

New Therapy for Severe Cystic Acne

Isotretinoin, 13-*cis*-retinoic acid (Accutane, Hoffmann-LaRoche), is brightening the bleak outlook for adolescents and young adults with nodular, cystic, and conglobate acne—a severe, scarring disease—that has resisted treatment with topical or systemic antibiotics, benzoyl peroxide, retinoic acid, and intralesional corticosteroids. Adolescents with less severe forms of acne who learn about the therapeutic triumphs of isotretinoin in severe recalcitrant nodular and cystic acne may assume that the drug also would be beneficial for them. Pediatricians should inform these adolescents that the drug has not been studied in, found effective for, or labeled for the treatment of typical acne.

Patients with multiple, active, deep dermal or subcutaneous cystic and nodular acne lesions are usually given 1 to 2 mg of isotretinoin per kilogram of body weight per day (although dosage as low as 0.05 mg/kg/d has been reported as beneficial), orally, in two divided doses for 15 to 20 weeks or until the cyst count decreases by 70%, if this happens sooner than 15 to 20 weeks. Use of this drug is associated with a reduction in sebaceous gland size and activity (a decrease in sebum excretion by as much as 75% to 90%), with inhibition of sebaceous cell differentiation, and with a reversion to prepubertal skin surface lipid composition. Although isotretinoin is expensive, a course of treatment usually clears the troublesome lesions and a prolonged remission often follows.

Side effects and alterations in patients' laboratory test results do occur; these appear to be lessened by reduction in dosage and to be fully reversible when the drug is discontinued. Vitamin A supplements may increase toxic effects from, and should not be taken with isotretinoin. Cheilitis is found almost universally. Conjunctivitis (frequently staphylococcal blepharokerato-conjunctivitis), dryness of the skin and nasal mucosa, epistaxis, and pruritus are common. Arthralgia and myalgia occur less frequently. Initial studies have indicated that plasma triglyceride levels increase in

25% of patients; therefore these levels should be measured before treatment and monitored at 1- or 2-week intervals thereafter; if there are high triglyceride levels, dietary manipulation or reduction of dosage should be considered. Decreased serum high density lipoprotein levels were found in 15% of patients and 7% had increased serum cholesterol levels. A recent report notes that serum lipids increase in nearly all patients, and do so at lower doses than those recommended for acne treatment. Elevated ESRs occur in 40% of patients, 13% have high platelet counts, and some have changes in other standard hematologic test results. In patients with keratinizing disorders given the drug in higher doses than used in acne, and for longer periods, skeletal hyperostosis has been observed.

An important consideration in the clinical use of isotretinoin is the observation that the drug is a teratogen in animals. Therefore, all patients should be informed of the drug's effects and sexually active female patients should be identified prior to treatment, counseled regarding the potential risks to the fetus if they become pregnant while receiving treatment, and given the drug only if they also use an effective form of contraception which should be continued 3 to 4 months beyond completion of treatment. Physicians may wish to document that patients were provided with this information. The drug does not appear to be mutagenic in humans, and it is not known whether the drug is excreted in breast milk.

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ANNOUNCEMENT OF THE PROGERIA INTERNATIONAL REGISTRY

An international registry of patients with the Hutchinson-Gilford progeria syndrome is being established to record all known cases of progeria in order to better determine the true nature, incidence and genetics of the disease, to follow the clinical course of patients with the disease, to determine prognosis, and to be able to offer summarized information and counseling to affected families and clinicians. A progeria newsletter will be distributed to interested individuals and families. Opportunities for progeria family gatherings are available. Strict confidentiality of personal data in the registry will be maintained. Any clinician or person who is aware of a living progeria patient is asked to communicate with: W. Ted Brown, MD, PhD; Director, Progeria Registry; Chairman, Department of Human Genetics; New York State Institute for Basic Research in Developmental Disabilities; 1050 Forest Hill Road; Staten Island, NY 10314.

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