MARCH 2023
Volume 27 - Issue 1

CAPE News

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

CONTENTS
Theme - Growth

Theme of the next issue- (June 2023) is THYROID DISORDERS

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EDITOR'S MESSAGE

It is a proud moment for us to present the next issue of CAPE News, that has been running successfully for more than 25 long years. CAPE News has showcased the achievements and hard work of the members of our vibrant body and presented academic content, for continued bonding and learning.It has contributed to the growth of pediatric endocrinology in India throughout its journey.

We begin with a big thank you to Dr Hemchand Prasad and members of Editorial Board (2021-22), who have made the newsletter rich in content and more attractive, simplifying our work already.

The new team has worked hard to carve this first issue of the year, with the focus on GROWTH. We have continued the comfortable style of the previous issues and have invited interdisciplinary learning pearls on the thematic topic. This issue also addresses the needs of young trainees with learning pearls from the ISPAE-PEP program and the vibrant trainees' section, the correct answers to which are eagerly awaited.

We hope you find this issue interesting and look forward to your continued support and contributions. The theme of the next issue will be THYROID DISORDERS.

With regards
Aashima Dabas

MESSAGE FROM THE ISPAE PRESIDENT

Dear members of ISPAE,

Greetings from the new EC Team of ISPAE for the years 2023-2024!

It is a privilege to write this message on behalf of the new Executive Council of ISPAE. We are looking forward to the next two years to implement new programs to improve the life of children with endocrine disorders. It is an honor to be a part of the EC during the exciting period of continuing IDEAL and BEST courses, which had been drafted and implemented during the previous EC's tenure to improve the delivery of healthcare to children with type 1 diabetes mellitus.

Exciting times are ahead for us with the biennial meeting of ISPAE at Bengaluru in November 2023. We hope to see all of you in person at the meeting.

It's time to thank the fantastic EC Team of ISPAE 2021-2022 for the fabulous things that had been initiated during their tenure. ISPAE - Aces monthly meetings, IDEAL and BEST courses are flagship programs that happened over the last couple of years.

The EC would be pleased at the updates from our members, including information on charitable and academic activities, and regular contribution to CAPE News.

Many thanks and kind regards,

Ahila Ayyavoo
President, ISPAE

Rakesh Kumar
Secretary, ISPAE

Sirisha Kusuma.
Joint Secretary, ISPAE

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WELCOME TO NEW MEMBERS

Life members

- Sasi Dharan (Pediatrician and Neonatologist)
- Amita Verma (Pediatric Endocrinology Fellow)

Associate Members

- Ms Rekha Negi
- Ms Muthumari P
- Ms Jayalakshmi V
- Dr Abraham Kodiatte (DM Endocrine resident)
- Dr Anil Vedwal
- Dr Sakthivel Sivasubramanian (DM Endocrinology)
- Ms Palak Kapoor

DOWN MEMORY LANE : JOURNEY OF CAPE NEWS

Anju Virmani, Director, Pediatric Endocrinology, Max Smart Super Specialty Hospital, & Endocrinologist, Madhukar Rainbow Children Hospital, Delhi

The venerable team of Dr Meena Desai and Dr Prisca Colaco organized the initial pediatric endocrine conferences in Mumbai and performed the initial magic of persuading the Indian Academy of Pediatrics that endocrinology was an important sub-speciality which deserved its own Chapter, thanks to the awesome, path-breaking work done by them at the Bai Jerbai Wadia Hospital. Thus was born the Pediatric & Adolescent Endocrinology Chapter of the IAP.

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BEST WISHES FOR A WONDERFUL 2008!

NOTICE OF THE ANNUAL GENERAL BODY MEETING

DEVELOPMENTAL ORIGINS OF HEALTH & DISEASE (DOHaD)

When the baby moved from Dr Desai's nurturing in Mumbai to Delhi, with Dr PSN Menon as Chairperson and I as Secretary-Treasurer, we felt a newsletter would be useful to keep all members in touch, as well as to reach out to others in the field. Dr P Raghupathy designed the lovely logo. My husband suggested *Chapter of Adolescent & Pediatric Endocrinology News*- CAPE News - and the name stuck! So started the journey… Whenever I met friends and colleagues, my questions as Secretary and Editor were standard: "Please will you contribute an article on xxx topic for the next CAPE News?" or "Hope you will remember to send this news to us?" or "I hope you are getting CAPE News?" or "Oh, what is your new address?" or the distressed one "How come you are *still* not a member of our Chapter?... Yes, of course, if you give me the membership money, I will give you the receipt right now, I have the receipt book." It seems just yesterday that I was reminding members to send in their article or news

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item, typing and compiling it all together, and three times a year, making printouts, photocopying and making sets to staple together, then writing each address by hand, sticking the postage stamps, making bundles region-wise to put in the different boxes at the main post office, and hoping there would not be too many returned undelivered. As the children grew up, they would often be pressed into helping out their mother in this labor of love!

Then came the major milestone when due to the huge, meticulous effort put in primarily by Dr Vijayalakshmi Bhatia, the Chapter also became the Indian Society of Pediatric & Adolescent Endocrinology. CAPE News was newsletter for Chapter and Society; it retained its name as it had become a 'brand'. It did become more colorful, as ISPAE developed our own website, held our own biennial meetings, including the PET School (name suggested by Dr Anju Seth), which was the first of it's kind in India, and evoked much interest, as other IAP Chapters later followed suit. In 2013, Dr Archana Arya took over from me as Editor, and a term later, Dr Vijayasarathi, while the newsletter grew from strength to strength. The paper version was stopped, and only soft copies were sent to all members. This made it possible to expand it, and add features like photo quiz and PedEndoScan. Dr Rakesh Kumar changed the frequency from 3 times a year to quarterly from 2020, and made it more packed with content and color! In the last 2 years, Dr Hemchand changed each issue to have a theme, and added more sections, making for the vibrant pot pourri you have all enjoyed so much. This was also the period in which the IDEAL course meant adding many non-physician members, making ISPAE itself more varied and dynamic, which is naturally reflected in CAPE News.


