

# Ambophyllin, an office-dispensed tablet for asthma, contains triamcinolone

Michael W. Yocum, MD, David A. Khan, MD, Richard G. Van Dellen, MD,  
and Nai-Siang Jiang, PhD Rochester, Minn.

Causes of Cushing's syndrome include Cushing's disease, ectopic adrenocorticotrophic hormone, or corticotropin-releasing hormone production, excessive adrenal hypersecretion, and exogenous glucocorticoid administration.<sup>1</sup> We examined two adult patients with asthma and Cushing's syndrome who were not known to be taking exogenous corticosteroids. Both were taking a proprietary pill labeled ambophyllin provided by a physician in Mexico. We analyzed an ambophyllin tablet and found it to contain triamcinolone. We present the case reports and a discussion of the implications of this information.

## CASE REPORTS

### Case 1

A 52-year-old man sought consultation for increased bruising and "stretch marks" about his abdomen. The subject had had asthma for 6 years, requiring 10 mg/day of prednisone, theophylline, and albuterol aerosol. He visited a physician in Mexico who prescribed a proprietary drug, ambophyllin, twice daily. This physician stated that ambophyllin contained no corticosteroid. With ambophyllin, the patient improved and had stopped taking theophylline, albuterol, and prednisone for the 3 previous years.

The patient was 68 inches tall and weighed 217 pounds. Physical findings included a blood pressure of 150/102 mm Hg, cushingoid habitus, and purple striae over the lower abdomen and axillary folds. There was a hyperinflated chest with decreased breath sounds and wheezes on forced expiration.

Laboratory findings included a hemoglobin of 15.9 gm/dl and a leukocyte count of  $12.2 \times 10^9/L$ . Pulmonary-function testing revealed an FVC, 2.8 L (4.22 L); FEV<sub>1</sub>, 2.06 L (3.39 L); forced expiratory flow rate between 25% and 75% of FVC, 1.4 L/sec (3.2 L/sec); and single breath diffusing capacity, 36% or 125% of predicted. The FEV<sub>1</sub> increased 11% after isoproterenol administration. Morning cortisol was 1.5 µg/dl (7 to 25 µg/dl), evening cortisol

#### Abbreviation used

HPLC: High-performance liquid chromatography

was 1.0 µg/dl (2 to 14 µg/dl), and serum corticotropin was 7 pg/ml (0 to 60 pg/ml). Twenty-four-hour urine-free cortisol was 14 µg (5 to 55 µg); cortisone, 47 µg; and triamcinolone, 309 µg.

The ambophyllin tablets were extracted with methanol. On a HPLC column, the unknown tablet was identified by comparison of its retention time and ultraviolet spectrum with authentic corticosteroid controls (Fig. 1, A and B). Four different ambophyllin tablets revealed triamcinolone in concentrations of 3.5, 4.2, 3.6, and 4.2 mg per tablet.

Ambophyllin was changed to prednisone, 10 mg/day and beclomethasone dipropionate aerosol was begun.

### Case 2

A 72-year-old woman sought consultation for severe osteoporosis. She had suffered fractures of her right wrist, hip, and her left femur. For previously treated Graves' disease, she required sodium levothyroxine (Synthroid; Flint Laboratories, Deerfield, Ill.), 0.15 mg daily. Asthma was diagnosed in 1978, and she required prednisone through 1982 in doses from 20 to 30 mg/day plus theophylline, inhaled beclomethasone, and albuterol aerosols. In 1982, she visited the same physician in Mexico (case 1) and was prescribed ambophyllin twice daily. She did not know ambophyllin contained corticosteroids but believed it controlled her asthma with only occasional inhaled albuterol use.

She was 144 cm tall and 43.6 kg in weight, and her blood pressure was 160/80. Physical findings revealed a cushingoid appearance, subcutaneous atrophy with ecchymoses, dorsal kyphosis, 3+ pitting edema, and hyperactive tendon reflexes.

