

# Hypertension Diagnosis Often Missed in Children

BY MITCHEL L. ZOLER  
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NEW ORLEANS — A diagnosis of hypertension was missed in 85% of children with high blood pressure in a study of 287 youngsters who were examined at two university-based, pediatric clinics.

The problem with diagnosing hypertension in kids is that there are too many threshold pressures for most physicians to keep straight, Charlene K. Mitchell, M.D.,

said at the annual meeting of the Southern Society for Pediatric Research.

Because the threshold for diagnosing hypertension varies by age, height, and gender, there are a total of 420 different diastolic and systolic pressures that determine whether a particular child has high blood pressure, said Dr. Mitchell, a pediatrician and internist at the University of Louisville (Ky.).

The total is 420 because there are 15 different age-specific threshold pressures for children aged 3-17 years, 7 different height-specific threshold pressures between the 5th and 95th height percentiles, different thresholds for girls and boys, and different thresholds for diastolic and systolic pressure.

The threshold criteria for borderline hypertension would add another 120 pressure thresholds for diagnosing hypertension.

"The numbers are chopped up too much. It's far too complex for easy man-

agement," Dr. Mitchell said. "If physicians must always look on a table every time they check a blood pressure, we'll continue to see underdiagnosis."

Her solution to the number surfeit is to cluster several ages with a single diagnostic pressure threshold. However, eventually she would like to have study results establish pressure thresholds for diagnosing hypertension that are empirically derived, rather than based on statistics. If the diagnostic criteria are simplified, physicians will be much more likely to identify hypertension in children much more often, Dr. Mitchell said.

"We need to be much more aggressive about recognizing hypertension in children than we are now," she added.

Her study was designed to assess physician accuracy at identifying hypertension in children aged 3-17 years being seen for routine, well-child visits from July 31 to Aug. 15, 2003. Of the 287 children examined, 90 (31%) had hypertension by current standards, and 35 (12%) had borderline hypertension. But only 15% of those with hypertension were diagnosed by their examining physicians.

The results also showed that physicians were more likely to diagnose hypertension in children with a higher body mass index (BMI).

The children who were correctly diagnosed as hypertensive were, on average, in the 92nd percentile for BMI. Those who had unrecognized blood pressure elevations were, on average, in the 76th percentile for BMI. ■

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**Ezetimibe:** The pharmacokinetics of ezetimibe in adolescents (10 to 18 years) have been shown to be similar to that in adults. Treatment experience with ezetimibe in the pediatric population is limited to 4 patients (9 to 17 years) with homozygous sitosterolemia and 5 patients (11 to 17 years) with HoFH. Treatment with ezetimibe in children (<10 years) is not recommended.

**Simvastatin:** Safety and effectiveness of simvastatin in patients 10-17 years of age with heterozygous familial hypercholesterolemia have been evaluated in a controlled clinical trial in adolescent boys and in girls who were at least 1 year post-menarche. Patients treated with simvastatin had an adverse experience profile generally similar to that of patients treated with placebo. **Doses >40 mg have not been studied in this population.** In this limited controlled study, there was no detectable effect on growth or sexual maturation in the adolescent boys or girls, or any effect on menstrual cycle length in girls. Adolescent females should be counseled on appropriate contraceptive methods while on therapy with simvastatin (see CONTRAINDICATIONS and PRECAUTIONS, Pregnancy). Simvastatin has not been studied in patients younger than 10 years of age, nor in pre-menarchal girls.

**Geriatric Use:** Of the patients who received VYTORIN™ (ezetimibe/simvastatin) in clinical studies, 792 were 65 and older (this included 176 who were 75 and older). The safety of VYTORIN was similar between these patients and younger patients. Greater sensitivity of some older individuals cannot be ruled out. (See CLINICAL PHARMACOLOGY, Special Populations and ADVERSE REACTIONS.)

**ADVERSE REACTIONS:** VYTORIN has been evaluated for safety in more than 3800 patients in clinical trials. VYTORIN was generally well tolerated. Table 1 summarizes the frequency of clinical adverse experiences reported in ≥2% of patients treated with VYTORIN (n=1236) and at an incidence greater than placebo regardless of causality assessment from 3 similarly designed, placebo-controlled trials.