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Theme: Calcium Disorders

And now its time for another team, and another perspective. The start of our wonderful scientific journal JPED, means that we will move back to the primary function of news, leaving heavy academic content to the Journal. We have much more news to share, as we increase the crucial aspects of advocacy to our sterling contribution to academics in the arena of pediatric endocrinology in India.

The last 25 years have indeed been eventful. We look forward to not just 25 more years, but indeed many decades of growing, evolving, with change as the only constant! Long live our ISPAE, its newsletter, and now its infant Journal!

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GUIDELINES/ Mini Review

Growth Hormone Deficiency- Perspectives of the Growth Hormone Research Society International.

Medha Mittal, Associate Professor, Chacha Nehru Bal Chikitsalaya, Delhi.

Diagnosis of growth hormone (GH) deficiency (GHD) should be based on a combination of auxologic, clinical, and laboratory data.[1] The perspective of the **Growth Hormone Research Society International** is summarized and the newer developments in this field highlighted.

GH provocative tests should be performed in the fasting state after excluding or adequately treating hypothyroidism and hypogonadism. The provocative agents used may be glucagon, clonidine, arginine, L-Dopa and GH releasing peptide-2. Insulin tolerance test may also be performed with appropriate monitoring for hypoglycemia. Non-response to two agents is recommended for diagnosis, though stimulation with a single agent may suffice for diagnosis in cases with high suspicion. Peak GH levels < 3ng/mL suggest severe GH deficiency in the presence of supportive clinical, laboratory and imaging information. The threshold for a confirmatory diagnosis is suggested (though not recommended) as peak GH level <7 ng/mL. Sex steroid priming may be performed when development is earlier than Tanner 3, to improve the specificity of the GH response. However, the exact doses of sex steroid, the age at which to begin priming, and the cut offs for the GH response obtained post-priming, are not yet standardized.

Insulin like growth factor 1 (IGF-1) forms an important component of evaluation (and guide to treatment) of GHD, with low values suggestive of GHD and values >0SDS excluding the diagnosis. The measurement should be performed using a reliable assay, with reference ranges based on age, gender, pubertal status and systemic disease. Further, values are difficult to interpret in children less than three years of age; IGF binding protein 3 is considered a more reliable biomarker in this age group.

Magnetic Resonance Imaging (MRI) of the hypothalamus and pituitary gland should be performed in all patients diagnosed to have GHD. This detects anatomical defects of the pituitary, brain tumors or other neurological disorders and predicts other associated pituitary hormone abnormalities, the need of genetic testing and the likelihood of persistent GHD. MRI may not be needed if GH provocative tests are normal. Pituitary size should be interpreted in the context of pubertal status as the size increases during puberty. Findings such as absent or hypoplastic anterior pituitary, an ectopic posterior pituitary, and hypoplasia of the stalk support the diagnosis of GHD.

Genetic tests may be undertaken when the phenotype suggests a high likelihood of a genetic cause, as in familial cases, specific syndromic forms of multiple pituitary hormone deficiencies, severe short stature (<-3SD for the population or >3SD lower than mid parental height), body disproportion and/or skeletal dysplasia, and SGA with inadequate catch-up growth. Karyotyping should be performed to rule out Turner syndrome in girls. FISH or microarray in a different cell type than blood cells (e.g., buccal smear or cells in urine) should be considered in those with report of 46XX and strong suspicion of Turner syndrome. In others, single nucleotide polymorphism (SNP) array followed by whole exome sequencing may be the preferred approach. Tests for methylation disorders may be ordered in children with SGA.

Newer Developments

- Macimorelin, a ghrelin agonist that stimulates release of GH, has received approval as a diagnostic test in adults. It has the advantages of oral administration, few side effects and high sensitivity and specificity. An open label group comparison trial has also been performed in children between 2 and 18 years of age with similar encouraging results.[2] The peak GH levels occurred between 15 and 60 minutes.

- Long-acting GH - Once weekly lonapegsomatropin, somatrogon and somapacitan have demonstrated non-

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inferior height velocities and similar safety profiles to daily GH in children with GHD in standard phase III clinical trials.[3] Long term surveillance studies are needed to demonstrate further safety profile.

- Oral Ghrelin analogs (such as LUM-201/MK677) have potential usefulness in children with hypothalamic GHD and mild pituitary dysfunction. Given their orexigenic effects, they could also be effective in non-GHD children with low body mass index (BMI), such as SGA, idiopathic short stature, Silver Russell Syndrome and Noonan Syndrome.

- The C-natriuretic peptide analog, vosoritide, has received approval in August 2021 for the treatment of achondroplasia in children more than 2 years of age, after genetic confirmation of the diagnosis.[4] CNP is expressed in the growth plate and regulates chondrocyte proliferation and differentiation. Vosoritide acts by binding to a receptor called natriuretic peptide receptor B, inhibiting downstream signaling pathways of the overactive *FGFR3*gene.[4]

GH treatment for Prader Willi Syndrome- GH treatment for cases of PWS has been approved since 2000. Treatment should be started after genetic confirmation of the diagnosis.[5] Doses are based on body surface area, starting from 0.5mg/m^2 and increasing over 3-6 months to 1.0 mg/m^2. GH provocative testing is not necessary before initiating treatment. IGF-1 serves as a useful biomarker for monitoring treatment. One must rule out severe obesity, uncontrolled diabetes, severe obstructive sleep apnea, active cancer, and active psychosis, before initiating GH treatment. Other management interventions like dietary modifications and hormonal therapies must continue alongside.

