



대한소아내분비학회
Korean Society of Pediatric Endocrinology

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Editor-in-Chief: Jung Sub Lim

Editorial Board Member: Hae Woon Jung, Hwa Young Kim, Eun Byoul Lee,
Moon Bae Ahn, Hye Jin Lee, Yoo Jin Lindsey Chung

Words from the President

I would like to wish all members a very happy new year. The past 2 years have been difficult with the ongoing COVID-19 pandemic. COVID-19 has had a significant impact on all aspects of our lives, in all parts of the world. While the KSPE has also been affected, I am grateful that we have been able to overcome challenges to succeed in our mission dedicated to advancing research, communication, education, and clinical practice in the field of pediatric endocrinology. The KSPE's 2021 symposiums and scientific meetings were completed as scheduled. Moreover, our society's publication, *Annals of Pediatric Endocrinology & Metabolism (APEM)*, has received and published exceptional studies, resulting in growth of the journal's impact factor and expectations for listing in the SCIE. 2022 is an important year. The 12th Biennial Scientific Meeting of the APPES will be taking place in Seoul in October. Since APPES 2008, this will be the second time KSPE will be hosting an APPES meeting. I anticipate APPES 2022 will be another successful meeting that will provide latest information and updates throughout the field of pediatric endocrinology. Furthermore, I believe it will be a great opportunity for all members to connect and engage with international researchers with similar goals and interests in pediatric endocrinology. I wish you and your family a meaningful year filled with peace and joy. While the situation is unpredictable, I am confident that we will overcome these difficulties through our individual efforts and collaborative co-work. KSPE and the International Committee strive to help you in achieving your goals and I ask for continued support and active participation. I thank all our colleagues who contributed to this issue of the newsletter and I wish all members of KPSE good health, success and happiness this year.

Jin Soon Hwang (President of KSPE, Ajou University Hospital)

Editor's Note

Greetings to all KSPE and international members. COVID-19 has brought many uncertainties and changes, especially in the field of medicine. Many scientific meetings were cancelled or postponed in the beginning of the pandemic, which was unprecedented. However, societies have adapted by embracing virtual and hybrid methods, by which sharing and communication with international researchers have endured. I hope all members continued success in their own fields of interest, and continue on to a fruitful year in 2022. In this 10th newsletter, we reflect on the KSPE 2021 Fall Symposium that was conducted virtually. We also introduce the latest hot topics in pediatric endocrinology and metabolism. 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 within the bounds of social distancing. We also have great hopes for APPES 2022, the 12th Biennial Scientific Meeting which will be taking place on October 5-8 at Conrad Seoul, Korea. I express my deepest gratitude and appreciation for the members 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. Thank you and I wish a happy new year for all.

Lim Jung Sub (International Committee Director, Korea Cancer Center Hospital)

Reflections on KSPE's 2021 Fall Symposium

In the aftermath of the coronavirus pandemic, KSPE's 2021 Fall symposium was successfully held virtually, on October 22. A total of 246 members participated in the meeting. The invited speaker of the plenary lecture, Professor Dokyoon Kim of the University of Pennsylvania, spoke about the development and application of the data integration approach in improving the ability to diagnose, treat and prevent complex disease using bioinformatics technology in his lecture entitled "Translational research using electronic health record-linked biobank data." The meeting then moved onto the symposium "New mechanisms and pathophysiology of congenital endocrinopathies." Updated diagnostic approaches and treatment with a focus on congenital endocrine diseases was discussed in detail by specialists in the field. Professors Yoo-Mi Kim, Young Ah Lee, Chongkun Cheon, Ja Hye Kim, and Hyo-Kyoung Nam focused on recent updates in skeletal dysplasia, hypothyroidism, diabetes, disorders of sex differentiation, and adrenal insufficiency, respectively. The talks highlighted genetic diseases related to endocrinopathies that the clinician should be focused on during the neonatal period. The talks also provided practical tips and guidelines that could help in differential diagnosis and treatment. The symposium was followed by a ceremony to award the presenters of outstanding abstracts. Members awarded for the oral presentation were Hwal Rim Jeong (Differentially expressed Exosomal miRNA; potential biomarker for catch-up growth in small for gestational age), Min Jae Kang (The characteristics of DNA methylation pattern in children born small for gestational age who failed to catch-up growth), Yunsoo Choe (Prenatal and childhood exposures to endocrine disrupting chemical and early

