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Korean Society of Pediatric Endocrinology

KSPE

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Words from the President

Dear members and colleagues,
I am pleased to announce the publication of the 9th issue of the Korean Society of Pediatric Endocrinology (KSPE) International Newsletter. In the past year, the COVID-19 pandemic has changed the world, setting new standards in every field. Although we went through tough times due to the pandemic, we successfully completed the KSPE's 2020 Fall Symposium and many scientific meetings virtually online. Currently the KSPE International Committee continues to provide many programs to improve the capabilities and skills of our members in areas of communication with international researchers, the latest medical knowledge, clinical practice, and education. 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. 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. Thank you very much.
Jin Soon Hwang (President of KSPE, Ajou University Hospital)

Editor's Note

Greetings to all members of the KSPE community. It gives me great pleasure to release the ninth issue of our society's International Newsletter. Last year was a year filled with uncertainties due to the COVID-19 pandemic, with many scientific meetings being cancelled or postponed. However, we were able to adjust our ways to the pandemic, with adoption of virtual meetings that allowed for opportunities to continue sharing research. In this newsletter, we reflect on the KSPE 2020 Fall Symposium that was conducted online. We also introduce the latest reviews and guidelines 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. 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.
Lim Jung Sub (International Committee Director, Korea Cancer Center Hospital)

Reflections on KSPE's Fall Symposium

After a weary beginning to 2020 with pandemic related cancellations and postponements, the KSPE's 2020 Fall Symposium was successfully held virtually, on October 23. A total of 240 members participated in the meeting, which was an increase from the number of participants in the previous year. The invited speaker of the plenary lecture, Professor Yong Man Han of the Korea Advanced Institute of Science and Technology, showed us the forefront of alternative β cell sources for diabetes therapy in his lecture entitled "Functionality of pancreatic islet-like organoids generated from pluripotent stem cells." The ability of human pluripotent stem cell derived endocrine cells to form clusters and to express pancreatic β cell like properties including endocrine hormone expression and glucose-responsive insulin production was demonstrated. Moreover, the ability of these endocrine cell clusters to regulate blood glucose levels when transplanted into diabetic mice was met with the promise of future therapeutic potential in the treatment of diabetes.
The meeting then moved onto the symposium "Transitional care of endocrine disorders from childhood to adult." Current issues and practical methods to approach transitional care for a broad range of pediatric patients was discussed in detail by specialists in the field. Professor Young Ah Lee, Professor Hae Sang Lee, Professor Jin-Ho Choi, Professor Hyo-Kyoung Nam, and Professor Ju Young Yoon focused on the issues and methods of transitional care for patients with childhood-onset growth hormone deficiency, type 1 diabetes mellitus, congenital adrenal hyperplasia, Turner syndrome, and childhood survivors of cancer therapy, respectively. The talks highlighted the issues that the clinician should be focused on during the time of transition from adolescence to adulthood for each of the disorders, and also emphasized the problems and difficulties in maintaining treatments during this time. The talks also provided practical tips and guidelines that could help optimize the transition to adult care. The symposium was a reminder that our pediatric patients are ever-changing and growing, and provided much insight into the need to prepare the patient, the family and ourselves, for a smooth transition to continued success in adult care.
The symposium was followed by a ceremony to award the presenters of outstanding abstracts. Members awarded for the oral presentation were Jungmin Ahn (Targeted Next-Generation Sequencing Panel-based mutation screening of 96 Korean

pediatric patients with idiopathic short stature and isolated growth hormone deficiency), Hyo-Kyoung Nam (Serum vascular endothelial growth factor-A (VEGF-A) levels according to pubertal state and body weight in girls), Kim Yoo-Mi (The association of pubertal onset in female rat and olfactory exposure of lavender oil), Yun Jeong Lee (The relationship between iodine status and thyroid function in congenital hypothyroidism with eutopic thyroid gland), and Yunha Choi (Mutation analysis of the COL1A1 and COL1A2 genes and genotype-phenotype correlation in patients with osteogenesis imperfecta). Winners of the KSPE research fund were also announced. The KSPE research fund was awarded to Young Ah Lee (Familial hypercholesterolemia; a prospective children's cohort study for early genetic diagnosis and treatment) and Yoo Jin Chung (Chronic exposure to a mixture of environmental endocrine disrupters in Casper zebrafish: its effects on sex differentiation and development and its relationship to precocious puberty). Although the in-person connections were missing, the fall conference was a great success. The platform provided a great way to share new research and ideas, and to come together to continue in our shared interests and goals towards innovative research and expert patient care in pediatric endocrinology.

