

FOCUS ON PEDIATRIC ENDOCRINOLOGY

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Vitamin D Supplements: How Much Is Too Much?

The mother was just trying to ensure that her infant was getting optimal nutrition. She'd been giving her baby 400 IU/mL of vitamin D daily. When it came time to buy more, she purchased a formulation that contained 400 IU per drop. Unaware of the change in concentration, she continued to give her child 1mL, resulting in a daily vitamin D intake of 12,000 IU — 30 times greater than the daily vitamin D requirement recommended by the American Academy of Pediatrics (AAP) and the Pediatric Endocrine Society (PES).

This true story represents just one scenario demonstrating how easy it can be for a child to receive too much vitamin D. Long hailed for its beneficial effects on bone health, this “wonder vitamin” has, in recent years, been touted for other possible health benefits, ranging from lowered blood pressure to enhanced immunity. So it's not surprising that many parents are giving supplements to their children. But when enough turns into too much, vitamin D toxicity may result.

“There's much research suggesting that vitamin D has effects beyond the bones, so more people are supplementing now than ever before,” says Maria Vogiatzi, MD, Chief of Pediatric Endocrinology at NewYork-Presbyterian Hospital/Phyllis and

David Komansky Center for Children's Health and Associate Professor of Clinical Pediatrics at Weill Cornell Medical College. “But many people use doses that are higher than those traditionally used. There are so many formulations out there that it can be

easy to give a much higher dose than intended.”

To shed light on the issue, the Drugs and Therapeutics Committee of the Pediatric Endocrine Society reviewed the safety of currently recommended high vitamin D doses as well as reported cases of pediatric intoxication, and proposed recommendations for the monitoring of children receiving vitamin D supplements and those with evidence or suspicion of intoxication. The report, authored by Dr. Vogiatzi (a committee member) was published in the *Journal of Clinical Endocrinology & Metabolism* (2014;99:1132-1141).

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Diagnosing PCOS in Teens Is No Easy Task

Irregular periods, acne, and excess body hair are all hallmarks of polycystic ovary syndrome (PCOS). But they are also common — and normal — among girls entering adolescence. How can physicians tell the difference?

Helping to facilitate the diagnosis is Aviva Sopher, MD, Assistant Attending Physician at NewYork-Presbyterian/Morgan Stanley Children's Hospital and Assistant Professor of Pediatrics at Columbia University College of Physicians and Surgeons. “The criteria for PCOS that apply to adults — hirsutism, abnormal levels of androgens in the blood, irregular menstrual cycles, and an elevated number and appearance of ovarian follicles — may not apply to adolescents,” she explains. “It can be misleading to use these criteria to diagnose



Increased acne is so common in the teenage years that it is not a reliable indicator of polycystic ovary syndrome.

PCOS in adolescent girls.”

It's important to make a diagnosis of PCOS because the syndrome is associated with metabolic derangements: metabolic syndrome, dyslipidemia, increased liver fat (which can rarely progress to cirrhosis), insulin resistance, and a higher risk of type 2 diabetes. Dr. Sopher is leading work at NYP/Morgan Stanley Children's to refine the diagnosis of PCOS in adolescents, using magnetic resonance imaging to assess ovary size and the number of follicles more clearly than abdominal ultrasound, as well as blood markers such as anti-Müllerian hormone. Girls in the

first two years after the onset of menses are more likely to have irregular menstrual cycles, so that criterion may not be a useful indicator of PCOS in this group. In a small case-control study (J

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Sizing Up the Benefits of Adolescent Weight Loss Surgery

Peer pressure. A challenging high school course load. Bodily changes that come with adolescence. It's hard being a teenager. Morbidly obese teenagers struggle with much more. Not only may they be subject to ridicule by their peers, but they have serious health risks that include type 2 diabetes, dyslipidemias, hypertension, and metabolic syndrome (MeS).

Researchers have found that weight loss surgery not only helps these young patients reduce their body mass index (BMI), but also lowers the risk of these complications. That's good news, because studies have demonstrated a dose-dependent relationship between adolescent BMI and morbidity and mortality in adulthood.

