

FDA Approves Recommended Changes to iPLEDGE Rules

BY ALICIA AULT

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As expected, the Food and Drug Administration has relaxed some of the rules for prescribing the acne drug isotretinoin, including eliminating the 23-day lockout period for women of childbearing potential.

Women still must have their initial prescription filled within 7 days of their first office visit or they will be prevented from getting the drug for 23 days. But the restriction no longer will apply to succeeding prescriptions.

Dermatologists, drugmakers, and professional organizations such as the American Academy of Dermatology had encouraged the FDA to make that change to the iPLEDGE program that governs isotretinoin prescribing.

At a meeting in August, the FDA's Dermatologic and Ophthalmic Drugs and Drug Safety and Risk Management advisory committees voted unanimously in support of eliminating the 23-day lockout and several other changes, which the agency also approved. Those included:

▶ Starting the 7-day window for the ini-

tial prescription for those of childbearing potential from the date of pregnancy testing, instead of the date of the office visit.

▶ Extending the prescription window from 7 days to 30 days for men and for women not of childbearing potential.

▶ Modifying the list of acceptable secondary forms of contraception to include male condoms with or without spermicide.

The changes will be effective Dec. 2. Updated materials will be sent to pharmacies and prescribers before then, said Roche Laboratories Inc., one of the isotretinoin manufacturers. The others are Mylan Laboratories Inc., Ranbaxy Laboratories Ltd., and Barr Pharmaceuticals Inc.

The committee members said iPLEDGE seemed to be interfering with the doctor-patient relationship and had not, despite all its restrictions, eliminated pregnancies. From March 2006 to March 31, 2007, there were 122 pregnancies in 91,894 women of childbearing potential who received a prescription.

There were 37 pregnancies in April, May, and June 2007, and 19 pregnancies outside the iPLEDGE program, Roche officials noted at the meeting. ■

Hair Biopsy Might Assist in Diagnosing Trichotillomania

BY SHERRY BOSCHERT

San Francisco Bureau

SAN FRANCISCO — Few patients will admit that they compulsively pull out their hair, but a hair biopsy can help make the diagnosis of trichotillomania, Dr. Pearl C. Kwong said at a meeting sponsored by Skin Disease Education Foundation.

Clinically, the missing hair may be barely noticeable or may show signs of regrowth, such as uneven hair lengths. In contrast, hairs lost from alopecia areata will be about the same length if they regrow. If a patient picks hair from a favored area of the scalp, a "Friar Tuck" sign can be a clue to trichotillomania, she said. Patients usually have no skin abnormalities elsewhere.

Both children and adults with this impulse control disorder typically deny hair-pulling, and parents may be unwilling to accept a possible diagnosis of trichotillomania, said Dr. Kwong, a dermatologist in Jacksonville, Fla.

A hair biopsy can help with diagnosis. On histology, a high frequency of telogen hairs and a high frequency of non-inflamed catagen hairs are typical.

Accurate data on the prevalence of trichotillomania are hard to get because people hide the disorder, but it is estimated to affect 8 million people in the United States. The mean age of onset seems to be 8 years in boys and 12 years in girls, and 1%-2% of college students have experienced or currently have symptoms. Adults with trichotillomania

often report that the disorder started at a young age, even as young as 1 year old, and it is more likely to be diagnosed in women than in men.

In infants or young children, pulling or twisting the hair usually is self-limited and is a benign form of trichotillomania. It may be a sign of psychosocial stress or an underlying psychological problem, however, and can become a chronic condition.

Adolescents and adults diagnosed with trichotillomania tend to have a poorer prognosis, with chronic remissions and exacerbations. Patients may avoid social situations or have GI complaints. "There's usually underlying psychopathology in that family," Dr. Kwong said.

Although scalp hair is the most common target, hair-pulling may focus on any hairy parts of the body, including eyelashes, eyebrows, or hair in pubic, perirectal, or armpit areas.

In young children, treat trichotillomania as a short-term habit disorder by cutting the hair very short (like a crew cut in boys) and applying Vaseline to the hair. "They stop because it's so slippery they can't pull," Dr. Kwong said.

Referral to psychiatry, psychology, or developmental and behavioral pediatrics should be considered, especially in patients older than young children. Trichotillomania has been associated with obsessive control disorder, personality disorders, body dysmorphic disorder, schizophrenia, and mental retardation.

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IgA Presence Confirms Henoch-Schönlein Cases

BY BARBARA J. RUTLEDGE

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BUENOS AIRES — Diagnosing Henoch-Schönlein purpura requires a small-vessel biopsy to confirm the presence of IgA, Dr. Thomas G. Cropley said at the 21st World Congress of Dermatology.