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1. Collett-Solberg PF, Ambler G, Backeljauw PF, et al. Diagnosis, Genetics, and Therapy of Short Stature in Children: A Growth Hormone Research Society International Perspective. Horm Res Paediatr. 2019;92(1):1-14.
2. Csákváry V, Ammer N, Bagci EB, et al. Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Macimorelin in Children with Suspected Growth Hormone Deficiency: An Open-Label, Group Comparison, Dose-Escalation Trial. Horm Res Paediatr. 2021;94(7-8):239-250.
3. Miller BS. What do we do now that the long-acting growth hormone is here? Front Endocrinol (Lausanne). 2022 22;13:980979.
4. Duggan S. Vosoritide: First Approval. Drugs. 2021 Nov;81(17):2057-2062.
5. Deal CL, Tony M, Höybye C, Allen DB, Tauber M, Christiansen JS; 2011 Growth Hormone in Prader-Willi Syndrome Clinical Care Guidelines Workshop Participants. Growth Hormone Research Society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader-Willi syndrome. J Clin Endocrinol Metab. 2013 Jun;98(6):E1072-87.

MINIREVIEW

Growth concern in preterm or SGA: Pediatric Endocrinologist opinion

Aaradhana Singh, Associate Professor, Department of Pediatrics, UCMS & GTBH, Delhi

Small for gestational age (SGA) is defined as a weight and/or length less than or equal to 2 SDS below the mean for gestational age[1]. Intrauterine growth restriction (IUGR) describes a pathophysiological condition of inhibited fetal growth in utero as indicated by at least 2 antenatal ultrasounds, whereas SGA refers to a statistically defined condition at birth, regardless of the cause.

Problems in SGA - Poor height velocity (HV) leading to adult height (AH) below target height, i.e., short stature; early development of metabolic disorders like obesity, diabetes, and cardiovascular diseases; pubertal issues including precocious puberty, exaggerated premature adrenarche, early menarche and faster progression of puberty are commonly encountered problems in SGA.

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Catch-up growth (CUG) and short stature in SGA - Catch-up growth is defined as HV greater than the median for chronological age and gender, for reaching a height > -2SDS or >3rd centile. Most infants who are born SGA achieve a normal height following a period of CUG before the age of 2 years[2]. However, approximately 10-15% of infants who are born SGA fail to achieve CUG, and those who do not achieve this within 2 years have a high risk of short stature in later life. In a study by Khadilkar et al in Pune, 29% SGA in upper socioeconomic strata had short stature at 2 years and 17% at 5 years, while in the lower socioeconomic group, 54% were short at 2 years and 46% at 5 years[3]. A child born SGA should have measurements of length, weight, and head circumference every 3 monthly for the first year of life and every 6 monthly thereafter. Those who do not manifest significant CUG in the first 6 months of life or those who remain short by 2 years of age may have other conditions that limit growth. These should be identified and managed. The preterm SGA infant can take four or more years to achieve a height in the normal range.

Pathophysiology of short stature in SGA -The various factors responsible for poor CUG in SGA are: low spontaneous GH secretion rate, disturbed GH secretion pattern, low serum IGF-1 levels, low IGF-BP3 levels, and low leptin levels[4]. IGF-1 resistance is also a contributory factor to poor catch up growth[5]. Although children with short stature who were born SGA frequently have GH levels lower than normal, most are not usually classified as being GH deficient by recognized criteria.

Genetic/syndromic SGA with short stature - Russell Silver syndrome (RSS) is characterized by triangular facies, relative macrocephaly, body asymmetry, protruding forehead and low BMI. Noonan syndrome: facial dysmorphism, ptosis, congenital heart disease and cryptorchidism. ACAN syndrome: short stature, rapidly advancing bone age during puberty and early onset osteoarthritis. Seckel syndrome: bird-headed face, microcephaly, intellectual disability. Cornelia de Lange syndrome: low anterior hairline, synophrys, anteverted nares, maxillary prognathism, long philtrum. Pseudohypoparathyroidism: obesity, intellectual disability, brachydactyly, round face.

Growth hormone (GH) therapy of SGA children: Indications as shown in box below :

	US, Food and Drug Administration (FDA)	European Medicines Agency (EMA)
Age of starting treatment	2 year	4 year
Height SDS at start of therapy	< -2.0	< -2.5
Height velocity at start	Not mentioned	< 0 SDS
Mid parental height (MPH) consideration	Not mentioned	< - 1.0 SDS

Treatment objectives: Increase the HV, normalize AH.

Dosage:

FDA: 66µg/kg/day (0.2 IU/kg/day based on a conversion factor of 1 mg = 3 IU).

EMA: 35 µg/kg/day (0.1 IU/kg/day).

International SGA Advisory Board: 66µg/kg/day (0.48 mg/kg/week).

International Societies of Pediatric Endocrinology and Growth Hormone Research Society 2006 consensus meeting: 35–70 µg/kg/day .

Response to GH treatment in SGA:

Mean height gain has been found to be 1.5 SDS in treated and 0.25 SDS in untreated children born SGA. Mean AH was -1.5 SDS for GH treated and - 2.5 SDS for untreated subjects, with a mean SDS difference of - 0.9 SDS.

Determinants of GH therapy:

1- High dose vs. low dose GH: Higher dose achieves better response.

2- Early vs. late start of therapy: Earlier start achieves better response.

3- Long term vs. short term therapy (duration): Longer duration achieves better height.

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4- Intermittent vs. continuous therapy: Continuous therapy is more effective.
5- Mid parental height: The greater the MPH, the greater the increase in AH.

Benefits of GH therapy other than height improvement:

- Improves body composition (decrease in fat mass and increase in lean body mass), blood pressure, and lipid metabolism.
- Increases bone mineral density.
- Intelligence and psycho-social functioning.

Monitoring: Same as that for other indications, including:

- HV and change in height SDS every 6mo - 1 yr.
- Serum IGF-1 level after 6 mo of start of therapy and yearly thereafter. As SGA babies may have IGF-1 insensitivity, IGF-1 levels above + 2 SDS may be needed for effective growth.
- Serum levels of thyroid hormones (T4, TSH) annually.
- Routine evaluation of metabolic parameters like lipid profile and blood sugar is recommended only if risk factors such as obesity and family history exist.
- Bone age assessment is not useful during GH therapy in SGA.

Discontinue GH therapy - When HV is < 2cm/yr.

Safety of GH therapy in SGA: GH has a safety profile and tolerability that compares well with that of GH in other approved indications.