Hae Woon Jung (Kyunghee University Medical Center)

Latest reviews and guidelines on pediatric endocrinology and metabolism

Thyroid

Trotsenburg Pv, Stoupa A, Léger J, Rohrer T, Peters C, Fugazzola L, Cassio A, et al. Congenital Hypothyroidism: A 2020-2021 Consensus Guidelines Update-An ENDO-European Reference Network Initiative Endorsed by the European Society for Pediatric Endocrinology and the European Society for Endocrinology. *Thyroid*. 2021;31(3):387-419.

Congenital hypothyroidism (CH) can be defined as dysfunction of the hypothalamic-pituitary-thyroid (HPT) axis present at birth, resulting in insufficient thyroid hormone (TH) production. In this consensus guideline, the various neonatal screening approaches for CH as well as the etiology (also genetics), diagnostics, treatment, and prognosis of both primary and central CH are included. In the section of neonatal screening of CH, CH screening for early detection and treatment is beneficial to prevent irreversible neurodevelopmental delay and optimize its developmental outcome and recommend worldwide. The incidence of CH partly depends on screening strategy, the incidence of primary CH lies between 1 in 3000 and 1 in 2000. The most sensitive test for detecting primary CH is measurement of thyrotropin (TSH) and when financial resources are available, adding measurement of total or free thyroxine (fT4) is recommended to screen for central CH. There are several biochemical criteria used in the decision to start treatment for CH. First of all, a newborn with an abnormal neonatal screening result should be referred to an expert center and confirmed by confirmatory testing with serum fT4 and TSH. If the serum fT4 concentration is below and TSH clearly above the age-specific reference interval, then levothyroxine (LT4) treatment should be started immediately. If the serum TSH concentration is >30 mU/L at confirmatory testing, treatment should be started, even if fT4 is normal. If the serum TSH concentration is 6-20 mU/L, the decision is open to the clinician whether start LT4 treatment immediately or re-evaluate 1 to 2 weeks later. If the serum fT4 is low, and TSH is low, normal or slightly elevated, the diagnosis of central CH should be considered and before starting LT4 treatment, intact adrenal function should be confirmed. The start of LT4 treatment should not be delayed due to thyroid gland imaging studies. Radioisotope scanning with or without the perchlorate discharge test, ultrasonography, or both studies are recommended. The LT4 starting dose should be up to 15 μg/kg per day. Infants with severe CH, defined by a very low pretreatment serum fT4 (<5 pmol/L) or total T4 concentration in combination with elevated TSH, should be treated with the highest starting dose (10-15 μg/kg per day). Infants with mild CH (fT4 > 10 pmol/L in combination with elevated TSH) should be treated with the lowest initial dose (~10 μg/kg per day); in infants with pretreatment fT4 concentrations within the age-specific reference interval, an even lower starting dose may be considered (from 5 to 10 μg/kg per day). For monitoring treatment in CH, the first clinical and biochemical follow-up evaluation should take place 1 to 2 weeks after the start of LT4 treatment and subsequent evaluations should take place every 2 weeks until complete normalization of serum TSH is achieved. Thereafter, the evaluation frequency can be lowered to once every 1 to 3 months until the age of 12 months. Any reduction of the LT4 dose should not be based on a single higher-than-normal fT4 concentration, unless TSH is suppressed or there are signs of overtreatment. If no definitive diagnosis of permanent CH was made, diagnostic re-evaluation of the HPT axis after the age of 2 to 3 years is indicated. Outcomes of neonatal screening and early treatment should be periodically evaluated in all children with CH, including psychomotor development and progress at school. Children and adolescents with primary CH due to dyshormonogenesis may develop goiter and nodules. Serum TSH

should be carefully targeted to the lower part of normal range and periodic ultrasound investigation is recommended. There are more detailed informations for genetics of CH, genetic counseling, and antenatal management in this consensus guideline.
Yoo Jin Chung (Myongji Hospital)

Adrenal gland

Woodcock T, Barker P, Daniel S, Fletcher S, Wass JAH, Tomlinson JW, Misra U, et al. Guidelines for the Management of Glucocorticoids during the Peri-operative Period for Patients with Adrenal Insufficiency. *Anaesthesia*. 2020;75(5):654-663.

