



BY ALAN  
ROCKOFF, M.D.

## UNDER MY SKIN

# Computer Correspondence

Ah, Monday morning. Time to check e-mails from far-flung patients. Miranda, a music major at Michigan, will remind me about her mometasone. Murray's mellowing on Minocin in Morocco.

Goodness, that inbox has certainly filled up over the weekend. What's this? Mortgage rates are that low? Wouldn't you know it—we just refinanced!

Look, I've been preapproved for credit. We have enough credit cards already, thanks.

Hmm, I knew they're importing medications from Canada and Mexico, but what kind of quality controls do they have in Bulgaria? Let's see, they're running a special on phentermine. Looks like a good price. I wonder what phentermine is. What else do they have ... narcotics, anxiolytics ... never mind. Why no topical steroids?

Finally, an e-mail from a patient! Don't recognize the name, though. I think I'd remember someone named Dirk Cen-

tagord. He's just canceling an appointment ... what's this? This Dirk sure needs an editor. What kind of message is, "stethoscope mercy brunhilde huzzah buffalo carson allure?"

Now what? Look, I'm a physician, so don't expect me to believe you can change the size of anything with a cream. Besides, size doesn't matter. It does? She would? I never thought about it. ... More drugs for sale. Judging by TV ads and cyberpromotions, half the world has fungal toenails and the other half has erectile dysfunction.

Another patient confirming an appointment. ... Thelma Fontenot? A Rolex for \$9.95? I wonder if it's genuine.

OK, knock it off—I got the mortgage stuff already. And phentermine, too. I'm just going to delete this stuff. Mortgage, delete. Credit cards, delete. Viagra, delete. Latin gibberish, delete. This is fun! Levitra, Cialis, Vicodin, delete, delete, delete. Ha! Hold on a second. ... I think one of those messages I just deleted was the one I was waiting for from Miranda in Michigan. Great, how am I going to find it in the 3,000 messages in the deleted folder?

It's too bad. E-mail could be such a nice

way to communicate. No phone tag, no trying to find a good time to call in a different time zone, no interruptions in the middle of patients. I installed a spam filter, but it worked so well that I couldn't even e-mail myself from home. How would I know if a patient tried to reach me and got his or her message blocked?

Now what? Great, first they enlarge you, then they shrink you back down. Alice in Wonderland had nothing on these guys. A revolutionary new diet pill that makes you lose up to 30 pounds in 30 days or less, automatically while you sleep? Body wrap at home to lose 6-20 inches in 1 hour! Put lindane under that overnight, and the scabies mites won't even find you in the morning.

Gustavo Fontenot? Must be Thelma's cousin from Caracas. ... What? "Sehr geehrte Damen und Herren, die Weih-nachtszeit naht und haben wir sicherlich noch einen guten Tipp!" Hey, Gustavo, I'll give you a guten Tipp in your guten Keester! A monkeypox on all the Fontenots. ...

Another canceled appointment? Hey, fool me once—Paris Hilton is not a real name! Video? What video?

More credit card come-ons. Look at that, they're coming in bunches, 5 in a row, 10 in a row, 50, same message. More mortgages, 10, 20, 50, REFINANCE NOW, REFINANCE NOW, REFINANCE NOW. ... Buy a Rolex, buy a Seiko, buy Vicodin, buy Cialis. The e-mails are like locusts, I can't kill them fast enough. ... I don't want any of those drugs! Nobody by that name missed an appointment! I'm not going to update personal information for a bank I never heard of! I'm not shrinking or enlarging anything! How am I supposed to respond to marion allegiant asphalt tally-ho torture confrontation? I refuse to answer Verzieren Sie die Uhr mit einer Gravur und sie warden! They're coming faster and faster. ... I can't see the screen ... everything's going black. OK, that's it, I'm bailing out, I'm deleting the whole Outlook. Mayday! Mayday! SOS! Abort! Abort! Control! Select All! Alt! DELETE, DELETE, DELETE. ...

Darn—I think I deleted Murray. ■

DR. ROCKOFF practices dermatology in Brookline, Mass. To respond to this column, write Dr. Rockoff at our editorial offices or e-mail him at [sknews@elsevier.com](mailto:sknews@elsevier.com).

## GUEST EDITORIAL

### The Quandary That Is Called the FDA

In the wake of the Vioxx scandal, the Food and Drug Administration has suddenly become the whipping boy of both the press and Congress, a combination that is certainly hard to beat. A feeding frenzy has erupted, with charges coming from inside and outside the agency.