References

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3. Khadilkar VV, Mandlik RM, Palande SA, et al. Growth status of small for gestational age Indian children from two socioeconomic strata. Indian J Endocrinol Metab. 2016;20(4):531-535.
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Growth concern in preterm or SGA: Neonatologist opinion

Pankaj Kumar Mohanty, Additional Professor & Head, Dept of Neonatology, AIIMS, Bhubhaneshwar

Preterm and SGA babies are vulnerable to early postnatal growth failure. Unlike other developing nations, India's birth cohort has more SGA preterm than AGA preterm infants. The incidence in the Southeast Asia region is 34% vs. 11% in developed nations[1]. SGA is based on the cross-sectional evaluation of infants and defined as birth weight (BW) < 10thpercentile of population-specific BW for specific gestational age or <- 2 SD. IUGR, used interchangeably with SGA, is the failure to obtain a growth potential in utero. IUGR applies to neonates born with clinical features of malnutrition and in-utero growth retardation, irrespective of their BW. Catch-up growth (CUG) or failure is linked to the intrauterine growth curve. Postnatal growth failure is defined as a weight < 10thcentile at 36 weeks corrected gestational age (GA) or a decrease in z-score of > 2 between birth and 36 weeks corrected GA[2]. About 10% of children born SGA fail to show CUG, and account for approximately 20% of all cases of short stature during adult life.

Within the SGA population, three subgroups exist: (i) infants with low weight but standard length for GA, (ii) infants with low length but normal weight for GA, and (iii) infants with low weight and length. Preterm IUGRs are

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more vulnerable to growth failure, metabolic syndrome, and mortality in later life. Infants who experience rapid CUG are at risk of developing metabolic syndrome, whereas those without CUG may end up with short stature. Medical conditions, male sex, and postnatal steroid administration (conflicting evidence) are linked to poor CUG in the preterm SGA subgroup of infants.

Preterm SGA neonates have lower postnatal growth trajectories of weight, height, and head circumference but fetuses with growth restriction intra-uterine (defined by ultrasound parameters or reduced growth velocity) are likely to have CUG, mainly in height, after birth[3]. Fetal growth velocity (GV) should be followed to determine at-risk infants who will have fetal growth restriction (FGR) and its complications. Leptin concentration, which is a marker of fat mass, is lower in SGA newborns. Leptin receptors are expressed in several tissues, which also regulate growth hormone-IGF axes. Leptin secretion occurring in the first year of life could be a critical metabolic marker of fetal programming. Appropriate calorie and protein intake can increase the sensitivity of leptin and modulate the GV as well [4]. Fetuses with IUGR are likely to have CUG, mainly in height.

Growth in fetal life and the neonatal period typically depends upon maternal intake, fetal insulin, and GH/IGF-1 intracellular signaling. Insulin resistance, deranged glucose homeostasis, and idiopathic hyperglycemia lead to failure of CUG. Plasma levels of IGF-1 are in SGA babies who fail to show CUG. Preventive aspects must be given importance. Managing maternal nutrition (diet, folic acid, calcium, and iron supplementation), preventing and treating maternal anemia, and antepartum (serial doppler studies) and intrapartum monitoring are important. The biophysical profile is mandatory in assessing a baby's condition in utero. Investigation for the etiology of fetal growth restriction (serum and urine testing for toxoplasmosis and cytomegalovirus) should be considered. Placental pathology to rule out infection/vasculopathy is useful. Good delivery room practices at birth (NRP protocol, maintaining normothermia, gentle ventilation, and preventing hypoxia) and early initiation of breast feeding whenever possible (late preterm SGA babies) should be practised. The metabolic triangle of hypoxia, hypothermia, and hypoglycemia should be prevented as far as practicable.

Preterm/ SGA infants often lose energy and protein in the first week of life despite caloric and protein supplementation, which causes growth failure even with active regimens of parenteral and early enteral feeding. Early initial feeding according to protocol, colostrum feeding in preterms, minimal enteral nutrition, maintaining normothermia, and normoglycemia are essential. Fortification of breastmilk (HMF) or formula for increased calories may be needed in the newborn period or into the first year of life for adequate growth in the preterm/ SGA population.

However, rapid weight gain during the first two years of life has been associated with obesity and abnormal body composition later in life, with more visceral and abdominal fat and less lean body mass in children born SGA. So high energy formulas and other growth supplements should be optimized according to need. The "developmental origins of health and diseases (DoHaD)" may be seen in IUGR neonates in adulthood. The most accepted hypothesis is the thrifty phenotype (Barker's) hypothesis, which proposes that the early-life environment has a long-term effect in later life. Type 2 diabetes, ischemic heart disease, kidney and liver disease, obesity, hypercholesterolemia, syndrome X, early onset osteoporosis, and Alzheimer's disease may be seen. IUGR infants should be regularly followed up for growth and development, with regular blood pressure checks, echocardiography if indicated, nutritional assessments, growth monitoring (using modified Fenton and subsequently Intergrowth/ WHO charts) and neurodevelopmental assessments.

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Journal of Pediatric Endocrinology and Diabetes (Official Journal of ISPAE)

THE THREE BEST ARTICLES [2022; Vol 2: Issue 2]- Available at: https://ispae-jped.com/

- Amit Kumar Gupta, Neerja Gupta. Genetics for the pediatric endocrinologists - Primordial short stature in children and adolescents. [DOI: 10.25259/JPED_38_2022]
- Ahila Ayyavoo, Abhimati Ravikulan, Raghupathy Palany. Treatment of diabetic ketoacidosis with subcutaneous regular insulin in a non-ICU setting is effective and economical: A single-center experience. [DOI: 10.25259/JPED_19_2022]
- Seema Gaonkar, Arvind Shenoi, Santhosh Olety Sathyanarayana, Arun Kumar Namachivayam, D. Malathi Raja, Nilesh Rao. A study on normalization of hypothyroxinemia in neonates below 34 weeks of gestation. [DOI: 10.25259/JPED_4_2022]

PEDENDOSCAN

Compiled by — Richa Arora, Consultant Pediatric Endocrinologist, New Delhi

1. Xiaoping Luo, Sha Zhao, Yu Yang, et al. Long-acting PEGylated growth hormone in children with idiopathic short stature. Eur J Endocrinol. 2022 Oct 13;187(5):709-718.doi: 10.1530/EJE-22-0449.