Laboratory findings included a hemoglobin of 12.9 gm/dl and a leukocyte count of  $9.3 \times 10^9/L$ . Morning and evening serum cortisols were <1 µg/dl. A cortrosyn stimulation test demonstrated a baseline cortisol of 1.6 µg/dl, increasing to 5.6 and 7.2 µg/dl. Pulmonary-function testing demonstrated FVC, 0.75 L (2.22 L); FEV<sub>1</sub>, 0.61 L (1.82 L); and forced expiratory flow rate between 25% and 75% of FVC, 0.6 L/sec (2 L/sec). FEV<sub>1</sub> increased 24% after

From the Departments of Allergic Diseases and Internal Medicine, and Clinical Chemistry, Mayo Clinic, Rochester, Minn.

Reprint requests: Michael W. Yocum, MD, Mayo Clinic, 200 First St. SW, Rochester, MN 55905.

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## RETENTION TIME OF AUTHENTIC GLUCOCORTICOIDS

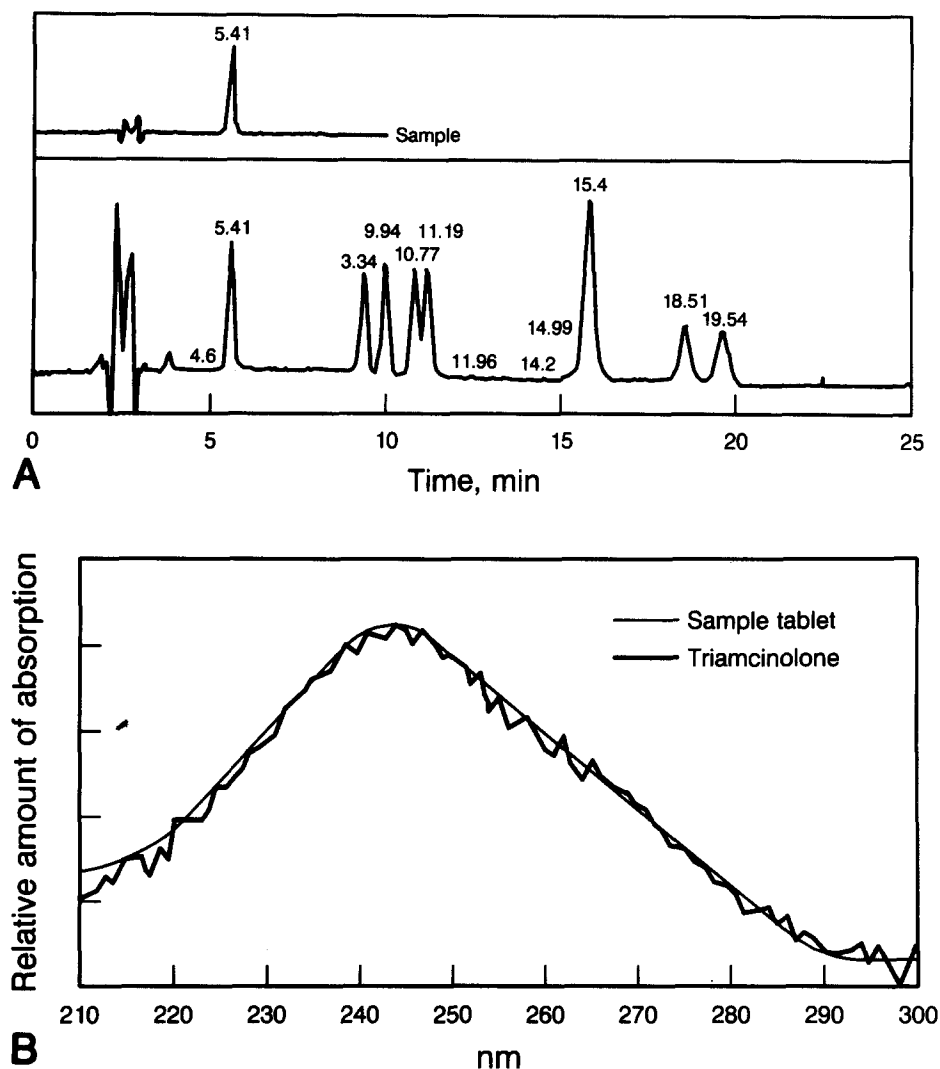


**FIG. 1. A,** Retention times in minutes of glucocorticoids: triamcinolone, 5.41; prednisolone, 9.34; cortisol, 9.94; fludrocortisone, 10.77; cortisone, 11.15; internal standard, 15.74; betamethasone, 18.50; and dexamethasone, 19.54. **B,** Ultraviolet spectrum of triamcinolone and the sample tablet.

inhaled isoproterenol. The serum thyroxine was 12.8  $\mu\text{g/dl}$ , and thyroid-stimulating hormone was suppressed. X-ray of the thoracolumbar spine revealed osteoporosis with compression fractures.

