SEPTEMBER 2023
Volume 27 - Issue 3

CAPE News

Newsletter of
The Indian Society for Pediatric and Adolescent Endocrinology (ISPAE)

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EDITOR'S MESSAGE

Dear ISPAE members,

It is a proud moment to present this issue of CAPE News that is loaded with **A**cademics, **A**ccolades and **A**nnouncements (3A)! This issue on Puberty and Endocrine diseases in systemic or chronic disorders contains three excellent reviews. In addition, 3Ds in the form of **D**rug Corner, **D**iagnostics corner and History corner (**D**ate) will be interesting reads.

The '*Haute*' of this issue is the majestic announcement of the prestigious ISPAD award for the ISPAE-IDEAL program. Please do read the message from ISPAE President and the IDEAL Core Committee.

The Organizing Committee of ISPAE 2023 at Bengaluru eagerly waits to greet us for the 8th biennial ISPAE Conference from 17-19 Nov 2023. I hope most of you have started to finalize your travel plans. The Biennial Meeting of the Asia Pacific Pediatric Endocrine Society (APPES) will be the next big academic feast to be organized by ISPAE at New Delhi from 2-5 Oct 2024. Please remember to block these dates in your calendar!

I thank all our ISPAE members who have added to this academic venture through their words and Karma! I eagerly look forward to your contributions for the next issue, which will be on “Childhood Diabetes”. Please remember to share your achievements and good work.

Hope you enjoy this issue.

Best wishes,

Aashima Dabas

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MESSAGE FROM THE ISPAE PRESIDENT

Dear friends,

Greetings!

Plenty of exciting achievements have been happening at ISPAE since the last CAPE NEWS edition.

IDEAL (ISPAE. Diabetes Education and Learning) has been selected for the award of "Innovation in Pediatric Diabetes Care Award 2023" by the International Society for Pediatric and Adolescent Diabetes (ISPAD). This is a matter of great pride for the IDEAL initiative. The dedication of the core committee members, Dr Shaila Bhattacharyya, Dr Aspi Irani, Dr Anju Virmani, Dr Santosh Olety, Dr Sirisha Kusuma Boddu, Dr Preeti Singh, Ms Sheryl Salis is remarkable that made this possible. The core committee members had the unstinting support of a huge team of committed faculty of Pediatric Endocrinologists from around India and the World, the current Executive Committee, Dr Pallavi and Mr Harsh Kohli. Each member of the faculty has devoted a lot of their time and worked with passionate zeal to improve the care of children with diabetes across India. This award is an acknowledgement of their dedication and passion.

Another interesting quarterly online educational series "Pediatric Endocrinology for practicing Pediatricians - PEPP" has been initiated by ISPAE with the support and benevolence of the Indian Academy of Pediatrics (IAP). The first meeting was on "Thyroid Disorders in children" and discussed practical aspects of management of thyroid disorders. Special thanks to Central IAP under the dynamic leadership of Dr Upendra Kinjawadekar and his team for their unwavering support.

Pediatric Endocrinology for Postgraduates (PEP) is also a quarterly academic activity that provides interactive learning opportunity to students and fellows and is being appreciated.

The ISPAE-ACES will be celebrating 25th edition of the series on the 14 October 2023 between 7-9pm IST. The topic for this meeting is 'Skeletal Dysplasia' and will have two case presentations and interesting lectures by Prof Amaka Offiah from Sheffield and Dr Mamta Muranjan from Mumbai.

ISPAE members are conducting a lot of charitable activities in different parts of the country to improve care for children with endocrine issues. The ISPAE Charity awards have been enhanced in the recent past. We applaud and encourage this gesture of our members.

ISPAE is in the process of initiating several new programs in the next few months which will be unveiled soon.

We are expecting all of you at the academic feast during the biennial conference of ISPAE at Bengaluru from 17-19 November, 2023.

Wishing you all a happy, safe and merry Diwali!

On behalf of ISPAE-EC 2023-2024,

Dr Ahila Ayyavoo.

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WELCOME NEW ISPAE MEMBERS

Life Members
• Dr Padmini Karnam, Vijaywada • Dr Shamkiran K, Bengaluru • Dr Sukanya Priyadarshini, New Delhi • Dr Afreen Khan, Noida • Dr Deepika Relangi, Bengaluru • Dr Savita Khadse, Navi Mumbai • Dr Bharani A Ramalingam, Kozhikode • Dr Jayati Jhala, Mumbai • Dr Shikha Swaroop, Patna • Dr Meenakshi Subramaniam, Nagpur • Dr Vasu Burli, Kurnoor • Dr Suganthi Venugopal, Coimbatore • Dr Nisha Kalai, Vellore • Dr Sandeep Paimode, Pune • Dr Gunavathy Krishnan, Tiruchirappalli • Dr SpalchenGonbo, Leh
Associate Members
• Dr Rahul Gupta, New Delhi • Dr Tapan Wadhwa, Rohtak

Trainees' Section, June 2023 Issue - Answers

PART 1: THE PICTORIAL QUIZ ANSWERS-

1) ECTOPIC THYROID GLAND
2) DYSHORMONOGENESIS- ORGANIFICATION DEFECT

ACROSS	DOWN
1-PENDRED	2- DE QUERVAIN
6-GRAVES	3- TSH RECEPTOR
8- DUOXA2	4- PSAMMOMA BODIES
9- PAPILLARY	5- MCCUNE ALBRIGHT
10-AGRANULOCYTOSIS	7- THYROGLOBULIN
13-QUEBEC	11- STELLWAG
14-SLC5A5	12- ECTOPIC
15- WOLFF -CHAIKOFF EFFECT	16- FOXE1

Winner: Dr JAYASHRI MN – Fellow, Pediatric Endocrinology, BCHI JJMMC, Davangere: CONGRATULATIONS!!

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ISPAD awards IDEAL the 2023 "Innovation in Pediatric Diabetes Care"


Sirisha Kusuma Boddu, *Pediatric Endocrinologist, Rainbow Hospitals, Hyderabad, &*
Anju Virmani, *Director, Pediatric Endocrinology, Max Smart Super Specialty Hospital, Delhi*

Great News! We are elated to announce that **IDEAL** has been **awarded ISPAD's prestigious "Innovation in Pediatric Diabetes Care" Prize** for the year **2023**. It will be officially presented to us at the ISPAD annual conference to be held in October in Rotterdam.

IDEAL's incredible journey from a hesitant, virtual course started for the first time in the world, to a confident, ISPAD Award-winning, one-of-a-kind training program, would not have been possible without the expertise, dedication and hard work of the IDEAL Faculty and the intense involvement of the Trainees. We would like to use this opportunity to express our gratitude to each Faculty member for their knowledge, commitment, and hard work toward building and conducting the IDEAL course. We sincerely hope to receive their continued support in conducting IDEAL and developing sorely needed spin-offs in advancing awareness and advocacy in the pediatric diabetes space.

We are equally grateful to the Trainees, now certified PDEs and IDEALites, who have worked so hard during the program, and who continue to teach and motivate us. It is gratifying to hear the news of their winning awards, accolades and appreciation, as they work in different parts of India, improving diabetes care for children, adolescents, and adults with T1D.

Together we IDEALites are becoming a force moving toward the betterment of the children of our country and around the world. This award will serve as a motivation for all of us to continue to work harder.

Sincere thanks to ISPAD from the IDEAL Core Committee:

Anju Virmani

Shaila Bhattacharyya

Santhosh Olety

Sirisha Kusuma Boddu

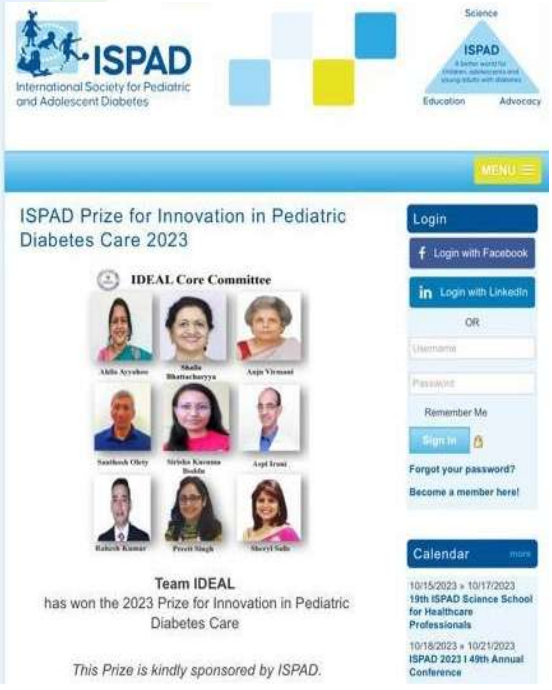
Preeti Singh

Sheryl salis

Aspi Irani

Ahila Ayyavoo

Rakesh Kumar



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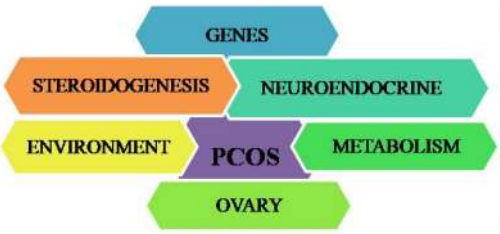
INTERNATIONAL EVIDENCE - BASED GUIDELINES (2023) ON POLYCYSTIC OVARIAN SYNDROME IN ADOLESCENCE

***Tejasvi Sheshadri**, Consultant Pediatric and Adolescent Endocrinologist;*
Sparsh Super Speciality Hospital, Shishuka Children's Hospital, Bangalore

Polycystic ovary syndrome (PCOS) is a long-term complex, heterogeneous, familial disorder. The clinical symptoms, including hyperandrogenism and chronic anovulation, typically develop during adolescence.

Pathophysiology-



- Androgen excess is a key feature, observed in approximately 60-80% of patients.
- Hirsutism results from excessive androgen production, whose chief source is the ovaries in the majority, followed by the adrenals.
- The elevated androgen concentrations suppress sex hormone-binding globulin (SHBG), concentrations contributing to higher free testosterone concentrations.
- The balance between androgens, AMH and FSH is disrupted, leading to follicular arrest. Abundant LH drives the theca cells to produce androgens, but FSH concentrations and conversion of androgens to estradiol are insufficient, resulting in failure to select a dominant follicle, thus there is chronic anovulation.
- Insulin resistance (IR) and hyperinsulinemia are common findings in women with PCOS, independent of their degree of adiposity, body fat topography, and androgen levels.
- In PCOS, the IR is tissue-selective. Resistance to the metabolic actions of insulin has been reported primarily in skeletal muscle, adipose tissue, and liver; while sensitivity to insulin actions on steroidogenesis persists in the adrenal and ovary.
- While early studies attributed the IR in PCOS to obesity, subsequent studies demonstrated the existence of IR in lean PCOS women. Puberty itself is associated with transient IR and hyperinsulinemia. Insulin can synergize with LH to increase theca cell androgen production. Insulin can also decrease the hepatic synthesis of SHBG, increasing circulating free androgens. Additionally, insulin may directly stimulate the activity of ovarian P450c17 and P450scc enzymes to promote ovarian androgen steroidogenesis.
- *Neuroendocrine Alterations*- Although not mandatory for diagnosis, a hallmark of PCOS is the presence of deregulated secretion of the gonadotropins, LH and FSH, which control ovarian steroidogenesis, follicular dynamics, and ovulation. Perturbed kisspeptin/KNDy and GABA signaling has been implicated in PCOS.
- *Genetics and epigenetics*- Studies of monozygotic and dizygotic twins have indicated moderate heritability of PCOS. The role of DENND1A in ovarian theca cell steroidogenesis is being investigated. The PCOS susceptibility allele in the FSHB gene is also associated with lower circulating FSH levels. Aromatase and LHCGR is another candidate gene in PCOS.
- *Altered Sympathetic Nerve Activity*- Many of the common clinical symptoms of PCOS are associated with chronic increased activity of the sympathetic nervous system.

