

## Functional abnormalities of the LES found by TNE

Patrick S. Enriquez, MD  
Jacob T. Cohen, MD  
Gregory N. Postma, MD  
James A. Koufman, MD

We summarize two cases of abnormalities of the lower esophageal sphincter (LES) that were examined by transnasal esophagoscopy (TNE).

### Case reports

**Patient 1.** A 22-year-old white woman—a professional singer—was evaluated for chronic hoarseness. Laryngopharyngeal reflux injury was noted on transnasal fiberoptic laryngoscopy. On TNE, the LES was found to be incompetent, as it allowed for unimpeded passage of the esophagoscope through the gastroesophageal junction as well as obvious reflux of gastric contents into the esophagus (figure 1, A). Esophageal manometry revealed an LES pressure of 8 mmHg (normal: 10 to 45) with complete postswallow relaxation pressure at the gastric baseline (figure 1, B). A pH study detected episodes of abnormal pharyngeal reflux.

**Patient 2.** A 47-year-old white man complained of substernal heaviness and dysphagia while eating solids. Findings on transnasal fiberoptic laryngoscopy were suggestive of laryngopharyngeal reflux. During TNE, the examiner experienced difficulty passing the scope through the tight LES despite air insufflation and irrigation (figure 2, A). Peristaltic contractions were strong and prolonged. No mucosal lesions were seen. Esophageal manometry detected a mild hypertensive resting LES pressure of 47 mmHg with incomplete relaxation at 16 mmHg residual pressure (normal relaxation pressure: <8 mmHg above the gastric baseline) and distal esophageal amplitudes greater than 180 mmHg (normal: 30 to 180) (figure 2, B). These findings were diagnostic of a “nutcracker esophagus.” A 24-hour, double-probe, ambulatory pH study revealed multiple pharyngeal acid exposures.

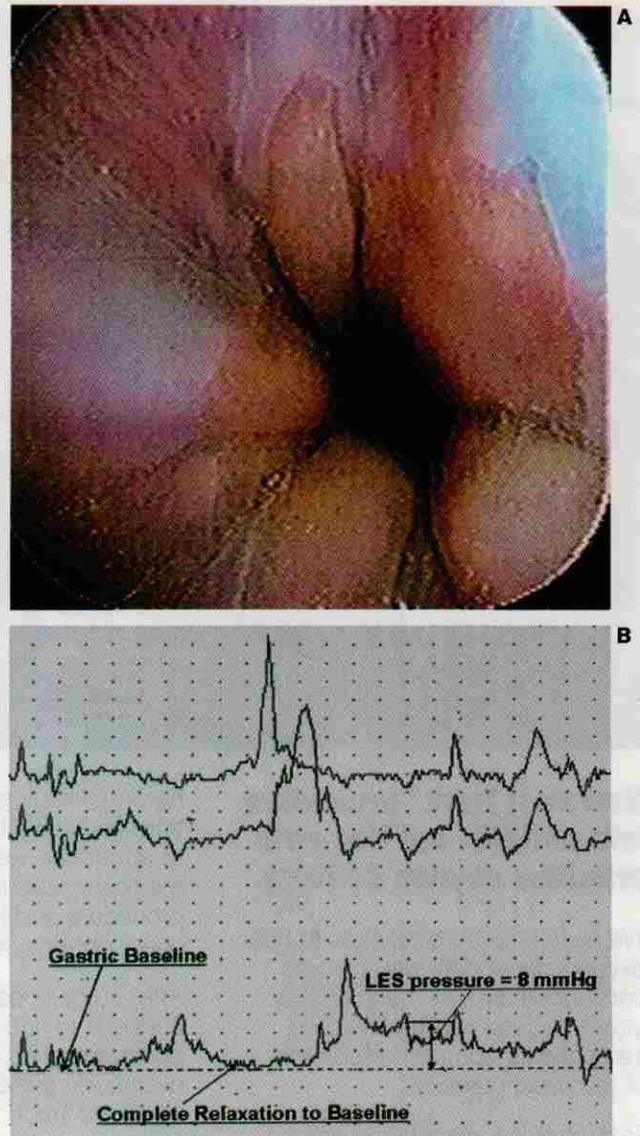


Figure 1. Patient 1. A: TNE shows the wide aperture of the LES. B: Esophageal manometry reveals that the LES pressure is low.

