

Confocal Laser Microscopy Gaining Momentum

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MONTREAL — Formation of an international confocal microscopy group, software that aids the detection and mapping of skin lesions, and introduction of a handheld device are among recent advances to aid in the diagnosis of lentigo maligna and other lesions in real time.

Researchers hope widespread adoption of confocal laser microscopy progress will permit further early diagnoses of cutaneous melanoma and other lesions at the bedside. "It is critical to do biopsies early. If you believe cancer starts from a single cell, you can diagnose it early [with confocal laser microscopy]. That is what we are working on now," Dr. Richard Langley said.

Described as a "living skin biopsy" by some, microscopy is not new. Pathologists have employed the intensely focused light to examine tissue specimens since the 1950s, he said. There is a limitation in live patients, however. "We cannot go through

confocal versus dermoscopy [97% vs. 89%, respectively]. The specificity was about the same [83% vs. 84%]," Dr. Langley said. "We missed one melanoma with the confocal technology, so it was not perfect."

For dermatologists accustomed to reading cross-sectional biopsies, it may take an adjustment to recognize the clusters of melanocytes, Dr. Langley said. "You have to retrain your eye to look differently—you are looking from above. Also, it is in black and white, not color, like we're used to."

Indicative of the growing interest in this technology is the formation of the International Confocal Microscopy Working Group, launched at the February 2008 American Academy of Dermatology annual meeting in San Antonio. The group aims to form an international network of medical professionals working with confocal laser microscopy and to promote education, training, and additional research about the technology.

New software for microscopy also

emerged in the past year (Electronic Zoom, Lucid Inc.). The video-capture software allows dermatologists or dermatopathologists to map a lesion and tag an area of interest. "You start with a macro image and, if you see an area you want to focus on, the software can be engaged," Dr. Langley said.

Another advance is the availability of a hand-held confocal microscopy device (VivaScope 3000, Lucid). Dr. Langley had no relevant financial disclosures. ■

Luxiq®

(betamethasone valerate) Foam, 0.12%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Rx Only
For Dermatologic Use Only
Not for Ophthalmic Use

CONTRAINDICATIONS

Luxiq is contraindicated in patients who are hypersensitive to betamethasone valerate, to other corticosteroids, or to any ingredient in this preparation.

PRECAUTIONS

General: Systemic absorption of topical corticosteroids has caused reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for those products.

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. (See **PRECAUTIONS-Pediatric Use.**)

If irritation develops, Luxiq should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing a failure to heal rather than noting a clinical exacerbation, as with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic patch testing.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, use of Luxiq should be discontinued until the infection has been adequately controlled.

Information for Patients: Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.

2. This medication should not be used for any disorder other than that for which it was prescribed.

3. The treated scalp area should not be bandaged or otherwise covered or wrapped so as to be occlusive unless directed by the physician.

4. Patients should report to their physician any signs of local adverse reactions.

5. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician.

Laboratory Tests: The following tests may be helpful in evaluating patients for HPA axis suppression:

ACTH stimulation test
A.M. plasma cortisol test
Urinary free cortisol test

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of betamethasone valerate.

Betamethasone was genotoxic in the *in vitro* human peripheral blood lymphocyte chromosome aberration assay with metabolic activation and in the *in vivo* mouse bone marrow micronucleus assay.

Pregnancy Category C: Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women. Therefore, Luxiq should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Because many drugs are excreted in human milk, caution should be exercised when Luxiq is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and an absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS

The most frequent adverse event was burning/itching/stinging at the application site; the incidence and severity of this event were as follows:

Product	Total incidence	Incidence and severity of burning/itching/stinging		
		Maximum severity		
		Mild	Moderate	Severe
Luxiq Foam n=63	34 (54%)	28 (44%)	5 (8%)	1 (2%)
Betamethasone valerate lotion n=63	33 (52%)	26 (41%)	6 (10%)	1 (2%)
Placebo Foam n=32	24 (75%)	13 (41%)	7 (22%)	4 (12%)
Placebo Lotion n=30	20 (67%)	12 (40%)	5 (17%)	3 (10%)

Other adverse events which were considered to be possibly, probably, or definitely related to Luxiq occurred in 1 patient each; these were paresthesia, pruritus, acne, alopecia, and conjunctivitis.

The following additional local adverse reactions have been reported with topical corticosteroids, and they may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximately decreasing order of occurrence: irritation; dryness; folliculitis; acneiform eruptions; hypopigmentation; perioral dermatitis; allergic contact dermatitis; secondary infection; skin atrophy; striae; and miliaria.

Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

OVERDOSAGE

Topically applied Luxiq can be absorbed in sufficient amounts to produce systemic effects. (See **PRECAUTIONS**)

WARNING

FLAMMABLE. AVOID FIRE, FLAME OR SMOKING DURING AND IMMEDIATELY FOLLOWING APPLICATION. Keep out of reach of children. Contents under pressure. Do not puncture or incinerate container. Do not expose to heat or store at temperatures above 120°F (49°C).

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A hand-held confocal microscopy device is one recent dermoscopy advancement.

a patient's skin, so we deal with reflective light. We still have confocal concepts, but we have real-time results," Dr. Langley said at the annual conference of the Canadian Dermatology Association.

Dr. Langley and his colleagues were the first to report use of confocal laser microscopy in a series of 40 dermatology patients with superficial melanoma (*J. Am. Acad. Dermatol.* 2001;45:365-76).

Others have since validated that microscopy distinguishes between malignant and benign lesions *in vivo*. To date, studies include more than 400 patients, said Dr. Langley of Dalhousie University, Halifax, N.S.

Last year, he and his associates published the first prospective study to compare microscopy with dermoscopy. "We decided to see if we can do a prospective, blinded, single-institution study," he said.

They assessed 125 patients with suspicious pigmented lesions using both technologies, followed by a confirmatory biopsy (*Dermatology* 2007;215:365-72). They detected a total of 88 melanotic nevi and 37 melanomas. "Sensitivity was higher with