Clinical Features

- Hirsutism is defined as excessive, coarse, terminal hairs, distributed in a male fashion. PCOS is the most common cause of hirsutism in adolescence.
- Mild hirsutism may be a sign of androgen excess when associated with menstrual irregularities.
- Moderate or severe inflammatory acne, unresponsive to topical therapy, may require investigation for androgen excess.
- Isolated acne and/or female pattern hair loss should not be considered diagnostic criteria for PCOS in adolescence.
- Irregular menstrual cycles (<21 or >45 days) beyond 1 to <3 years after menarche, 3 years post-menarche with <8 cycles/year or <21 or >35 days cycle; 1 year post-menarche any 1 cycle>90 days; or primary amenorrhea in girls after 15 years of age or >3 years post-thelarche.

Diagnosis: Laboratory and other work-up

- Biochemical hyperandrogenism should be defined based on the methodology used, as no clear cut-off for testosterone concentrations exists for adolescents. Biochemical evidence of hyperandrogenism based on elevations of total and/or free testosterone, measured in a reliable reference laboratory and preferably by LC-MS/MS method, is preferred to direct immunoassays.
- ***Polycystic Ovarian Morphology (PCOM)***
  - Adolescents- Measurement of ovarian volume, follicle number, and uterine dimensions may be useful in the evaluation of amenorrhea, but is not needed.
  - Adults- The follicle number per ovary is a reliable marker; ≥ 20 in at least 1 ovary is a threshold of PCOM; ovarian volume & follicle number per cross-section are other parameters.
- ***Biomarkers of PCOS***
  - The use of AMH, T/DHT ratios, and specific proteins or micro RNA as biomarkers of PCOS has not been validated in adolescents.
  - AMH can be used in place of ultrasound as a biomarker for diagnosis in adults, but not in adolescents.
  - Glycemic status should be evaluated using oral glucose tolerance test in all adolescents with PCOS (regardless of age and BMI) and reassessed every 1-3 years as per metabolic risk profile.
  - IR, compensatory hyperinsulinemia, or obesity should not be considered as diagnostic criteria for PCOS in adolescents.
- Women with PCOS have higher risk of obstructive sleep apnea; and endometrial hyperplasia or cancer (pre-menopausal period).
- Increased risk of metabolic syndrome and hypertension is seen in fathers and brothers of women with PCOS; the risk is inconclusive in first degree female relatives.
- PCOS affects quality of life, mental health and psychosexual functions.

Treatment

- Lifestyle intervention
  - Combination of calorie restricted diets, behavioral treatment, and exercise.
  - Combined weight loss and physical exercise are the first-line therapy in overweight and obese girls. They decrease androgen levels, normalize menstrual cycles, and improve markers of cardiometabolic health.
  - Extremely obese adolescents respond poorly to lifestyle intervention.
  - In normal-weight girls, increasing physical activity is effective in reducing the development of metabolic syndrome.
- Local Therapies/Cosmetic
  - Cosmetic hair-removal methods for hirsutism include bleaching, chemical epilation, plucking, waxing, shaving, electrolysis, and laser hair removal.
  - Photoepilation is the first-line management of localized hirsutism in PCOS. Diode and alexandrite lasers are preferred. The alexandrite laser is superior to IPL methods in facial hirsutism.
  - Topical eflornithine is recommended as an adjuvant to photoepilation in girls aged 16 years or older, with laser-resistant facial hirsutism, or as monotherapy in those whom photoepilation is not indicated.
  - The use of topical finasteride is not recommended based on existing data.

Additive Pharmacological Modalities

- **Metformin:** Beneficial effects are seen in overweight or obese adolescents with PCOS, but only short-term data are available. In non-obese adolescents with PCOS and hyperinsulinemia, metformin improves ovulation and testosterone level.
- **Anti-Androgens:** Two types of anti-androgens are used in the management of PCOS: androgen receptor blockers like spironolactone, flutamide, and the third generation progestin, cyproterone acetate, and inhibitors of 5-alpha reductase such as finasteride. Anti-androgens reduce features of androgen excess more than metformin in monotherapy. Spironolactone is the most commonly used, though data on efficacy compared to flutamide are limited. Anti-androgens should only be used when contraceptive measures are guaranteed.
- **Oral Contraceptive Pills:** Combination OCP containing an estrogen component and a progestin component address multiple concerns in adolescents with PCOS. Increased SHBG and decreased LH release due to the estrogen leads to a decreased free androgen index, and the progestin allows suppression of endometrial proliferation and regular withdrawal bleeding. OCP improve acne and hirsutism, and reduce menstrual irregularity. There are no high-quality RCTs of specific OCP formulations for adolescents with PCOS to help decision-making in this population, and no specific formulation can be recommended over another.
- **Combination Treatments:** Where available, low-dose combinations of insulin-sensitizing and anti-androgenic generics normalize cardiovascular risk and body composition and result in a more favorable posttreatment pattern of circulating androgens and ovulation rates than OCP intake. Inositol can be advised in PCOS to improve metabolic profile after discussing limited clinical benefits with its use.

Reproductive Aspects- In some adolescents with or at risk for PCOS, normal ovulatory function may exist or emerge with time and present as ovulatory adolescent PCOS.

Transition- PCOS therapy in adolescence should aim at decreasing hepato-visceral adiposity, enhancing central fat loss, and thus attenuating pregestational oligo-anovulation, while reducing gestational complications such as diabetes mellitus, preeclampsia, and preterm delivery.

Reference: *Teede HJ, Tay CT, Laven JJE, et al. Recommendations From the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. J Clin Endocrinol Metab. 2023;108(10):2447-2469. doi:10.1210/clinem/dgad463*

PUBERTAL INDUCTION IN BOYS FOR FERTILITY PRESERVATION- ENDO ERN GUIDELINES

Richa Arora*, Consultant Pediatric Endocrinologist, New Delhi*

Puberty is the physiological process during which secondary sexual characteristics develop. Apart from physical changes, there are also changes in body composition, brain, cardiovascular and skeletal development. In boys, the first sign of pubertal development is an increase in testis volume, ≥4 mL which occurs at an average age of 11 years, and should appear before the age of 14 years. This is typically followed by the development of pubic and axillary hair. Peak height velocity usually coincides with a testis volume of about 10-12 mL, followed by change in voice [1]. The assessment of the hypothalamic-pituitary-gonadal (HPG) axis includes the quantification of serum gonadotropins, FSH and LH, and gonadal sex steroids, testosterone (T) in boys. Gonadal peptides like inhibin B, AMH and insulin-like factor 3 may add useful information about the gonadal Sertoli & Leydig cell function [2]. A karyotype should be considered in boys with hypergonadotropic hypogonadism and who do not have a predisposing past history of testicular damage.

Puberty induction: The child needs to be informed about the medical condition in a continuous and age-appropriate process [3]. Parents need to be informed and counseled of the challenges their child will encounter during pubertal induction. All such boys should be treated by a multidisciplinary team including pediatric endocrinologist, adult endocrinologist, psychologist, urologist, geneticist, surgeon and nurse specialist, depending on the situation and specific requirement. Pubertal induction should be commenced in boys with a high risk of hypogonadism by the age of 12 years if there are no signs of pubertal development [4].

Testosterone is the most widely used agent, started as intramuscular injection of T esters (enanthate, propionate or cypionate) at 10% of the adult dose to allow physiological induction. The dose is increased by 25-50 mg every 6 months, to achieve an adult dose in 2-3 years. The adult dose consists of injection of testosterone 250 mg every 3 weeks. This regimen allows for developmental of sexual characteristics and sexual function.

Although effective in inducing pubertal signs and symptoms, T formulations neither stimulate testicular growth nor induce spermatogenesis. It is still unclear whether T therapy for pubertal induction hinders future development of testes, or likelihood of spermatogenesis, if gonadotropins are used in adulthood.

Gonadotropins are now being increasingly used for the additional advantage of fertility preservation. The standard protocol is biweekly/ weekly injections of human chorionic

gonadotropin (hCG) along with FSH, over 12-24 months [5]. This protocol has been shown to promote spermatogenesis and achieve fertility. Different treatment protocols with gonadotropins can be used to induce puberty in adolescent males with hypogonadotrophic hypogonadism (HH): exogenous hCG alone or in combination with recombinant FSH. However, evidence consistently suggests that combination therapy with recombinant FSH (rFSH)/hCG is significantly more effective than hCG alone, both for inducing spermatogenesis and increasing testicular volume. Some evidence suggests that pre-treatment with rFSH, followed by the combination with hCG or GnRH is even more effective in optimising Sertoli cell maturation, and is able to induce spermatogenesis even in extremely small testes, with cryopreservation of these sperm for ensuring the future fertility of these patients. This approach mimics the physiological elevation of FSH during spontaneous pubertal development. As this treatment involves use of multiple weekly injections, it should be discussed with the patient and parents before commencing therapy.

It is recommended to switch to T replacement treatment (TRT) in boys with HH after the completion of pubertal induction. The combination of rFSH and hCG therapy for 6-24 months results in testicular growth in almost all and spermatogenesis in 80-95% of patients without undescended testes. The shift from FSH/hCG therapy to testosterone should occur after sperm analysis. In case there is sufficient sperm in the ejaculate, sperm cryopreservation (banking) should be considered, particularly in severe oligospermia. In cases with azoospermia, i.e. 'poor responders' to gonadotropin stimulation, testicular sperm extraction (TESE) procedure might be considered. A brief therapy withdrawal (i.e. 4 months) after the conclusion of pubertal induction with gonadotropins, and before the start of TRT, might be considered to verify a spontaneous recovery of the HPG axis in HH. It is recommended to monitor treatment every 3-6 months during puberty induction. Regular follow-up with clinical parameters, patient's satisfaction and bone density, with yearly measurements of FSH and LH is suggested.

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TURNER SYNDROME - BEYOND KARYOTYPE

***Medha Mittal**, Department of Pediatrics, Chacha Nehru Bal Chikitsalaya, New Delhi*

Turner Syndrome (TS) has an incidence of 25-50 per 100,000 females and is due to the absence of all or part of the second sex chromosome (X or Y). About 45% have monosomy (45XO) and 12-20% have structural alterations, including isochromosome and ring chromosome. The rest have mosaicism as 45X/46XX, 45X/46XY and further variations [1].

While typical stigmata aid diagnosis of TS (as in homogeneous 45XO), the phenotypic presentation is quite variable and may influence early detection. The consistent features of TS are short stature and premature ovarian insufficiency; primary amenorrhea, kidney malformations, hearing loss are less frequent [3]. The mosaic 45X/46XX group has the least co-morbidities [2]. Thyroid disease, liver dysfunction and hearing loss increase with age, though less often in mosaics and least in XY mosaics. Spontaneous menarche is more likely in those with X short arm deletion. Those with isochromosome have the lowest incidence of congenital heart disease (bicuspid aortic valve) and severe hearing loss. The presence of ring chromosome is associated with a high incidence of short stature and metabolic defects (high HbA1c, liver enzymes). The finding of short fourth metacarpals is less frequent in 45X/46XX mosaics, but consistently present in those with isochromosome of the long arm of X. The presence of Y chromosome is a risk for gonadoblastoma and requires bilateral gonadectomy on follow-up.

