

News Release

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Press conference time: May 16, 4:30 p.m. in the ATS Press Room (E-1)

Poster session time: 1:30-4:00 p.m. May 18 Location: CC-Room 353-355 (Third Level), Morial Convention Center

High-Fat Meals a No-No For Asthma Patients

ATS 2010, NEW ORLEANS— People with asthma may be well-advised to avoid heavy, high-fat meals, according to new research. Individuals with asthma who consumed a high-fat meal showed increased airway inflammation just hours after the binge, according to Australian researchers who conducted the study. The high fat meal also appeared to inhibit the response to the asthma reliever medication Ventolin (albuterol).

"Subjects who had consumed the high-fat meal had an increase in airway neutrophils and TLR4 mRNA gene expression from sputum cells, that didn't occur following the low fat meal," said Dr. Lisa Wood, Ph.D., research fellow of the University of Newcastle. "The high fat meal impaired the asthmatic response to albuterol. In subjects who had consumed a high fat meal, the post-albuterol improvement in lung function at three and four hours was suppressed."

The research will be presented at the ATS 2010 International Conference in New Orleans.

Asthma prevalence has increased dramatically in westernized countries in recent decades, suggesting that environmental factors such as dietary intake may play a role in the onset and development of the disease. Westernized diets are known to be relatively higher in fat than more traditional diets.

High dietary fat intake has previously been shown to activate the immune response, leading to an increase in blood markers of inflammation. However, the effect of a high fat meal on airway inflammation, which contributes to asthma, had not been investigated.

Researchers recruited 40 asthmatic subjects who were randomized to receive either a high-fat, high-calorie "food challenge", consisting of fast food burgers and hash browns containing about 1,000 calories, 52 percent of which were from fat; or a low-fat, low-calorie meal consisting of reduced fat yogurt, containing about 200 calories, and 13 percent fat.

Sputum samples were collected before the meal and four hours afterward, and analyzed for inflammatory markers.

Subjects who had consumed the high-fat meal had a marked increase in airway neutrophils and TLR4 mRNA gene expression. TLR4 is a cell surface receptor that is activated by nutritional fatty acids: TLR4 'senses' the presence of saturated fatty acids, and prompts the cell to respond to the fatty acids as if they were an invading pathogen, releasing inflammatory mediators. While the study didn't definitively distinguish between high fat and high energy, this increase in TLR4 activity suggests that dietary fat is important to the effects.

Subjects who had consumed the high fat meal also had reduced bronchodilator response as measured by $FEV_{1\% predicted}$ and FEV1/FVC%, when compared to those had consumed the low-fat meal.

"This is the first study to show that a high fat meal increases airway inflammation, so this is a very important finding," said Dr. Wood. "The observation that a high fat meal changes the asthmatic response to albuterol was unexpected as we hadn't considered the possibility that this would occur."

The mechanism by which a high fat meal could change the bronchodilator response requires further investigation.

"We are designing more studies to investigate this effect. We are also investigating whether drugs that modify fat metabolism could suppress the negative effects of a high fat meal in the airways," said Dr. Wood. "If these results can be confirmed by further research, this suggests that strategies aimed at reducing dietary fat intake may be useful in managing asthma." "A High Fat Challenge Enhances Innate Immune Responses in Asthmatic Airways" (Session C103, Tuesday, May 18, 1:30-4:00 p.m., CC-Room 353-355 (Third Level), Morial Convention Center; Abstract 2474)

*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.

A high fat challenge enhances innate immune responses in asthmatic airways

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RATIONALE: Dietary fat activates innate immune responses, leading to an increase in systemic inflammation. However, the effect of dietary fat on airway inflammation has not been investigated. We hypothesised that a high fat intake may lead to increased airway neutrophilia in asthma. The aim of this study was to examine the effect of a high fat versus low fat food challenge on airway inflammation in asthma.

METHODS: Non-obese subjects with asthma were randomized to receive a high fat/ high energy (HF) (n=14) or low fat/ low energy (LF) (n=16) food challenge. 16 obese subjects also received a HF challenge. Subjects on the HF challenge consumed a meal containing 4480 kJ, including 52% of energy (60g) from fat. Subjects on the LF challenge consumed a meal containing 840 kJ, including 13% of energy (3g) from fat. At baseline, hypertonic saline challenge and clinical assessment were performed. Induced sputum samples were collected at baseline and at 4 hours. Airway inflammatory markers included induced sputum total and differential cell counts, IL-8 and neutrophil elastase, measured by commercial assay. TLR4 mRNA expression from sputum cells was measured using RT-PCR.

RESULTS: At 4 hours after the food challenge, subjects on the HF challenge, had a significantly higher increase in % sputum neutrophils (16.4 (4.4 (SEM)) % vs 3.4 (4.1) %, p = 0.044) and higher fold increase in TLR4 mRNA expression (2.06 (1.3-5.4 (IQR)) vs 1.00 (0.6 – 1.4), p = 0.037), compared to the LF challenge. Subjects on the HF challenge also had an impaired bronchodilator response, with a lower increase in FEV1/FVC% at 4 hours compared to the LF challenge (1.0 (-2.0-2.6 (IQR)) % vs 4.5 (2.7-6.8) %, p = 0.001). There were no differences in the responses of obese vs non-obese asthmatics to the HF challenge.

CONCLUSION: A high fat/ high energy challenge causes an increase in airway inflammation and suppresses bronchodilator response in asthma. Strategies aimed at reducing dietary fat intake may be useful in reducing inflammation in asthma.