Investigators at NewYork-Presbyterian/Morgan Stanley Children Hospital reported that weight loss surgery (laparoscopic adjustable gastric banding) was associated with reductions in waist circumference, BMI, systolic and diastolic blood pressure, and C-reactive protein (*J Obesity*. 2011;2011:906384) in morbidly obese 14-18-year-olds who had the surgery. Significant weight loss and improvements in MeS components were observed 6 months and one year following the surgery. The incidence of MeS declined 56.8 percent after 6 months and 69.6 percent after 12 months. Moreover, gastric banding was as effective in morbidly obese adolescents with metabolic syndrome at baseline as it was in those without MeS.

"Our findings add to the literature documenting the effectiveness of weight loss surgery to achieve not only weight loss, but also to resolve comorbidities like metabolic syndrome in morbidly obese adolescents," says Ilene Fennoy, MD, Attending Physician at NYP/Morgan Stanley Children's, Professor of Pediatrics at



Columbia University College of Physicians and Surgeons, and the senior author of the study, which was also directed by Jeffrey L. Zitsman, MD, Director of Adolescent Bariatric Surgery and Associate Professor of Surgery. "These findings are important, because metabolic syndrome that progresses into adulthood can raise the risk of cardiovascular disease and type 2 diabetes." The investigators later reported that the long-term effects of gastric banding persist, showing in a

three-year follow-up study that morbidly obese adolescents can lose weight successfully and experience continued improvements in their health (*Surg Obes Relat Dis*. 2014;Jun 5).

Today, adolescents having weight loss surgery at NYP/Morgan Stanley Children's are offered sleeve gastrectomy instead of gastric banding, because it appears to be more effective. With sleeve gastrectomy, a portion of the stomach is removed, including the part responsible for producing ghrelin, the "hunger hormone." The NYP/Morgan Stanley Children's investigators found that patients who underwent sleeve gastrectomy experienced faster weight loss and a better improvement in blood glucose levels than those who had gastric banding.

There is one potential disadvantage of weight loss surgery in adolescents, however: vitamin D deficiency. Many obese teens are already vitamin D deficient, including some with secondary hyperparathyroidism (*ISRN:Obesity*. 2013;Feb 24). Drs. Fennoy and Zitsman and their colleagues are now studying the effects of weight loss surgery on vitamin D status and bone health.

To learn more about weight loss surgery at the Center for Adolescent Bariatric Surgery at NYP/Morgan Stanley Children's, call (212) 305-8862.

Diagnosing PCOS in Teens Is No Easy Task (continued from page 1)

Pediatr Endocrinol Metab. 2014 Jul 8), Dr. Sopher and her colleagues showed that levels of anti-Müllerian hormone were higher among girls ages 13-21 with PCOS and correlated with androgen levels and ovarian size, indicating that this blood test could serve as a useful adjunct to other PCOS diagnostic methods.

To assess the risk of fatty liver disease in adolescents with PCOS, she is directing a clinical trial of non-obese adolescents ages 13-21 with and without PCOS to study the link between liver fat and PCOS. Results to date indicate that insulin resistance is more common in the girls with PCOS and that this population may have more liver fat even though they are not obese. Girls diagnosed with fatty liver disease may continue to a randomized Phase III placebo-controlled study to assess the efficacy of six months of metformin treatment.

When to Suspect Adolescent PCOS

Doctors should suspect PCOS in an adolescent patient in:

- Girls with an unusual excess of hair in places where they wouldn't expect it, such as the face, chin, stomach, and back.
- Girls with irregular menstrual cycles close to amenorrhea more than two years after the onset of menses, although other causes should be ruled out (such as anorexia, high levels of exercise, or another hormonal imbalance).
- Girls who develop pubic hair and axillary hair before the age of 8, who may progress to PCOS when they reach adolescence.

To learn more about the clinical trial of fatty liver disease in adolescents with PCOS or to refer a patient for this study, call (212) 305-1518.

Can Antidepressants Reduce Bone Mass in Adolescents?

