Consensus Statement on the Use of Gonadotropin-Releasing Hormone Analogs in Children
Jean-Claude Carel, Erica A. Eugster, Alan Rogol, Lucia Ghizzoni and Mark R. Palmert
Pediatrics 2009;123:e752; originally published online March 30, 2009;
DOI: 10.1542/peds.2008-1783

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/123/4/e752.full.html
Consensus Statement on the Use of Gonadotropin-Releasing Hormone Analogs in Children

Jean-Claude Carel, MD, PhD,* Erica A. Eugster, MD,b Alan Rogol, MD, PhD,c,e Lucia Ghizzoni, MD,d Mark R. Palmert, MD, PhD,f, on behalf of the members of the ESPE-LWPES GnRH Analogs Consensus Conference Group

OBJECTIVE. Gonadotropin-releasing hormone analogs revolutionized the treatment of central precocious puberty. However, questions remain regarding their optimal use in central precocious puberty and other conditions. The Lawson Wilkins Pediatric Endocrine Society and the European Society for Pediatric Endocrinology convened a consensus conference to review the clinical use of gonadotropin-releasing hormone analogs in children and adolescents.

PARTICIPANTS. When selecting the 30 participants, consideration was given to equal representation from North America (United States and Canada) and Europe, an equal male/female ratio, and a balanced spectrum of professional seniority and expertise.

EVIDENCE. Preference was given to articles written in English with long-term outcome data. The US Public Health grading system was used to grade evidence and rate the strength of conclusions. When evidence was insufficient, conclusions were based on expert opinion.

CONSENSUS PROCESS. Participants were put into working groups with assigned topics and specific questions. Written materials were prepared and distributed before the conference, revised on the basis of input during the meeting, and presented to the full assembly for final review. If consensus could not be reached, conclusions were based on majority vote. All participants approved the final statement.

CONCLUSIONS. The efficacy of gonadotropin-releasing hormone analogs in increasing adult height is undisputed only in early-onset (girls ≤6 years old) central precocious puberty. Other key areas, such as the psychosocial effects of central precocious puberty and their alteration by gonadotropin-releasing hormone analogs, need additional study. Few controlled prospective studies have been performed with gonadotropin-releasing hormone analogs in children, and many conclusions rely in part on collective expert opinion. The conference did not endorse commonly voiced concerns regarding the use of gonadotropin-releasing hormone analogs, such as promotion of weight gain or long-term diminution of bone mineral density. Use of gonadotropin-releasing hormone analogs for conditions other than central precocious puberty requires additional investigation and cannot be suggested routinely.

PEDIATRICS 2009;123:e752–e762

Gonadotropin-releasing hormone analogs (GnRHas) are standard of care for treatment of central precocious puberty (CPP). However, despite a favorable record of safety and efficacy, significant questions remain regarding their use. The European Society for Pediatric Endocrinology (ESPE) and the Lawson Wilkins Pediatric Endocrine Society (LWPES) convened a consensus conference to examine GnRHa therapy in pediatric patients. We did not address whether historically defined normal ages for the onset of puberty should be modified but used the
operational definition of precocious puberty as puberty beginning before 8 years of age in girls and 9 years of age in boys.

METHODS

Participant Selection
Consideration was given to equal representation from North America (United States and Canada) and Europe, an equal male/female ratio, and a balanced spectrum of professional seniority and expertise.

Process
Thirty participants were put into 1 of 6 groups with assigned topics and designated chairpersons. Each participant prepared a summary of the literature regarding a question that was distributed before the conference (held over 3 days in November 2007). Each group revised the summaries and presented them to the full conference. If consensus could not be reached, conclusions were made on the basis of a vote of all participants. This report is organized around the questions that were addressed; it has been approved by the participants and endorsed by the LWPES and ESPE.

