

ADHD Affected 9.5% of Children in 2007-2008

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FROM THE ANNUAL MEETING OF THE
AMERICAN ACADEMY OF CHILD AND
ADOLESCENT PSYCHIATRY

NEW YORK – The prevalence of attention-deficit/hyperactivity disorder among children and adolescents rose to its highest level in 2007-2008, with 9.5% of children and adolescents ever diagnosed, according to a federally sponsored national

telephone survey covering more than 70,000 American children and adolescents.

Although the reasons behind the increased prevalence of attention-deficit/hyperactivity disorder (ADHD) remain unclear, the increase over the 7.8% rate of ever-diagnosed ADHD in 2003-2004 reached statistical significance and appears real.

"We think something is going on," Melissa L. Danielson said, while pre-

senting a poster at the meeting. Explanations might include increased awareness of the diagnosis, and more children and adolescents undergoing formal evaluation, she said. Backing up the national finding are data on ADHD prevalence in each individual state. Prevalence rates rose in almost every state, and in 13 states recent increases reached statistical significance, she said in an interview.

The National Survey of Children's

VITALS

Major Finding: During 2007-2008, U.S. children and adolescents aged 4-17 years had a 9.5% prevalence rate of ever having attention-deficit/hyperactivity disorder, a significant increase from the 7.8% rate in 2003-2004.

Data Source: The National Survey of Children's Health, a random-sample telephone survey of parents with data on more than 70,000 U.S. children and adolescents aged 4-17 years run by the Centers for Disease Control and Prevention.

Disclosures: Ms. Danielson said that she had no conflicts of interest.

Health, run by the Centers for Disease Control and Prevention, receives its primary funding from the Department of Health and Human Services. In 2007 and 2008, a randomly selected sample of U.S. parents answered a telephone survey about their children's health. Parents answered four questions about ADHD: Did they have a child aged 4-17 years who ever received a diagnosis of the disorder? Did their child have a current diagnosis? Is the ADHD mild, moderate, or severe? Does the child receive medication?

Extrapolated survey results showed that in 2007-2008, 4.1 million American children and adolescents had a current diagnosis, 7.2% of the 4- to 17-year-old population (less than the 9.5% ever diagnosed with ADHD). Of these, two-thirds – 2.7 million – received medical treatment for their ADHD, and parents said that 570,000 (14%) of their kids had severe ADHD. About half had mild ADHD, with the remaining patients having what their parents described as moderate disorder. Subgroups with significantly less-severe ADHD included girls and adolescents aged 15-17.

Boys, adolescents aged 15-17 years, and multiracial and non-Hispanic children all had significantly higher prevalence rates of current ADHD relative to their respective comparator subgroups. Sex, race, and ethnicity had no linkage with medication use, but medication treatment occurred less often in the 15- to 17-year-olds, said Ms. Danielson, a statistician on the Child Development Studies team of the CDC in Atlanta.

Children aged 11-14 years had the widest medication use, 73%, while adolescents aged 15-17 had the lowest rate of medication use, 56%, a statistically significant difference. Children aged 11-14 years with severe disease had a roughly 90% rate of medical treatment; teens aged 15-17 years with mild ADHD had the lowest medication rate, about 50%.

Children and teens with a concurrent diagnosis of disruptive behavior disorder had a statistically significant, 50% adjusted, relative increased rate of receiving medical treatment for their ADHD and also had a significantly higher prevalence of current, severe ADHD. More than 30% of children with the concurrent diagnosis had severe ADHD. ■

• *Insulin initiation and intensification of glucose control*

Intensification or rapid improvement in glucose control has been associated with a transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy, and acute painful peripheral neuropathy. However, long-term glycemic control decreases the risk of diabetic retinopathy and neuropathy.

• *Lipodystrophy*

Long-term use of insulin, including LANTUS, can cause lipodystrophy at the site of repeated insulin injections. Lipodystrophy includes lipohypertrophy (thickening of adipose tissue) and lipatrophy (thinning of adipose tissue), and may affect insulin absorption. Rotate insulin injection or infusion sites within the same region to reduce the risk of lipodystrophy. [See *Dosage and Administration* (2.1)].

• *Weight gain*

Weight gain can occur with insulin therapy, including LANTUS, and has been attributed to the anabolic effects of insulin and the decrease in glucosuria.

• *Peripheral Edema*

Insulin, including LANTUS, may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

• *Allergic Reactions*

Local Allergy

As with any insulin therapy, patients taking LANTUS may experience injection site reactions, including redness, pain, itching, urticaria, edema, and inflammation. In clinical studies in adult patients, there was a higher incidence of treatment-emergent injection site pain in LANTUS-treated patients (2.7%) compared to NPH insulin-treated patients (0.7%). The reports of pain at the injection site did not result in discontinuation of therapy.

Rotation of the injection site within a given area from one injection to the next may help to reduce or prevent these reactions. In some instances, these reactions may be related to factors other than insulin, such as irritants in a skin cleansing agent or poor injection technique. Most minor reactions to insulin usually resolve in a few days to a few weeks.

Systemic Allergy

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including LANTUS and may be life threatening.

