

# Hybrid Type Diabetes Found in 18% of Obese Kids

BY CHRISTINE KILGORE  
Contributing Writer

WASHINGTON — A preliminary look at the children referred for participation in a large treatment trial of type 2 diabetes in overweight and obese youth shows that the children not only have a high prevalence of hypertension and dyslipidemia, but a high incidence of autoantibody positivity as well, investigators reported at the annual scientific sessions of the American Diabetes Association.

The findings add to those of other studies suggesting that a significant number of children with apparent type 2 diabetes mellitus also may have diabetes autoim-



**The number of youth with diabetes autoimmunity with characteristics of type 2 diabetes is likely higher.**

DR. KLINGENSMITH

munity consistent with type 1 diabetes, reported Dr. Georgeanna J. Klingensmith, director of pediatric clinics at the Barbara Davis Center for Childhood Diabetes in Aurora, Colo.

Approximately 18% of the 535 children screened for inclusion thus far in the 15-center, National Institutes of Health-sponsored Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study were found to be positive for diabetes autoimmunity. The children, who were racially and ethnically diverse, were considered by their pediatric endocrinologists to have type 2 diabetes.

The number of youth with diabetes autoimmunity in conjunction with characteristics of type 2 diabetes is likely much higher, however, because some potential study participants were locally prescreened for autoantibodies and were not even sent to the TODAY study investigators. The presence of islet cell autoimmunity is an exclusion criterion for the study, Dr. Klingensmith said.

Indeed, other studies have reported higher rates of what some physicians and investigators are now calling “double,” “hybrid,” or “type 3” diabetes.

Investigators of a large British study, for instance, reported almost 10 years ago that 33% of 157 young adults with type 2 diabetes were found to be positive for diabetes-associated antibodies. And, just this year, investigators of a German study reported that 36% of 128 children thought to have type 2 diabetes also had diabetes-associated antibodies, Dr. Klingensmith said.

Dr. Ingrid M. Libman of the Children’s Hospital in Pittsburgh said in another presentation that the “spectrum” of diabetes now presenting in youth presents treatment dilemmas.

“If insulin therapy preserves B-cell function, should all patients that phenotypically look like type 2 but have antibodies be treated with insulin?” she asked. “And should patients [with type 1 and obesity]

be treated with insulin sensitizers?”

There have been few studies on treatment for “double” diabetes, she continued. Children who are registered in the Allegheny County Registry for diabetes and the Children’s Hospital Registry who have characteristics of both type 1 (antibodies and/or ketones and diabetic ketoacidosis, for instance) and type 2 (obesity and/or acanthosis nigricans) are being treated in their communities with either insulin alone or with insulin and an