Evaluation of Evidence
Preference was given to articles written in English with long-term outcome data published between 1990 and 2007. The US Public Health grading system1 was used to grade the evidence and strength of the recommendations.2 Grading was reviewed by the full conference under the guidance of a methodologist/biostatistician. This report is not a practice guideline; nonetheless, we aimed to adhere to modified appraisal of guidelines research and evaluation (AGREE) criteria.3

INITIATION OF GnRHa THERAPY FOR CPP

Clinical Criteria
The most important clinical criterion for GnRHa treatment is documented progression of pubertal development, which is based on the recognition that many patients with CPP have a slowly progressive or nonprogressive form and achieve adult height (AH) within their target range without GnRHas.4-7 Accelerated growth velocity and skeletal maturation are other features of sustained and/or rapidly progressing CPP.8 However, some patients with slowly progressive CPP and advanced bone age (BA) reach normal AH without intervention.9

Conclusions: Progressive pubertal development and growth acceleration should be documented over a 3- to 6-month period before GnRHa therapy. This observational period may not be necessary if the child is at or past Tanner stage III (breast), particularly with advanced skeletal maturation (CIII).

Adopted Children
Boys and girls adopted internationally are at risk of CPP, although data are limited for boys.10,20 Response to GnRHas in adopted girls with precocious or early normal puberty seems comparable with that seen in nonadopted girls.11 Adopted children may be at increased risk of emotional and behavioral problems,23 but no data are available to demonstrate that GnRHa therapy improves psychological well-being.24

Conclusions: Although international adoption constitutes a risk factor for CPP, adopted children should be treated no differently than nonadopted children with CPP (CIII).

Hormonal Criteria
Luteinizing hormone (LH) measurements are the most valuable biochemical parameter for the diagnosis of CPP.
Because prepubertal LH levels are <0.1 IU/L, LH assays used should have a detection limit near 0.1 IU/L.25-27 In 1 study of normal children, basal LH levels distinguished prepubertal (LH < 0.2 IU/L) and pubertal males with 100% sensitivity and specificity, but 50% of the girls with Tanner stage 2 breasts had levels in the prepubertal range.27

LH can be measured after stimulation with GnRH (single serum sample at 30–40 minutes27-29) or with a GnRHa such as aqueous leuprolide (single sample at 60 minutes30,31). Peak LH values show an overlap between prepubertal and early pubertal children. As with basal LH, variability among assays and paucity of normative data have hampered the development of diagnostic cutoffs for CPP, although an (assay-specific) prepubertal limit of peak LH at 3.3 to 5.0 IU/L has been suggested.25,27,28

LH levels provide more information than those of follicle-stimulating hormone (FSH). However, the stimulated LH/FSH ratio may help differentiate progressive CPP (which tends to have higher LH/FSH ratios) from nonprogressive variants that do not require GnRHa therapy.32-34

For estradiol, the most sensitive measurements (tandem mass spectrometry) have shown that prepubertal levels may be <1 pg/mL (3.7 pmol/L) and undetectable with commonly available assays.35 Thus, in non–mass spectrometry assays, measurable estradiol only confirms relatively advanced puberty. Similarly, testosterone assays with detection limits of >10 ng/dL may not discriminate prepubertal from early pubertal levels.36 For estradiol and testosterone, the laboratory used must have a defined prepubertal range.

Conclusions: Sensitive assays with pediatric norms should be used and stimulation results interpreted depending on the agent used (BII). The same caveats are important if hormonal testing is used to monitor therapy (see below). Basal LH levels are useful screening tests and may be diagnostic (BII). Stimulated LH levels are important, but interpretation suffers from assay variability and absence of clear diagnostic cutoffs (BII). Gonadal sex-steroid levels can add information in support of the diagnosis but are not sufficient (BII).

**Pelvic Ultrasound**

Female patients with CPP have increased ovarian and uterine dimensions compared with prepubertal controls and girls with premature thelarche.37 For CPP, cutoff values for uterine length range from 3.4 to 4.0 cm. The presence of an endometrial echo is highly specific (~100%) but less sensitive (42%–87%).34 The cutoffs for a pubertal ovarian volume range between 1 and 3 mL (volume = length x width x height x 0.5233).38

Conclusions: Pelvic ultrasound is helpful in differentiating CPP from premature thelarche as an adjunct to GnRH stimulation (BII).