**Table 1\***  
Clinical Adverse Events Occurring in ≥2% of Patients Treated with VYTORIN and at an Incidence Greater than Placebo, Regardless of Causality

Body System/ Organ Class Adverse Event	Placebo (%) n=311	Ezetimibe 10 mg (%) n=302	Simvastatin** (%) n=1234	VYTORIN** (%) n=1236
<b>Body as a whole - general disorders</b>				
Headache	6.4	6.0	5.9	6.8
<b>Infection and infestations</b>				
Influenza	1.0	1.0	1.9	2.6
Upper respiratory tract infection	2.6	5.0	5.0	3.9
<b>Musculoskeletal and connective tissue disorders</b>				
Myalgia	2.9	2.3	2.6	3.5
Pain in extremity	1.3	3.0	2.0	2.3

\* Includes 2 placebo-controlled combination studies in which the active ingredients equivalent to VYTORIN were coadministered and 1 placebo-controlled study in which VYTORIN was administered.

\*\* All doses.

**Ezetimibe:** Other adverse experiences reported with ezetimibe in placebo-controlled studies, regardless of causality assessment: *Body as a whole - general disorders:* fatigue; *Gastrointestinal system disorders:* abdominal pain, diarrhea; *Infection and infestations:* infection viral, pharyngitis, sinusitis; *Musculoskeletal system disorders:* arthralgia, back pain; *Respiratory system disorders:* coughing.

**Post-marketing Experience:** The following adverse reactions have been reported in post-marketing experience, regardless of causality assessment:

**Hypersensitivity reactions,** including angioedema and rash; increased CPK; elevations in liver transaminases; hepatitis; thrombocytopenia; pancreatitis; nausea; cholelithiasis; cholecystitis; and, very rarely in patients taking an HMG-CoA reductase inhibitor with ezetimibe, rhabdomyolysis (see WARNINGS, Myopathy/Rhabdomyolysis).

**Simvastatin:** Other adverse experiences reported with simvastatin in placebo-controlled clinical studies, regardless of causality assessment: *Body as a whole - general disorders:* asthenia; *Eye disorders:* cataract; *Gastrointestinal system disorders:* abdominal pain, constipation, diarrhea, dyspepsia, flatulence, nausea; *Skin and subcutaneous tissue disorders:* eczema, pruritus, rash.

The following effects have been reported with other HMG-CoA reductase inhibitors. Not all the effects listed below have necessarily been associated with simvastatin therapy. *Musculoskeletal system disorders:* muscle cramps, myalgia, myopathy, rhabdomyolysis, arthralgias.

*Nervous system disorders:* dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, dizziness, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy, psychic disturbances. *Ear and labyrinth disorders:* vertigo.

*Psychiatric disorders:* anxiety, insomnia, depression, loss of libido.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included 1 or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, dermatomyositis, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, eosinophilia, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

*Gastrointestinal system disorders:* pancreatitis, vomiting. *Hepatobiliary disorders:* hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma.

*Metabolism and nutrition disorders:* anorexia. *Skin and subcutaneous tissue disorders:* alopecia, pruritus. A variety of skin changes (eg, nodules, discoloration, dryness of skin/mucous membranes, changes to hair/nails) have been reported.

*Reproductive system and breast disorders:* gynecostasia, erectile dysfunction. *Eye disorders:* progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Abnormalities:** elevated transaminases, alkaline phosphatase, γ-glutamyl transpeptidase, and bilirubin; thyroid function abnormalities.

**Laboratory Tests:** Marked persistent increases of serum transaminases have been noted (see WARNINGS, Liver Enzymes). About 5% of patients taking simvastatin had elevations of CK levels of 3 or more times the normal value on 1 or more occasions. This was attributable to the noncardiac fraction of CK. Muscle pain or dysfunction usually was not reported (see WARNINGS, Myopathy/Rhabdomyolysis).

**Concomitant Lipid-Lowering Therapy:** In controlled clinical studies in which simvastatin was administered concomitantly with cholestyramine, no adverse reactions peculiar to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with simvastatin or cholestyramine.