Continued on page 500

# CIPRO<sup>®</sup> HC OTIC

ciprofloxacin HCl  
and hydrocortisone  
otic suspension

What a difference a day makes.

www.ciprohc.com



Continued from page 498

## Get patients pain-free almost a full day sooner.<sup>1</sup>

- CIPRO<sup>®</sup> HC Otic ends ear pain 19.2 hours faster than a fluoroquinolone with no steroid
- The only steroid/fluoroquinolone combination for otitis externa
- Convenient 3•2•7 dosing (3 drops, 2 times/day for 7 days)

### BRIEF SUMMARY

#### CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

#### INDICATIONS AND USAGE

CIPRO<sup>®</sup> HC OTIC is indicated for the treatment of acute otitis externa in adult and pediatric patients, one year and older, due to susceptible strains of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Proteus mirabilis*.

#### CONTRAINDICATIONS

CIPRO<sup>®</sup> HC OTIC is contraindicated in persons with a history of hypersensitivity to hydrocortisone, ciprofloxacin or any member of the quinolone class of antimicrobial agents. This nonsterile product should not be used if the tympanic membrane is perforated. Use of this product is contraindicated in viral infections of the external canal including varicella and herpes simplex infections.

#### WARNINGS

##### NOT FOR OPHTHALMIC USE. NOT FOR INJECTION.

CIPRO<sup>®</sup> HC OTIC should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving systemic quinolones. Serious acute hypersensitivity reactions may require immediate emergency treatment.

#### PRECAUTIONS

**GENERAL:** As with other antibiotic preparations, use of this product may result in overgrowth of nonsusceptible organisms, including fungi. If the infection is not improved after one week of therapy, cultures should be obtained to guide further treatment.

#### Information for Patients:

If rash or allergic reaction occurs, discontinue use immediately and contact your physician.

Do not use in the eyes.

Avoid contaminating the dropper with material from the ear, fingers, or other sources.

Protect from light.

Shake well immediately before using.

Discard unused portion after therapy is completed.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Eight *in vitro* mutagenicity tests have been conducted with ciprofloxacin, and the test results are listed below:

- Salmonella/Microsome Test (Negative)
- E. coli* DNA Repair Assay (Negative)
- Mouse Lymphoma Cell Forward Mutation Assay (Positive)
- Chinese Hamster V79 Cell HGPRT Test (Negative)
- Syrian Hamster Embryo Cell Transformation Assay (Negative)
- Saccharomyces cerevisiae Point Mutation Assay (Negative)
- Saccharomyces cerevisiae Mitotic Crossover and Gene Conversion Assay (Negative)
- Rat Hepatocyte DNA Repair Assay (Positive)

Thus, 2 of the 8 tests were positive, but results of the following 3 *in vivo* test systems gave negative results:

- Rat Hepatocyte DNA Repair Assay
- Micronucleus Test (Mice)
- Dominant Lethal Test (Mice)

Long-term carcinogenicity studies in mice and rats have been completed for ciprofloxacin. After daily oral doses of 750 mg/kg (mice) and 250 mg/kg (rats) were administered for up to 2 years, there was no evidence that ciprofloxacin had any carcinogenic or tumorigenic effects in these species. No long term studies of CIPRO<sup>®</sup> HC OTIC have been performed to evaluate carcinogenic potential.

Fertility studies performed in rats at oral doses of ciprofloxacin up to 100 mg/kg/day revealed no evidence of impairment. This would be over 1000 times the maximum recommended clinical dose of otolopical ciprofloxacin based upon body surface area, assuming total absorption of ciprofloxacin from the ear of a patient treated with CIPRO<sup>®</sup> HC OTIC twice per day.

Long term studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical hydrocortisone. Mutagenicity studies with hydrocortisone were negative.