These guidelines aim to ensure that patients with adrenal insufficiency are identified and adequately supplemented with glucocorticoids during the peri-operative period. There are two major categories of adrenal insufficiency: 1) primary adrenal insufficiency, which is due to diseases of the adrenal gland (failure of the hormone producing gland), and 2) secondary adrenal insufficiency, which is due to deficient adrenocorticotropin hormone (ACTH) secretion by the pituitary gland, or deficient corticotropin-releasing hormone (CRH) secretion by the hypothalamus (failure of the regulatory centers). Patients taking physiological replacement doses of corticosteroids for either primary or secondary adrenal insufficiency are at significant risk of adrenal crisis and must be given stress doses of hydrocortisone during the peri-operative period. Daily doses of prednisolone of 10–15 mg/m2 hydrocortisone equivalent or greater in children may result in hypothalamo–pituitary–adrenal axis suppression if administered for more than 1 month by oral, inhaled, intranasal, intra-articular or topical routes. This chronic administration of glucocorticoids is the most common cause of secondary adrenal suppression, sometimes referred to as tertiary adrenal insufficiency. Children with adrenal insufficiency are more vulnerable to problems with glycemic control than adults and require frequent blood glucose monitoring. They can be treated with a bolus of hydrocortisone at induction of anesthesia (2 mg/kg for minor or major surgery under general anesthesia) followed by an immediate continuous infusion of hydrocortisone, or alternatively with a bolus at induction followed by subsequent four hourly IV boluses of hydrocortisone (2 mg/kg) in the postoperative period. The period of fasting should be minimized (no more than 6 hours) and patients with adrenal insufficiency should be prioritized on routine surgical operating lists. When enteral intake is established, the patient should receive double the normal dose of hydrocortisone for 48 hours, and this should then be reduced to standard hydrocortisone doses once stability has been achieved. Pediatric endocrinologists must remember the symptoms and signs of acute adrenal insufficiency so that inadequate supplementation or undiagnosed adrenal insufficiency can be detected and treated promptly. Delays may prove fatal.
Moon Bae Ahn (Seoul St. Mary's Hospital)

Diabetes Mellitus

American Diabetes Association. Children and Adolescents: Standards of Medical Care in Diabetes-2021. *Diabetes Care*. 2021;44(Suppl 1):S180-S199.

The annual "Standards of Medical Care in Diabetes" published by the American Diabetes Association has been updated for the current year. The revisions to the chapter on children and adolescents include new information regarding continuous glucose monitoring (CGM) for glycemic control in type 1 diabetes. New recommendations on physical activity in youth with prediabetes and type 2 diabetes and on considering social determinants in treatment decisions had been added to this year's guidelines. To summarize these new recommendations, real-time CGM in conjunction with insulin therapy is a useful tool to lower and/or maintain A1C levels and/or reduce hypoglycemia when used properly. Intermittently scanned CGM in conjunction with insulin therapy can be useful to replace self-monitoring of blood glucose. CGM metrics derived from CGM use over the most recent 14 days (or longer for patients with more glycemic variability), including time in ranges (within target, below target, and above target), are recommended to be used in conjunction with A1C whenever possible. Youth with prediabetes and type 2 diabetes, like all children and adolescents, should be encouraged to participate in at least 60 minutes of moderate to vigorous physical activity daily (with muscle and bone strength training at least 3 days/week) and to decrease sedentary behavior. Providers should assess for food security, housing stability/homelessness, health literacy, financial barriers,

and social/community support and apply that information in making treatment decisions of type 1 and type 2 diabetes.
Hye Jin Lee (Hallym University Kangnam Sacred Heart Hospital)

Obesity/Lipids

Bendor CD, Bardugo A, Pinhas-Hamiel O, Afek A, Twig G. Cardiovascular Morbidity, Diabetes and Cancer Risk among Children and Adolescents with Severe Obesity. *Cardiovasc Diabetol*. 2020;19(1):79.

Severe obesity among children and adolescents is a significant global public health concern. The prevalence has markedly increased over the last decades, becoming common in many countries. Identifying substantial risk for severe obesity and its deleterious cardiovascular sequelae is of great clinical and public health importance. This systematic review reports on (i) the association between severe obesity and the prevalence of cardiovascular risk factors, diabetes and cancer in cross-sectional studies and (ii) the relationship between severe obesity and incident cardiometabolic, cancer and mortality in longitudinal studies. A systematic search was conducted using PubMed, to identify relevant articles published through October 20, 2019. Sixty studies were included in this review, of which 10 (17%) were longitudinal. The inclusion of studies in this review was not limited to a specific definition of severe obesity.