**Central Nervous System Imaging**

CPP may be a sign of central nervous system pathology. Unsuspected intracranial pathology has been reported in 8% of girls39,40 and 40% of boys41 without neurologic findings or neurofibromatosis. The percentage of children with unsuspected intracranial pathology decreases with age.39-41 Only 2% to 7% of girls who have onset of CPP between the ages of 6 and 8 years have unsuspected pathology, and only ~1% have a tumor such as a glioma or astrocytoma.39,40 Factors that may decrease the likelihood of finding a tumor include racial/ethnic background, family history of CPP, and adoption.

Conclusions: All boys with CPP and girls with CPP at <6 years of age should have a head MRI. It is controversial whether all girls who develop CPP between 6 and 8 years of age require head MRI. Girls with neurologic findings and rapid pubertal progression are more likely to have intracranial pathology and require an MRI examination (BII).

### AVAILABLE GnRHs AND THERAPEUTIC REGIMENS FOR CPP

#### Currently Available Therapeutic Regimens

All available GnRHa are effective despite their different routes of administration, dosing, and duration of action (Tables 1–3).42,43 The depot preparations are preferred be-

**TABLE 1 Characteristics of GnRHas**

<table>
<thead>
<tr>
<th>Rapid Acting</th>
<th>Monthly Depot</th>
<th>3-mo Depot</th>
<th>12-mo Implant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td>3–4 times daily (intranasal) or every day (subcutaneous)</td>
<td>Every 28 d</td>
<td>Every 90 d</td>
</tr>
<tr>
<td><strong>Peak serum concentrations</strong></td>
<td>10–45 min</td>
<td>4 h</td>
<td>4–8 h</td>
</tr>
<tr>
<td><strong>Onset of therapeutic suppression</strong></td>
<td>2–4 wk</td>
<td>1 mo</td>
<td>1 mo</td>
</tr>
<tr>
<td><strong>Advantage</strong></td>
<td>Quick on/off</td>
<td>Dosing and efficacy well studied</td>
<td>Fewer injections and fewer compliance concerns</td>
</tr>
<tr>
<td><strong>Disadvantage</strong></td>
<td>Multiple daily doses needed/ compliance very difficult</td>
<td>Painful injections/suboptimal compliance</td>
<td>Painful injection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GnRHa</th>
<th>Administration</th>
<th>Starting Dose, per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nafarelin</td>
<td>Nasal spray</td>
<td>800 µg twice</td>
</tr>
<tr>
<td>Buserelin</td>
<td>Nasal spray</td>
<td>20–40 µg/kg</td>
</tr>
<tr>
<td>Buserelin</td>
<td>Subcutaneous</td>
<td>1200–1800 µg</td>
</tr>
<tr>
<td>Leuprolide</td>
<td>Subcutaneous</td>
<td>50 µg/kg</td>
</tr>
<tr>
<td>Deslorelin</td>
<td>Subcutaneous</td>
<td>4–8 µg/kg</td>
</tr>
<tr>
<td>Histrelin</td>
<td>Subcutaneous</td>
<td>8–10 µg/kg</td>
</tr>
<tr>
<td>Triptorelin</td>
<td>Subcutaneous</td>
<td>20–40 µg/kg</td>
</tr>
</tbody>
</table>
TABLE 3  Depot GnRHa Formulations42,47,48

<table>
<thead>
<tr>
<th>Depot Preparation</th>
<th>Brand Name</th>
<th>Starting Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goserelin</td>
<td>Zoladex LA</td>
<td>3.6 mg every month or 10.8 mg every 3 mo</td>
</tr>
<tr>
<td>Buserelin</td>
<td>Suprefact depot</td>
<td>6.3 mg every 2 mo</td>
</tr>
<tr>
<td>Leuprolide</td>
<td>Enantone or Lupron-depot</td>
<td>3.75 mg every month or 11.25 mg every 3 mo</td>
</tr>
<tr>
<td></td>
<td>Prostap SR</td>
<td>3.75 mg every month</td>
</tr>
<tr>
<td></td>
<td>Lupron depot PED</td>
<td>7.5, 11.25, or 15 mg every month (0.2–0.3 mg/kg per mo) or 11.25 mg every 3 mo</td>
</tr>
<tr>
<td>Triptorelin</td>
<td>Decapeptyl, Gonapeptyl</td>
<td>3 or 3.75 mg every month or 11.25 mg every 3 mo</td>
</tr>
<tr>
<td>Histrelin</td>
<td>Supprelin LA</td>
<td>50 mg implant every year</td>
</tr>
</tbody>
</table>

