

# Partners Asthma Center Faculty Newsletter

*Excellence in asthma care for children and adults*



*Brigham and Women's  
Hospital*

*Massachusetts General  
Hospital*

*Faulkner Hospital*

*Newton-Wellesley  
Hospital*

*North Shore Medical  
Center*

## Dr. Jack Elias to Visit Partners Asthma Center

Dr. Jack Elias, Waldemar Von Zedtwitz Professor of Medicine and Chief of Pulmonary and Critical

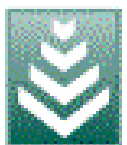


Care Medicine at Yale University School of Medicine, will visit Partners Asthma Center on January 13 and 14, 2005.

He will be speaking at ***Asthma Grand Rounds*** on Friday morning, January 14. In his honor, we will have a Partners Asthma Center dinner at the Hampshire House

on Thursday evening, January 13. Spouses/significant others are invited.

We will arrange for research presentations and clinical case discussions on Friday morning, 10:00 a.m.—1:00 p.m., at Brigham and Women's Hospital, and a lunch in the Ingram Library at the Brigham Pulmonary Division offices at 1:00 p.m. prior to his departure. The science, clinical discussions, and food are open to all!



# Salmeterol and the FDA: What Should We Tell our Patients?

Just when it seemed that telephone calls about the flu vaccine were beginning to taper off, our patients have begun calling about the safety of salmeterol (Serevent), an issue raised on the front pages of the *Boston Globe* and elsewhere. We are being asked repeatedly, is it safe for me to take my Serevent (and by extension, my Advair)? Here's the answer that I propose we offer in our patient newsletter, *Breath of Fresh Air*. Please let me know if you feel otherwise, at [cfanta@partners.org](mailto:cfanta@partners.org).

## **Salmeterol (Serevent): Is It Safe?**

In October, Merck Pharmaceuticals decided to withdraw its pain reliever and anti-inflammatory medication, rofecoxib (Vioxx), from the market. Post-marketing studies (that is, studies conducted after the medication had been approved for sale by the Food and Drug Administration [FDA]) found that use of Vioxx for 18 months or more was associated with a significant increase in the risk of heart attacks and strokes.

In the wake of this decision, the FDA is now being asked to review the safety of other prescription medications that were originally approved for sale in the United States but for which additional safety information has since become available. One of the five medications publicly mentioned for review is salmeterol (Serevent). Salmeterol is widely used to treat asthma and chronic obstructive pulmonary disease (COPD). Salmeterol is available for inhalation by Diskus device, either alone or in combination with an inhaled steroid, fluticasone (Flovent). The salmeterol-fluticasone combination inhaler, called Advair, is the most widely prescribed controller medication for asthma in the United States.

### ***Studying the safety of Serevent***

Why are there safety concerns about Serevent? In 1996, two years after FDA approval of Serevent, its manufacturers, GlaxoSmithKline, embarked on a large-scale experiment to assess the safety of Serevent. They felt the need to demonstrate its safety because of concerns that had been raised about potential harmful effects from regular use of this entire group of medications, called beta-agonist bronchodilators. Thousands of patients with asthma were asked to participate in this study, in which one group was given Serevent to take twice-daily and the other group received a placebo inhaler. Both groups of patients were advised to take their other usual asthma medications as they had before. The study lasted just over 6 months, and the question asked was: were there any differences in harmful respiratory outcomes in the two groups; that is, did one group have more asthma deaths or near-deaths (respiratory failure requiring use of a ventilator) than the other group?

The study, called the SMART study as an acronym for Salmeterol Multi-center Asthma Research Trial) was stopped in 2002 after approximately 26,000 persons with asthma (of the intended 60,000) had been enrolled. The study was stopped because of a trend toward more asthma deaths (13 vs. 4) and life-threatening asthma events (36 vs. 23) in the Serevent-treated group. When the scientists conducting the study examined subgroups of patients, they found the following disturbing results:

- among African-Americans, more deaths and near-deaths from asthma occurred in those given Serevent than in those given placebo; and

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- among patients with asthma not using an inhaled steroid as a preventive (controller) medication, again more deaths and near-deaths from asthma occurred in those given Serevent than in those given placebo. Only 38% of the African-Americans who participated in the study used an inhaled steroid.

