# Erosive Oral Lichen Planus May Flag Genital Lesions

BY BETSY BATES
*Los Angeles Bureau*

PORTLAND, ORE. — Gingival lichen planus, particularly forms that are erosive, ulcerative, or bullous, should raise the red flag of suspicion about the presence of genital lesions, Dr. Roy S. Rogers III said at the Pacific Northwest Dermatological annual scientific meeting.

"The gynecologists usually don't ask about the mouth or look there. The dentists certainly don't ask about the vulva, nor do they look there. Neither do the ENT [ear, nose, throat] physicians," said Dr. Rogers, professor of dermatology at the Mayo Clinic in Rochester, Minn.

"It's really up to us to be the internist and externist [in order to diagnose extraoral lichen planus]," he said.

Studies suggest that genital lesions are present in 1 of 5 women and 1 in 20 men with oral lichen planus.

When oral lesions are reticular, linear, and feature papular and plaquelike lesions, "these are low-hanging fruit and are rather easy to deal with," he said.

In fact, many such lesions are asymptomatic and discovered by a dentist during a routine examination.

It is lesions that are atrophic, erosive, ulcerative, and/or bullous that can be extremely painful, often with extraoral manifestations. "They require our very expert care," Dr. Rogers said.

Vulvovaginal lesions may be eroded, leading in some cases to desquamatous vaginitis. Known as vulvovaginal-gingival syndrome, this form of the disease is chronic and may involve other areas of the body, including the skin, scalp, nails, ear canal, and esophagus.

Much rarer, but clinically similar, is peno-gingival syndrome in men, which is characterized by desquamative gingivitis and penile involvement.

Histopathology and immunopathology usually have findings typical of classic lichen planus lesions.

Therapy can be challenging, but may include the topical immunomodulator tacrolimus, systemic and topical corticosteroids, hydroxychloroquine, cyclosporine, dapsone, griseofulvin, interferon α-2b, retinoids, and mycophenolate mofetil.

Topical tacrolimus is particularly effective in reducing symptoms of both oral and vulvar lichen planus, which is a T cell–mediated disorder, he said.

Studies performed by Dr. Rogers' group at the Mayo Clinic found that the application of topical tacrolimus produced meaningful symptomatic improvement in 33 of 37 patients with oral lichen planus and 15 of 16 patients with vulvar lichen planus within about 1 month (Arch. Dermatol. 2004;140:1,508-12; Arch. Dermatol. 2004;140:715-20).

Burning and stinging were reported in roughly one-third of patients but became less pronounced over time.

In both studies, discontinuation of treatment resulted in a return of lesions; however, they were less severe and could be controlled with reinitiation of tacrolimus treatment.

Meticulous oral hygiene is critically important to control perioral disease, because patients tend to develop secondary candidiasis that may become koebnerized from poor oral hygiene, Dr. Rogers said.

Patients with oral lichen planus face a 1% lifetime risk of malignant transformation of their lesions. "Tell them you want them to be seen every 6 months by their dentist and/or by you," he said.

Dr. Rogers reported no financial disclosures. ■

# Recurrence Is Common Following Surgery for Pelvic Organ Prolapse

TUCSON, ARIZ. — There is a substantial recurrence rate following surgery for pelvic organ prolapse, particularly in the context of cystocele repair, University of Washington researchers reported at the annual meeting of the Society of Gynecologic Surgeons.

Dr. Michael Fialkow and associates examined records for 142 women who underwent surgery primarily for pelvic organ prolapse in 1993 and were then followed for up to 10 years.

A total of 36 recurrent cases were identified during the 1,050 woman-years studied, for an overall recurrence rate of 3.43 per 100 woman-years.

"A cystocele was the most common site of both primary (87%) and recurrent (75%) prolapse … which is consistent with previous literature documenting the difficulty of repairing this condition durably," the investigators noted in a poster presented at the meeting.

More than half of the recurrences—21 of 36—developed at the same site as the original prolapse, but 11 patients developed prolapse at a new site and 4 had evidence of recurrent prolapse at the original site and a new occurence elsewhere.

Of note, just 6 patients opted for a surgical repair following recurrence, whereas 16 opted for conservative management, and 14 had no documented management of the recurrent prolapse.