#### Pregnancy: Teratogenic Effects. Pregnancy Category C:

Reproduction studies have been performed in rats and mice using oral doses of up to 100 mg/kg and IV doses up to 30 mg/kg and have revealed no evidence of harm to the fetus as a result of ciprofloxacin. In rabbits, ciprofloxacin (30 and 100 mg/kg orally) produced gastrointestinal disturbances resulting in maternal weight loss and an increased incidence of abortion, but no teratogenicity was observed at either dose. After intravenous administration of doses up to 20 mg/kg, no maternal toxicity was produced in the rabbit, and no embryotoxicity or teratogenicity was observed.

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.

Animal reproduction studies have not been conducted with CIPRO<sup>®</sup> HC OTIC. No adequate and well controlled studies have been performed in pregnant women. Caution should be exercised when CIPRO<sup>®</sup> HC OTIC is used by a pregnant woman.

**Nursing Mothers:** Ciprofloxacin is excreted in human milk with systemic use. It is not known whether ciprofloxacin is excreted in human milk following topical otc administration. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric use:** The safety and efficacy of CIPRO<sup>®</sup> HC OTIC have been established in pediatric patients 2 years and older (131 patients) in adequate and well-controlled clinical trials. Although no data are available on patients less than age 2 years, there are no known safety concerns or differences in the disease process in this population which would preclude use of this product in patients one year and older. See **DOSE AND ADMINISTRATION**.

#### ADVERSE REACTIONS

In Phase 3 clinical trials, a total of 564 patients were treated with CIPRO<sup>®</sup> HC OTIC. Adverse events with at least remote relationship to treatment included headache (1.2%) and pruritus (0.4%). The following treatment-related adverse events were each reported in a single patient: migraine, hypesthesia, paresthesia, fungal dermatitis, cough, rash, urticaria, and alopecia.

NDC 0065-8531-10

CIPRO<sup>®</sup> is a registered trademark of Bayer AG.

Licensed by Bayer AG.

Manufactured by Bayer Corporation

Rx Only

U.S. Pat. Nos. 4,670,444; 4,844,902

5,843,930; and Pat. Pending

Revised January, 1999

CHC06-0199

# Alcon

ALCON LABORATORIES, INC.  
Fort Worth, Texas 76134

www.alconlabs.com

#### Reference:

1. Pistorius B, Westberry K, Drehobl M, et al. Prospective, randomized, comparative trial of ciprofloxacin otc drops, with or without hydrocortisone, vs. polymyxin B-neomycin-hydrocortisone otc suspension in the treatment of acute diffuse otitis externa. *Infect Dis in Clin Pract.* 1999;8:387-395.

©2003 Alcon, Inc.

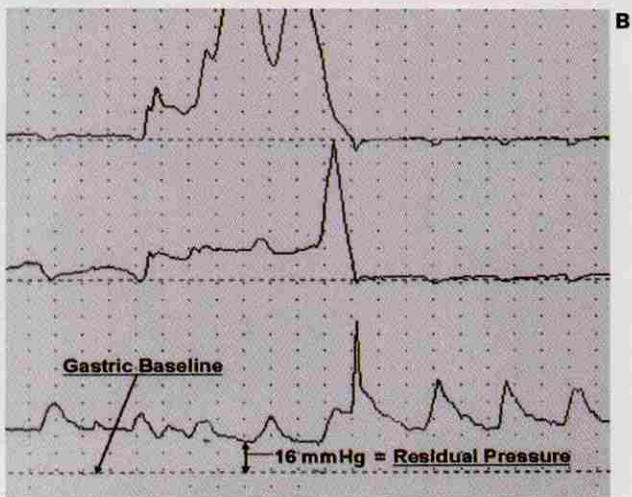


Figure 2. Patient 2. A: TNE reveals that the LES is tight. B: Esophageal manometry shows that pressures are at the high end.

## Discussion

TNE is a safe in-office procedure that allows for the direct visual examination of the esophageal and gastric mucosa. With experience, the examiner can become more familiar with the nuances of sphincter tone and peristalsis. Experience coupled with a good clinical history makes TNE a useful tool for diagnosing esophageal motility disorders.