Before continuing with our interpretation of these results, we need to acknowledge that publication of this newsletter, *Breath of Fresh Air*, is made possible in part by a generous educational grant from the makers of Serevent, GlaxoSmithKline.

### What accounts for these findings?

The explanation for the findings in the SMART study – why Serevent was associated with more bad asthma outcomes – is unknown. Some have speculated that taking an effective bronchodilator (to open the breathing passageways by relaxing the bronchial muscles) without taking an anti-inflammatory medication (to prevent swelling of the walls of the bronchial tubes and excess mucus production) can lead to life-threatening asthmatic attacks because one is deceived into feeling that one's breathing is satisfactory while all the while the breathing passageways become more swollen and clogged. Other explanations are possible, however, and future research will be needed to answer this question of "why?"

As a result of the findings from the SMART study, a warning was added to the informational insert provided with each package of Serevent and Advair inhalers.

**WARNING:** *Data from a large placebo-controlled US study that compared the safety of salmeterol (SEREVENT Inhalation Aerosol) or placebo added to usual asthma therapy showed a small but significant increase in asthma-related deaths in patients receiving salmeterol (13 deaths out of 13,174 patients treated for 28 weeks) versus those on placebo (4 of 13,179). Subgroup analyses suggest the risk may be greater in African-American patients compared to Caucasians.*

Additional advice in the package insert suggests that

*Patients should not stop SEREVENT or ADVAIR therapy for asthma or SEREVENT for COPD without physician/provider guidance since symptoms may recur after discontinuation.*

The question that may now go before the FDA is: should anything more be done to ensure patient safety, including potentially removing Serevent and Advair from the market?

### What would you recommend?

Imagine that you are a member of the advisory board reviewing this information. You know of the concerns about the safety of Serevent, and you know too of the benefits of its use in combination with anti-inflammatory medications – fewer symptoms, improved lung function, fewer asthmatic attacks, and avoidance of the need for higher doses of inhaled steroids. You know that literally millions of people feel that they have been greatly helped by these drugs. What would you advise?

We at Partners Asthma Center continue to prescribe Serevent and Advair. We feel that the benefits outweigh the potential risks. We do not recommend that Serevent be used unless a patient with asthma is also taking a regular anti-inflammatory medication. And we believe that the best protection against life-threatening asthmatic attacks is not removal of long-acting beta-agonist bronchodilators from the market but good medical follow-up, knowledge about asthma and about the warning signs of severe asthmatic attacks, and a plan of action in the event that you suffer a severe asthmatic attack. Remember that the bad outcomes in the SMART study were life-threatening asthmatic attacks. You can remain safe from such attacks with good medicines and good medical care.

## Other Partners Asthma Center Events and News

### **Asthma Grand Rounds**

**Friday, January 14, 8:30 a.m.**

*New Therapeutic Targets in Asthma*

**Dr. Jack Elias**

Location: BWH Bornstein Family Amphitheater  
Videoconferencing: MGH (Lawrence House)  
NSMC (MAC-4, Davenport)

### **News from the Asthma Educators' Institute**

The *Becoming an Asthma Educator* course on Nov. 13 at NSMC attracted nearly 100 participants (despite the snowfall!). Congratulations to **Dr. Philip Thielhelm** and to all participating faculty from the allergy and pulmonary groups at NSMC.

**Dr. Ivan Soto-Arapé** has extended the outreach of Partners Asthma Center to Uphams Corner Health Center in Dorchester. He provides pulmonary and asthma consultations once per month, and will begin spirometry testing on-site with technical support from Jacqueline Rodriguez-Louis.







Partners Asthma Center

*Excellence in asthma care for children and adults*

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Partners Asthma Center  
75 Francis Street  
Boston, MA 02115  
Phone: 1-800-9PARTNERS  
Fax: (617) 732-7421  
Email: [asthma@partners.org](mailto:asthma@partners.org)

*Save the Date:*  
Dinner to honor Visiting Professor, *Dr. Jack Elias*  
**Thursday, January 13**  
**Hampshire House, Boston**



*Water lilies, Summer, 2004*