Metabolic syndrome was suggested to be more prevalent in children with severe than mild obesity, with only a few studies that focused on elucidating whether severe obesity carried an increased cardiometabolic risk over mild obesity. The prevalence of at least one cardiometabolic risk factor in children with severe obesity ranged from 67 to 86%. In dyslipidemia, higher prevalence and increasing trends of abnormal values were observed with increasing BMI categories. Data on tracking of blood pressure from childhood to adulthood demonstrated a strong correlation and a higher prevalence of youth-onset hypertension in children with severe obesity. Data show that youth with type 2 diabetes are at risk for earlier onset and more aggressive progression of diabetes-related complications than adults with type 2 diabetes and youth with type 1 diabetes. Compared to adults with matched BMI and metabolic risk profile, adolescents with severe obesity were shown to have more advanced liver disease, characterized by higher prevalence of definitive NASH (62% vs. 25%, P = 0.009) and fibrosis (83% vs. 29%, P = 0.002), and also higher systemic inflammatory markers. A change in BMI during puberty was associated with an up to twofold increased risk for heart failure. A recent longitudinal study from a nationwide cohort showed a strong association of adolescent BMI with elevated risk of cardiomyopathy in adulthood, especially dilated cardiomyopathy. The point estimates for total cardiovascular mortality were 4.3 (2.7–6.9) vs. 3.4 (2.8–4.2), and for all-cause mortality 2.0 (1.7–2.3) vs. 1.7 (1.6–1.9) with BMI higher than 35 kg/m2 compared to those with BMI of 30–35 kg/m^2.

Children with severe obesity are at greater risk for dyslipidemia, hypertension, type 2 diabetes and fatty liver disease than children with mild obesity. Cardiovascular disease and risk factors are intensified in severe compared to mild obesity, and appear at earlier ages. In summary, significant cardiovascular morbidity and higher risk of all-cause mortality have been reported in children and adolescents with severe obesity. The alarming increase in the prevalence of severe obesity, specifically among very young children, is likely to pose major challenges for the future burden of cardiometabolic disease.
Yoo Jin Chung (Myongji Hospital)

Klinefelter syndrome

Zitzmann M, Aksglaede L, Corona G, Isidori AM, Juul A, T'Sjoen G, Kliesch S, et al. European Academy of Andrology Guidelines on Klinefelter Syndrome Endorsing Organization: European Society of Endocrinology. *Andrology*. 2021;9(1):145-167.

Klinefelter syndrome (KS) is the most common sex chromosomal disorder in men, affecting patients with both hypogonadism and infertility. Nevertheless, no international guidelines have been available for KS. These guidelines, provided by the European Academy of Andrology, make recommendations regarding the care of patients with KS in various developmental stages ranging from childhood, adolescence, to adulthood. For pre-pubertal boys with KS, biennial general physical examinations including testicular evaluations were recommended. Suspected neurological or psychiatric deficits should be examined by respective specialists. Testosterone supplementation during infancy or early childhood is not recommended except in cases of micropenis. For adolescents with KS, giving information on fertility issues to patients and/or his parents is considered a good clinical practice. Assessment of Tanner stages and growth profile (height, weight, waist circumference, body proportions), signs and symptoms of hypogonadism, and measurements of testosterone and gonadotropins are recommended prior to the

predicted start of puberty and at individually determined intervals thereafter. Testosterone supplementation is recommended in cases of delayed puberty and/or signs and symptoms of hypogonadism (with low-normal testosterone and supra-normal LH serum concentrations 2 SD, according to age-related references), after fertility issues have been addressed. For adults with KS, semen analysis, sperm cryopreservation and/or testicular biopsy for testicular sperm extraction (TESE) (in cases of confirmed azoospermia) are recommended in all patients who wish for paternity. Education on lifestyle and yearly assessment of weight, waist circumference, blood pressure, fasting glucose, HbA1c and lipid profile and adequate treatment are recommended. For management of bone health, DXA analysis and fracture risk assessment with determination of vitamin D levels at the first visit and then on an individual basis are proposed.

Hwa Young Kim (Seoul National University Hospital)

Down syndrome

Tsou AY, Bulova P, Capone G, Chicoine B, Gelaro B, Harville TO, Martin BA, et al. Medical Care of Adults with Down Syndrome: A Clinical Guideline. *JAMA*. 2020;324(15):1543-1556.