Most of the phenotypic features are related to loss of genes on the short arm of the X chromosome. The haploinsufficiency of *SHOX* (short stature homeobox) containing gene located on Xp22.23 in the pseudoautosomal region of the sex chromosome is responsible for many skeletal changes, including short stature and short fourth metacarpal. This gene is expressed in cells of first and second pharyngeal arches, middle portions of limbs and distal part of forearm bones and wrist bones. It is a transcription regulator and its function is dosage dependent. The presence of both copies of this gene in mosaics explains the lower proportion of brachymetacrpia, unlike the higher frequency seen in isochromosome X [1].

Recent studies have reported the role of epigenetic mechanisms and differential methylation of various genes that affect phenotype expression like *TIMP1* causing bicuspid aortic valve disease, *IL3RA* related to immune function, *KDM6A* associated with gonadal dysgenesis, among others [1]. Imprinting of genes would further explain the phenotypic variation that exists even within monosomy in 45XO females.

Diagnosis: A peripheral blood lymphocyte karyotype, examining at least 20 cells, is essential to diagnose TS [4]. However, a conventional karyotype could miss low-level mosaicism or the presence of cells containing a Y chromosome. It is therefore recommended to perform cytogenetic analysis on 50 cells. Amongst homogeneous 45XO cases (diagnosed on 20 cell karyotype), 20% were detected as 45 X/46XX mosaics when additional buccal cell FISH analysis was performed [3]. The rate of abnormal cells can also vary from one tissue to another (blood lymphocytes versus amniotic, buccal, skin, gonadal or urinary cells). A FISH analysis on a buccal smear is less invasive and could be performed either after a 45XO diagnosis or as an alternative to standard karyotype [5]. It is not only less invasive, but is also better correlated to the karyotype in gonads as compared to blood lymphocytes. A larger number (100-200) of cells are routinely examined in FISH. X and Y specific centromeric probes used include DXZ1(Xp11.1-q11.1) and DYZ3(Yp11.1-q11.1). Alternately, PCR could be used with primers specific to Y sequences using genomic DNA from peripheral blood, oral epithelial cells or hair roots. The presence of Y chromosome is reported in 10-12% of patients of TS. However, with the presence of isoXq or Xp without mosaicism, there is seldom need for checking for Y chromosome. In cases of ring X chromosomes, microarray analysis may be performed to check for presence of the XIST gene [5]. As per recommendations, the diagnosis of TS should not be considered in females with one X chromosome and a deletion on the other X distal to Xq24 and in women over 50 years with less than 5% cells with 45XO [4].

TS should be suspected in all girls with short stature. A varied genotype-phenotype correlation exists and DNA analysis by advanced methods could be helpful to assess for mosaicism and timely detection of any Y chromosome material.

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PUBERTAL ISSUES IN SMALL FOR GESTATIONAL AGE


Sangita Yadav, *Professor, and* ***Alankrita Goswami,*** *Resident; Hamdard Institute of Medical Science and Research, New Delhi.*

Growth and puberty are often affected in children born small for gestational age (SGA). SGA babies have a tendency to gain excessive fat during catch-up-growth, and are prone to develop precocious pubarche, precocious adrenarche and an earlier start of puberty (though within the normal range) compared to their AGA peers. [1]. Age at menarche may be earlier by 5-6 months, and the pubertal progression may be slightly faster[2]. Hvidt et al found that girls born SGA with catch-up of 1-unit increase in z-score for length in infancy had earlier puberty, compared to infants without catch-up-growth. They also had menarche1.6-2.3 months earlier than those born AGA [3].

Growth during puberty in SGA: This has an implication on final adult height (AH) in view of accelerated tempo. The pubertal growth spurt may occur earlier during pubertal transition, and the period of growth may be shortened [4].Linear growth during puberty in SGA children is based on accelerated skeletal maturation, leading to earlier closure of growth plate, and lower AH, i.e the adolescent growth spurt is less intensive and shorter, in the earlier stage of sexual maturation, and results in a shorter period of growth[5].

SGA children with catch-up-growth also have predisposition to obesity. Obese children have increased levels of leptin, which promote GH secretion through various mechanisms like more receptors for growth hormone (GH) and higher levels of insulin-like-growth-factor-1 (IGF-1). The earlier pubertal maturation in SGA girls ensues from a mismatch between reduced prenatal weight gain i.e. reduced adipogenesis and lesser capacity for safe lipid storage, the accelerated postnatal weight gain augments lipogenesis, and thus need for lipid storage. This mismatch, with accelerated postnatal weight gain, is associated with an increased risk of early onset of insulin resistance and dyslipidemia, exaggerated adrenarche and premature pubarche, earlier age at menarche, and higher incidence of polycystic ovary syndrome **(Box 1**).

Several studies have shown no significant difference in fertility between adults born SGA or AGA; normal gonadal function was found in several SGA cohorts [4].

Box 1. Hormonal Changes in SGA with Catch up

- Leptin produced by the adipose tissue could be the link between obesity and earlier puberty in SGA girls. Leptin can lead to premature activation of GnRH pulse generator, thus affecting gonadotropin secretion and central initiation of puberty.
- Excessive weight gain decreases the levels of sex hormone binding globulin (SHBG), and increases the bioavailable estradiol and other sex steroids, that lead to onset of puberty.
- Adrenal androgens get converted to estrogen by the aromatase enzyme in adipose tissue, thus adding to the pool of available estrogens that further contributes to early onset of puberty.
- High BMI promotes insulin resistance and hyperinsulinemia, that simulate secretion of luteinizing hormone (LH) and promote androgen secretion. The androgens contribute to early puberty by stimulating GnRH secretion.

Treatment Implications:

Treatment with GH influences growth but may have limited influence on the onset and duration of puberty and the pubertal height gain, regardless of the GH dose. The addition of gonadotropin-releasing hormone agonist (GnRH) treatment to GH treatment does not leads to gain in weight and fat mass, and decrease in bone turnover and bone mineral density. There is now evidence that rules out evidence of long-term negative effects of this combination treatment [4]. Cognitive functioning, problematic behavior, self-perception and quality of health were similar in young adults born SGA following combined GH/GnRHa treatment compared with those treated with GH only.

To conclude, catch-up growth in SGA children is associated with higher BMI in prepubertal and pubertal periods as well as with an earlier appearance of menarche and adolescent height spurt. Catch-up growth allows the children to compensate for a low birth weight, but has far-reaching consequences in the form of increased risk of rapid fat accumulation and faster transition to puberty. Thus, SGA children are at risk for having compromised pubertal growth and maturation, and need long-term metabolic and endocrine monitoring.

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HISTORY OF TESTOSTERONE DISCOVERY: A TALE OF CURIOSITY, RAPACITY AND CYNICISM

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Observations of the effects of androgen ablation are an old story. As early as 200 years BC, Romans knew that castrating roosters made them more hen-like, less aggressive and fatter. Then it took almost another 2000 years for the great Scottish surgeon *John Hunter* to report in 1771 that castrated roosters (capons) could recover some of their lost maleness after testicular implantation. There are no references of his work in this area, only reports from attendees at his lectures. His reported observations took almost another 80 years (1849) to be confirmed by *Adolph Berthold*, who discovered that testicular action was correlated to circulating blood fractions - now known as the androgen hormone family.

A great deal of interest developed after *Dr Charles E. Brown-Séquard* made a presentation in 1889 on how self-administration of a liquid prepared by him from animal gonads led to improvement in his own physical strength, intellectual capacity and sexual vigor. Scientists all over the world started hearing about Brown-Sequard's incredible discovery, and began experimenting in the hope of truly discovering the “Elixir of Life.” Doctors bought guinea pigs in record numbers to conduct experiments of what was known as the “Brown-Sequard operation”, then aiming to restore the suspected substances produced by the male gonads by implanting segments or whole organs in different locations. These techniques were eventually found to be useless.

In 1927 in Chicago, *Lamuel McGee* and *Fred C. Koch* extracted 20 gm of a substance from almost 20 kg of bulls' testes, that “when injected into castrated animals restored their maleness” but this did not receive much attention from the scientific community. It was *Ernst Laqueur* and his team in Amsterdam obtaining larger amounts of the substance which caught wide attention. They named it “testosterone” from the words testicle, sterol and the suffix of ketone.

By 1935, almost simultaneously and independently, three teams led by *Adolf Butenandt, Kàroly Gyula* and *Leopold Ruzicka* reported their successful efforts to synthesize testosterone. For their work on androgens, *Butenandt* and *Ruzicka* received the Nobel Prize for Chemistry in 1939. Butenandt had to wait until the end of the war to accept the award, which he finally received in 1945.

After synthesis of the hormone, injectable preparations for human use were developed, and shortly before the onset of World War II, clinical trials on testosterone were underway. Interest grew in the use of testosterone for a variety of conditions, varying from sexual difficulties to the prevention of benign prostatic hypertrophy. Testosterone substitution became so widely prescribed that, by the mid 1940s, warnings were already being published in medical journals about its indiscriminate use and abuse. Injectable preparations, at regular but frequent intervals, were the norm in the early days of testosterone therapy before the availability of depot preparations. In 1988, USA banned the use of steroids for non-medical purposes and in 1999, the World Anti-Doping Agency was formed to detect and prevent misuse.

Currently, there is a plethora of delivery forms of testosterone available, with their own advantages and drawbacks, ranging from buccal, to transdermal preparations, to subdermal implants.

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DIAGNOSIS CORNER - ANTI-MULLERIAN HORMONE

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Anti-Müllerian Hormone (AMH),a dimeric glycoprotein, is a member of the transforming growth factor-β (TGF-β) family of cytokines. AMH plays a significant role in differentiation of reproductive structures. In males, AMH is produced by Sertoli cells from the 7th week of gestation, and triggers the involution of Müllerian ducts, allowing for testicular development. In females, AMH is produced by ovarian granulosa cells of antral and pre-antral follicles from the 36th week of gestation, and plays a role in the control of ovarian follicle growth.

In healthy males, AMH concentrations are very high from birth to puberty, after which they decrease significantly but in general remain higher than those seen in females. The expression of AMH secretion in the male fetus is genetically regulated and is stimulated by Follicle Stimulating Hormone (FSH). Later, with the onset of puberty, the increase in concentration of intratesticular testosterone inhibits the secretion of AMH by acting on the newly expressed Sertoli cell androgen receptor.

In healthy females, AMH is low at birth and rises slowly through infancy. During minipuberty, gonadotropins stimulate growth of ovarian follicles. AMH is detectable in the sera of infant girls, reaching peak concentrations around 3.5 months of age. In mid-childhood, low serum concentrations of AMH can be measured, especially with highly sensitive AMH assays. This is by virtue of continual recruitment of the primordial follicle pool to small follicles independent of FSH stimulation, even during the quiescent period of ovarian activity. Levels increase further at puberty and then remain relatively stable until the mid-to-late 20s when they begin to fall, becoming undetectable at menopause. Minor fluctuations of AMH around pubertal onset have been observed, but overall, AMH concentrations are stable through pubertal development which indicates an individual set-point of ovarian activity. Studies describing the variations of AMH show that its levels slightly rise until about 9y of age, followed by a decline from 9y to ~ 15y of age and then an increase. Healthy, early postmenarcheal girls have an average AMH level of 37.13 ± 2.14 pmol/L (5.2 ± 0.3 ng/mL). Overall, serum AMH concentrations reflect the number of small antral follicles throughout life [1].

