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Korean Society of Pediatric Endocrinology

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Table of contents

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Words from the President

Dear members,
I am pleased to announce the publication of the 11th issue of the Korean Society of Pediatric Endocrinology (KSPE) International Newsletter. Since its establishment in 1995, KSPE has made great strides in both academics and research. With current membership nearing 300 members, our society continues to grow and make an impact through greater academic interaction, research, continuing education and public health campaigns.
This year is an important year, with our society hosting the soon upcoming APPES 2022 meeting in Seoul. The meeting will be hosted in hybrid format, with both in-person and online attendees. With the hard work of members of the organizing committee, I am sure that the meeting will be a success in providing a dynamic forum for many researchers to get together and exchange ideas and forge new connections.
KSPE and the International Committee strive to help you in achieving your goals and I ask for continued support and active participation from our members. Finally, I would like to express my heartfelt gratitude to the International Committee director and staff members who have contributed to publication of the newsletter and to international exchange. Thank you very much.
Jin Soon Hwang (President of KSPE, Ajou University Hospital)

Editor's Note

Greetings to all members of the KSPE community. I am greatly pleased to be sharing with you the 11th issue of the International Newsletter. In this newsletter, we reflect on the 2022 Spring Symposium, which was held as an in-person meeting this past May. It was a welcome change from the previous recent meetings that were held online. In this issue we also introduce the latest reviews and guidelines in pediatric endocrinology and metabolism, to help our members in clinical practice. Moreover, we hope that the schedule of forthcoming international conference in endocrinology and related fields serves to help navigate another year of scientific exchange and collaboration. The APPES 2022 meeting is fast approaching, and we welcome all attendees to Seoul, either in-person or virtually. I would like to express my deepest gratitude and appreciation for everyone who contributed their time and effort in the making of this newsletter, including the president, KSPE members, and the members of the KSPE international committee.
Jung Sub Lim (International Committee Director, Korea Cancer Center Hospital)

Reflections on KSPE's 2022 Spring Symposium

The KSPE's 2022 spring symposium was successfully held on May 20 at BEXCO, Busan. It was the first face-to-face conference since the beginning of the COVID-19 pandemic. The meeting provided grounds for members of the society to meet in quite some time. Professor Reiko Horikawa, the Director of the Japanese National Centre for Child Health and Development, presented the types, mechanisms, and the results of clinical trials of long-acting growth hormones during the invited lecture entitled "Long-acting growth hormone: now and the future." The second invited lecture entitled "Artificial Intelligence (AI) for healthcare: prediction, interpretability, mullti-modality" was given by Dr. Edward Choi (Kim Jaechul Graduate School of AI, Korea Advanced Institute of Science and Technology). Dr. Choi introduced the concept of AI and explained how it can be used in clinical care, specifically using the electronic health records. The meeting then moved onto the symposium "Digital health care and precision medicine in pediatric endocrinology". Professor Jieun Lee discussed the details of digital health technology for type 1 diabetes management. The molecular and genetics-based approaches for precision medicine in monogenic and type 2 diabetes were discussed by Professor Jung-Eun Moon. Precision medicine in obesity, thyroid cancer and reproductive endocrinology were discussed in detail by Professors Yumi Kim, Young Ah Lee, and Jin-Ho Choi, respectively. The talks focused on the genetic background as well as practical clinical guidelines of the diseases by specialists of each field. The symposium was followed by the KSPE academic awards ceremony. The winners were as follows: Hwal Rim Jeong for the KSPENDO Award; Yun Jeong Lee for the Emerging Researcher Award; Jae Hyun Kim and Jung-Eun Moon for the Outstanding Paper Awards. Following the awards ceremony, the retirement ceremony for Professor Byung Kyu Suh of The Catholic University of Korea, Seoul St. Mary's Hospital was held. Professor Suh gave a highly motivating lecture of his past journey as a clinician, researcher, and educator. The spring symposium was a great success in the sharing of knowledge and ideas for better research and clinical care.
Hye Jin Lee (Hallym University, Kangnam Sacred Heart Hospital)

Latest reviews and guidelines in pediatric endocrinology and metabolism

Obesity

Cudaa S and Censani M, Progress in pediatric obesity: new and advanced therapies. Curr Opin Pediatr. 2022;1;34(4):407-413.