Animal studies show that serotonin regulates bone mass. Selective serotonin reuptake inhibitors (SSRIs) increase systemic and central nervous system levels of serotonin and may lead to bone loss. Prior research has shown that people age 65 and older who take SSRIs have an increased incidence of fractures and osteoporosis. Now a new study shows that SSRIs may also reduce bone mass in adolescents and young adults — the first such investigation to explore this relationship. The results were reported at the 2014 annual meeting of the Endocrine Society.

One study showed that adolescent users of SSRIs experienced an average bone loss of 5 to 10 percent.

Maria Vogiatzi, MD, Chief of Pediatric Endocrinology at NewYork-Presbyterian Hospital/Phyllis and David Komansky Center for Children's Health and Associate Professor of Clinical Pediatrics, in collaboration with Ryan T. Demmer, PhD, of the Columbia University Mailman School of Public Health, examined data from the 2006-2010 National Health and Nutrition

Examination Survey. Of 4,303 subjects aged 12 to 20 for whom demographic, anthropometric, DEXA, and prescription medication data were available, 62 individuals were taking SSRIs.

After adjusting for age, gender, height, body mass index, socioeconomic status, and physical activity levels, SSRI use remained a statistically significant predictor of bone mass, with SSRI users experiencing an average bone loss of 5 to 10 percent. Specifically, SSRI use correlated with a decrease in bone mineral density and bone mineral content in the femoral neck, total femur, and lumbar spine. Moreover, data suggested that bone loss increased with longer duration of SSRI use.

Concludes Dr. Vogiatzi, "This study serves as a basis for further studies. It does not provide the final answer regarding the link between bone loss and SSRIs, but it does indicate that there is a clinical issue here that needs to be addressed and studied further," says Dr. Vogiatzi.



Vitamin D Supplements: How Much Is Too Much? (continued from page 1)

Spotting Vitamin D Toxicity

Vitamin D is a hormone that regulates calcium absorption from the gut. Children experiencing vitamin D toxicity typically demonstrate hypercalcemia. Symptoms may include poor appetite, weight loss, abdominal pain, constipation, and vomiting, which in time may progress to dehydration and central nervous system changes. Increased calcium excretion in the urine also raises the risk of kidney stones.

How much is too much is a subject of debate. The AAP and PES both recommend 400 IU per day for children ages 0-18, while the Institute of Medicine recommends 400 IU daily for infants up to age 1 and 600 IU for those 1-18. The Endocrine Society recommends 400-1,000 IU for the first year of life and 600-1,000 IU for the rest of childhood. The recommendations for patients at risk for vitamin D deficiency are different still, while the European Food Safety Authority and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition have no vitamin D recommendations at all for children over age 1. The upper levels of intake also differ from group to group. These differences reflect the ongoing debate about what constitutes optimal or adequate vitamin D levels for skeletal health; the discussion has generated confusion among treating physicians and the public.

What Physicians Can Do

The Pediatric Endocrine Society paper recommends:

1. Becoming aware of vitamin D formulations and counseling patients about their use.
2. Monitoring children receiving vitamin D supplements in the upper dose ranges (such as treatment of vitamin D deficiency) through serum testing of 25-hydroxyvitamin D (25OHD). 25OHD levels of up to 100 ng/mL are considered acceptable; a level over 100 ng/mL signals vitamin D excess; and a level of 150 ng/mL or more indicates vitamin D intoxication.
3. Considering vitamin D intoxication in the differential workup of children with hypercalcemia or hypercalciuria.
4. Treating vitamin D toxicity with the recognition that it may take several weeks for high 25OHD levels to resolve. Initial treatment includes ceasing supplementation, followed by hydration and diuretics to increase calcium excretion. Some children whose intoxication persists despite this therapy may need glucocorticoids and calcitonin; bisphosphonates; or even hemodialysis (when other treatments have failed).

"Physicians should be aware that there are parents giving their children supplements at the higher levels of intake," says Dr. Vogiatzi. "These recommendations should help provide some guidance to avoid, recognize, and treat vitamin D toxicity."



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