

# Secondhand Smoke Raises Boys' Blood Pressure

BY M. ALEXANDER OTTO

FROM THE ANNUAL MEETING OF THE  
PEDIATRIC ACADEMIC SOCIETIES

DENVER – There's a new reason to keep children away from secondhand smoke: It raises systolic blood pressure in boys, a University of Wisconsin, Madison, study suggests.

However, the mean increase was minimal – just 1.6 mm Hg – when researchers compared boys exposed to secondhand smoke with those who were not. “For an individual child, that's not necessarily something you would worry

link between secondhand smoke and blood pressure changes in children. Secondhand smoke already is known to decrease lung growth, increase the risk for sudden infant death, and cause respiratory problems in children, among other factors.

Conversely, Dr. Baumgartner and her colleagues also discovered that girls exposed to secondhand smoke had slightly lower systolic blood pressure than did

other girls, a mean of 1.8 mm Hg.

“I think there could be something going on there, but we are not sure what it is,” she said.

“It's actually supported in the academic literature” that smoking raises blood pressure in males but can have the opposite effect in females.

She hesitated to call female sex a protective factor, because the drop in blood pressure could signal some other dele-

terious effect of smoke exposure.

In their cross-sectional retrospective analysis, the researchers mined National Health and Nutrition Examination Survey data from 1999-2006, identifying 6,421 children aged 8-17, 52% girls, 34% white, 27% Mexican American, and about 32% exposed to secondhand smoke.

They defined exposure as having at least one smoker in the house and by



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**Tobacco smoke exposure raised BP in boys, but lowered it in girls.**

about” in the short term, lead investigator and environmental health research fellow Jill Baumgartner, Ph.D., said the meeting.

Still, elevated blood pressure in childhood can lead to adult hypertension and, “We found a similar [blood pressure] effect for children exposed to really low levels as for children exposed to higher levels, [reinforcing] the notion that there really is no acceptable exposure level for secondhand smoke,” she said.

The study by Dr. Baumgartner and her colleagues is the first to demonstrate a

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of first symptomatic or asymptomatic AFib recurrence<sup>1</sup>

- Absolute difference in recurrence rate of about 11% at 1 year ( $P < 0.001$ ; primary endpoint)
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of MULTAQ patients were free of symptomatic AFib recurrence vs 54% on placebo at 1 year ( $P < 0.001$ ; secondary endpoint)<sup>1</sup>

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in CV hospitalization or mortality, the combined primary endpoint ( $P < 0.0001$ , entirely attributable to CV hospitalizations)<sup>2,3</sup>

\*Relative risk reduction (RRR) observed over the study period (median 22-month treatment and follow-up; minimum 12 months, maximum 30 months).<sup>2,3</sup>

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### Important Safety Information

MULTAQ is contraindicated in patients with NYHA Class IV heart failure, or NYHA Class II–III heart failure with a recent decompensation requiring hospitalization or referral to a specialized heart failure clinic. In the ANDROMEDA Study, a greater than two-fold increase in mortality was observed in this unstable population (see full boxed WARNING).

**Important Update:** Hepatocellular liver injury, including acute liver failure requiring transplant, has been reported in patients treated with MULTAQ in the postmarketing setting. A liver injury section has been added to the Important Safety Information.

Please see additional Important Safety Information and brief summary of Prescribing Information, including boxed WARNING, on adjacent pages.

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## VITALS

**Major Finding:** Exposure to secondhand smoke increases the blood pressure of boys aged 8-17 by a mean of 1.6 mm Hg.

**Data Source:** National Health and Nutrition Examination Survey

**Disclosures:** Dr. Baumgartner said she has no disclosures. The study was funded by an Academic Pediatric Association Young Investigators Grant.

serum cotinine levels of 0.01-14 ng/mL. Children with levels above 14 ng/mL were excluded because that level of the nicotine metabolite indicates that they themselves smoke. Having a smoker in

body mass index, physical activity, survey year, health insurance, household income, and potassium, caffeine, and sodium intake.

There was no dose-response relation-

the house strongly correlated with cotinine levels.

Through matching and statistical adjustments, the researchers controlled for a range of confounding variables, including age, sex,

ship between cotinine levels and blood pressure. Elevations were similar in boys and drops similar in girls across cotinine levels.

In exposed boys, increases in systolic blood pressure ranged from 1 to 1.9 mm Hg. In exposed girls, drops ranged from 1.5 to 2.6 mm Hg. Both results were statistically significant.

"If you looked at higher doses, you might see a dose response, but in this range of exposure, because it's so low" it wasn't apparent, Dr. Baumgartner said.

The next step is a longitudinal study

to see whether blood pressure changes vary with variations in secondhand smoke exposure.

"We are also trying to better understand the biologic drivers of tobacco smoke and blood pressure in kids," she said.

In the meantime, "If you are physician and have a parent coming in saying 'I am reducing the amount I'm smoking,' we are showing that's not quite enough. [They] need to stop smoking, because even at really low levels, exposure is having an effect on kids and their blood pressure," she said. ■

## Important Safety Information for MULTAQ®

### Contraindications

#### WARNING: HEART FAILURE

MULTAQ is contraindicated in patients with NYHA Class IV heart failure, or NYHA Class II–III heart failure with a recent decompensation requiring hospitalization or referral to a specialized heart failure clinic.