The patient refused to stop the use of ambophyllin despite our warning that it contained a corticosteroid.

### DISCUSSION

When patients present with Cushing's syndrome and no history of exogenous corticosteroid usage, several possibilities exist. The patient may have endog-

enous hypersecretion of steroids or could be taking steroid surreptitiously or unknowingly. The presence of exogenous corticosteroids is discernible by the suppression of morning and evening serum cortisols, suppressed serum adrenocorticotrophic hormone levels, suppressed 24-hour urine-free cortisols, and the presence of urine cortisol-interfering substances.<sup>1</sup> HPLC can be used for analysis of corticosteroids in the urine.<sup>2-4</sup> Comparison of urine chromatographs with known steroids can identify the corticosteroid present. The suspected tablet can also be identified by HPLC.<sup>5</sup>

The magnitude of the occult prescribing of triamcinolone is unknown. Unfortunately, the patients are unaware that ambophyllin contains a steroid. Since the patients derived some amelioration of their chronic illness from ambophyllin, their belief in what they consider a "wonder drug" is understandable. It is difficult to dissuade these patients from continued use of ambophyllin without proof that it is a corticosteroid. These patients are susceptible to Addisonian crises during medical or surgical stress. There is no historical data to inform the physician that a patient receiving ambophyllin is taking triamcinolone. Hopefully, this article will alert physicians that the proprietary, office-dispensed drug, ambophyllin contains triamcinolone.

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## Proteinases in extracts of the storage mite, *Aleuroglyphus ovatus*

Thomas B. Edwards, MD, Walter L. Trudeau, BA (MOD),  
Enrique Fernández-Caldas, PhD, Dong K. Lee, MD,  
Mitchel J. Seleznick, MD, and Richard F. Lockey, MD Tampa, Fla.

Storage mites are sources of allergens associated with allergic rhinitis and asthma by skin test, RAST, and nasal and bronchial challenges.<sup>1</sup> Storage-mite species, such as *Glycyphagus*, *Acarus*, and *Tyrophagus*, contain proteinases, esterases, lipase, glycosidases, cellulase, amylase, lysozyme, and chitinase.<sup>2</sup> *Der p* I and *Der f* I, the major allergens of the house dust mites, *Dermatophagoides pteronyssinus* (*Dp*) and *D. farinae* (*Df*), have been identified as cysteine proteinases.<sup>3</sup> Trypsin-like serine proteinases, some of which are allergenic, are also contained in house dust mite extracts.<sup>2, 4</sup>

This study investigated the proteinase activity in extracts of the storage mite, *Ao*, which is commonly

### Abbreviations used

|              |                                                        |
|--------------|--------------------------------------------------------|
| <i>Ao</i> :  | <i>Aleuroglyphus ovatus</i>                            |
| <i>AoB</i> : | <i>Aleuroglyphus ovatus</i> body                       |
| SCM:         | Spent culture medium                                   |
| UCM:         | Unspent culture medium                                 |
| OD:          | Optical density                                        |
| E-64:        | Trans-epoxysuccinyl-L-leucylamido-(4-guanidino)-butane |

found in farming environments. Positive skin tests and RASTs to *Ao* have been demonstrated in house dust-allergic individuals in the United States.<sup>5</sup>

*Ao* was cultured in glass containers at 75% relative humidity on autoclaved rodent chow. Cultures were sieved through a 125  $\mu$ m screen to obtain a feces-rich filtrate. *Ao* was then cultured on this filtrate to exhaustion. After 2 months, the culture was sieved through a 75  $\mu$ m screen to obtain the SCM. The SCM and the UCM were defatted and air-dried, homogenized, and extracted for 20 minutes in Tris HCl, 0.1

From the Division of Allergy and Immunology, University of South Florida College of Medicine, and James A. Haley Veterans Hospital, Tampa, Fla.

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Reprint requests: Enrique Fernández-Caldas, PhD, Division of Allergy and Immunology, c/o VA Hospital (VAR 111 D), 13000 Bruce B. Downs Blvd., Tampa, FL 33612.

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