* No data are available on the use of the 22.5-mg 3-month depot in children.

cause of improved compliance.44,46 In most children, monthly injections adequately suppress the gonadotropin axis, but some children require more frequent injections or higher-than-standard doses. The 3-month formulations are comparable with monthly dosing, but no randomized comparative trial is available. In 1 prospective trial, 7.5 mg of leuprolide monthly suppressed LH more effectively than 11.25 mg every 3 months, although sex-steroid concentrations were equivalently inhibited.60 The 50-mg histrelin-acetate implant provides sustained suppression for 12 months.51,52

Conclusions: A variety of GnRHa formulations are available and efficacious. The choice of a particular agent depends on patient and physician preference and on local marketing approval (CIII).

Treatment Monitoring
Progression of breast or testicular development is suggestive of treatment failure,52–56 but progression of pubic hair may indicate normal adrenarche. Growth velocity, height SD score (SDS), and BA advancement should decline during treatment. Vaginal bleeding may occur after the first administration of GnRHAs, but subsequent bleeding suggests lack of efficacy or incorrect diagnosis. Markedly decreased growth velocity (less than or equal to 894 Ebsco Subs 22827242 on January 24, 2012pediatrics.aappublications.orgDownloaded from pedig
Treatment Duration
Several studies have reported a direct relationship between treatment duration and AH, and an inverse relationship between age at pubertal onset or at initiation of therapy and AH. However, deciphering the respective influences of age at onset of puberty, age at initiation of therapy, and treatment duration is problematic, because these variables are interrelated. Undue delay in initiation of therapy (≥1–2 years) may compromise AH.

Parent/Patient Preference, Anticipated Time of Menarche, CA, and BA
In the studies we examined, wishes of the patient and family and the physician’s decision were stated as deciding factors for cessation of treatment. The mean age at treatment discontinuation ranged from 10.6 to 11.6 years, with mean BA ranging from 12.1 to 13.9 years and mean age at menarche of ~12.3 years. Discontinuation at a CA of ~11.0 years and a BA of ~12.0 years has been associated with maximum AH. However, BA is not an appropriate single variable, because a BA of ~12.0 years can be observed at different CAs and because BA is unreliable for predicting height gain after treatment. One study has suggested that height gain after treatment may be higher for those with early (<6 years) versus late treatment.

Height and Growth Velocity
Although growth velocity during therapy and height at interruption of therapy are positively associated with AH, they cannot be used as independent factors for deciding when to stop treatment. For a child with unexplained marked deceleration of growth, consideration might be given to stopping treatment or to introducing adjunct therapies.

Conclusions: There is insufficient evidence to rely on any one clinical variable (CA, duration of therapy, BA, height, target height, growth velocity) to make the decision to discontinue treatment (CIII). Therefore, it is reasonable to consider these parameters and informed parent and patient preferences, with the goal of menarche occurring near the population norms (CIII).

OUTCOMES OF GnRHa THERAPY FOR CPP
Reproductive Function
Follow-up studies have been performed with girls in their late teens and women up to 31 years in 1 study and have reported that ovarian function was not impaired. Menses began 2 to 61 months after the end of treatment. Regular ovarian cycles occurred in 60% to 96% of the patients, without differences from reference populations. Infertility has not been reported. Of 28 reported pregnancies, 7 were terminated and 21 resulted in healthy children. Three small studies showed no differences from controls in gonadal function for boys at the ages of 15 to 18 years. Paternity rates have not been reported.

Conclusions: The available data suggest that gonadal function is not impaired in girls treated with GnRHAs (BII). Nevertheless, available data are limited. Long-term data on fecundity and ovarian reserve of treated patients with CPP are needed.