This multicenter, phase II study was done to evaluate the safety and efficacy of weekly PEGylated-recombinant human growth hormone (PEG-rhGH) in 360 children with idiopathic short stature (ISS) in China. Subjects were randomized 1:1:1 (120 children in each group) to weekly s.c. injections of PEG-rhGH 0.1 (low-dose (LD) group) or 0.2 mg/kg/week (high-dose (HD) group) or control group for 52 weeks. The primary end point was change (Δ) in height SD score (HT-SDS) from baseline to week 52. Secondary end points were height velocity (HV), bone maturity, insulin-like growth factor-1 (IGF-1) SDS, and IGF-1/insulin-like growth factor-binding protein-3 (IGFBP-3) molar ratio. At week 52, mean (SD) change in HT-SDS was 0.56 (0.26), 0.98 (0.35), and 0.20 (0.26) in the LD, HD, and control groups, respectively (within-group and inter-group $P < 0.0001$). Statistically significant values of HV, IGF-1, IGF-1/IGFBP-3 ratio, and IGF-1 SDS at week 52 from baseline were noted in treatment groups. There were clear dose-dependent responses for all auxological variables. PEG-rhGH was well tolerated throughout the treatment period. **Fifty-two-week treatment with PEG-rhGH 0.1 or 0.2 mg/kg/week achieved significant improvement in HT-SDS and other growth-related variables, including HV, IGF-1 SDS, and IGF-1/IGFBP-3 ratio, in a dose-dependent manner. Both doses were well tolerated with similar safety profiles.**

2. Mohamad Maghnie, Michael B Ranke, Mitchell E Geffner et al.Safety and Efficacy of Pediatric Growth Hormone Therapy: Results From the Full KIGS Cohort. JClin Endocrinol Metab. 2022 Nov 25;107(12):3287-3301. doi: 10.1210/clinem/dgac517.

Kabi/Pfizer International Growth Database (KIGS) is a large, international database (1987-2012) of children treated with recombinant human growth hormone (rhGH) in real-world settings. This paper looked at the safety and efficacy of rhGH (Genotropin [somatropin]; Pfizer) in children with growth disorders from the full KIGS cohort (n=83 803 [58% male]). Disorders included idiopathic GH deficiency (IGHD; 46.9%), organic GHD (10.0%), small for gestational age (SGA; 9.5%), Turner syndrome (TS; 9.2%), idiopathic short stature (ISS; 8.2%), and others (16.2%). Median rhGH treatment duration was 2.7 years and observation 3.1 years. SAEs occurred in 3.7% of patients and death in 0.4%. The most common all-causality SAEs were recurrence of craniopharyngioma (0.2%), neoplasm (benign, malignant or unspecified - 0.1%), cancer (0.1%); and scoliosis (0.1%). Median first-year delta height-SD score (SDS) (Prader) in prepubertal patients was 0.66 (IGHD), 0.55 (ISS), 0.58 (TS), and 0.71 (SGA). Median gains in near adult height SDS were 1.79 (IGHD), 1.37 (ISS), and 1.34 (SGA) for boys, and 2.07 (IGHD), 1.62 (ISS), 1.07 (TS), and 1.57 (SGA) for girls. **Data from KIGS shows that rhGH is safe and increases short-term height gain and adult height across GHD and non-GHD conditions.**

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3. Soliman A, Rogol AD, Elsiddig S, Khalil A, et al. Growth response to growth hormone treatment in children with GH deficiency and those with idiopathic short stature based on their pretreatment insulin-like growth factor 1 levels and at diagnosis and IGF-1 increment on treatment. *Pediatr Endocrinol Metab. 2021 Jul 22;34(10):1263-1271.doi: 10.1515/jpem-2021-0389.*

In this study, authors looked at whether children with ISS or with GHD with variable pretreatment IGF1 standard deviation score (IGF1SDS) have different IGF-1 and growth responses to recombinant human growth hormone (rhGH) therapy. They compared the effect of GH therapy (0.035-0.06 mg/kg/day) on linear growth and weight gain per day (WGPD) in children with ISS and those with GHD with low pretreatment IGFISDS (IGF SDS < -1.5) and compared them with age-matched prepubertal children with ISS and GHD with normal pretreatment IGF1SDS. An untreated group of children with ISS served as the control group. The height SDS (HtSDS) at presentation of children with ISS and low pretreatment IGF1SDS was significantly lower compared to the normal IGFI group. The age, body mass index (BMI), BMISDS, peak GH response to clonidine provocation and bone age did not differ between the two study groups. After 1 year of treatment with rhGH, IGF1SDS increased significantly in both groups ($p<0.05$). The increase in the HtSDS and WGPD were significantly greater in the lower pretreatment IGF1SDS group. The IGF1SDS, BMISDS, HtSDS and difference between HtSDS and mid-parental HtSDS were significantly greater in the rhGH treated groups vs. the not treated group. The WGPD and increment in BMI were significantly greater in children who had low pretreatment IGF1SDS. There was a significant increase in the IGF1SDS in the two treated groups ($p<0.05$), however, the WGPD was greater in the pretreatment low IGF1SDS. **IGFI deficiency represents a low anabolic state. Correction of IGFI level (through rhGH and/or improved nutrition) in short children (ISS and GHD) was associated with increased linear growth and weight gain, denoting significant effect on bone growth and muscle protein accretion.**

4. Han Saem Choi, Ahreum Kwon, Junghwan Suh et al. Effect of long-acting growth hormone treatment on endogenous growth hormone secretion in prepubertal patients with idiopathic short stature: A preliminary study. Growth Horm IGF Res. 2022 Jul 8;66:101486.doi:10.1016/j.ghir.2022.101486