breast development in 8-year-old girls: A prospective cohort study), Soojin Hwang (A Comparison of Whole Exome Sequencing to Targeted Panel Sequencing in Patients with Disorders of Sex Development), Moon Bae Ahn (The Role of Fetuin-A-to-Adiponectin Ratio in Obese Children and Adolescents with Diabetes Mellitus), and Ahreum Kwon (Sleep timing is one of the Risk for Obesity in Adolescents: Korean National Health and Nutrition Examination Survey VII). Winners of the KSPE research fund were also announced. The KSPE research fund was awarded to In Hyuk Chung (Birth weight, parenting environment, maternal factors and childhood obesity viewed through health check-up for infant and toddler) and Chongkun Cheon (A study on the correlation between diabetes and depression using the Down syndrome critical region gene 1). As the conference was held in a hybrid format due to the COVID-19 pandemic, face-to-face interactions were sorely missed. However, the fall conference was a great success and the upgraded platform allowed for acquisition of new knowledge, sharing of new ideas, and effective communication. The meeting allowed us to come together to continue in our shared interests and goals for innovative research and expert patient care in pediatric endocrinology.

Yoo Jin Chung (Myongji Hospital)

Hot topics in endocrinology at 2021 conferences (ENDO, ESPE, APPES)

ENDO 2021 (March 20-23)

Reproductive Endocrinology

Presentation: Management of endocrine complications of adolescent eating disorders

Speaker: Madhusmita Misra (Massachusetts General Hospital and Harvard Medical School)

Anorexia Nervosa (AN) is common low-weight eating disorder associated with many endocrine changes, which is primarily adaptive to preserve energy expenditure. Changes in GH-IGF1 axis (\uparrow GH, \downarrow IGF-1), H-P-A axis (\uparrow cortisol), H-P-T axis (\downarrow T3) and other hormones (\downarrow insulin, leptin, oxytocin, \uparrow ghrelin, PYY) occurred in patients with AN, leading to interruptions in the H-P-G axis (functional hypothalamic amenorrhea) and impaired bone metabolism. Adolescence is an important period during which peak bone mass is achieved. Adolescent girls with AN showed decreased accrual peak bone mass and higher prevalence and incidence of fractures. Endocrine guidelines recommend that baseline BMD be measured by DXA in any adolescent or woman with 6 or more months of functional hypothalamic amenorrhea. Earlier screening is recommended if there is a history of suspicion of severe nutritional deficiency and/or skeletal fragility. Several mechanisms may contribute to impaired bone health in AN. First, lower lean mass and higher marrow adipose tissue is associated with lower BMD. Secondly, despite increases in GH secretion overnight, IGF-1 levels were significantly decreased and osteocalcin levels were not increased in AN patients compared to controls, which may mean presence of GH resistance. Third, functional hypogonadotropic hypogonadism is common in AN. Estrogen inhibits osteoclast induced bone resorption and promotes bone formation. Oral ethinyl estradiol may have an IGF-1 suppressive effect (hepatic first pass), thus, transdermal estradiol replacement may be effective in improving bone outcomes. The guideline suggest short-term use of transdermal 18- β E2 with cyclic oral progestin if menses do not resume after 6-12 months of a reasonable trial of nutritional, psychological and exercise intervention. Fourth, higher cortisol levels and other altered appetite regulating hormones including higher ghrelin, PYY or lower leptin levels also affect bone health in AN patients. To summarize, low bone density is prevalent in AN, associated with a higher risk of fracture. Mechanisms of low bone density includes alteration of body composition and many endocrine changes. Management involves an interdisciplinary treatment team to optimize weight gain and menstrual recovery, optimizing calcium and vitamin D status, and estrogen replacement after 6-12 months of lifestyle intervention. Continuous use of transdermal 17 β -estradiol (100 mcg) with cyclic progestin for 12 days of each month is recommended.

