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News Release

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Session C29: Sensations in the Lung: Coughing and Constricting Tuesday, May 19, 2015, 9:30 a.m. – 11:30 a.m. Location: Colorado Convention Center

One Exposure to E-Cigarette Use Diminishes Cough Reflex Sensitivity

ATS 2015, DENVER—With just one exposure to electronic-cigarette (e-cigarette) vapor, participants in a study of 30 healthy subjects demonstrated a diminishment of cough reflex sensitivity. The study was presented at the 2015 American Thoracic Society International Conference.

"Although e-cigarettes have become popular worldwide, very little is known about their effect on the respiratory system. There has been no other research to our knowledge on the effect of ecigarette use on the sensitivity of the cough reflex," said lead author Peter Dicpinigaitis, MD, Professor of Clinical Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, N.Y.

The cough reflex stimulates cough to protect the upper respiratory system from the entrance of foreign material. Cough challenge testing is a standard research tool used to measure cough reflex sensitivity. In previous work, Dr. Dicpinigaitis and fellow researchers have shown that chronic tobacco cigarette smokers have reduced cough reflex sensitivity. The researchers theorized that the reduced sensitivity was caused by chronic cigarette smoke-induced desensitization of the airway cough receptors.

The 30 subjects in the current study were healthy adult lifetime nonsmokers. Researchers measured cough reflex sensitivity with the use of capsaicin, the pungent extract of red pepper. Capsaicin has been shown to safely and reproducibly induce cough in previous studies. The capsaicin cough challenge involved inhalation of single breaths of ascending doubling

concentrations of capsaicin until the concentration induced five or more coughs, which is called C_5 , was reached. Subjects underwent cough challenge at baseline (day 1), 15 minutes after they were exposed to an e-cigarette (day 2), and then 24 hours later (day 3). The e-cig "vaping" session for each patient involved 30 puffs of the disposable e-cigarette Blu (Lorillard Technologies), with each puff 30 seconds apart. This provided an exposure of 1.5 to 1.8 mg of nicotine, which is approximately that of one tobacco cigarette.

Cough reflex sensitivity was significantly diminished in subjects compared with baseline. However, 24 hours after the e-cig exposure, cough reflex sensitivity returned to baseline. The mean log C₅ at baseline was 0.50 ± 0.48 (SD), compared with 0.79 ± 0.62 15 minutes after e-cigarette exposure and 0.55 ± 0.53 at one day after exposure.

"We still need to understand the clinical significance of this effect and investigate the consequences of chronic e-cigarette exposure," Dr. Dicpinigaitis said.

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* Please note that numbers in this release may differ slightly from those in the abstract. Many of these investigations are ongoing; the release represents the most up-to-date data available at press time.

Abstract 62793 Effect of Electronic Cigarette Use on Cough Reflex Sensitivity Type: Scientific Abstract Category: 01.06 - Airway Responsiveness and Cough: Physiology and Functional Mechanisms (RSF) Authors: <u>P.V. Dicpinigaitis</u>, A. Lee Chang, A.J. Dicpinigaitis; Albert Einstein College of Medicine and Montefiore Medical Center - Bronx, NY/US

Abstract Body

Rationale: We have previously shown that chronic smokers of tobacco cigarettes have reduced cough reflex sensitivity to capsaicin compared with healthy nonsmokers, presumably on the basis of chronic cigarette smoke-induced desensitization of airway cough receptors (Eur Respir J 2006:28:786-90). The electronic cigarette (e-cig) is a device that delivers nicotine-containing vapor to the lungs without the products of combustion of tobacco and other substances found in standard tobacco cigarettes. Although e-cigs have gained widespread use worldwide, little is known about their effect on the respiratory system, and nothing, to our knowledge, about their effect on the sensitivity of the cough reflex. Capsaicin, the pungent extract of red pepper, has been shown to induce cough in a safe, dose-dependent, and reproducible manner. Thus, capsaicin

cough challenge has become an important research tool to measure the effect of an intervention on cough reflex sensitivity.

Methods: Healthy adult lifetime nonsmokers underwent cough reflex sensitivity measurement employing capsaicin cough challenge at baseline (day 1), 15 minutes after an e-cig exposure (day 2), and again 24 hr later (day 3). Capsaicin cough challenge involves inhalation of single breaths of ascending doubling concentrations of capsaicin until the concentration inducing 5 or more coughs (C_5) is attained. An e-cig "vaping" session consisted of 30 puffs of a disposable electronic cigarette (Blu, Lorillard Technologies, Greensboro, NC, USA) 30 seconds apart, thus providing an exposure of 1.5-1.8 mg nicotine, approximating that of one tobacco cigarette.

Results: 30 subjects (15 female) completed the study. After electronic cigarette exposure, cough reflex sensitivity was significantly diminished (i.e., C_5 was significantly increased) compared to baseline. This effect was transient, as demonstrated by the enhancement of cough reflex sensitivity back to baseline levels 24 hr after the e-cig exposure. Mean log C_5 at baseline was $0.50\pm0.48(SD)$; 15 minutes after electronic cigarette exposure 0.79 ± 0.62 ; and 24 hr subsequently 0.55 ± 0.53 . Employing mixed-effects modeling and after correcting for multiple comparisons using the Tukey-Kramer approach, the difference between log C_5 at baseline and post e-cig exposure was significant (p<0.0001) as was the difference between post e-cig use and 24 hours later (p=0.0002).

Conclusions: The present study demonstrates that a single, acute exposure to electronic-cigarette vapor significantly diminishes cough reflex sensitivity. The clinical significance, if any, of the transient, acute effect that we have demonstrated, as well as the consequences of chronic electronic cigarette exposure remain to be elucidated.