Long-acting growth hormone (LAGH) is emerging as a new preparation for treatment of short stature. This study aimed to determine whether 12-month treatment with LAGH in patients with idiopathic short stature (ISS) had an effect on the nocturnal endogenous growth hormone (GH) secretion, metabolic consequences and efficacy. Participants included 10 GH-naïve prepubertal children with idiopathic short stature (ISS), of whom one patient was withdrawn due to own decline during study. Participants were randomized on a 1:1 ratio to receive either a daily GH (0.37 mg/kg/week) or once-weekly LAGH (0.7 mg/kg/week) over a 12-month period. Nocturnal endogenous GH secretory profiles obtained from 12-h blood samplings at 30-min interval were assessed at baseline and 2 weeks after the completion of GH treatment. Post-treatment changes in height velocity, height standard deviation score (SDS), metabolic parameters, and adverse events were measured. A total of 4 patients received LAGH, and 5 patients received daily GH. Nocturnal endogenous GH secretory profiles, such as mean serum GH concentrations, frequency, amplitude, interpulse interval of spontaneous GH secretory bursts, and mass of GH released per secretory burst were similar at baseline and after 12-month treatment in both groups. The efficacy and safety after LAGH treatment for 12 months were similar to those of daily GH. **These findings indicated that LAGH does not suppress endogenous GH secretion, and can be used for treatment of non-GH deficient short stature with similar efficacy and safety compared to daily GH. These may contribute to define and develop treatment and follow-up protocols for LAGH use in ISS patients**.

5. Rosenberg AG, Passone CGB, Pellikaan K, et al. Growth Hormone Treatment for Adults With Prader-Willi Syndrome: A Meta-Analysis. JClin Endocrinol Metab. 2021 Sep 27;106(10):3068-3091.doi: 10.1210/clinem/dgab406.

Features of Prader-Willi syndrome (PWS) overlap with features of growth hormone (GH) deficiency, like small hands and feet, short stature, increased body fat, and low muscle mass and strength. In children with PWS, GH treatment (GHt) improves physical health and cognition. GHt is recommended in children with PWS, but not in adults. The authors aim to provide an overview of the current knowledge on GHt in adults with PWS. Medline, Embase, and the

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Cochrane Central Register of Controlled Trials databases were searched. The study selection included randomized clinical trials (RCTs) and nonrandomized (un)controlled trials (NRCTs) that reported data for adults with PWS, who received GHt for at least 6 months. Nine RCTs and 20 NRCTs were included. Body composition improved during 12 months of GHt with an increase in mean (95% CI) lean body mass of 1.95 kg (0.04 to 3.87 kg) and a reduction of mean (95% CI) fat mass of -2.23% (-4.10% to -0.36%). BMI, low-density lipoprotein cholesterol levels, fasting glucose levels, and bone mineral density did not change during GHt. There were no major safety issues. **GHt appears to be safe and improve body composition in adults with PWS, which is speculated to perhaps reduce cardiovascular morbidity.**

DRUG CORNER

Long Acting Growth Hormone

Ruchi Shah, Consultant Pediatric Endocrinologist, Endokids Clinic, Ahmedabad

Growth hormone (GH) can restore normal growth in children with growth hormone deficiency (GHD). Since the half-life of GH is short, it requires daily subcutaneous injection, which can be cumbersome for the child and family. The GH Research Society published, after a closed meeting of 55 international scientists, their perspective on long acting GH (LAGH) therapy in 2016[1] - "LAGH compounds may represent an advance over daily GH injections because of increased convenience and differing phamacodynamic properties, providing the potential for improved adherence and outcomes." Two new molecules of LAGH are currently approved for adults with GHD, and are in trials for pediatric patients.

Somapacitan (SOGROYA® - NovoNordisk A/S) is a reversible albumin binding GH. Reversible endogenous binding to albumin delays its elimination, a technique which has been used for other molecules like insulin detemir, GLP 1 molecules liraglutide and semaglutide etc. Studies comparing efficacy of once-weekly GH with Norditropin have shown similar efficacy to once-daily treatment in children with primary GHD and SGA failing to catch up.[2,3] Overall it was well tolerated and no participant discontinued due to serious side effects. These studies included 3 centers from India. The dose used was 0.16 mg/kg/week, compared to 0.034 mg/kg/day of daily GH. However, GHD secondary to tumors, radiotherapy or syndromes like Turner, Prader Willi were not included. It will be launched in India in 2024 and may be costlier than daily therapy.

Somatrogon (NGENLA® - Pfizer Inc.) is a GH molecule fused with a C-terminal peptide from β-hCG. It is already approved for use in pediatric GHD in Canada, Australia, Japan and most European countries. In a randomized, open label Phase 3 study, Somatrogon showed similar HV-SDS compared to daily Genotropin in 224 prepubertal primary GHD patients.[4] The doses used were 0.25, 0.48 and 0.66 mg/kg/week compared to 0.034 mg/kg/day of Genotropin, with the highest dose group being most comparable to daily therapy. **LAGH was perceived to be better by the study participants since it replaces the need for daily injections. I**t will be launched by the end of this year in India. Since **the burden of the treatment cost is still on the family in most patients, its use will be limited by affordability.**

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1. Christiansen JS et al. Growth Hormone Research Society perspective on the development of long-acting growth hormone preparations. Eur J Endocrinol. 2016;174(6):C1-8.
2. Miller BS et al. Weekly Somapacitan is effective and well tolerated in children ith GH deficiency: The Randomized Phase 3 REAL4 Trial. J Clin Endocrinol Metab. 2022;107(12):3378-3388.
3. Juul A et al. Somapacitan in children born small for gestational age: a multi-centre, open-label, controlled phase 2 study. Eur J Endocrinol. 2023;188(1):lvac008.
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BIOCHEMISTRY CORNER

Biochemical diagnosis of acromegaly

Aashima Dabas, Associate Professor, Department of Pediatrics, Maulana Azad Medical College, New Delhi