This review article discusses new medical and surgical options for the treatment of children and adolescents with obesity. The impact of COVID-19 on this vulnerable population as well as the recent availability of the screening tests for rare genetic causes of obesity were also reviewed. The prevalence of obesity in childhood is increasing, with associations to the COVID-19 pandemic. Obese children are at high risk for severe COVID-19 infection requiring ICU admission and mechanical ventilation. More therapeutic options have been available for the treatment of youth with obesity since 2020, including 2 anti-obesity medications that were approved by the FDA. The GLP-1 receptor agonist, liraglutide, was approved for chronic weight management of children aged 12 and older who have obesity defined by specific BMI cut-offs for age and sex that correspond to a BMI of 30kg/m^2 or higher for adults. Semaglutide is another GLP-1 receptor agonist which is administered weekly and is currently not approved for use in adolescents for the treatment of obesity. However, the STEP-4 Teen trial is closing in March 2022. Setmelanotide is a melanocortin-4 (MC4R) receptor agonist developed for the treatment of obesity. In November 2020, setmelanotide was approved by the FDA for patients 6 years and older with obesity due to three rare genetic conditions: POMC deficiency, PCSK1 deficiency, and LEPR deficiency confirmed by genetic testing demonstrating variants in proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or Leptin Receptor (LEPR) genes considered pathogenic, likely pathogenic, or of uncertain significance. It is also in clinical trials for other rare genetic disorders associated with obesity. These disorders include Bardet-Biedl Syndrome, Alstrom Syndrome, POMC and other MC4R pathway heterozygous deficiency obesity, and POMC epigenetic disorders. Genetic screening for rare genetic causes of obesity had been widely available. Most of the genetic testing is based on mutations in genes involved in the MC4R pathway which modulates appetite regulation. Children with genetic causes of obesity frequently present with severe hyperphagia, defined as an obsession and almost complete preoccupation with food. In addition to the hope of treatment with a new pharmacotherapeutic agent that may help individuals with genetic mutations, patients may also benefit from increased knowledge about their condition and reduced social stigma.

Hye Jin Lee (Hallym University, Kangnam Sacred Heart Hospital)

Bone and calcium metabolism

Lee YA, Kwon A, Kim JH, Nam HK, Yoo JH, Lim JS, Cho SY, Cho WK, Shim KS. Clinical practice guidelines for optimizing bone health in Korean children and adolescents. Ann Pediatr Endocrinol metab. 2022;27(1):5-14.

The Committee on Pediatric Bone Health of the Korean Society of Pediatric Endocrinology has developed evidence-based clinical practice guidelines for optimizing bone health in Korean children and adolescents. Osteoporosis is now increasingly recognized in younger adults due, in part, to the longer survival of chronically ill children and children with osteoporosis are at a high risk of skeletal morbidity not only during youth, but also in adult life. Numerous factors that affect bone mineral deposition and bone mass formation are largely divided into two groups: nonmodifiable factors including genetics, sex, and ethnicity and modifiable factors including nutrition, exercise, lifestyle, body weight, body composition, and hormonal status. Low bone mineral density (BMD) is the preferred term for dual-energy x-ray absorptiometry reports in children when the BMD z-score is ≤-2.0. Osteoporosis in children is defined as the presence of ≥1 vertebral compression fracture in the absence of local disease or high-energy trauma. It may also be defined as the presence of both a clinically significant fracture history and a BMD z-score ≤-2.0. There are primary and secondary causes of reduced bone mass and increased fracture risk. Primary osteoporosis (osteogenesis imperfecta, idiopathic juvenile osteoporosis etc.) occurs due to intrinsic skeletal defects originating from genetic or idiopathic causes, while secondary osteoporosis (endocrine, neuromuscular, connective tissue, gastrointestinal, hemato-oncologic, renal, nutritional disorders and medication use) results from chronic systemic illnesses in children due to either the effects of the disease process or the treatment on the skeleton. DXA should be performed for any pediatric patients at risk of primary or secondary bone disease to decrease the risk of clinically significant fractures. If follow-up DXA is indicated, the minimum interval between scans should be 6–12 months. In terms of management, adequate nutritional intake, weight-bearing exercise, reduced sedentary activities, maintaining proper body mass index as well as lean body mass, and balanced hormonal status should be adequately