You Joung Heo (Ewha Womans University Mokdong Hospital)

Diabetes Mellitus

Presentation: Best medical practices in obesity and type 2 diabetes mellitus in kids

Speaker: Seema Kumar (Mayo Clinic)

With increasing obesity in children, health issues including type 2 diabetes are arising as challenges in the field of pediatric endocrinology. Although there is consensus among clinicians on the necessity of managing obesity to prevent associated medical problems in sustained or aggravated obesity, medications for obesity in children are much limited. Furthermore, the methods

by which obesity should be treated is not firmly established. This presentation was impressive because the author presented a well-formed guideline for evaluating obesity and suggested consequent approaches for obesity treatment. The guideline was appropriately specific, such that clinicians could get an idea of managing obesity in the long term. The presentation is expected to help the pediatric endocrinologist in the practicalities of obesity management in children in the outpatient clinic. Furthermore, the author overviewed the recent approach for treating type 2 diabetes in children. The TODAY study, a very large prospective which has reported on complications in youth-onset type 2 diabetes, was analyzed with deep consideration. In terms of medications in T2DM, the presenter not only dealt with metformin but also discussed liraglutide, a GLP-1 receptor agonist that was recently approved by the FDA. Overall, the presentation was informative and easy to understand. I appreciated the presenter's effort in relaying upcoming knowledge in obesity and type 2 diabetes in children and adolescents.

Sung Eun Kim (St. Vincent hospital, the Catholic University of Korea Bundang Medical Center)

ESPE 2021 (September 22-26)

Diabetes Mellitus

Plenary lecture: New drugs for treatment of youth with type 2 diabetes

Speaker: William V. Tamborlane (Yale University School of Medicine)

Type 2 diabetes mellitus (T2DM) is characterized by increased insulin resistance and decreased insulin secretion in both pediatric and adult patients. Although the pathophysiology of T2DM in pediatric and adult groups is not different, no new drugs based on randomized controlled studies, excepting metformin, had been approved for use in pediatrics for more than 20 years. Recruiting children for T2DM trials has been difficult because there are relatively few children with T2DM in Europe and most patients in the United States are disadvantaged (lack of follow-up visits due to parents' working, poor compliance with taking medications, common use of anti-psychotics due to depression and/or behavior problems). Fortunately, stand-alone pharmacodynamics or pharmacokinetics studies are no longer required prior to phase 3 studies because early pharmacodynamics/kinetics studies showed uncommonly high concentrations of exposure drugs in pediatrics with T2DM. Also, there were similarities between of weight and BMI of adults and physically mature adolescents. As such, the pediatric diabetes consortium (PDC) was established to improve the care of adolescents through efforts of making drugs with proven effectiveness in adults available to youth with T2DM. PDC centers have been involved in clinical trials such as the Ellipse study (liraglutide; a GLP-1 agonist), Exenatide Q week study, Boehringer Ingelheim Dinamo study (empagliflozin vs linagliptin), Takeda Alogliptin study, Novo Nordisk pioneer teens study (semaglutide; oral form of GLP-1 agonist), and others. Thanks to PDC centers, newly approved drugs for adolescents with T2DM are in the pipeline.