Role of AMH in Males:

- Since AMH is the product of the Sertoli cells in the testes of males, a positive assay is evidence of the presence of testes, useful in cryptorchidism and disorders of sex development.
- In cases of hypogonadotropic hypogonadism, both prepubertal and pubertal males are likely to have low AMH levels due to decreased FSH stimulation. In the postpubertal period, AMH levels are elevated for age consequent to insufficient testosterone, however, the levels will still be lower than expected for the patient's Tanner stage, reflecting the lack of FSH stimulation. The treatment of such patients with FSH results in increased AMH concentrations [2].
- AMH is being investigated as a test for differentiating hypogonadotropic hypogonadism from constitutional delay of puberty (CDP). Patients with CDP, or with defective androgen production or sensitivity, exhibit high prepubertal AMH levels.
- In patients with primary hypogonadism such as Klinefelter's syndrome, AMH levels reflect the degree of testicular dysfunction. They maintain normal AMH levels during infancy, which

decreases with age, as Sertoli cell function reduces from mid-puberty, resulting in high FSH and small testis volume.

- Role in precocious puberty: Precocious puberty in males including central precocious puberty (CPP) and gonadotropin-independent forms such as familial male limited precocious puberty are associated with low AMH secretion for age due to rise in intratesticular testosterone. Gonadotropin-releasing hormone (GnRH) analog therapy normalizes AMH to prepubertal values, suggesting that the Sertoli cell maturation in early puberty may be reversible, and AMH could potentially serve as an additional tool for diagnosis of precocious puberty and treatment efficacy [3].

Role of AMH in Females:

- In prepubertal females, AMH can help localize the source of virilization: raised levels are found in testicular tissue-induced virilization, while levels are normal in congenital adrenal hyperplasia.
- Granulosa Cell Tumors (GCT)**:** AMH, along with inhibin B, can be used as a marker of diagnosis, treatment efficacy, tumor progression and recurrence. Prepubertal girls with GCT usually present with adnexal mass and features of hyperestrogenism and precocious puberty.
- Turner syndrome: AMH is an excellent indicator of premature ovarian insufficiency in these patients. AMH levels will be low in girls with Turner syndrome. Unlike blood gonadotropin levels that vary across the menstrual cycle, AMH has the advantage of a relatively stable blood concentration, therefore providing an attractive marker of premature ovarian failure.
- Primary ovarian insufficiency (POI): AMH has been proposed as a potential biomarker of ovarian reserve in childhood to determine possible candidates for fertility preservation, and the timing of such interventions in children and adolescents at risk of POI. In mid-childhood, serum concentrations of AMH predicted the number of ovarian follicles as the girls reached puberty and adolescence. AMH < 4 pmol/L has been reported as predictive of POI in adolescents and adult patients [4].
- Biomarker for ovarian reserve in cancer patients: AMH can provide a particularly useful marker of ovarian reserve in the prepubertal population, where FSH is not a reliable measurement.
- Polycystic ovary syndrome: Adolescents and adult females with PCOS exhibit higher AMH concentrations as compared to controls which correlates with ovarian volume and androgen level. This high AMH concentration is consequent to increased number of small AMH producing follicles resulting from altered gonadotropin secretion. AMH reduces follicle growth as well as intrafollicular aromatase activity and thereby inhibits estradiol production from small growing ovarian follicles.
- Precocious puberty marker in girls: AMH may be useful in differentiation of CPP and premature thelarche (PT). Females with PT, ages 1-3y, exhibited lower AMH levels that negatively correlated with FSH compared with age-matched controls. In contrast, girls with CPP showed similar AMH levels as healthy age-matched controls at baseline, with negative correlation to FSH. AMH levels in patients with CPP were lower than in patients with PT in direct comparison studies [5].

Conclusion

Despite much work on AMH, little is known about the clinical implications of individual serum AMH concentrations during childhood and adolescence. More studies are required to substantiate it's clinical implications. The lack of reliable standardized values of AMH during childhood is a limitation in using the clinical biomarker for assessment of puberty related conditions.

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DRUG CORNER - ANTIANDROGENIC PROGESTINS

***Ruchi Shah**, Pediatric Endocrinologist, Endokids Clinic, Ahmedabad*

The term **progestogen** is used for any steroid hormone with progestational effect, which includes progesterone (the natural steroid produced from the corpus luteum) and progestins (synthetic derivatives with progestational activity).Many effects of progestins are based on their effects on other steroid receptors like the Estrogen Receptor (ER), Androgen Receptor (AR), Glucocorticoid Receptors (GR) or Mineralocorticoid Receptor (MR).

After the discovery of the molecular structure of progesterone in 1934, various generations of progestins have been developed, most of them19-nortestosterone derivatives, which have androgenic side effects, ranging from severe to mild. Later, different progestins (also referred to as 4th generation progestins) with potent anti-androgenic effects became available [1]. The most potent anti-androgenic progestins are cyproterone acetate(CPA)(highest), dienogest, drospirenone(DRP) and trimegestone, in that order. These molecules are antagonists of 5α-reductase and also competitively block testosterone from binding to AR, decreasing androgen effect.

The two most commonly used molecules used in adolescents amongst the above are CPA and DRP. CPA is quite useful for adolescent girls with features of significant hyperandrogenism. It is banned in the US due to rare case reports of hepatotoxicity [2]. DRP, an analog of spironolactone, has anti-mineralocorticoid effects and has the potential to reduce BP and LDL levels and increase HDL levels as well. These drugs are used in the following indications:

1. ***Polycystic Ovarian Syndrome:*** Adolescents with suspected PCOS with prominent symptoms of hyperandrogenism, benefit from combined oral contraceptive pills containing low dose ethinyl estradiol (EE) (35 mcg or less) with an anti-androgen progestin. All progestins inhibit LH

and subsequently the production of androgens by the ovarian theca cells, and increase the hepatic clearance of testosterone. They also compete at the receptor sites with androgens and thus exert a more profound clinical anti-androgenic effect. They are associated with less seborrhea, acne, hirsutism and androgenic loss of hair and increased skin collagen content. Commonly used progestins are CPA and DRP.

2. ***Acne:*** Yaz®, containing ethinyl estradiol (20 mcg) and DRP (3 mg) is amongst the only 3 OCPs approved by FDA for treatment of acne. Other anti-androgen progestin combinations were found equally effective in reducing acne in few studies, especially CPA 2 mg combined with EE 35 µg (Diane-35®, Ginette-35, MY pill® etc). However, the efficacy of OCPs over other non-hormonal treatment for acne has not been proven consistently [3].
3. ***Adolescent contraception/anovulatory uterine bleeding*:**
   - Combined with estrogen: should be considered in an adolescent with PCO morphology or hyperandrogenism. In adolescents without such coexisting symptoms, OCPs containing norgestrel, levonorgestrel or norethindrone are preferred for their stronger ovulation inhibition effect. DRP 3 mg is available with both 20 µg EE (Yaz®) and 30 µg EE (Yasmin®).
   - Progestin only pill (POP): DRP only 4 mg pill (Slynd®) is available to be taken continuous for 24 days followed by 4 days of inactive pills. Compared to other POPs like desogestrel, norethindrone and norgestrel, this preparation offers more flexibility (POPs need to be taken at the exact same time everyday throughout the 24 days; chances of pregnancy are higher with missed doses since progestins are cleared faster than estrogens).
4. ***Late pubertal transgender female adolescents***: Pretreatment with CPA followed by estrogen administration in transgender female adolescents who are assigned male gender at birth, and in whom GnRH analogs/ gonadectomy are not feasible, achieves good decline in testosterone levels[4].

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CASE REPORT - CENTRAL PRECOCIOUS PUBERTY MANIFESTING IN A CASE OF HYDROCEPHALUS



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Central precocious puberty (CPP) in girls is most often idiopathic but can occasionally be caused by lesions of the central nervous system. We present a case of CPP secondary to acquired hydrocephalus in a 9 year-old girl.

Case Report: Bilateral breast enlargement was noticed in a girl aged 8y3mo, with onset of pubic hair growth and bleeding per vaginum observed in the next 7 months. The child was adopted at 2 weeks of life, following post-partum maternal death. She was one of twins delivered at 32 weeks of gestation by normal vaginal delivery and needed nearly 15 days of NICU care. At 3 months of age, she was diagnosed with communicating hydrocephalus, considered probably secondary to preterm sequelae. She underwent ventriculoperitoneal (VP) shunt insertion at 5 months of age. She was noted to have delayed developmental milestones and bilateral hearing loss, and developed seizure disorder at 5y of age. With a VP shunt malfunction at age 7y, her seizures recurred and she underwent a shunt revision. Subsequently she was seizure-free for 2y, and a follow-up CT brain revealed non-progression of hydrocephalus.

On examination, she had plagiocephaly, weight 35 kg (75-90thcentile), height 135.3cm (50-75th centile), BMI 19.2 (overweight, 1.13 Z-score). Tanner sexual maturity rating showed breasts stage 3 and pubic hair stage 2. Her height age was 9.6y, and bone age was 12.7y. Baseline FSH was 5.52 mIU/ml, LH 2.21µIU/ml, Estradiol 28 pg/ml - all in the pubertal range, indicative of CPP. She was started on GnRH analog treatment and advised regular follow-up.

Discussion: Hydrocephalus represents a diverse group of conditions resulting from impaired circulation and/or absorption of CSF. In addition to neuropsychiatric symptoms, intellectual disability and seizures, children with hydrocephalus are at risk of developing endocrine issues such as short stature and CPP. Precocious puberty is seen in both congenital and acquired hydrocephalus, with the prevalence ranging from 10-62%in different case series [1]. Girls were more affected (52%) than boys (21%) in a study of children with hydrocephalus secondary to meningomyelocele [2].

Hydrocephalus-related CPP appears to be less prevalent than amenorrhea [3]. The possible explanation for the association of both amenorrhea and CPP with hydrocephalus is the unphysiological variations in intracranial pressure on different areas of the hypothalamus-pituitary axis. CPP in hydrocephalus is due to enhanced gonadotrophin secretion, which may disrupt the inhibitory signals including endogenous opioids and dopamine. This in turn leads to removal of chronic inhibition of the GnRH pulse generator and subsequent premature activation of the HPG axis [3]. The effect of shunting on precocious puberty is unclear - CPP can occur before or after shunting, as well as in arrested hydrocephalus. Pubertal maturation was observed to occur considerably earlier in patients with shunted hydrocephalus [4].

To conclude, prematurity, hydrocephalus and repetitive VP shunting accounted for CPP in the index child. In children with hydrocephalus, regular monitoring of growth and pubertal status is essential.

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PEDSENDOSCAN

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Österbrand M, Fors H, Norjavaara E. Pharmacological treatment for pubertal progression in boys with delayed or slow progression of puberty: A small-scale randomized study with testosterone enanthate and testosterone undecanoate treatment. Front Endocrinol (Lausanne). 2023;14:1158219.