IgA deposits in vessel walls, along with prominent extracutaneous manifestations, are the hallmarks of Henoch-Schönlein purpura (HSP), a specific type of small-size vessel vasculitis that is the most common vasculitis syndrome in children, often occurring after a respiratory tract infection.

In recent years, three different sets of classification criteria have been proposed, the oldest of which does not list IgA deposition in its diagnostic criteria. In 1990, the American College of Rheumatology published its classification of Henoch-Schönlein purpura (*Arthritis Rheum.* 1990;33:1114-21), requiring four diagnostic criteria:

▶ Palpable purpura, defined as slightly raised "palpable" hemorrhagic skin lesions not related to thrombocytopenia;

▶ Age less than 20 years at disease onset;

▶ Bowel angina, or diffuse abdominal pain, which might include bloody diarrhea;

▶ Presence of granulocytes in vessel walls.

"There is no mention of immunofluorescence or IgA here," said Dr. Cropley. The ACR definition is based only on histopathology and clinical symptoms. Dermatologists were not involved in developing the classification system, which has been criticized for the "lack of dermatological insight," said Dr. Cropley, professor of medicine in the division of dermatology at the University of Massachusetts, Worcester.

A group of physicians that included rheumatologists, nephrologists, and pulmonologists (but not dermatologists) convened in Chapel Hill, N.C., in 1994 and developed consensus guidelines for the diagnosis of various forms of vasculitis, including HSP (*Arthritis Rheum.* 1994;37:187-92). "[This] definition of Henoch-Schönlein purpura requires the presence of vasculitis with IgA-dominant immune deposits affecting small vessels, which they defined as capillaries, venules, or arterioles," said Dr. Cropley. The definition noted that the vasculitis typically involves skin, gut, and glomeruli and that the condition is associated with arthralgias or arthritis. "IgA is part of the definition, but there are still many other areas of 'looseness' in this definition."

In 2006, the European League Against Rheumatism and the Paediatric Rheumatology Society published Classification Criteria for Henoch-Schönlein purpura (*Ann. Rheum. Dis.* 2006;65:936-41). In their definition, the presence of palpable purpura is a mandatory criterion, and at least one of the following four features must be present: diffuse abdominal pain; biopsy-proved predominant IgA deposition; acute arthri-

tis in any joint or arthralgia; and renal involvement (hematuria and/or proteinuria).

The epidemiology of HSP is well described. In the United States, the incidence is about 10 cases per 10,000. About 75% of cases begin in childhood, with an equal prevalence in males and in females. The disease is often preceded by a respiratory tract infection, but no typical or unique pathogen has been associated with it, said Dr. Cropley.

Adult cases are less likely to be associated with an antecedent infection, and the prevalence is higher in men than in women.

Differential diagnosis of Henoch-Schön-



Even in the presence of palpable lesions, vessel biopsy is required to diagnose Henoch-Schönlein purpura.

lein purpura includes other forms of small-size vessel vasculitis causing palpable purpura, such as Wegener's granulomatosis, IgG leukocytoclastic vasculitis, and microscopic polyangiitis. Other IgA-associated vasculitides should also be considered, including IgA rheumatoid factor-associated small-vessel vasculitis and acute hemorrhagic edema of infancy.

The question of whether or not the presence of IgA predicts an increased likelihood of renal involvement is unanswered. An epidemiologic study of HSP showed renal involvement occurred in one-third of the children with the disease (*Kidney Int.* 1998;53:1755-9). Significant independent risk factors for chronic renal disease in these patients were severe abdominal symptoms, prolonged purpura, and decreased factor XIII activity. But the prognostic significance of IgA status could not be evaluated in the study, because the researchers used the 1990 ACR diagnostic criteria of Henoch-Schönlein purpura.

IgA deposition is a defining criterion of Henoch-Schönlein purpura in the two most recent diagnostic guidelines. Patients with the condition may have a poorer prognosis concerning renal involvement than patients with other forms of small-vessel vasculitis. As such, Dr. Cropley recommended a biopsy for immunofluorescence and histopathology, if possible, in patients who seem to have Henoch-Schönlein purpura. Serum IgA levels have been shown to correlate with the risk of IgA nephropathy in adults with Henoch-Schönlein purpura; thus, monitoring serum IgA level over time may help identify patients at particular risk of chronic renal disease. He reports no conflicts of interest. ■