Dr. Fialkow of the university's department of obstetrics and gynecology and another investigator disclosed that they have participated in the speaker's bureau for Pfizer Inc., which makes products used in the treatment of pelvic organ prolapse.

The study's coinvestigators represented the Center for Health Studies of the Group Health Cooperative and the department of epidemiology at the University of Washington, Seattle.

**—Betsy Bates**

## DRUGS, PREGNANCY, AND LACTATION

# Morphine Poisoning via Breast Milk

Last month, my associates and I published a case report of an apparently healthy full-term newborn who died at 13 days from morphine poisoning. The cause was determined to be a genetic polymorphism in the mother, which made her an ultrarapid metabolizer of codeine to morphine, via cytochrome P450 2D6 (CYP2D6).

The coroner investigating the death contacted us after detecting an extremely high blood morphine level in the baby, because the mother had been taking codeine for episiotomy pain and had been breast-feeding. We suspected the mother might have the polymorphism, identified in recent years in a population subgroup. In one case involving ultrarapid CYP2D6 metabolism, a healthy man almost died from morphine poisoning when he received codeine for dental pain (N. Engl. J. Med. 2004;351:2827-31).

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Genetic testing of the mother, father, baby, and extended family members identified the mother (and maternal grandmother) as ultrarapid CYP2D6 metabolizers, but not the baby. Frozen breast milk had a morphine level far higher than described in the literature: 87 ng/mL, vs. the typical level of 1.9-20.5 ng/mL associated with maternal doses of 60 mg of codeine every 6 hours (Lancet 2006;368:704).

Overall, there has been the perception that codeine is safe for the baby during breast-feeding. The few studies that have evaluated breast milk in women taking codeine have not found high morphine levels, and the American Academy of Pediatrics and other authoritative bodies list codeine as compatible with breast-feeding.

In most cases, this remains true. But considering the common practice of prescribing codeine for pain after childbirth with episiotomy or by cesarean section, many babies may be at risk. The prevalence of ultrarapid metabolizer status ranges from 1% in Denmark and Finland to 10% in Greece and Portugal to 29% in Ethiopia.

A genetic test is commercially available, but it is expensive and is currently not routinely performed. Other options all have pros and cons. One could withhold codeine in the postpartum period, but codeine is sometimes clearly needed for pain.

Using a nonsteroidal anti-inflammatory drug and avoiding codeine when breast-feeding eliminates the risk of toxicity in the baby, but may not adequately control pain. Using a lower dose of codeine minimizes potential toxicity to the baby, but may not provide sufficient pain control for the mother, and the dose could still be too high if she is an ultrarapid metabolizer. Another option is to avoid breast-feeding while taking codeine, but the baby would lose the benefits of breast-feeding.

In our case the mother took codeine until the child died at 13 days, which is longer than usual. This suggests that use for no more than 2-3 days is advisable. In retrospect, there were clinical signs hinting that the mother was an ultrarapid metabolizer: Despite being on a low dose of codeine, in combination with paracetamol, she was somnolent and constipated, and the dose had to be reduced on the second day of treatment.

Be alert for signs and symptoms suggesting that a patient is an ultrarapid metabolizer, including somnolence, sleepiness, dizziness, and constipation. The metabolism to morphine by CYP2D6 is responsible for most of the analgesic and CNS depressant effects of codeine.

Why have cases like this one not been previously reported? I suspect such cases may not be as rare as we thought, but not all the cases are as tragic because the mothers do not take codeine for as long a time. For example, in a paper we published more than a decade ago on outcomes in babies exposed to drugs in breast milk, 25 women reported taking codeine while breast-feeding, and in five cases their babies were described as being sleepy. An abstract from a 1984 meeting described apnea in premature babies who were being breast-fed, which resolved as soon as their mothers stopped taking codeine. Interestingly, their symptoms began at about day 7, which was also the case in our report, suggesting it takes time for morphine to accumulate in the milk to dangerous levels.

Eventually, this is the type of pharmacogenetic information everyone will be aware of and will have available when presenting for medical care. For now, we are conducting a large case-control pharmacogenetic study funded by Genome Canada on babies who were breast-fed while the mother was using codeine to better define the scope of this issue.

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