The study evaluated pubertal progression with six injections of testosterone enanathate (TE), 75 mg i.m./month (1/3-1/5 of adult dose), compared with two injections of testosterone undecanoate (TU), 250 mg i.m./3 months (1/4 of adult dose). Both treatments were well tolerated. Twelve of 14 (86%) TU-treated boys and 12/12 in the TE group reached the primary outcome, which was testicular enlargement ≥8 ml after 12 months. **The study supported that both TE and TU had similar effects in terms of pubertal progression.**

Wu C, Zhang X, Yan F, et al. Does vitamin D have a potential role in precocious puberty? A meta-analysis. Food Funct. 2023;14(11):5301-5310.

A meta-analysis was conducted to evaluate differences in vitamin D concentration between subjects with precocious puberty and normal subjects, the risk of precocious puberty in subjects with low vitamin D levels, and the effect of supplementation of vitamin D on subjects with precocious puberty on medication. Those with precocious puberty had lower serum vitamin D levels than normal population, with standardized mean difference -1.16 ng/mL (95% CI -1.41 to -0.91 ng/mL). Lower level of vitamin D was associated with risk of precocious puberty (OR, 95% CI 2.25, 1.66 to 3.04). Compared with gonadotropin-releasing hormone analog (GnRHa) intervention alone, subjects receiving GnRHa + vitamin D intervention had significantly lower luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estradiol levels and bone age, and higher predicted adult height. **Vitamin D showed an association in precocious puberty. Further well-powered studies are needed to confirm the findings.**

Jabari M. Trans Dermal Testosterone Compared to Intramuscular Testosterone for Young Males with Delayed Puberty: A PRISMA Guided Systematic Review. Int J Gen Med. 2023;16:733-744.

The authors conducted a systematic review to evaluate the right formulation of testosterone (TE) for young males with delayed puberty. This study points out the favorable effects of transdermal TE treatment in boys, while the existence of the vast gap in research needs to be acknowledged. **Quality of life, cardiac events, metabolic parameters, coagulation profiles, are important aspects of treatment that are overlooked and under evaluated in most studies.**

Shokri B, Heidarianpour A, Shokri E. Effect of Exercise and Detraining on Signs of Puberty and Selected Inflammatory Markers in Girls with Precocious Puberty. Med Sci Sports Exerc. 2023;55(7):1133-1142.

The authors examined the effects of aerobic exercise and detraining on adiponectin, resistin, tumor necrosis factor alpha (TNF-α), white blood cell, and pubertal signs (uterine length, ovarian volume,LH and FSH) in girls with central precocious puberty (CPP). Girls with CPP had lower adiponectin (P = 0.01) and higher TNF-α levels (P = 0.001) than healthy girls. In CPP + EX

(exercise) group, after 12 weeks, body weight and fat mass decreased, and adiponectin increased significantly (P = 0.02). Resistin (P = 0.02), TNF-α (P = 0.02), neutrophils (P = 0.01), and signs of puberty significantly (P < 0.05) decreased. In the CPP group, no significant change was observed in any of the parameters; only LH (P = 0.0001), and uterine length and ovarian volume (P = 0.003, P = 0.001) decreased after 12 and 16 weeks, respectively. The authors concluded that **aerobic exercise can have a positive effect on the state of inflammation and pubertal signs. Positive effects remain after 4 weeks of detraining.**

Hobbs AK, Cheng HL, Tee EYF, Steinbeck KS. Menstrual Dysfunction in Adolescents with Chronic Illness: A Systematic Review. J Pediatr Adolesc Gynecol. 2023;36(4):338-348.

The authors aimed to identify the impact of chronic illness on the age of menarche and menstrual cycle in adolescents: 43 papers met the inclusion criteria: 27 papers focused on type 1 diabetes (T1D), 8 papers on adolescents with cystic fibrosis, the remaining on inflammatory bowel disease, juvenile idiopathic arthritis, celiac disease, and chronic renal disease. Metanalysis of 933 patients with T1D vs. 5244 controls demonstrated a significantly later age of menarche in T1D (by 0.42 years; P ≤ .00001) and significant association between higher HbA1c and insulin dose (IU/kg) and later age of menarche. **There was evidence of delayed menarche and some evidence of irregular menses in those with cystic fibrosis and T1D.**

Learning Pearls - 24th ISPAE Aces Meeting : Bone Disorders (24th June)

*Compiled by **Zalak Upadhyay**, Consultant Pediatric Endocrinologist, Endocare for Kids, Rajkot, Gujarat*

Experts: Professor Zulf Mughal, Manchester, UK & Professor Rajesh Khadgawat, AIIMS, Delhi

The discussion mainly involved non-nutritional rickets (like VDDR type IA, IB, 2A, 2B, hypophosphatemic) and osteoporosis in children. Early identification and treatment are essential to reduce the risk of associated complications. Biochemistry and genetic analysis should be done whenever possible. Treatment compliance and long term follow up are necessary for better outcome.

VDDR Rickets: The goals of treatment are to maintain serum calcium in the low normal range; provide enough calcium (intravenous if required) to suppress PTH; maintain serum phosphorus in the normal range and perform periodic monitoring of urinary calcium / creatinine ratio (target < 4mg/kg/day).

Autosomal dominant hypocalcemia Type 1 The administration of calcium and calcitriol may worsen hypercalciuria and nephrocalcinosis, so a better option is giving subcutaneous rhPTH 1-34 infusion (with aid of pumps). However, this treatment is very cumbersome, and is not licensed for use in children. In mice, it has been reported to increase the risk of bone cancers. The alternative medicine- ***Encaleret*** (oral calcilytic drug) is well tolerated with no serious adverse effects. It is a negative modulator of calcium sensing receptor (CaSR), which increases serum calcium and decreases urine calcium excretion.

X linked Hypophosphatemic Rickets (XLH)- Conventional therapy is with phosphorus (25-50mg/kg/day in 5-6 divided doses, with calcitriol/alphacalcidiol, with well repleted vitamin D3 store. This conventional treatment has problems like poor adherence to treatment, abdominal pain and

diarrhea due to phosphorus salts, possibility of causing secondary hyperparathyroidism, nephrocalcinosis, and inadequate healing with the need for surgery to correct limb deformities.

Burosumab monoclonal antibody to FGF23, showed promising results in the dose of 0.8 mg/kg given subcutaneously fortnightly. Burosumab improved serum phosphorus level, TmP/GFR, $1,25(OH)_2D$ and ALP, linear growth and pain scores. Corrective surgery may not be required when Burosumab is given in the early years.

Hypophosphatasia - is usually managed with supportive management like physiotherapy and pain relief, with treatment for hypercalcemia and seizures (pyridoxine). ***Asfotase alfa***, a recombinant bone-targeted treatment, improves mineralization and improves survival. It is believed to be a game changer in the management of hypophophatasia. Asfotase alfa (40 or 100 mg/ml concentration) is given subcutaneously in the dose of 2-3 mg/kg thrice weekly (i.e. 6-9 mg/ kg/ week).

Pediatric Osteoporosis is defined as

- Presence of one or more vertebral compression fractures (Genant Grading adopted now in children for grading vertebral fractures)- osteoporosis confirmed, no BMD required.
- If no vertebral compression fractures, presence of both clinically significant fracture history and BMD score Z score ≤ - 2.0. A clinically significant fracture history is defined as the presence of two or more long bone fractures by age 10y, and or three or more long bone fractures by age 19y.

Confirmation of osteoporosis- Bone mineral density is performed by DXA. The following sites are checked in infants and children:

- Infants/ young children 0-5 years- DXA Lumbar spine
- Spine and Total Body Less Head (TBLH)- preferred sites
- Forearm and femur neck- not very useful
- Follow up DXA- minimum interval of 6-12 months
- Short stature or growth delay- spine and TBLH, BMC and aBMD adjusted.

Causes of Pediatric osteoporosis:

- *Primary*- Osteogenesis imperfecta, Bruck syndrome, Hypophosphatasia, Idiopathic juvenile osteoporosis
- *Secondary*- causes like leukemia and chemotherapy, renal failure, use of glucocorticoids, neuromuscular disorders.

Management

- Treat the underlying cause- helps to improve secondary osteoporosis
- Adequate supplementation of calcium and vitamin D3 is important
- Promote physical activity
- Treat any other hormonal deficiency.

Bisphosphonates are given for the treatment of pediatric osteoporosis (to be given till epiphyseal fusion in primary cause of osteoporosis)

- Pamidronate or zolendronic acid can be used for treatment .

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- Pamidronate given at maximum dose of 9 mg/kg/year for children > 3y of age, 3 mg/kg divided equally over 3 days given every 4 months. Zolendronic acid- maximum dose of 0.1 mg/ kg/ year given as 2 equal doses (0.05 mg/ kg) every 6 months in children > 2y of age and 0.025 mg/ kg every 3 months for children < 2y of age.
- Bisphosphonates have adverse effects like febrile effects, height concerns, osteonecrosis of jaw and atypical fractures, though very few have been reported.
- Further clinical trials in osteogenesis imperfecta that hold promise in the future with Setrusumab and Romosozumab (monoclonal antibody that binds and inhibits sclerostin).

IDEAS: Initiative for Diabetes Education and Awareness for Schools

Sirisha Kusuma Boddu, *Pediatric Endocrinologist, Rainbow Hospitals, Hyderabad; Joint Secretary ISPAE*

As the number of school-going children with type 1 diabetes (T1D) increases rapidly, it becomes imperative to ensure that schools provide reasonable conditions for their self-care activities so that their safety and well-being are not compromised. Only when provided with equal opportunities to study and progress, can these children become happy and productive members of society - assets rather than liabilities. We are heartened by steps taken in the right direction, like the recent directive by NCPCR, to ensure care during examinations and otherwise also. At this juncture, we are faced with the challenge of equipping teachers and other school personnel with the basic knowledge of childhood diabetes. Here, the numbers must be kept in mind: in 2022, there were almost 15 lakh schools in India, of which over 12 lakh were rural, with over 95 lakh teachers.

Under the "ISPAE School Resources" project, we prepared a PowerPoint presentation of information necessary for school personnel to manage T1D in school. Some of us ISPAE members - a few pediatric endocrinologists and T1D educators - started discussing how to get this across to the relevant teachers most effectively, within our very limited resources of time, effort, and money. Realizing that physical presentations in schools have minimal reach, we decided to go the virtual way and target teachers who had students with T1D in their class, reaching them through the T1D children and their families. We contacted as many parents as we could, via announcements in T1D WhatsApp groups across the country, asking them to request their child's teacher/s to attend this session.

The first ever IDEAS session was held on **6th August** (the first Sunday of the month) from **10-11.30 am**, on the Zoom platform, to enable interested teachers to attend without interfering with their work schedule. The School PPT was presented in an interactive mode by pediatric

endocrinologists Drs Sirisha Boddu and Preeti Singh, and diabetes educator Dr Shuchy Chugh, moderated by Drs Anju Virmani and Santhosh Olety, and supported (organizational and logistical help) by Ms Sheryl Salis, Mr Harsh Kohli, and Mr Lakshminarayana. We are delighted to share that the response to this 90-minute program was overwhelming: soon into the session, we realized our limitation of not being able to accommodate more than 100 participants. Teachers and Principals of schools from all over India joined in, expressed their thoughts, gave suggestions, and provided very positive feedback, which was heartening. They said that this would be very useful for all teachers faced with the challenge of looking after children with T1Din school, by giving them the necessary knowledge and confidence.