Acromegaly presents as the other extreme of disorders of stature, resulting from hypersecretion of growth hormone. It is associated with co-morbidities like sleep apnea syndrome, type 2 diabetes mellitus, debilitating arthritis, carpal tunnel syndrome, hyperhidrosis, and hypertension. The phenotype includes tall stature, somatic overgrowth and disfigurement with accompanying risk for premature morbidity. The majority of patients have a GH-secreting adenoma evident by elevated levels of GH and IGF-1, with a small proportion having mixed tumors that secrete GH and prolactin. An elevated level of GH is likely, but random measurements of GH are seldom helpful. The 2014 Endocrine Society guideline[1] on management of acromegaly advised against the measurement of random GH for the diagnosis of acromegaly, due to the episodic nature and pulsatile release pattern of GH from the pituitary. Instead, serum IGF-1 levels should be measured in those with a pituitary mass: levels are elevated in acromegaly, and serve as a marker of GH hypersecretion and function. Other factors like nutrition, fasting and chronic systemic illness will affect the IGF-1 levels. However, IGF-1 levels should not be interpreted for diagnosis of acromegaly only in the presence of morbidities, as they are commonly prevalent in the population in general.

The role of the GH suppression test has been evaluated in confirming the diagnosis of acromegaly using the oral glucose challenge test (OGTT) that stimulates hypothalamic somatostatin secretion. A GH level of <1 ug/L two hours after a glucose load of 75 gm suggests a normal GH response (GH suppression). However, a GH that fails to get suppressed with glucose challenge is suggestive of GH hypersecretion. The cutoff level of GH was revised from ≥ 1 ug/L to ≥ 0.4 ug/L with availability of newer GH assays. Recent concerns have been on defining the optimum threshold of hyperglycemia to consider the glucose challenge test as confirmatory. A study by Bugalho et al reported this threshold as 120 mg/dL, suggesting a repeat GH suppression test for peak glycemic value below 120 mg/dL[2]. Other concerns in interpreting the OGTT-GH suppression test include coexistent diabetes/ hyperglycemic states, age, catabolic illness, malnutrition, renal or hepatic failure, or ongoing treatment with somatostatin receptor ligands (octreotide, lanreotide). Discordant GH levels after OGTT and IGF-1 levels mandate repeat testing, after excluding physiological and pathological illnesses that can cause transient suppression of the pituitary. Also, additional testing using 24-hour GH profile, and measurement of IGF-BP3 levels may be helpful[3].

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HISTORY CORNER

Compiled by Ruchi Shah, Consultant Pediatric Endocrinologist, Endokids Clinic, Ahmedabad

The forgotten superhero of science: Choh Hao Li.

The person who was the first to purify and synthesize most pituitary hormones, Choh Hao Li (1913-1987) was born in Guangzhou (Canton), China, to Kan Chi Li and Mew Shing Twui. He was the fourth of fourteen siblings, all of whom became successful scholars. He received his Bachelor of Science degree at the University of Nanking in 1933 and taught chemistry there for two years, before entering the PhD program in organic chemistry at the University of California, Berkeley, where he then served as faculty for several decades. He established the Hormone Research Laboratory (HRL) and when he retired in 1983, he simply established another lab at UCSF where he worked till just a few weeks before his death. HRL was the training ground for more than 300 visiting scholars, postdoctoral associates,

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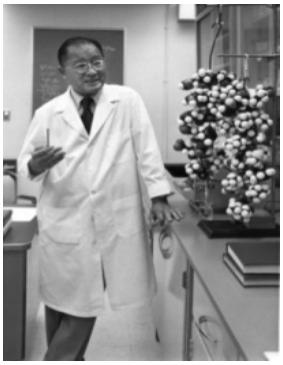

and graduate students, who went on to become leading figures in protein hormone chemistry and endocrinology.

In 1938, when he started his own research, none of the anterior pituitary hormones had been identified chemically. In the next 5 decades, Li published 1,100 papers, and was the first, or among the first, to purify and determine the amino acid structure of the anterior pituitary hormones - adrenocorticotropin (ACTH), lutropin (LH), follitropin (FSH), melanotropin (MSH), lipotropin, prolactin, and most notably, somatotropin (STH or growth hormone), and beta-endorphin. Li was a pioneer not only in the chemical synthesis of melanotropins, corticotropins, endorphins, lipotropin and GH, but also the synthesis of biologically active peptides and proteins and analogues of the natural species. One of the side products of GH that Li studied turned out to be a growth factor active in cell cultures, and was named insulin-like growth factor-1. Li also contributed heavily to the development of techniques and methods for protein chemists. The biological properties and clinical applications of these hormones were also extensively studied in his laboratory, so that by the time of his death the production of genetically engineered GH and its widespread clinical use had become a reality.

Even the purest lab preparations of hormones generally had biological activities overlapping those of other hormones. Although most workers explained this by cross-contamination, Li felt that the activities overlapped because portions of the structures were homologous from one hormone to the next. The second notion that fascinated him was that biologically active fragments could be derived from hormones because qualitatively the basis for activity resided in a limited region of the molecule, while other regions modulated the basic activity. His notions are well proven today.

He received several awards, and was nominated at least twice for the Nobel prize. A great believer in working hands on, he was also generous in acknowledging the contributions of others, not just students but even lab staff, who would even be included as his co-authors. He also would freely share his hormone preparations with fellow scientists across the world. He married Annie Lu on Nanchang, in 1938, and discussed his research and publications with her on daily basis. Their three children became a cardiac surgeon, a veterinarian and an architect. As a man of sharp intellect, discipline, hands on involvement, a scientist and a teacher, he has left behind a body of knowledge and a shining example for future generations.

PATIENT CORNER

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

Abdu Rozik

Abdu Rozik is a Tajik singer, musician, boxer and internet blogger who shot to fame after being a contestant in the Indian reality show Big Boss. Nineteen year old Abdu Rozik, whose real name is Savriqul Muhammadroziqi, was born to a gardener family on 23 September 2003 in Tajikistan. He holds the record for being the world's smallest singer, with a height of 94 cms (3'1"). He was diagnosed to have severe GHD in childhood, but because his family could not afford GH therapy due to financial constraints, he remained stunted. However,he did not let his medical condition affect him. He has also participated in MMA fights with Hasbulla, his friend who also suffers from GHD. Abdu Rozik who currently has more than 2.7 million followers and 8 awards, continues to inspire people around the world with his songs and charming personality. (images.arcpublishing.com/thenational)

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IDEAL- Journey so far!