BMI and Correlates of Metabolic Syndrome
Childhood obesity is associated with earlier pubertal development in girls, and early sexual maturation is associated with increased prevalence of overweight and obesity. There has been concern that GnRHa therapy may affect BMI. Eleven studies addressed BMI outcome in girls with CPP, 2 included boys, and 1 included girls with early puberty (onset at the ages of 8 and 9 years). Before GnRHa treatment, mean BMI SDS was above average in girls with CPP in all studies, whereas results were split in boys. The combined analysis indicates that BMI SDS did not increase after treatment irrespective of age at presentation. At AH, mean BMI SDS ranged from 0.1 to 1.7, with an overall slight decrease from pretreatment BMI. No reports regarding metabolic syndrome and GnRHa treatment were identified.

Conclusions: Above-average BMI is frequent at diagnosis of CPP. Long-term GnRHa treatment does not seem to cause or aggravate obesity, as judged from BMI (BII). Studies of body composition and fat distribution are needed.

Bone Mineral Density
Bone mineral density (BMD) may decrease during GnRHa therapy. However, subsequent bone mass accrual is preserved, and peak bone mass does not seem to be negatively affected by treatment. There is some suggestion that discontinuation of treatment in girls with a BA of ≤11.5 years may lead to greater BMD and that, as in all adolescents, optimum calcium and vitamin D intake and skeletal-loading exercise may positively influence bone mass.

Conclusions: Young adults treated with GnRHAs for CPP in childhood ultimately accrue BMD within the normal range for age (BII).

Risk of Polycystic Ovarian Syndrome
The possibility that CPP is a first manifestation of polycystic ovarian syndrome (PCOS) has been raised. PCOS occurred in 0% to 12% of girls with CPP followed prospectively compared with 5% to 10% in the general population. Single studies have reported (1) an increased average ovarian size after CPP resulting from hypothalamic hamartoma, (2) a higher prevalence of exaggerated adrenarche in patients with CPP than in controls, and (3) the occurrence of signs of PCOS 0.5 to 4.0 years after menarche.

Conclusions: Follow-up of treated or untreated girls with CPP into the midteenage years suggests that the development of PCOS (BII) or polycystic ovary morphology (CIII) is not clearly different from that in the general population. Premature adrenarche and early childhood insulin resistance are potential risk factors for PCOS, but it is not clear if the presence of these conditions along
with CPP increases the eventual risk of PCOS (CIII). Longitudinal data through adolescence are needed.

**PSYCHOSOCIAL DEVELOPMENT**

Potential psychological consequences of CPP, including risk for emotional distress and problem behavior, are often used to justify treatment with GnRHas. Hormonally induced behavioral changes (eg, aggression, sexuality) that occur during normal puberty may occur earlier in children with CPP, perhaps consistent with the hormonal effects on brain development observed in rodents.98

Limited data are available regarding psychological consequences of CPP, and the few existing studies have limitations that have yielded inconsistent conclusions.99

In 2 studies examining psychological functioning in girls with CPP before and after treatment,24,100 no consistent patterns of change were observed. GnRHas have been suggested to adversely affect mood and cognition in adults,101 but similar effects have not been evaluated in children.

Conclusions: There is little evidence to show whether CPP leads to psychological or behavioral problems or whether treatment with GnRHas are associated with improved psychological outcome (CIII). Thus, no recommendations related to psychosocial outcomes are possible. Controlled studies with standardized instruments are needed.

**USE OF GnRHas FOR CONDITIONS OTHER THAN CPP**

**Gonadal Protection for Children Undergoing Chemotherapy**

Infertility represents one of the main long-term consequences of chemotherapy. Studies that evaluated the effects of ovarian suppression by GnRHas during chemotherapy in adult and adolescent patients have yielded inconsistent results.102–104

Prospective, randomized trials in adult women are ongoing (see NCT00196846, NCT00908844, NCT00380406, NCT00068601 at http://clinicaltrials.gov/).

Conclusions: Routine use of GnRHas for gonadai protection in children undergoing chemotherapy cannot be suggested (CIII).