We are confident that our focused, no/ low cost, approach would generate awareness of T1D in those teachers who need it most. They are also most likely to retain the information given, as this is not just a theory session for them, but a resource to handle a situation they are already dealing with. We emphasized that they can always look up the PPT later any time they want to, as it is freely available on the ISPAE website. We plan to conduct more such sessions on a regular basis in the future, using a combination of Zoom and YouTube, to widen our audience. We look forward to your support for informing as many T1D families as possible, and for conducting sessions.

IDEAS, in summary, is a sustainable mode of educating teachers about T1D self-care, as it can reach out widely, without consuming much time or expense.

AWARDS/ ACHIEVEMENTS

Dr V Soundaram, Consultant Pediatric Endocrinologist at Apollo Children's hospital and Apollo Proton Cancer Center, Chennai, completed her ESPE Clinical fellowship at King's College, London, in August 2023. She acquired good experience in diabetes technology, bariatric clinics, and CAH management.

Dr Aashima Dabas, Associate Professor, Dept of Pediatrics, Maulana Azad Medical College, New Delhi, completed her ESPE Clinical Fellowship in August 2023 at Royal Manchester Children's Hospital, Manchester, in August 2023. This provided an opportunity to observe advanced diagnostics and management of both common and rare endocrine disorders.

Dr Deepika Harit, Professor, Dept of Pediatrics, University College of Medical Sciences, Delhi, was awarded the Allan Drash fellowship at the Barbara Davis Center for Childhood Diabetes, Colorado, in April 2023. It provided a wonderful combination of clinical and research experiences, including the latest cutting-edge technology and innovations in T1D.

Mr Paras Devani was honored by an Award of Excellence to Diabetes Educators by Diabetes Research Solutions (DRS) & Dr Mohan's National Diabetes Educator Program (NDEP) at ITC Maratha, Mumbai, on 2nd Sept 23. Twenty Diabetes Educators were selected for this award from more than 1000 educators across India.

Publication: A Hindi translation of a patient handbook on 'Puberty and hormonal management in children with disabilities' will be released at the ISPAE website soon. The handbook is produced under an educational grant from the Australasian Paediatric Endocrine Group (APEG).

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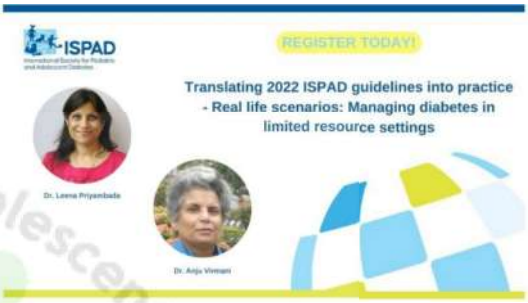
ACTIVITIES BY ISPAE MEMBERS

ISPAD Webinar: Translating 2022 ISPAD Guidelines into practice - Real life scenarios: Managing diabetes in limited resource settings

***Leena Priyambada**, Consultant Pediatric Endocrinologist, Rainbow Children's Hospital, Hyderabad, &*

***Anju Virmani**, Director, Pediatric Endocrinology, Max Smart Super Specialty Hospital, New Delhi.*

***Moderator: Graham Ogle,** General Manager, Life For A Child (LFAC)*



In the ISPAD Educational Webinar series on the 2022 ISPAD guidelines, a webinar on Management of T1D in Limited Resource Settings was held on September 14, 2023. Based on this new chapter in the Guidelines, the webinar discussed managing diabetes in young people working with financial, educational, logistic, and other constraints, whether in diagnosis, insulin therapy, monitoring at home or in the clinic, coping with acute and chronic complications, handling toddlers, adolescence, and school, and providing psychological support. It received a record number of registrations nearly 400 registrations, and generated much discussion and questions. The recording is available at the ISPAD website, ispad.org

CME Program on Congenital Hyperinsulinism

***Shaila Bhattacharyya,** Consultant Pediatric Endocrinologist, Manipal Hospitals, Bengaluru, &*

***Pratik Shah**, Consultant Pediatric Endocrinologist, Royal London Children's Hospital - Bart's Health NHS Trust*

Dr Pratik Shah (MBBS, DCH, FRCPCH, PhD) visited various centers in India during July-August 2023. He has keen interest in all forms of glucose disorders, including rare and syndromic forms of hypoglycemia/diabetes and ketotic hypoglycemia. Few glimpses of his visit:

Bengaluru: A CME on latest updates about Congenital Hyperinsulinism (CHI) organized by Dr Shaila Bhattacharyya, supported by Manipal Hospitals, at Sterlings Mac hospital. The session was attended by adult and pediatric endocrinologists and fellows. Neonatologists, pediatricians and nuclear medicine consultants also participated. It was followed by 6 interesting case discussions by pediatric endocrinologists and fellows.

Mumbai: A two days program, including OPD for all monogenic forms of hypo- and hyperglycemia, followed by a unique support group meeting was held for patients with CHI and their families. They were educated regarding the condition, its diagnosis, prognosis, management and emergency management. Parents participated in an interactive quiz.

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Ahmedabad: Fourteen patients attended a specialty OPD arranged at Endokids Clinic by Drs Shalmi Mehta and Ruchi Shah. It was followed by a talk on managing hypoglycemia in neonates and older children, especially for residents. Dr Pratik Shah gave his insight on many other difficult cases.

Vadodara: 10 patients with genetic forms of diabetes or CHI visited the OPD organized by Cure Hormones, Vadodara, by Dr Riddhi Patel. A conference on complex glucose disorders was well attended by pediatricians.

Some of the developments during his visit:

- Samples for genetic testing of all forms of monogenic diabetes mellitus and hyperinsulinism genes can be sent to Madras Diabetes Research Foundation (MDRF) free of cost. Contact person: Dr Radha Venkatesan (radharv@yahoo.co.in, mathi.dale@gmail.com)
- National guidelines for management of CHI are being developed in collaboration with ISPAE, IAP and NNF, for the use of pediatricians and pediatric endocrinologists, with special reference to Indian circumstances.
- National Conference on Glucose Disorders in Children to be organized.
- Development of CHI Parent Support Group in India for families' support as well as creating information leaflets in various regional languages.

*(Compiled by **Trishya Reddy**, Fellow, Pediatric Endocrinology, Manipal Hospitals, Bengaluru and **Ruchi Shah**, Consultant Pediatric Endocrinologist, Endokids, Ahmedabad)*

World Obesity Day Celebrations

***Priti Phatale**, Pediatrician, and **Hemant Phatale**, Endocrinologist and Diabetologist, Samrat Endocrine Institute, Aurangabad*

Multiple events were organized as part of World Obesity Day celebrations on the theme of "Changing perspectives: Let's talk about Obesity":

1. Release of an information brochure on Obesity in regional languages by renowned orthopedic surgeon & senior IMA member Dr Sachin Saoji & Mr Ulhas Shiurkar, Director of Deogiri Institute of Engineering & Management Studies. Over 50 persons attended this awareness campaign.
2. Awareness campaign at school levels: Over 700 persons, children to policymakers, including various stakeholders, were made aware about obesity & its co-morbidities.The schools covered were Shri Saraswati Bhuvan High School and Dr Desarda Public School. An Awareness Campaign was also conducted from 94.3 MY FM, a popular radio station of Aurangabad.

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Workshop on Type1 Diabetes

Sweet Souls, Vijaywada

This was a successful, informative, interactive workshop conducted on July 9, 2023 at Fortune Murali Park, Vijayawada, by a team from Sweet Souls and Association of Clinical Endocrinologists - of doctors, certified diabetes educators, and people with T1D, comprising Dr. Murli Krishna G, IDEALites Lakshminarayana V, Sree Divya A, Nithin S, Karthik N, as well as Naveen, Madhuri, Harshini, Sirisha, Lithika and family, and Karthik's wife Bindhu. Approximately 65 people attended the workshop, shared their experiences and knowledge, on various topics related to diabetes management. The participants learnt through each other's experiences. Each session was followed by a quiz.

Inauguration of RL Jalappa Diabetes Center For Children, Kolar, Karnataka

Tejasvi Sheshadri, *Consultant Pediatric and Adolescent Endocrinologist, Sparsh Super Speciality Hospital, & Shishuka Children's Hospital, Bangalore*

The inauguration of RL Jalappa Diabetes Center for Children in RL Jalappa Hospital and Research Center, Kolar, Karnataka, was done on 6 May 2023. This is the first super-specialty T1D clinic in and around Kolar district. It provides multidisciplinary care for children with T1D with a highly qualified team including Dr Sudha Reddy (HOD Pediatrics), Dr Tejasvi Sheshadri (Pediatric Endocrinologist), Ms Ayesha Mulani (Nutritionist and Diabetes Educator), Ms Kavya (Diabetes Educator). The chief guests at the inauguration included Dr Prasanna Kumar and Dr Sanjay Reddy (Endocrinologists at Center for Diabetes and Endocrine Care (CDEC) and Primer Academy of Medical Sciences (PAMS)), Dean and Principal of Devraj Urs Medical College, Kolar. In association with CDEC and PAMS, this clinic is providing free insulin pens, glucometers, glucometer strips, cooling pouches and diabetes education material. Since the inauguration in May 2023, 30 children with T1D have been enrolled.

Workshop on Common Endocrine Disorders in Children

Medha Mittal, *Associate Professor, Pediatrics, Chacha Nehru Bal Chikitsalaya, New Delhi*

The workshop was organized as a post conference workshop to Pediatric Conference of North India, 2023 in association with IAP Delhi on Sep 24, 2023. Forty-five delegates registered for the workshop. The faculty included Dr Anju Seth, Dr Vandana Jain, Dr Ravindra Kumar, Dr Rajni Sharma, Dr Aashima Dabas, Dr Preeti Singh, Dr Medha Mittal, Dr Aaradhana, Dr Anjali Verma, Dr Ruchi Mishra. IAP Delhi President Dr Anurag Agarwal and Vice President Dr Mukesh graced the

occasion. The workshop highlights included case discussions and hands - on case based activities in small groups, case presentations by residents and MCQ quiz. Common pediatric endocrine conditions were discussed including disorders of growth, puberty, adrenal, thyroid, diabetic ketoacidosis and hypoglycemia.

PEPP series: Webinar on Thyroid disorders in childhood

An online event was held on 05 September at the dIAP platform as a part of the PEPP as a part of the Pediatric Endocrinology for Practising Pediatricians series, an IAP-ISPAE venture. The program included case presentations on acquired and congenital hypothyroidism, with a lecture on thyroid disorders in childhood by Dr Ahila Ayyavoo.