So Yoon Jung (Soonchunhyang University Seoul Hospital)

APPEs 2021 (November 26-28)

Presentation: Pubertal induction regimens: current recommendations

Speaker: Joanna Tung Yuet Ling (Hong Kong Children's Hospital)

To help timely maturation of external and internal genitalia and development of secondary sexual characteristics, pubertal induction is mainly needed in 3 groups: 1) primary gonadal dysfunction 2) hypogonadotropic hypogonadism 3) constitutional delay in growth and puberty. Pubertal induction in girls consist of low-dose estrogen administration starting at 10 years old or 11 to 12 years old in Turner syndrome. It should be followed by full 2-3 years of unopposed estrogen administration, except for older girls with late diagnosis over the age of 13, who need a faster induction period of 2 years. Among several types of estrogens, 17-beta-estradiol is the most safe and effective. Theoretically, transdermal estrogen is better than oral estrogen, but there is a lack of concrete evidence. Hence, whether to treat transdermally or orally should be decided on in consideration of the patient's preferences, characteristics, local drug availability and cost. In boys, pubertal induction should be started at 12 to 13 years with low doses of testosterone followed by gradual increases to adult doses. Among various forms of testosterone, intramuscular intermediate-acting testosterone esters and oral testosterone undecanoate are commonly used for testosterone replacement therapy (TRT). Intramuscular intermediate-acting testosterone esters should be started at a dose of 50mg every 4 weeks and escalated by 50 mg per month every 6-12 months over 2-3 years until adult doses of 200-250 mg every 2 to 4 weeks are reached. For oral testosterone undecanoate, starting doses are 40mg on alternative days for 3 months, then 40mg every day for 6-12 months, followed by increases every 6 months to 2-3 times daily, until full adult doses of 40-80 mg 2-3 times daily are reached. During TRT

in adolescents, monitoring for serum testosterone level in mid-normal range is required as well as hematocrit monitoring. When hematocrit is over 0.54, TRT should be stopped until hematocrit decreases to a safe level, at which point treatment should be restarted at a reduced dose. In patients with Klinefelter syndrome (KS), TRT usually starts in mid-to-late puberty since testosterone rises initially in early puberty but eventually declines. The option of cryopreservation and/or surgical sperm retrieval should be discussed before initiation of TRT in KS patients. For hypogonadotropic hypogonadism (HH) patients, hCG monotherapy, combined gonadotropin treatment (hCG and FSH) or sequential gonadotropin therapy (FSH monotherapy → combined FSH and hCG) might be considered with the additional aim of inducing testicular enlargement. In conclusion, physicians need to individualize pubertal induction therapy for each patient considering co-morbidities, height, fertility and personal preferences.

Yunsoo Choe (Seoul National University Children's Hospital)

Presentation: New technology in diabetes management

Speaker: Elizabeth Davis (Perth Children's Hospital)

As 100 years has passed from the discovery of insulin, it is timely to consider the advances in care for children and adolescents living with diabetes. At this Plenary session, Dr. Elizabeth Davis discussed the latest technology in pediatric diabetes care for blood glucose monitoring and insulin delivery, including closed loop systems. She also provided practical suggestions in integrating education and management in clinical care, during an era of constantly changing diabetes technology. Most pediatric endocrinologists are familiar with continuous glucose monitoring (CGM), as it is now widely used in the pediatric diabetic population. CGM benefits younger children and their caregivers in terms of increased quality of life. Recent randomized control trials have also shown better glycemic control with CGM. Furthermore, a longitudinal study has shown that longer use of CGM has a higher OR for HbA1c <7%. Insulin pumps are less commonly used than CGM, and its use varies around the world. It is important to not prejudge who will benefit from the insulin pumps, and the biggest impact of the outcome of insulin pumps was the "center effect", suggesting that education, rather than the machine, may be most important in terms of outcomes. Automated insulin delivery (AID), also known as an artificial pancreas, is a closed loop system consisting of CGM, algorithm, and an insulin pump. There are currently 3 commercially available AID systems and about 5 more AID systems in the pipeline. The glycemic control of the AID system reported so far have been similar (time in range around 70% and HbA1c around 7%). Dr. Davis emphasized that the clinician (not industry) should choose the system best for each person with diabetes before ordering the device with consideration of the patient's lifestyle, education, current familiarity/comfort (use of previous devices), resources available, and cost (insurance). The expectations of an AID system are 1) learning curve for the systems to adapt for 2-3 weeks, 2) actions needed to keep the system working should be educated, 3) personal control to 'give up control', 4) glycemic outcomes of 70% time in range, and 5) still need basics of diabetes self-management. The role of clinicians is 1) assessing bolus behavior and diabetes self-management, 2) adjusting insulin doses, 3) reinforcing good diabetes self-management behavior, 4) education on best use of device, and 5) reinforcing expectations of AID systems. For the health care professional (HCP) there has been a steep increase in the learning needed to support young people using these new technologies. HCPs have had to upskill in the new reporting software, advisors, and in some cases the technology that facilitate database benchmarking.