**Increasing AH of Children With Idiopathic Short Stature**

The effect of GnRHa therapy on AH has been evaluated in girls with idiopathic short stature (ISS) and normal puberty (8–10 years of age), with a mean gain compared with predicted height of 0 to 4.2 cm.†† In boys with rapidly progressing puberty, GnRHa therapy increased AH compared with predicted height.5 The effects of combined GH and GnRHa therapy in children with ISS are controversial,111 with mean gains of 4.4 to 10 cm with combination therapy versus −0.5 to 6.1 cm in untreated controls.112,113 In these studies, one cannot definitively separate the effects of GH from GnRHas. In 2 randomized studies of adopted girls with normal puberty, GnRHas plus GH was compared with GnRHas alone, with a 3-cm height gain demonstrated with combination therapy.22,114

Disadvantages of the use of GnRHas in children with ISS include absence of pubertal growth acceleration, delayed puberty with potential psychosocial disadvantage, and decreased BMD. Long-term follow-up studies are lacking.

Conclusions: GnRHa therapy alone in children with ISS and normally timed puberty is minimally effective in increasing AH, may compromise BMD, and cannot be suggested for routine use (DII). Combined GnRHa and GH therapy leads to a significant height gain but may have adverse effects. Routine use of GnRHas in children with ISS being treated with GH cannot be suggested (CIII).

**Increasing AH of Children Born Small for Gestational Age**

Short children born small for gestational age (SGA) usually have a normal pubertal timing, although some of them have rapidly progressing puberty, and may be treated with GH.92,115 Data on the additional effect of GnRHas are limited.113

Conclusions: Routine use of the combination of GnRHas and GH in children born SGA cannot be suggested (CIII).

**Increasing AH of Children With Severe Hypothyroidism**

Some children with severe hypothyroidism are at risk for rapid progression through puberty and diminished AH. In the only study available, combined GnRHas and levothyroxine and levothyroxine alone produced similar gains in height SDS.116

Conclusions: Routine use of combined therapy with GnRH and levothyroxine cannot be suggested (CIII).

**Increasing AH of Children With GH Deficiency**

Some children with GH deficiency are short at the start of puberty and at risk for short adult stature. Retrospective studies that evaluated the addition of GnRHas to GH involved a limited number of subjects and provided controversial results.117–119 Three prospective studies that reported near-AH or AH have shown an ~1-SD height gain,120–122 possibly without detrimental effect on BMD.123

Conclusions: Routine use of combined therapy with GnRH and GH in GH-deficient children with low predicted AH at onset of puberty cannot be suggested (CIII).

**Increasing AH of Children With Congenital Adrenal Hyperplasia**

One nonrandomized study examined the effect of combined GH and GnRHa treatment on AH in 14 children with congenital adrenal hyperplasia (CAH) and normal or precocious puberty and found a 1-SD increase in AH in comparison with standard treatment for CAH.124

Conclusions: Additional studies are needed to determine if GnRHa therapy alone or in combination with GH should be used in children with CAH and low predicted AH. Routine use of GnRHas for CAH cannot be suggested (CIII).

**Children With Autism**

Conclusions: Despite 1 controversial article reporting that GnRHas may benefit behavioral symptoms in chil-
dren with autism, the consensus is that there is no current evidence for GnRHa therapy for this indication (CIII).

CONCLUSIONS
Several important observations emerged from this conference. Despite a considerable body of literature on the use of GnRHas, few rigorously conducted and controlled prospective studies are available from which to derive evidence-based recommendations. Most of our conclusions are categorized as CIII, a level of evidence that underscores the need for additional research in key areas such as the psychosocial effects of GnRHa treatment for CPP. The efficacy in increasing AH is undisputed only in early-onset progressive CPP, which highlights the need to increase our knowledge of the pathophysiology and normal limits of puberty and of the physical and psychosocial consequences of treated and untreated CPP. Our systematic review also highlighted the lack of objective evidence for commonly voiced concerns such as the propensity for GnRHas to promote weight gain or to lead to long-term diminution of BMD. Use of GnRHas for conditions other than CPP requires additional investigation and cannot be routinely suggested.

ACKNOWLEDGMENTS
Each participant to the conference provided a conflict-of-interest disclosure that is available on request. A portion of the funding for the conference was provided by pharmaceutical companies that produce and market GnRH agonists (Ferring, Indevus, Ipsen, TAP). Representatives from these companies did not participate in any deliberations, did not contribute to the content of the report, and did not review or comment on the report before publication.