IDEALITES CORNER

Hyderabad Marathon

Activity 1- Three IDEALites - Divya Akula, Karthik N, and Lakshminarayan V**,** ran the NMDC Hyderabad marathon on 27 August 2023. Divya ran the full 42 km, Lakshminarayan the half marathon i.e. 21 km, while Karthik completed a run of 10 km. This was Divya's first official full marathon of 42.2 km, that too within a year of her starting running. The motivation to run started in Aug 2022, after interviewing Sridhar and Girish, both of whom have T1D. When they started, they would gasp even after a run of 100 meters. During the practice journey, they learnt to analyze the change in blood glucose, using CGMS, and ran daily with a very motivating running group @ecilrunners. Completing the NMDC marathon was a special milestone, as it is the 2nd largest and toughest in India. Few comments:

@Divya*- "Running is fun, yet absolutely therapeutic! It helps in maintaining BGs and fitness, both physical and emotional fitness".*

@Lakshminarayan- *"I find running a marathon is a great way of creating awareness of both my challenges i.e. blindness and T1D. There is a lot of self-satisfaction, and a great improvement in my physical and mental health. Being an IDEALite, I see running on insulin as a part of "Diabetes Education", and find an opportunity to teach people with T1D how to manage blood glucose during physical activity. If you are able to run successfully, it's a great sign of your successful diabetes management!"*

@Karthik- *"Running or physical activity with T1D is always difficult due to sudden changes in blood glucose levels. However, gaining proper knowledge about my diabetes from fellow T1Ds, experienced doctors and my own experience, along with the use of modern technologies such as sensors, and CGM transmitters, and most importantly, my being part of the 'Sweet Souls' support group and an IDEALite, all helped. I was able to manage my running/ physical activity perfectly well, achieving great glycemic control and losing unhealthy weight. I feel active throughout the day."*

Activity 2- Sree Divya- Excited to share the remarkable journey of Ms Sree Divya, who achieved the feat of completing 100 days of running with the ECIL Runners, all while managing her T1D and a full-time job. Her dedication teaches us that individuals with T1D can greatly benefit from incorporating consistency into their routines. Her achievement serves as a poignant reminder that giving up is not an option. The consistent effort she invested in her running regimen, sugar checks, and vigilant monitoring has proven that challenges can be overcome with unwavering dedication. Divya's accomplishment underscores the profound impact of consistency in every facet of life. Let's draw inspiration from Divya's journey and integrate the power of consistency into our routines. Whether it's pursuing our goals, managing our health, or making positive changes, a steadfast commitment can lead to remarkable outcomes.

Yog Dhyan Foundation (YDF) Activities: *July to September 2023*

Dr Anil Vedwal*, Chief Functionary, YDF, Delhi*

YDF is an Indian trust established in 1985 with the mission to ensure a quality of life for children and their families living with Type 1 Diabetes (T1D). Our activities in this quarter (July-Sept 2023) included an HbA1c Camp, a Special Yoga Session to strengthen body and mind, a Millets Training Program with the support of PPHF, our monthly online meeting "Look, One Virtual Event" (on Zoom), a Fund Raiser for a sick young person with T1D, and an educational play on managing T1D well, enacted by 5 children under age 10y. These underscore the YDF commitment to improve the quality of life of those living with T1DM and their families.

July 2023: An HbA1c blood test camp cum special yoga session was held. More than 200 children participated, with each child getting an A1c and complete review of records of SMBG, insulin correction, nutritional value of diet, regularity of physical exercise, and reinforcement of diabetes education and counselling. The yoga session educated the children and families about how physical exercise, breathing and meditation techniques help maintain good health, whether with or without diabetes. It was an exciting session for all, as it included birthday celebrations and delicious food; concluding as usual with providing of free diabetes supplies (insulin, glucostrips, syringes, pen needles).

August 2023: In keeping with the UN declaring 2023 as the International Year of Millets as proposed by the Government of India, YDF and PPHF organized a Millets Training Program. The emphasis on millets being a healthier option than regular grains and also ecologically beneficial to India, was useful for the T1D families, particularly those with Celiac Disease.

"Look, One Virtual Event" connects children with T1D every 2nd Sunday with inspiring "T1D Heroes" and experts in various fields. This quarter our heroes were Ms Chhavi (a successful Diabetes Educator, career woman and active YDF volunteer), Ms Kanishka Vashisht (cardiac technician, non-invasive lab, happily married), and Ms Amarjeet Kaur (certified yoga instructor, mother). Our topics were 'A guide to supporting children with T1D in School' (panel discussion), 'Effective management of T1D within my budget' by Ms Bhumika Khurana, and 'The Role of Family in the Management of Type One Diabetes' by Dr Jyoti Kakkar. Other speakers/ panelists were Mr Harsh Kohli, Ms Pragati Johri, Dr Preeti Singh, Dr Anju Virmani, Dr Shivani Desai, Dr Shuchy Chugh, Ms Chhavi & Ms Renu.

September 2023: The last camp of this quarter ended with an exciting play by a group of five young children (<age 10y), who played the roles of 'Blood Glucose', 'Insulin', 'Subcutaneous muscles', 'Energy', and 'Oxygen' to help children with T1D understand the role of insulin and how to manage T1D better.

Through such initiatives, YDF is being able to improve the lives of many persons with T1DM.

Managing T1D: Striking a note of caution!

Dr Mudita Dhingra, *Pediatric Endocrinologist, Haryana &* ***Dr Anju Virmani****, Pediatric Endocrinologist, Delhi*

K, a 22y gentleman from Haryana, has T1D and celiac disease for over a decade. He would come to consult me only at times of crises, and had developed several problems like chronic diarrhea, malnutrition, moderate to severe anemia, retinopathy, neuropathy, short stature and delayed puberty. In August, he appealed for help through a piteous video that he had become very weak as his parents were neglecting his care, and he lacked financial and social support. He wanted to get admitted for a few days to get better, and then live by himself as he felt unwanted at home. He was also worried he had "blood cancer" because in the past he had received blood transfusions twice for severe anemia.

I reached out to the IDEALites with this appeal for immediate care and long-term rehabilitation, and got an immediate response, with several donations from Rs 100 to Rs 5000. Dr Vedwal of Yog Dhyan Foundation (YDF) contacted him, offering free diabetes care supplies through a neighbor of K's who had experienced T1D in the family and agreed to help. K refused supplies, insisting he needed hospital admission and that he did not want to continue living with his parents. I immediately arranged admission in a local hospital, and the doctors there managed an episode of severe hypoglycemia he had the same evening. However, they felt they would not be able to manage such a complex situation, and suggested referral to PGI Chandigarh to which K enthusiastically agreed. Mr Harsh Kohli contacted T1D friends in Chandigarh to help try and get him admitted on an emergency basis the next day (Sunday), and arrange travel. Dr Vedwal sent money from his pocket to cover immediate costs (donation money comes in after a lag period).

However, after these arrangements were all made, spending considerable time, K suddenly changed his mind. Expressing disappointment that he had not recovered and diarrhea had not improved (in 36 hours), he got himself discharged, accompanied his father home, saying he would reconsider the need to visit PGI. He sent and deleted several videos, demanded much more money immediately, and evaded our talking to his family. When his SMBG logs were requested, it became evident he was not monitoring except when he felt hypoglycemic, and had no reviews or A1c/ other tests for almost 2 years. The frequent changes in history and information, the alternating moods of anger and guilt towards his parents, and the repeated demands for money, made us realize he was not mentally fit enough to manage on his own, and would need his family's support, no matter how despised.

Dr Vedwal requested their neighbor to get a clearer picture. She visited their home, and found that K and his father had already approached government agencies several times in the past and obtained help from them, but did not sustain self-care. She convinced them to visit PGI Chandigarh. However, instead of going on Sunday when help had been arranged, they chose to

wait till mid-week, did not take calls from Mr Kohli or his contacts, and returned home after refusing to wait in Chandigarh for the endocrine clinic till the next day.

In the following four weeks, K has continued to request for money on various grounds, sent only 5-6 BG values after much insistence, refused to comply with even basic medical advice like not injecting into extremely hypertrophic sites, and evading all efforts to improve self-care. Dr Vedwal continues to stay in regular touch and try in various ways to improve the situation. The experience has been disappointing - many hours spent, many people requested for help - but also valuable learning for us. We would like to share the precautions we did take, and some lessons we learnt, a few more obvious than others:

- Chronic, longstanding problems do not have easy or short-term solutions. A seemingly acute crisis is likely to have underlying deep-rooted, intractable issues.
- Lack of finances could be the expressed reason for a crisis, but may not be the only reason, or may not be the reason at all, with several underlying but unstated inter-personal factors involved.
- It may be wise to make multiple attempts to understand the ground realities before giving monetary help, to ensure hopes of monetizing the situation are not fulfilled/ encouraged.
- Financial help was provided cautiously. If the money had been sent as demanded, raising hopes for larger sums, we may have worsened his problems.
- We made sure donations came to an organization, rather than being collected by individual/s. We were fortunate in having YDF to channel donations.
- It was not possible for anyone of us to accompany him or take over his care. That responsibility rested with him and his family members.
- In situations where family members are/ are perceived to be a major part of the problem, seeking government i.e. institutional help as a first response may be preferable.
- For minors, in other instances, the Child Helpline has been very useful, but would only provide help to those under age 18y.

We hope these lessons will be of some use to our readers. Meanwhile, when trying to help beyond our professional capacity, we should be prepared mentally for partial or total failure and wasted efforts in some instances. It ought not deter us from trying to help the next person, the next time, while being careful to *primum non nocere* - firstly, do no harm.

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TRAINEES' SECTION

Tejasvi Sheshadri, *Consultant Pediatric and Adolescent Endocrinologist, Sparsh Super Speciality Hospital, & Shishuka Children's Hospital, Bangalore*

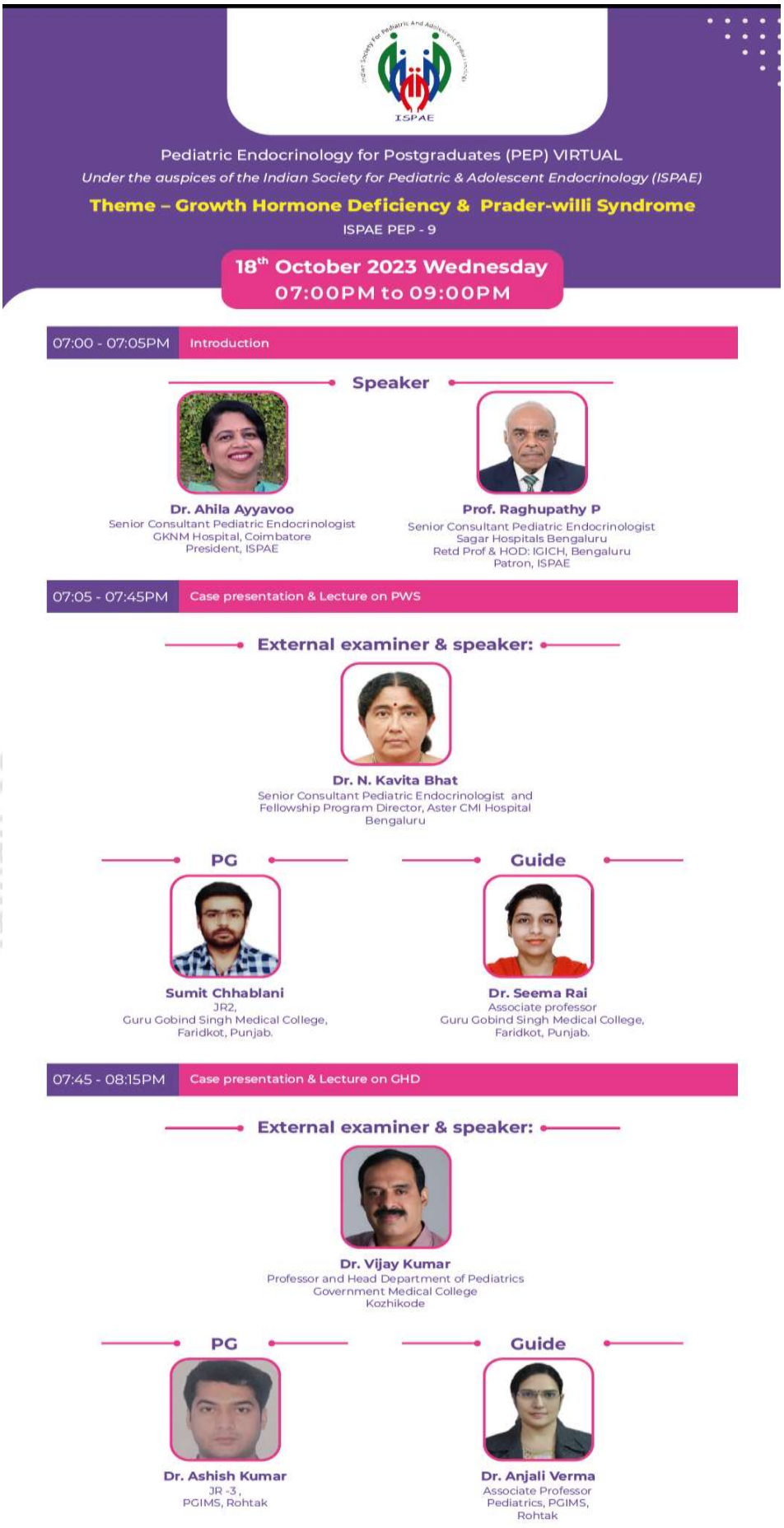
FACT OR FICTION? THE TRUE OR FALSE TRIVIA- Read the below statements carefully and answer if they are TRUE or FALSE