I, too, have been critical of the FDA at times and have expressed concern about some of its premature decisions and lack

of postapproval surveillance of drugs. Nevertheless, let's place some of the blame where it should be placed; there is enough to go around. The FDA, created in 1906 as part of the Pure Food and Drug Act, has gone through a number of iterations in response to changes in the industry it is intended to control and in the human beings it is expected to protect. In its nearly 100 years of life, drugs have become more complex, and Americans have grown older. The acceleration of technology and pharmacology that has occurred in the last half century has provided physicians and patients a breathtaking array of medical options to prolong and improve the quality of life. At the same time, many of these products have the potential to adversely affect the safety of those individuals who are the treatment targets.

It was but a short 12 years ago that Congress pressured the FDA to get into bed with the pharmaceutical industry in

order to expedite drug approval and get new drugs to market faster. The pharmaceutical industry convinced Congress that unless the drug approval process was not accelerated, thousands of patients would die. Examples of this threat have so far been illusory. Industry also convinced Congress that it cost them too much to bring products to market, many of which were "me too" drugs. As a result of these initiatives, the approval of

new molecular entities increased from 30 in 1991 to 53 in 1996. Now Congress, in its infinite wisdom, charges that the FDA has been too hasty and superficial with its drug approval process.

As medical therapy has changed in the last half century, so too has the role of the FDA in evaluating drugs' efficacy and safety. Mid-20th century medical therapy was focused on the treatment of episodic short-term diseases like pneumonia. Safety and efficacy could be measured in days or weeks.

Major changes occurred in the 1970s and 1980s that led to the consideration of drugs for the long-term prevention and treatment of chronic diseases that affect an increasingly aging population. Drugs and devices to treat atherosclerotic cardiovascular disease, hypertension, and diabetes mellitus were developed. Clinical trials suggested that drugs should be taken for a lifetime, and that could be a very

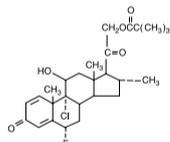
*Continued on following page*

## Cloderm<sup>®</sup> (clocortolone pivalate) Cream, 0.1%

### For Topical Use Only

**DESCRIPTION:** Cloderm Cream 0.1% contains the medium potency topical corticosteroid, clocortolone pivalate, in a specially formulated water-washable emollient cream base consisting of purified water, white petrolatum, mineral oil, stearyl alcohol, polyoxy 40 stearate, carboxymethylcellulose sodium, sodium hydroxide, with methylparaben and propylparaben as preservatives.

Chemically, clocortolone pivalate is 9-chloro-6 $\alpha$ -fluoro-11 $\beta$ , 21-dihydroxy-16 $\alpha$ -methylpregna-1, 4-diene-3, 20-dione 21-pivalate. Its structure is as follows:



### CLINICAL PHARMACOLOGY:

Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

**Pharmacokinetics:** The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses. (See **DOSE AND ADMINISTRATION**).

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

**INDICATIONS AND USAGE:** Topical corticosteroids are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

**CONTRAINDICATIONS:** Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

### PRECAUTIONS

**General:** 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.

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 receiving a large dose of a potent topical steroid applied to a large surface area or under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. 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 and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.

Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. (See **PRECAUTIONS - Pediatric Use**).

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

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, the corticosteroid should be discontinued until the infection has been adequately controlled.

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

- This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
- Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
- The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
- Patients should report any signs of local adverse reactions especially under occlusive dressing.

5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

**Laboratory Tests:** The following tests may be helpful in evaluating the HPA axis suppression:

Urinary free cortisol test

ACTH stimulation 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 topical corticosteroids.

Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

**Pregnancy Category C:** Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids 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:** It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities not likely to have deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

**Pediatric Use:** Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area body weight ratio.

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

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 following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence:

Burning  
Itching  
Irritation  
Dryness  
Folliculitis  
Hypertrichosis  
Acneiform eruptions  
Hypopigmentation  
Perioral dermatitis  
Allergic contact dermatitis  
Maceration of the skin  
Secondary infection  
Skin atrophy  
Striae  
Miliaria

**OVERDOSAGE:** Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS**).

**DOSE AND ADMINISTRATION:** Apply Cloderm (clocortolone pivalate) Cream 0.1% sparingly to the affected areas three times a day and rub in gently.

Occlusive dressings may be used for the management of psoriasis or recalcitrant conditions.

If an infection develops, the use of occlusive dressings should be discontinued and appropriate anti-microbial therapy instituted.

**HOW SUPPLIED:** Cloderm (clocortolone pivalate) Cream 0.1% is supplied in 15 gram, 45 gram and 90 gram tubes.

Store Cloderm Cream between 15° and 30° C (59° and 86° F). Avoid freezing.

Distributed by:

**HEALTHPOINT<sup>®</sup>**

Healthpoint, Ltd.  
San Antonio, Texas 78215  
1-800-441-8227

Reorder No. 0064-3100-15 (15g)  
Reorder No. 0064-3100-45 (45g)  
Reorder No. 0064-3100-90 (90g)

127825-0303