Hye Jin Lee (Hallym University Sacred Heart Hospital)

Title: Clock genes and bone - circadian rhythms of skeletal homeostasis

Speaker: Masanobu Kawai (Osaka Medical Center and Research Institute for Maternal and Child Health)

At the symposium session, Dr. Masanobu Kawai presented his study which demonstrated how circadian rhythms work and is related to skeletal homeostasis. The circadian clock system is an evolutionarily conserved system by which organisms adapt their metabolic activities to environmental inputs. However, lifestyles that may cause disruption between the internal circadian clock system and external rhythms are emerging. For example, data from night shift workers indicate an association between disrupted circadian clock systems and human disorders. These workers show increased mortality and morbidity from cardiovascular dyslipidemia and cancer. Night shift work is also associated with increased risk of osteoporotic fractures. It was found that the relative risk of osteoporosis was 1.35 times higher in shift workers than non-shift workers, possibly indicating that disruption of the circadian clock system may deteriorate skeletal metabolism. Other evidence is from circulation levels of bone metabolic markers, which exhibit diurnal rhythms. C-telopeptide of collagen Type 1 (CTX), which is a bone resorption marker, showed a rhythmical pattern in concentration with peaks at night time. Osteocalcin (OC) also showed a rhythmical pattern, but has a smaller amplitude than CTX. Serum calcium levels are also high during the night time in humans, however, the molecular

mechanisms that associate the circadian clock system and skeletal metabolism are largely unknown. Based on previous studies, this study hypothesized that the circadian clock system regulates calcium metabolism, especially calcium absorption, and affects skeletal homeostasis. In the molecular network of the clock system, the BMAL1 gene forms a protein complex with CLOCK. This protein complex stimulates the clock-controlled genes, inducing a cascade response and regulating circadian rhythm. In this study, the knock-out (Bmal1 int $-/-$) mouse showed disrupted circadian rhythmicity and impaired calcium absorption provoked compensatory elevation of parathyroid hormone levels and activated bone resorption. In addition, blocking circadian rhythmicity activated the sympathetic nervous system, which in turn stimulates bone resorption and suppresses bone formation. As a result, the study found reduced bone mass in these knock-out mice.

Min Jeong Jang (Seoul St. Mary's Hospital)

Experiences as a visiting scholar

Place: KAIST (Daejun, Korea)

Duration: Mar 2020 – Feb 2021



I worked as a visiting professor at the integrated lab of metabolism, obesity and diabetes (iMOD) at the graduate school of medical science and engineering (GSMSE) of KAIST for a year. KAIST GSMES is a specialized graduate school for those who have a medical license and who have a bachelor's or master's degree in the sciences and engineering. It was established to foster medical scientists in convergent studies to take leadership in the advancement of the life sciences. Dr. Hail Kim, the Chief of iMOD, has always been interested in serotonin signaling. The iMOD is currently focused on two important cells, hepatocytes and pancreas beta cells, which are first line in defense of maintaining normal blood glucose levels. The lab primarily studies molecular physiology

and conducts animal experiments using serotonin knockout mice models in order to study the regulation of differentiation and proliferation of hepatocytes and beta cells in glucose metabolism.