1) The first physical sign of puberty in boys is an increase in testicular volume to more than 3 ml.
2) Mini puberty lasts longer in female children.
3) Voice change in boys during puberty can happen as early as testicular volume of 4 ml.
4) A 15y old boy, in early to mid-puberty, presents with tender bilateral gynecomastia (3cm diameter). The first option in the management is treatment with an anti-estrogen (Tamoxifen).
5) Prepubertal testis consists mainly of Sertoli cells.
6) Critical body weight hypothesis or Frisch hypothesis states that to initiate puberty, girls need to reach a critical level of body weight.
7) One-third of girls with Turner syndrome have spontaneous thelarche.
8) The presence of polycystic ovarian morphology in an adolescent is necessary to make a diagnosis of PCOS.
9) The most common cause of hypergonadotropic hypogonadism in boys is Klinefelter syndrome.
10) Mosaic Turner with ring-X and isoXq are just as short as 45,XTurner children.
11) In the 'KNDy' model- Kisspeptin, Neurokinin B and Dynorphin are all excitatory peptides.
12) Hypothalamic hamartomas may be associated with gelastic seizures.
13) McCune-Albright syndrome is considered one of the causes of central precocious puberty due to premature GnRH activation.
14) Familial male-limited precocious puberty is due to germline activating mutations of the LH receptor gene.
15) The first line treatment for PCOS is oral contraceptive pills.

Please mail the answers to email: tejasviseshadri@gmail.com
Top three Winners (fastest responses) will be announced in the next issue

Contact us: editor.capenews@gmail.com

Please check the new video in Hindi by ISPAE on
NEWBORN SCREENING FOR
CONGENITAL HYPOTHYROIDISM
https://youtu.be/sBrqw9DCSs8?si=4z36J9yeC-aT9525


ISPAE
Pediatric Endocrinology for Postgraduates (PEP) VIRTUAL
Under the auspices of the Indian Society for Pediatric & Adolescent Endocrinology (ISPAE)
Theme – Growth Hormone Deficiency & Prader-willi Syndrome
ISPAE PEP - 9
18th October 2023 Wednesday
07:00PM to 09:00PM
07:00 - 07:05PM Introduction
Speaker
Dr. Ahila Ayyavoo
Senior Consultant Pediatric Endocrinologist
GKNM Hospital, Coimbatore
President, ISPAE
Prof. Raghupathy P
Senior Consultant Pediatric Endocrinologist
Sagar Hospitals Bengaluru
Retd Prof & HOD: IGICH, Bengaluru
Patron, ISPAE
07:05 - 07:45PM Case presentation & Lecture on PWS
External examiner & speaker:
Dr. N. Kavita Bhat
Senior Consultant Pediatric Endocrinologist and
Fellowship Program Director, Aster CMI Hospital
Bengaluru
PG
Guide
Sumit Chhablani
JR2,
Guru Gobind Singh Medical College,
Faridkot, Punjab.
Dr. Seema Rai
Associate professor
Guru Gobind Singh Medical College,
Faridkot, Punjab.
07:45 - 08:15PM Case presentation & Lecture on GHD
External examiner & speaker:
Dr. Vijay Kumar
Professor and Head Department of Pediatrics
Government Medical College
Kozhikode
PG
Guide
Dr. Ashish Kumar
JR -3 ,
PGIMS, Rohtak
Dr. Anjali Verma
Associate Professor
Pediatrics, PGIMS,
Rohtak

ISPAE 2023

BENGALURU

8th Biennial Meeting of

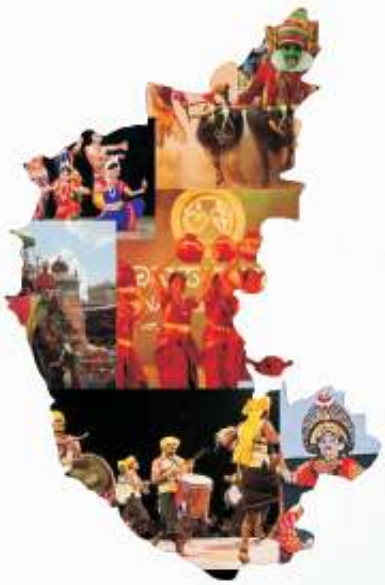
Indian Society for Pediatric and Adolescent Endocrinology (ISPAE)

17th - 19th November, 2023

Venue:

Hilton Garden Inn

Embassy Manyata Business Park, Bengaluru



ispae2023bangalore@gmail.com

www.ispae2023.com

REGISTRATION DETAILS

THREE DAY PROGRAM - 17 - 19 November, 2023, Bengaluru

Type	Upto 31st Oct 2023	Spot Registration
ISPAE Members	Rs. 14,000	Rs. 15,000
Non Members	Rs. 16,000	Rs. 17,000
Student* / Accompanying Person	Rs. 7,000	Rs. 7,000
International Delegates	US $ 200	

SINGLE DAY PROGRAM - 19th November 2023

Type	Upto 31st Oct 2023	Spot Registration
Registration for General Paediatricians and Practitioners	Rs. 5,000	Rs. 5,000

Registration fees inclusive of 18% GST

* Students (DM / M.Ch. / DNB / PDF / MD) should submit proof from the Head of the Department

Organising Committee

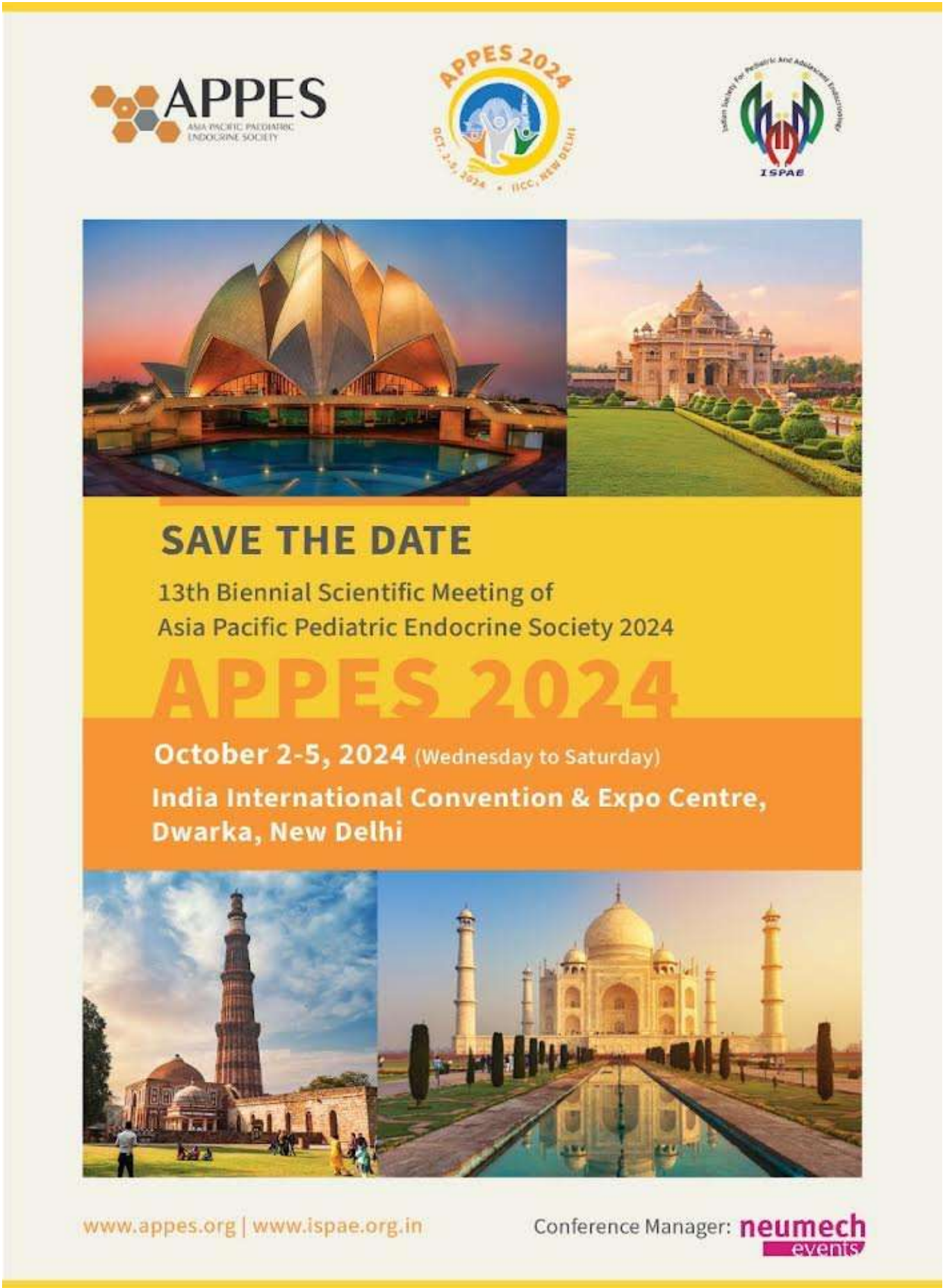
Dr. Raghupathy P
Chief Patron

Dr. Shaila Bhattacharyya
Organising Chairperson

Dr. Vani H.N
Organising Secretary

Dr. Pavithra Nagaraj
Joint Secretary

Scan QR Code to **REGISTER NOW**


APPES
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APPES 2024
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SAVE THE DATE
13th Biennial Scientific Meeting of
Asia Pacific Pediatric Endocrine Society 2024
APPES 2024
October 2-5, 2024 (Wednesday to Saturday)
India International Convention & Expo Centre,
Dwarka, New Delhi
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Conference Manager: neumech events