The following are members of the ESPE-LWPES GnRH Analogs Consensus Conference Group (in alphabetical order, with group chairs indicated by an asterisk) and are coauthors of this article: Franco Antoniazzi (Pediatric Clinic, Policlinico Giambattista Rossi, University of Verona, Verona, Italy); Sheri Berenbaum (Departments of Psychology and Pediatrics, Pennsylvania State University, University Park, PA); Jean-Pierre Bourguignon (Department of Pediatrics, University of Liège, Liège, Belgium); George P. Chrousos (First Department of Pediatrics, University of Athens, Athens, Greece); Joël Coste (Department of Biostatistics, Groupe Hospitalier Cochin-Saint Vincent de Paul and Université Paris-Descartes, Paris, France); Cheri Deal* (Endocrine Service, Sainte-Justine Hospital Research Center, University of Montreal, Montreal, Quebec, Canada); Liat de Vries (Institute for Endocrinology and Diabetes, Schneider Children’s Medical Center of Israel, Petah-Tikva, Israel, and Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel); Robert L. Rosenfield* (University of Chicago Priztker School of Medicine, Departments of Pediatrics and Medicine, Section of Pediatric Endocrinology, University of Chicago Comer Children’s Hospital, Chicago, IL); Dorothy Shulman (Department of Pediatrics, All Children’s Hospital/University of South Florida, Tampa, FL); Dennis Styne (Rumsey Chair of Pediatric Endocrinology, Professor of Pediatrics, University of California, Sacramento, CA); Maïthé Tauber (Unité d’Endocrinologie, Hôpital des Enfants, Toulouse, France); and Jan M. Wit (Department of Pediatrics, Leiden University Medical Center, Leiden, Netherlands).

We acknowledge Dr Christina Kanaka-Gantenbein (First Department of Pediatrics, University of Athens, Athens, Greece) for her help to Prof George P. Chrousos in the preparation of his contribution to the meeting.

REFERENCES
5. Lazar L, Pertzelan A, Weintrob N, Philip N, Kauli R. Sexual precocity in boys: accelerated versus slowly progressive pu-


20. Teilmann G, Pedersen CB, Skakkebaek NE, Jensen TK. Increased risk of precocious puberty in internationally adopted children in Denmark. *Pediatrics.* 2006;118(2). Available at: www.pediatrics.org/cgi/content/full/118/2/e391


46. Tuvemo T, Gustafsson J, Proos LA; Swedish Growth Hormone and central precocious puberty. *J Pediatr Endocrinol Metab.* 2000;13(suppl 1):687–693


49. Paterson WF, McNeill E, Young D, Donaldson MD. Auxological outcome and time to menarche following long-acting goserelin therapy in girls with central precocious or early puberty. *Clin Endocrinol (Oxf).* 2004;61:626–634


92. Rosenfield RL. Identifying children at risk of polycystic ovary syndrome. J Clin Endocrinol Metab. 2007;92(3):787–796


**Consensus Statement on the Use of Gonadotropin-Releasing Hormone Analogs in Children**

Jean-Claude Carel, Erica A. Eugster, Alan Rogol, Lucia Ghizzoni and Mark R. Palmert

*Pediatrics* 2009;123:e752; originally published online March 30, 2009; DOI: 10.1542/peds.2008-1783

| Updated Information & Services | including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/123/4/e752.full.html |
| References | This article cites 118 articles, 60 of which can be accessed free at: http://pediatrics.aappublications.org/content/123/4/e752.full.html#ref-list-1 |
| Citations | This article has been cited by 11 HighWire-hosted articles: http://pediatrics.aappublications.org/content/123/4/e752.full.html#related-urls |
| Subspecialty Collections | This article, along with others on similar topics, appears in the following collection(s): Office Practice http://pediatrics.aappublications.org/cgi/collection/office_practice |
| Permissions & Licensing | Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://pediatrics.aappublications.org/site/misc/Permissions.xhtml |
| Reprints | Information about ordering reprints can be found online: http://pediatrics.aappublications.org/site/misc/reprints.xhtml |