The average life expectancy of patients with Down syndrome has increased substantially, from 25 years in 1983 to 60 years in 2020. However, there have been no clinical guidelines for the care of adults with Down syndrome. The Global Down Syndrome Foundation Medical Care Guidelines for Adults with Down Syndrome Workgroup developed evidence-based clinical practice guidelines (14 recommendations and 4 statements of good practice) for multiple clinical areas including mental health, dementia, screening or treatment of diabetes, obesity, cardiovascular disease, osteoporosis, thyroid disease, atlantoaxial instability, and celiac disease. Overall, the evidence base was noted to be limited. Two recommendations about diabetes screening advocate earlier initiation of screening (using HbA1c or fasting plasma glucose) and shorter intervals of testing (every 3 years beginning at age 30 years for asymptomatic patients, and every 2-3 years beginning at age 21 years for patients with comorbid obesity), given the high prevalence and earlier onset of diabetes in this population. Three recommendations for obesity, cardiovascular disease, and osteoporosis agreed with existing guidance for individuals without Down syndrome. The guidelines advocate monitoring for BMI annually, assessing the appropriateness of statin therapy every 5 years starting at age 40, and evaluating for secondary causes of osteoporosis (hyperthyroidism, vitamin D deficiency, hyperparathyroidism, medications affecting bone health) in patients who sustain a fragility fracture. Screening for hypothyroidism was recommended every 1-2 years using a serum TSH, beginning at age 21.

Hwa Young Kim (Seoul National University Hospital)

Schedule of forthcoming international conferences in endocrinology and related fields

Pediatric Endocrine Society (PES) Annual Meeting
Date: April 30-May 3, 2021
Location: Virtual meeting

Interdisciplinary Symposium on Osteoporosis (ISO) 2021
Date: May 12-14. 2021
Location: Virtual conference

81st American Diabetes Association (ADA) Scientific meeting
Date: June 25-29, 2021
Location: Virtual meeting

11th International Prader-Willi Syndrome Conference
Date: July 6 - 10, 2022
Location: Limerick, Ireland

ESPE 2021
Date: September 22-26, 2021
Location: Virtual meeting

90th Annual Meeting of the American Thyroid Association
Date: September 30 - October 3, 2021
Location: Virtual Meeting

ISPAD 2021 – 47th Annual Conference
Date: October 13-16, 2021
Location: Lisbon, Portugal

EndoBridge 2021
Date: October 21 - 24, 2021
Location: Antalya, Turkey

The 55th Annual Scientific Meeting of JSPE
Date: October 28-30, 2021
Location: Sapporo, Hokkaido, Japan

11th Asia Pacific Paediatric Endocrine Society (APPES) Scientific Meeting
Date: November 25-28, 2021
Location: Kuala Lumpur, Malaysia

19th World Congress Insulin Resistance Diabetes and Cardiovascular Disease (WCIRDC)
Date: December 2-4, 2021
Location: Los Angeles, CA, USA

IDF Diabetes Complication Congress 2021
Date: December 6-11, 2021
Location: Virtual Congress

Endo 2022
Date: March 13-15, 2022
Location: Kyoto, Japan

International Congress of Neuroendocrinology
Date: August 7-10, 2022
Location: Glasgow, UK

Helpful English expressions in the clinic

A. Greeting the audience

- Good morning/afternoon and welcome. It is an honor to be presenting here for you today.
- Good morning/afternoon. I would like to thank the organizers for inviting me here today.
- Good morning/afternoon. Thank you all for attending this presentation. I am delighted for this opportunity to present today.

B. Introducing yourself

- Let me introduce myself. I am (name) from (institution) in (city), (country).
- Let me start by giving you a brief introduction about myself. I am (name) from (institution).

C. Stating the title/subject/topic of the presentation

- Today I would like to give you an overview about…
- As you can see on the screen, our topic today is…
- The title/subject/topic of my presentation/talk/speech today is…
- I am here today to speak to you about…

D. Stating the purpose/aim/objective

- Today I would like to present the results of my research. The main objectives are to…
- What I intend to do during this presentation is…
- The main purpose/aim/objective of this presentation is to…

E. Sequencing words for the flow of the presentation

- I'll begin with/I'll start off with…Then I'll move onto…After that, I'll be looking at…
- First/First of all, I would like to…Secondly/Then/Next…Thirdly/And then…Finally…

D. Summarizing and concluding remarks

- This brings the presentation to a conclusion/the end…
- I would like to wrap up this presentation with a brief summary…l

E. Questions

- I will now take any questions that you may have.
- I think we have time for a few questions now.
- I will be happy to answer any questions you may have.