**Adolescent Patients (ages 10-17 years):** In a 48-week controlled study in adolescent boys and girls who were at least 1 year post-menarche, 10-17 years of age with heterozygous familial hypercholesterolemia (n=175), the safety and tolerability profile of the group treated with simvastatin (10-40 mg daily) was generally similar to that of the group treated with placebo, with the most common adverse experiences observed in both groups being upper respiratory infection, headache, abdominal pain, and nausea (see CLINICAL PHARMACOLOGY, Special Populations and PRECAUTIONS, Pediatric Use).

## Ethnicity Affects Some Measures of Kawasaki

BY DOUG BRUNK  
San Diego Bureau

SAN DIEGO — African American children with Kawasaki disease are more likely to have higher documented fevers in the hospital, higher erythrocyte sedimentation rates, and higher C-reactive protein levels than their white counterparts, Ian C.

Balfour, M.D., reported in a poster session at an international Kawasaki disease symposium.

Although the disparity may be related to genetic differences between African Americans and whites, Dr. Balfour noted that more research is needed to further understand the association.

"At this time, I can't say there is a take-home message," Dr. Balfour, a pediatric cardiologist with St. Louis University, told FAMILY PRACTICE NEWS in an interview. "I think we need further study to determine why certain patients have higher erythrocyte sedimentation rates and higher levels of C-reactive protein."

For the study, which he called the first of its kind, Dr. Balfour and his associates reviewed the records of 124 children admitted to Cardinal Glennon Children's Hospital in St. Louis between Jan. 1, 1995, and Dec. 31, 2002, with a diagnosis of Kawasaki disease.

The investigators used analysis of variance and chi-squared testing to analyze

differences between African American and white children.

A greater number of African American patients presented with Kawasaki disease before age 6 years, compared with white patients (97.4% vs. 76.3%), but the difference was not statistically significant.

African American children had significantly higher mean fever upon hospital admission, compared with white children (102.2° F vs. 101.3° F).

The African American children also had significantly higher mean erythrocyte sedimentation rates (72.9 mm/hr vs. 55.9 mm/hr).

C-reactive protein levels also differed significantly between the two groups. African American children had mean C-reactive protein levels of 22.3 mg/L vs. 6.9 mg/L among their white counterparts.

Dr. Balfour noted that coronary artery involvement was similar between the two groups.

The symposium was sponsored by the American Heart Association. ■

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multiple clinical parameters in relation to ethnic origin.

Of the 124 children, 76 (61%) were white, 38 (31%) were African American, 7 (6%) were Asian, and 3 (2%) were from other ethnic groups. Age at presentation ranged from 2 to 11 years.

Because the number of Asian patients and those from other ethnicities was so small, Dr. Balfour only discussed clinical

## Exercise Program Lowered Diastolic BP in Preschoolers

BY BRUCE JANCIN  
Denver Bureau

ORLANDO, FLA. — It's never too early to make lifestyle changes aimed at reducing cardiovascular risk, findings from a new German study show.

A group of German preschoolers had significantly improved cardiovascular risk profiles as well as "tremendously" enhanced motor development, in response to a structured exercise program, Kerstin S. Ketelhut, M.D., re-

ported at the annual meeting of the American College of Cardiology.

Given the worsening epidemics of obesity and metabolic syndrome among people of all ages in industrialized countries and the worrisome implications for future cardiovascular disease rates, it's high time to focus more attention on the merits of regular exercise in nursery and elementary schools as a safe, effective, and low-cost intervention for primary cardiovascular prevention, argued Dr. Ketelhut of

the University of Potsdam (Germany).

She reported on a 2-year controlled study of the effects of introducing a regular exercise program to 160 youngsters when they were 3 years old and attending any one of 17 Berlin-area nursery schools; 105 classmates served as controls.

The program involved three 45-minute structured workout sessions per week. Study end points were changes in blood pressure, resting heart rate, body mass index, and perfor-

mance on standardized motor tests involving running, jumping, balance, and coordination.

At 2 years, mean diastolic blood pressure in the exercise-intervention group was 65.7 mm Hg, significantly lower than the 68.1 mm Hg in controls. Systolic blood pressure, heart rate, and body mass index didn't differ significantly between the two groups. But the exercise-intervention group scored markedly better than controls in all four domains of the standardized motor testing. ■

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