synchronized to optimize bone health. In order to enhance BMD, pharmacological treatment includes bisphosphonate and newer drugs such as teriparatide (recombinant human parathyroid hormone), strontium ranelate, and denosumab (monoclonal anti-RANKL antibody) which modulates bone formation and resorption. However, the effect and safety profiles of newer drugs in children are yet insufficient. Childhood bone mineral deposition can be a major determinant of BMD in later life, thus modifiable determinants of bone mass should be adequately maintained to optimize bone health in children and adolescents. The definition of osteoporosis in children is different from that in adults, and in pediatric patients with primary or secondary osteoporosis, underlying conditions should be treated first, and then conservative and pharmacologic therapies should be considered.

Moon Bae Ahn (Seoul St. Mary's Hospital, The Catholic University of Korea)

Disorders of sexual development and hypogonadism

A Nordenström, S F Ahmed, E van den Akker, J Blair, M Bonomi, C Brachet, et al. Pubertal induction and transition to adult sex hormone replacement in patients with congenital pituitary or gonadal reproductive hormone deficiency: an Endo-ERN clinical practice guideline. Eur J Endocrinol. 2022;186(6):G9-G49.

This guideline was endorsed by the European Society for Pediatric Endocrinology, the European Society for Endocrinology and the European Academy of Andrology. The aim was to create practice guidelines for clinical assessment and puberty induction in individuals with congenital pituitary or gonadal hormone deficiency. The guideline includes recommendations for puberty induction with estrogen or testosterone. Publications on the induction for puberty with follicle-stimulation hormone and human chorionic gonadotrophin in hypogonadotropic hypogonadism are reviewed. The expert panel recommends that pubertal induction or sex hormone replacement to sustain puberty should be cared for by a multidisciplinary team. Children with a known condition should be followed from the age of 8 years for girls and 9 years for boys. Puberty induction should be individualized but considered at 11 years in girls and 12 years in boys. 17β-estradiol is recommended for puberty induction in girls and adding progesterone is recommended after at least 2 years of treatment of puberty induction. For boys, testosterone is recommended for puberty induction and the treatment process depends on the diagnosis. Psychological aspects of puberty and fertility issues are especially important to address in individuals with sex development disorders or congenital pituitary deficiencies. The transition of these young adults highlights the importance of a multidisciplinary approach, to discuss both medical issues and social and psychological issues that arise in the context of these chronic conditions.

Yoo Jin Chung (Myongji Hospital)

Thyroid

M Klosinska, A Kaczynska, I Ben-Skowronek. Congenital Hypothyroidism in Preterm Newborns - The Challenges of Diagnostics and Treatment: A Review. Front Endocrinol (Lausanne). 2022;13:860862.

Congenital hypothyroidism (CH) is a disorder highly prevalent in premature neonates. As the survival rate of preterm newborns is constantly escalating, there is an increasing incidence of CH, with almost 50% occurrence. This review summarizes the current state of knowledge on CH in preterm infants. CH originates from multiple factors (e.g. maternal factors, perinatal and labor complications, genetic abnormalities, thyroid malformations, side effects of medications and therapeutic actions). CH in preterm neonates manifest clinically in a few distinctive forms: primary, permanent or transient, and secondary. Transient CH was mentioned to be more common in preterm neonates (with incidence of 1:1114) and may develop as a result of maternal exposure to antithyroid medications or fetal exposure to maternal antithyroid antibodies, untreated maternal hypothyroidism, and the use of iodine-based skin disinfectants on premature infants which can inhibit thyroxine production. In addition, hypothyroxinemia of prematurity prevails because of the immaturity of the hypothalamic-pituitary-thyroid axis and multiple other risk factors (such as, lower gestational age, maternal pre-eclampsia, respiratory distress syndrome, mechanical ventilation, and dopamine infusions). The repetition of neonatal screening that involves collection of a second blood specimen between the tenth and fourteenth days after birth were recommended in neonates at risk of CH (preterm, low birthweight, and sick infants). The initial dose of levothyroxine (L-T4) were suggested depending on the severity of the disease: 10–15 μg/kg/day in primary CH (increases in children with severe CH), 5-10 μg/kg/day in suspected central CH, and 1-2 μg/kg/day in diagnosed central CH. Reevaluations beyond the first 6 months of life were emphasized to assess the need or its absence for further therapy.