In a placebo-controlled study in patients with severe heart failure requiring recent hospitalization or referral to a specialized heart failure clinic for worsening symptoms (the ANDROMEDA Study), patients given MULTAQ had a greater than two-fold increase in mortality. Such patients should not be given MULTAQ.

- MULTAQ is also contraindicated in patients with second- or third-degree atrioventricular (AV) block or sick sinus syndrome (except when used in conjunction with a functioning pacemaker), bradycardia <50 bpm, QTc Bazett interval ≥500 msec or PR interval >280 msec, and severe hepatic impairment
- MULTAQ should not be given to patients who are or may become pregnant (Category X) or nursing. MULTAQ may cause fetal harm when administered to a pregnant woman
- MULTAQ should not be coadministered with strong CYP 3A inhibitors, such as ketoconazole, itraconazole, voriconazole, cyclosporine, telithromycin, clarithromycin, nefazodone, ritonavir, or drugs or herbal products that prolong the QT interval and might increase the risk of Torsade de Pointes, such as phenothiazine antipsychotics, tricyclic antidepressants, certain macrolide antibiotics, and Class I and III antiarrhythmics

### New or Worsening Heart Failure

Postmarketing cases of new onset and worsening heart failure have been reported during treatment with MULTAQ. Advise patients to consult a physician if they develop signs and symptoms of heart failure, such as weight gain, dependent edema, or increasing shortness of breath. If heart failure develops or worsens, consider the suspension or discontinuation of MULTAQ.

### Liver Injury

Hepatocellular liver injury, including acute liver failure requiring transplant, has been reported in patients treated with MULTAQ in the postmarketing setting. Advise patients treated with MULTAQ to report immediately symptoms suggesting hepatic injury (such as anorexia, nausea, vomiting, fever, malaise, fatigue, right upper quadrant pain, jaundice, dark urine, or itching).

Consider obtaining periodic hepatic serum enzymes, especially during the first 6 months of treatment. It is not known whether routine periodic monitoring of serum enzymes will prevent the development of severe liver injury. If hepatic injury is suspected, promptly discontinue MULTAQ and test serum enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase, as well as serum bilirubin, to establish whether there is liver injury. If liver injury is found, institute appropriate treatment and investigate the probable cause. Do not restart MULTAQ in patients without another explanation for the observed liver injury.

### Hypokalemia and Hypomagnesemia with Potassium-Depleting Diuretics

Hypokalemia and hypomagnesemia may occur with concomitant administration of potassium-depleting diuretics. Potassium levels should be within the normal range prior to administration of MULTAQ and maintained in the normal range during administration of MULTAQ.

### QT Interval Prolongation

MULTAQ induces a moderate (average of about 10 msec but much greater effects have been observed) QTc (Bazett) prolongation. If the QTc Bazett interval is ≥500 msec, MULTAQ should be stopped.

### Increase in Creatinine

Serum creatinine levels increase by about 0.1 mg/dL following MULTAQ treatment initiation. The elevation has a rapid onset, reaches a plateau after 7 days and is reversible after discontinuation. If an increase in serum creatinine occurs and plateaus, this increased value should be used as the patient's new baseline. The change in creatinine levels has been shown to be the result of an inhibition of creatinine's tubular secretion, with no effect upon the glomerular filtration rate.

### Drug-Drug Interactions

- Treatment with Class I or III antiarrhythmics or drugs that are strong inhibitors of CYP 3A must be stopped before starting MULTAQ (see Contraindications)
- Patients should be instructed to avoid grapefruit juice beverages while taking MULTAQ
- Calcium channel blockers and beta-blockers could potentiate the effects of MULTAQ on conduction
- Increased digoxin levels and gastrointestinal disorders have been observed when MULTAQ was coadministered with digoxin. Digoxin can also potentiate the electrophysiologic effects of MULTAQ (such as decreased AV-node conduction); the need for digoxin therapy should be reconsidered when prescribing MULTAQ. If digoxin treatment is continued, halve the dose of digoxin, monitor serum levels closely, and observe for toxicity
- Postmarketing cases of increased INR with or without bleeding events have been reported in warfarin-treated patients initiated with MULTAQ. Monitor INR after initiating MULTAQ in patients taking warfarin

### Adverse Reactions

In studies, the most common adverse reactions observed with MULTAQ were diarrhea, nausea, abdominal pain, vomiting, and asthenia.

**Please see brief summary of Prescribing Information, including boxed WARNING, on adjacent pages.**

**References:** 1. Singh BN, Connolly SJ, Crijns HJGM, et al; for the EURIDIS and ADONIS Investigators. Dronedarone for maintenance of sinus rhythm in atrial fibrillation or flutter. *N Engl J Med.* 2007;357:987-999. 2. MULTAQ® (dronedarone) Prescribing Information. Sanofi-aventis U.S. LLC; 2011, Bridgewater, NJ. 3. Hohnloser SH, Crijns HJGM, van Eickels M, et al; for the ATHENA Investigators. Effect of dronedarone on cardiovascular events in atrial fibrillation. *N Engl J Med.* 2009;360:668-678.