For the first three months, I was trained in several skills needed for basic experiments and animal handling with the help of PhD researchers. I personally found it much easier than studying abroad because of the lack of a language barrier. I proceeded to conduct animal experiments with HTR2b k/o mice and my study topic was how early pancreatic beta cell failure could influence diabetes onset and development of diabetic complications. While I had intended to research abroad, my course was altered initially by the fact that my wife was unable to join me and then by the COVID-19 pandemic. Thus, I decided on domestic training at KAIST in Daejun, which I believe in the end to be an exceptional choice. I rented a small apartment at KAIST with low cost, studying during the weekdays and spending time with family during the weekends. Life on campus was unique, safe, and overall very satisfactory especially during the COVID-19 pandemic. I would like to express my deepest gratitude to Professor Ho-Seong Kim for guiding me to this position and providing much support and encouragement.

Hyun Wook Chae (Yonsei University Gangnam Severance Hospital)



Schedule of forthcoming international conferences in endocrinology and related fields

15th International Conference on Childhood Obesity and Nutrition

Date: March 14-15, 2022

Location: London, United Kingdom

Endo 2022

Date: June 11-14, 2022

Location: Atlanta, GA, United States

International Congress of Neuroendocrinology

Date: August 7-10, 2022

Location: Glasgow, Scotland

Pediatric Endocrine Society (PES) Annual Meeting (PES 50th Anniversary)

Date: April 28-May 1, 2022

Location: Chicago, IL, United States

82nd American Diabetes Association (ADA) Scientific meeting

Date: June 3-7, 2022

Location: New Orleans, LA, United States and Virtual meeting

11th International Prader-Willi Syndrome Conference

Date: July 6-10, 2022

Location: Limerick, Ireland

ESPE 2022

Date: September 15-17, 2022

Location: Rome, Italy

ISPAD 2022 – 48th Annual Conference

Date: October 13-16, 2022

Location: Abu Dhabi, United Arab Emirates

91st Annual Meeting of the American Thyroid Association

Date: October 19-23, 2022

Location: Montreal, Quebec, Canada

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

Preparations for the forthcoming APPES 2022 in Seoul

The Inaugural Meeting for the 12th Biennial Scientific Meeting of the Asia Pacific Paediatric Endocrine Society (APPES) 2022 hosted by the Korean Society of Pediatric Endocrinology (KSPE)

On November 23, 2021, the local organizing committee (LOC) members of KSPE gathered for the inaugural meeting of the 12th Biennial Scientific Meeting of APPES 2022 which will be taking place on October 5-8 at Conrad Seoul, Korea. *Ho-Seong Kim* (Yonsei Univ.) was announced as the chairperson of the Seoul meeting, and all LOC members participated in discussions for an engaging and educational program. Since APPES 2008, this will be the second time an APPES meeting will be hosted by the KSPE. The LOC is looking forward to planning another successful meeting that is expected to provide the latest information and updates in all fields of pediatric endocrinology. Following the Fellows School at Bloomvista in Yangpyeong, APPES 2022 will consist of 4 plenary lectures, 16 symposia, 6 Meet the Expert sessions, and 5 oral presentation sessions including the Kaichi Kida session, presented by a mixture of expert regional and international speakers. The members of the LOC are *Kee-Hyoung Lee* (Vice chairperson, Korea Univ.), *Jin Soon Hwang* (Secretary general, Ajou Univ.), *Il Tae Hwang* (Deputy secretary general, Hallym Univ.), *Kye Shik Shim* (Treasurer, Kyung Hee Univ.), *Se Young Kim* (Vice treasurer, Bundang Jaesang General Hosp.), *Jin-Ho Choi* (Scientific committee, Ulsan Univ.), *Jung Sub Lim* (Publication committee, Korea Cancer Center Hosp.), *Young-Jun Rhie* (Social program committee, Korea Univ.), and *Kyung Hee Yi* (Public relation committee, Wonkwang Univ.). Registration will begin in early March. *Moon Bae Ahn* (Seoul St. Mary's Hospital, The Catholic University of Korea)