Hwa Young Kim (Seoul National University Bundang Hospital)

C Peters, N Schoenmakers. MECHANISMS IN ENDOCRINOLOGY: The pathophysiology of transient congenital hypothyroidism. Eur J Endocrinol. 2022;187(2):R1-R16.

Transient congenital hypothyroidism (TCH) refers to congenital hypothyroidism which spontaneously resolves in the first few months or years of life. Despite the prognostic importance of TCH and its increasing frequency, much remains unclear regarding its pathophysiology. This review clarified the definition of TCH, and summarized the process of thyroid hormone biosynthesis including the roles of known genetic and environmental determinants of TCH. Although it is not usually possible to distinguish individuals with permanent CH from those with TCH at the time of diagnosis, indicators of TCH were lower levothyroxine requirements throughout the course of treatment, lower TSH levels at diagnosis, and absence of TSH elevation during treatment. Additional predisposing factors included low birth weight, male sex, non-White ethnicity, prematurity and neonatal intensive care admission, and maternal thyroid disease. However, given the difficulties in predicting TCH, all children with thyroid gland in situ CH should be reassessed before the end of the third year of life. The suggested indications for treatment cessation included the absence of a definitive diagnosis of permanent CH, a daily dose of thyroxine ≤ 25 μg (consider if <3 μg/kg/day) and stable or decreasing dose requirements, without TSH rise on treatment. Potential contributors of the increases in TCH included the effects of increased ascertainment due to decreased screening cut points, the likely re-emergence of iodine deficiency in certain regions, altered genetic background or ethnicity of the screened population, and increased survival of preterm infants in some settings. For genetic causes of TCH, the association of TCH with DUOX2 and DUOXA2 mutations is well-recognized. When TCH is confirmed to be genetically mediated, the individual should be offered long-term monitoring for recurrent thyroid dysfunction, particularly during pregnancy.

Hwa Young Kim (Seoul National University Bundang Hospital)

Growth and puberty

C Hage, H Gan, A Ibba, G Patti, M Dattani, S Loche, et al. Advances in differential diagnosis and management of growth hormone deficiency in children. Nat Rev Endocrinol. 2021;17:608-624.

In this comprehensive review of the diagnosis and management of growth hormone deficiency (GHD) in children, the authors provide an up-to-date review of the clinical presentation, neuroimaging, genetic testing, management, adverse effects, and transitional care associated with GHD. The clinical presentation may differ according to the age at diagnosis and whether the deficiency in growth hormone (GH) is isolated or multiple. GHD in neonates can be isolated but it often presents as multiple pituitary hormone deficiency (MPHD), while GHD in childhood presents typically with persistent growth failure. The most common presentation in adolescents is growth retardation and delayed puberty. GH stimulation testing is required to assess GH secretory capacity, with 2 failed tests confirming a diagnosis of GHD. Recent guidelines suggest that the best assays should measure the 22kDA isoform of GH using highly sensitive chemiluminescence immunoassays. Other biochemical parameters such as IGF1 and IGFBP3 may provide additional information in the diagnosis of GHD. A genetic origin of GHD should be considered in the presence of parental consanguinity, positive family history, craniofacial or brain midline abnormalities or other syndromic features that suggest a genetic etiology. An approach in which extra-pituitary features point to a specific underlying diagnosis with subsequent candidate gene testing may prove useful. Brain MRI should be performed in children with GHD to avoid missing hypothalamic-pituitary abnormalities or tumors, with an assessment of the signal intensity, shape, size, and position of the anterior pituitary, posterior pituitary, pituitary stalk, and surrounding tissues. In addition to a high resolution sellar MRI, one or more survey sequences of the entire brain, a fluid attenuation inversion recovery and a diffusion-weighted imaging sequence in the axial plane is recommended. The established treatment of GHD is rhGH with daily injections. Several sustained-release GH preparations administered weekly have been developed, offering increased acceptance, tolerability and flexibility. Multiple potential adverse effects need to be monitored including intracranial hypertension with increased intraocular pressure, slipped capital femoral epiphysis, and progressive worsening of scoliosis. The existing evidence does not support a clear association between rhGH and risk of death, with contrasting results from different studies. The current guidelines for GH testing during the transition period agree on the need for retesting in patients with isolated GHD after stopping rhGH for at least 1 month. In those with MPHD, low IGF1 levels (<-2.0 SDS), documented genetic defects affecting pituitary function, and/or structural hypothalamic-pituitary defects, rhGH can be continued without interruption or retesting.