• *Antibody production*

All insulin products can elicit the formation of insulin antibodies. The presence of such insulin antibodies may increase or decrease the efficacy of insulin and may require adjustment of the insulin dose. In phase 3 clinical trials of LANTUS, increases in titers of antibodies to insulin were observed in NPH insulin and insulin glargine treatment groups with similar incidences.

6.2 Postmarketing experience

The following adverse reactions have been identified during post-approval use of LANTUS.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate reliably their frequency or establish a causal relationship to drug exposure.

Medication errors have been reported in which other insulins, particularly short-acting insulins, have been accidentally administered instead of LANTUS [See *Patient Counseling Information* (17) in the full prescribing information]. To avoid medication errors between LANTUS and other insulins, patients should be instructed to always verify the insulin label before each injection.

7. DRUG INTERACTIONS

A number of drugs affect glucose metabolism and may require insulin dose adjustment and particularly close monitoring.

The following are examples of drugs that may increase the blood-glucose-lowering effect of insulins including LANTUS and, therefore, increase the susceptibility to hypoglycemia: oral anti-diabetic products, pramlintide, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, propoxyphene, pentoxifylline, salicylates, somatostatin analogs, and sulfonamide antibiotics.

The following are examples of drugs that may reduce the blood-glucose-lowering effect of insulins including LANTUS: corticosteroids, niacin, danazol, diuretics, sympathomimetic agents (e.g., epinephrine, albuterol, terbutaline), glucagon, isoniazid, phenothiazine derivatives, somatropin, thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives), protease inhibitors and atypical antipsychotic medications (e.g. olanzapine and clozapine).

Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.

The signs of hypoglycemia may be reduced or absent in patients taking sympatholytic drugs such as beta-blockers, clonidine, guanethidine, and reserpine.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Subcutaneous reproduction and teratology studies have been performed with insulin glargine and regular human insulin in rats and Himalayan rabbits. Insulin glargine was given to female rats before mating, during mating, and throughout pregnancy at doses up to 0.36 mg/kg/day, which is approximately 7 times the recommended human subcutaneous starting dose of 10 Units/day (0.008 mg/kg/day), based on mg/m². In rabbits, doses of 0.072 mg/kg/day, which is approximately 2 times the recommended human subcutaneous starting dose of 10 Units/day (0.008 mg/kg/day), based on mg/m², were administered during

LANTUS® (insulin glargine [rDNA origin] injection) solution for subcutaneous injection

organogenesis. The effects of insulin glargine did not generally differ from those observed with regular human insulin in rats or rabbits. However, in rabbits, five fetuses from two litters of the high-dose group exhibited dilation of the cerebral ventricles. Fertility and early embryonic development appeared normal.

There are no well-controlled clinical studies of the use of LANTUS in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is essential for patients with diabetes or a history of gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. Insulin requirements may decrease during the first trimester, generally increase during the second and third trimesters, and rapidly decline after delivery. Careful monitoring of glucose control is essential in these patients.

8.3 Nursing Mothers

It is unknown whether insulin glargine is excreted in human milk. Because many drugs, including human insulin, are excreted in human milk, caution should be exercised when LANTUS is administered to a nursing woman. Use of LANTUS is compatible with breastfeeding, but women with diabetes who are lactating may require adjustments of their insulin doses.

8.4 Pediatric Use

The safety and effectiveness of subcutaneous injections of LANTUS have been established in pediatric patients (age 6 to 15 years) with type 1 diabetes [see *Clinical Studies* (14) in the full prescribing information]. LANTUS has not been studied in pediatric patients younger than 6 years of age with type 1 diabetes. LANTUS has not been studied in pediatric patients with type 2 diabetes.

Based on the results of a study in pediatric patients, the dose recommendation when switching to LANTUS is the same as that described for adults [see *Dosage and Administration* (2.3) and *Clinical Studies* (14) in the full prescribing information]. As in adults, the dosage of LANTUS must be individualized in pediatric patients based on metabolic needs and frequent monitoring of blood glucose.

8.5 Geriatric Use

In controlled clinical studies comparing LANTUS to NPH insulin, 593 of 3890 patients (15%) with type 1 and type 2 diabetes were ≥65 years of age and 80 (2%) patients were ≥75 years of age. The only difference in safety or effectiveness in the subpopulation of patients ≥65 years of age compared to the entire study population was a higher incidence of cardiovascular events typically seen in an older population in both LANTUS and NPH insulin-treated patients.

Nevertheless, caution should be exercised when LANTUS is administered to geriatric patients. In elderly patients with diabetes, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions. Hypoglycemia may be difficult to recognize in the elderly [See *Warnings and Precautions* (5.3)].

10. OVERDOSAGE

An excess of insulin relative to food intake, energy expenditure, or both may lead to severe and sometimes prolonged and life-threatening hypoglycemia. Mild episodes of hypoglycemia can usually be treated with oral carbohydrates. Adjustments in drug dosage, meal patterns, or exercise may be needed.

More severe episodes of hypoglycemia with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. After apparent clinical recovery from hypoglycemia, continued observation and additional carbohydrate intake may be necessary to avoid recurrence of hypoglycemia.

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