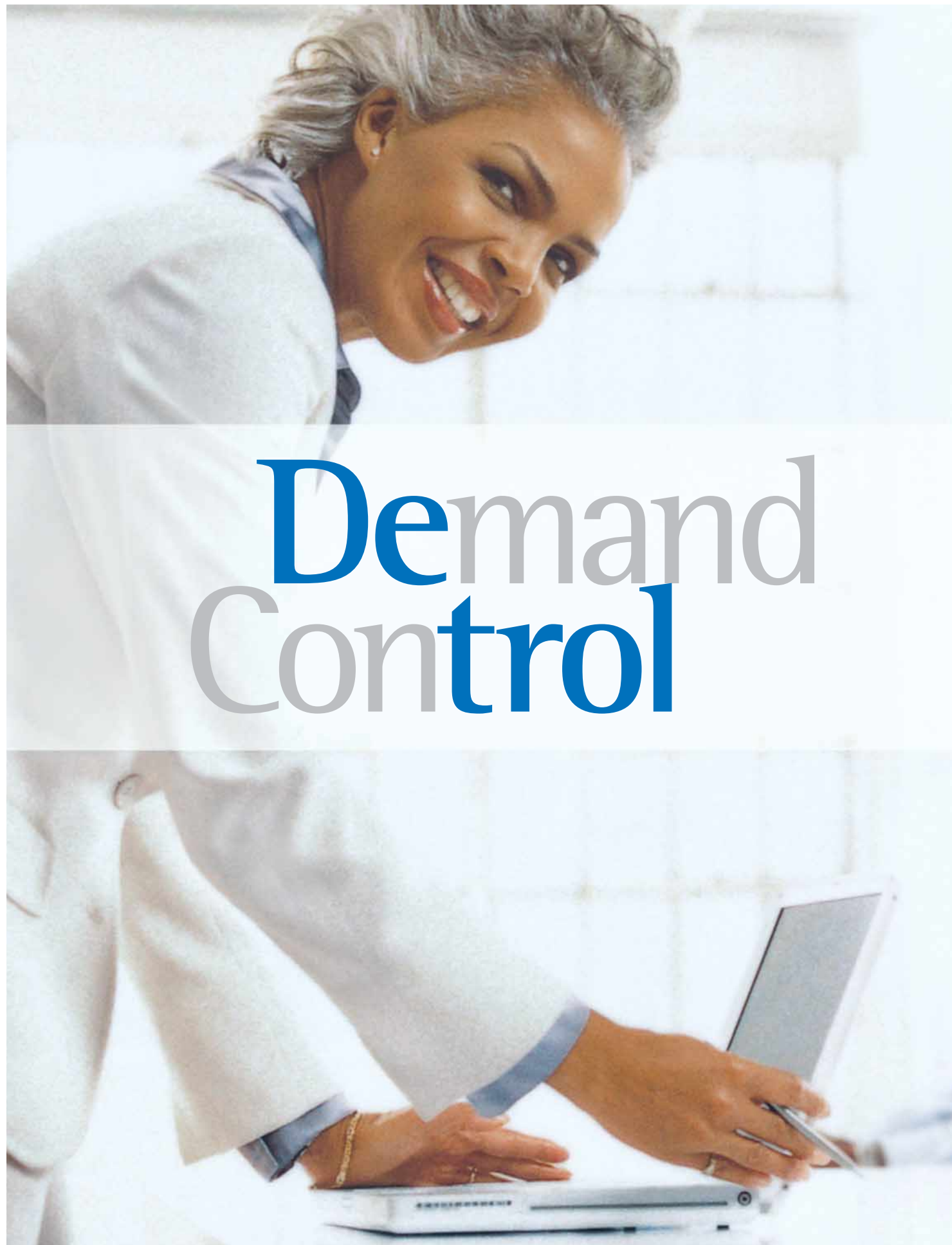
oral agent, mainly metformin, she said.

It is possible that obesity and insulin resistance may accelerate the presentation of type 1 diabetes in patients with type 2, said Dr. Libman.

The children being enrolled in the TODAY study, in addition to having an absence of islet cell autoimmunity, must have had diabetes for 2 years or less, be 10-17 years of age, and have a fasting C-peptide greater than 0.6 ng/mL and a body mass index at the 85th percentile or above.

Participants will be randomized to receive metformin alone, metformin and rosiglitazone, or metformin and intensive lifestyle therapy.

Of the 535 children who were screened for inclusion in the TODAY study, approximately 5% had only glutamic acid decarboxylase (GAD) autoantibodies and 6% had only IA-2 autoantibodies. Approximately 7% had both GAD and IA-2 autoantibodies. All told, 18% were positive for one or both of the antibodies measured.



Dr. Klingensmith and her coinvestigators also looked at the number of children who had very high titer antibody levels. They found that 12% of the children screened—and 65% of all antibody-positive children—were either positive for both autoantibodies or had antibody titers that were more than 300% above normal (above the cut-off point for positivity).

They found that there were no differences between the groups in age, gender, or duration of diabetes. Children with both antibodies, however, had lower C-peptide levels, BMI and triglyceride levels, as well as higher HDL cholesterol and HbA<sub>1c</sub> levels, and greater insulin use than

did children with no antibodies, Dr. Klingensmith said.

According to Dr. Neil H. White, director of the division of pediatric endocrinology and metabolism at St. Louis University who is also a TODAY study investigator, approximately 12% of the children were receiving insulin alone at the time of screening for the study, and almost 50% were receiving metformin only. Approximately 25% were receiving both. The remaining children were receiving other medications or no treatment at all.

