:950-952.
23. Saxena VN, Dogra J. Long-term oral azithromycin in chronic plaque psoriasis: a controlled trial [published online ahead of print March 19, 2010]. *Eur J Dermatol*. 2010;20:329-333.
24. Collin B, Vani A, Ogboli M, et al. Methotrexate treatment in 13 children with severe plaque psoriasis [published online ahead of print October 30, 2008]. *Clin Exp Dermatol*. 2009;34:295-298.
25. Kaur I, Dogra S, De D, et al. Systemic methotrexate treatment in childhood psoriasis: further experience in 24 children from India. *Pediatr Dermatol*. 2008;25:184-188.
26. Cordoro KM. Systemic and light therapies for the management of childhood psoriasis: part II. *Skin Therapy Lett*. 2008;13:1-3.
27. Gisondi P, Fantuzzi F, Malerba M, et al. Folic acid in general medicine and dermatology. *J Dermatolog Treat*. 2007;18:138-146.
28. Davis A, Krafchik BR. New drugs in pediatric dermatology. *Curr Opin Pediatr*. 1993;5:212-215.
29. Brecher AR, Orlow SJ. Oral retinoid therapy for dermatologic conditions in children and adolescents. *J Am Acad Dermatol*. 2003;49:171-182.
30. Lovell DJ, Reiff A, Ilowite NT, et al; Pediatric Rheumatology Collaborative Study Group. Safety and efficacy of up to eight years of continuous etanercept therapy in patients with juvenile rheumatoid arthritis. *Arthritis Rheum*. 2008;58:1496-1504.
31. Morbach H, Richl P, Stojanov S, et al. Tumor necrosis factor receptor 1-associated periodic syndrome without fever: cytokine profile before and during etanercept treatment [published online ahead of print April 19, 2009]. *Rheumatol Int*. doi:10.1007/s00296-009-0937-0.
32. Nielsen S, Ruperto N, Gerloni V, et al; Italian Pediatric Rheumatology Study Group. Preliminary evidence that etanercept may reduce radiographic progression in juvenile idiopathic arthritis. *Clin Exp Rheumatol*. 2008;26: 688-692.
33. Lovell DJ, Giannini EH, Reiff A, et al; Pediatric Rheumatology Collaborative Study Group. Long-term efficacy and safety of etanercept in children with polyarticular-course juvenile rheumatoid arthritis: interim results from an ongoing multicenter, open-label, extended-treatment trial. *Arthritis Rheum*. 2003;48:218-226.
34. Hawrot AC, Metry DW, Theos AJ, et al. Etanercept for psoriasis in the pediatric population: experience in nine patients. *Pediatr Dermatol*. 2006;23:67-71.
35. Mayser P, Mrowietz U, Arenberger P, et al. Omega-3 fatty acid-based lipid infusion in patients with chronic plaque psoriasis: results of a double-blind, randomized, placebo-controlled, multicenter trial. *J Am Acad Dermatol*. 1998;38:539-547.
36. Grattan C, Burton JL, Manku M, et al. Essential-fatty-acid metabolites in plasma phospholipids in patients with ichthyosis vulgaris, acne vulgaris and psoriasis. *Clin Exp Dermatol*. 1990;15:174-176.
37. Fahrer H, Hoeflin F, Lauterburg BH, et al. Diet and fatty acids: can fish substitute for fish oil? *Clin Exp Rheumatol*. 1991;9:403-406.
38. Lin YK, Yen HR, Wong WR, et al. Successful treatment of pediatric psoriasis with Indigo naturalis composite ointment. *Pediatr Dermatol*. 2006;23:507-510.