Hae Woon Jung (Kyung Hee University Medical Center)

Schedule of forthcoming international conferences in endocrinology and related fields

12th Asia Pacific Paediatric Endocrine Society (APPES) Scientific Meeting
Date: October 5-8, 2022
Location: Seoul, Korea and Virtual

91st Annual Meeting of the American Thyroid Association
Date: October 19-23, 2022
Location: Montreal, Quebec, Canada

ISPAD 2022 – 48th Annual Conference
Date: October 13-16, 2022
Location: Abu Dhabi, United Arab Emirates

EndoBridge 2022
Date: October 20 - 23, 2022
Location: Antalya, Turkey

The 55th Annual Scientific Meeting of JSPE
Date: November 1-3, 2022
Location: Yokohama, Japan

20th World Congress Insulin Resistance Diabetes and Cardiovascular Disease (WCIRDC)
Date: December 1-3, 2022
Location: Los Angeles, CA, United States

16th International Conference on Childhood Obesity and Nutrition
Date: February 20-21, 2023
Location: Madrid, Spain

Endo 2023 - The 105th Annual Meeting of Endocrine Society
Date: June 15-18, 2023
Location: Chicago, IL, United States

Pediatric Endocrine Society (PES) Annual Meeting
Date: MAY 5-8, 2023
Location: San Diego, CA, United States

83rd American Diabetes Association (ADA) Scientific meeting
Date: October 20-23, 2022
Location: Antalya, Turkey

ESPE 2023 – 61st Annual Meeting
Date: September 21-23, 2023
Location: The Hague, Netherlands

92nd Annual Meeting of the American Thyroid Association
Date: September 27-October 01, 2023
Location: Washington DC, United States

APPES 2022 in Seoul

The upcoming 12th Asia Pacific Paediatric Endocrine Society (APPES) Biennial Scientific Meeting is set to be held in Seoul during October 5-8. This is the second time the KSPE is hosting the scientific meeting, with the 5th meeting having taken place in Seoul in 2008. The upcoming meeting will provide a forum for members of the global pediatric endocrinology community to share knowledge in the "New era and big challenges in paediatric endocrinology." The conference will be hosted in a hybrid format (with both virtual and in-person attendance) with expectations for a dynamic and vibrant meeting despite the COVID-19 pandemic. We hope you will enjoy all aspects (academic and social) of this meeting. **More detailed information can be found on the APPES 2022 website (https://appes2022seoul.org/index.php)**.

Seoul is the capital of Korea as well as the heart of Korea's culture. Here are some historical and exciting places you may want to visit to experience the essence of K-culture.

A Guide to Seoul

<1> Gyeongbokgung Palace and National Palace Museum
Gyeongbokgung was the first royal palace of the Joseon dynasty, the last kingdom of Korea. You can experience the great history of the early Joseon dynasty that lasted for 200 years at the palace and surrounding areas.

<2> N Seoul Tower
N Seoul Tower is a landmark of Seoul, one of its most recognizable sights for the last 40 years, and a beloved romantic spot. Its fences are lined with numerous padlocks, each bearing a vow of unchanging love. Don't miss the Namsan cable car, which can take you to the N Seoul Tower, whilst providing a panoramic view of downtown Seoul on the way.

<3> Ikseon-dong
Here's a Hanok Neighborhood! Ikseon-dong is a center of Seoul's "newtro" (new and retro) boom, a gate in time where narrow alleyways crisscross through the neighborhood of quirky cafés, restaurants, bookstores, arcades, beer halls, accessory shops, and photography studios.

<4> Lotte World
Lotte World Adventure, a massive indoor amusement park connected to a subway station, department store, and hotel, was opened to the public on July 12, 1989. You can enjoy many of its attractions, including The Conquistador, the French Revolution rollercoaster, the Flume Ride, and the Gyro Drop. Get in Touch with the Korean People's Love for Festivities!

You can refer to more various places and detailed information on the official tourism information website of Seoul (https://english.visitseoul.net/index).

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