In terms of comorbidities, he reported, 26% had hypertension and almost 60% had dyslipidemia.

It remains to be seen whether diabetes autoimmunity will alter the clinical course of the disorder in youth with the clinical features of type 2 diabetes, Dr. Klingensmith said.

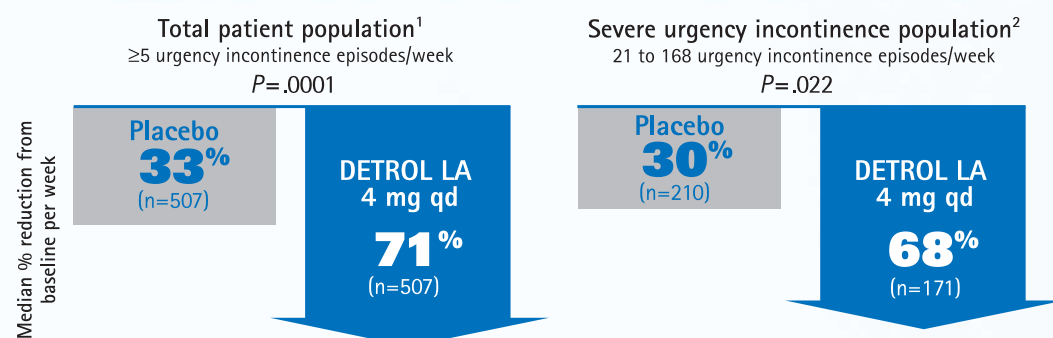
When it comes to the risk of conditions and complications traditionally associated with type 1 diabetes, it very well may, Dr. Libman warned.

Current guidelines, for instance, recommend screening for autoimmune thyroid disease in children with type 1 diabetes who, in contrast to those with type 2 diabetes, are known to have an increased frequency of thyroid antibodies and thyroid dysfunction. But a look at a

sample of children in the Pittsburgh registries shows that children with “double” diabetes may have the same prevalence of thyroid antibodies as do those with type 1 diabetes.

Twenty percent of 24 children with double diabetes (defined here as obese with diabetes antibodies) were positive for thyroid antibodies, as were 21% of 117 children with type 1 diabetes (lean with diabetes antibodies). The two groups had a similar incidence of hypothyroidism. A sample of 21 children with type 2 diabetes (obese with no diabetes antibodies) had neither problem, Dr. Libman reported. ■

## DETROL LA is the #1 prescribed brand for OAB\*— with **BIG REDUCTIONS** in OAB symptoms<sup>1,2</sup>



Van Kerrebroeck et al. *Urology*. 2001;57:414-421.<sup>1</sup>  
A 12-week, placebo-controlled OAB study.  
See full study description on next page.

Landis et al. *J Urol*. 2004;171:752-756.<sup>2</sup>  
A post hoc subgroup analysis of Van Kerrebroeck et al.  
See full study description on next page.

DETROL LA is indicated for the treatment of overactive bladder with symptoms of urge incontinence, urgency, and frequency. DETROL LA is contraindicated in patients with urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma and in patients who have demonstrated hypersensitivity to the drug or its ingredients. DETROL LA capsules should be used with caution in patients with clinically significant bladder outflow obstruction, gastrointestinal obstructive disorders, controlled narrow-angle glaucoma, and significantly reduced hepatic or renal function. Dry mouth was the most frequently reported adverse event (DETROL LA 23% vs placebo 8%); others (≥4%) included headache (DETROL LA 6% vs placebo 4%), constipation (DETROL LA 6% vs placebo 4%), and abdominal pain (DETROL LA 4% vs placebo 2%).

\*Source: IMS NPA, based on total US prescriptions of antimuscarinics for OAB from October 2001 to December 2005.

<sup>†</sup>Source: IMS Midas Global Sales Audit, Verispan longitudinal data, based on total prescriptions of DETROL and DETROL LA for OAB from April 1998 to December 2005.

74 million prescriptions<sup>†</sup>

once-daily  
**Detrol<sup>®</sup> LA**  
tolterodine tartrate  
extended release capsules

Please see important product information on next page.

**Improved Control. Less Bother.**