Compiled by Dr Preeti Singh, Associate Professor, Department of Pediatrics, Lady Hardinge Medical College and KSCH, New Delhi (On behalf of IDEAL Core Committee)

THE IDEAL FAMILY

"Teaching is more than imparting knowledge; it is inspiring change. Learning is more than absorbing facts; it is acquiring understanding."said William Arthur Ward. The magic of digital education through our IDEAL program has added a new dimension to learning in pediatric diabetes. Readers of this newsletter do not need to be convinced of the special role Pediatric Diabetes Educators can play in empowering children with T1D and their families, enhancing their ability to self-manage through knowledge and skills, motivation and support.

The IDEAL Core Committee with its team of over 50 experienced IDEAL faculty from across India, feel proud to have completed the training of 4 batches (of over 100 participants) since October 2021. Batches 1, 2, and 4 were for educators, that included nurses, dietitians, and others dealing with large groups of persons with T1D e.g., group admins; while batch 3 was for doctors, encompassing pediatricians, pediatric endocrine fellows and one physician with T1D. The presentations of our experience - in the annual ISPAD meeting (Abu Dhabi, 2022), our biennial ISPAE meeting (Chandigarh, 2022) and at PEDICON 2023 (IAP's 60th annual conference held jointly with IPA's 30th conference: Ahmedabad, 2023) - were highly appreciated. The phenomenal success truly belongs to our dedicated and committed team of IDEAL faculty and the trainees. The family tree of"IDEALITES"is growing slowly, not only in numbers but also in richness of knowledge, diversity in geography, and strength in networking across India, as we bond together in our striving to improve diabetes care in our children. The virtual platform has given us several advantages. It has kept our costs miniscule and our relevance to managing in resource limited settings, high. It has encouraged the participation of female trainees in large numbers. It has enhanced our ability to make our markandin reaching out to remote parts of our country, as the proportion of trainees from non-metros increases. In batch 4, the large proportion of trainees who have T1D or are T1D parents, added an important practical domain to learning and interaction during sessions, which was useful both to the trainees and the faculty. Though we mandated a minimum attendance of 80%, most of our trainees achieved over 90% attendance, testifying to their high level of motivation and sincerity. It has been a gratifying experience so far and the sentiments are reflected during each online certification ceremony.

Based on the critical inputs and the valuable feedback from all our trainees, faculty, and Exit examiners, and the audit of the trainees' performance, the Core Committee has decided to revamp and update the entire curriculum, focusing existing modules more sharply to meet the needs of the trainees. The vibrant team of IDEAL faculty has readily agreed to redo the herculean task , and update the modules in keeping with new emerging evidence and the recently released ISPAD 2022 Guidelines. We look forward to implementing the revised curriculum from batch 5.

We have received an enthusiastic and overwhelming response to the upcoming batch 5 application process. We are also fortunate to have received unqualified support from the new ISPAE EC led by Dr Ahila, and have begun batch 5 enthused and refreshed from 1st April 2023.

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LEARNING PEARLS

30th IPA CONGRESS & 60th PEDICON (19th-23rd February 2023)

Compiled by Dr Zalak Shah Upadhyay, Consultant Pediatric Endocrinologist, Endocare for Kids, Rajkot, Gujrat

'Hypocalcemia in neonates and children': Talk by Dr Zalak Upadhyay (Rajkot)

- Hypocalcemia defined as serum calcium levels < 7 mg/dL in preterms, <8 mg/dL in term infants, <8.5 mg/dL in children. (1 mmol/L is 4 mg/dL).
- Screen the mother for hypocalcemia if a neonate presents with low calcium levels.
- Check corrected calcium for low/ high albumin levels.
- Always measure complete calcium profile - serum calcium, phosphorus and ALP.
- Treatment of acute hypocalcemia - injection calcium gluconate and later shift to calcium infusion 0.5-1.5 mg/kg/h for 8-10 h (prepare 1mg/ml solution 990mg of 10% calcium gluconate i.e. 11 ampoules to NS/ D5 to prepare a solution upto 1000 ml.).
- In cases not responding to calcium infusion, check serum Magnesium because hypomagnesemia may lead to low PTH secretion or PTH resistance).
- Caution to transport blood sample on ice pack when sample collected for PTH as it degrades quickly, or separate the serum and freeze it for assaying later.
- Always assess PTH when calcium is low/ high, not when calcium levels are normal.
- In a case of vitamin D deficiency, calcium is low, phosphorus can be low/ normal with raised ALP.
- In a case of hypoparathyroidism, calcium is low and phosphorus is high (both move in opposite directions).

Approach to Precocious Puberty: talk by Dr Sahar Idibi (Syria)

- Definition: Appearance of secondary sexual characteristics before age 8 years in girls, 9 years in boys.
- Idiopathic in 80-90% of girls; and pathological in upto 50% of boys.
- Hormone levels- Estradiol > 20 pg/ml suggests pubertal; levels >100 pg/ml suggests ovarian tumors or cysts. Testosterone > 30 ng/dL suggests pubertal levels.
- Girls with premature thelarche show exaggerated rise in FSH after GnRH injection (GnRH stimulation).
- Suppressed LH and FSH with highly elevated estradiol point to peripheral precocious puberty (PPP).
- A definitive CPP diagnosis is confirmed by a brisk rise in LH 20-40 min after infusion of GnRH (100 mcg).
- CPP is treated with Leuprolide depot 0.25-0.3 mg/kg/mo, continued until progress of puberty is age appropriate or until bone age is 12.5 years.
- Nafarelin acetate (Synarel) is a agonist analogue of GnRH and can be used to treat CPP - if available. 1600 mcg/d intranasally divided as 2 sprays in each nostril BD.
- Treatment of PPP is mainly by addressing the underlying cause

Congenital hypothyroidism: talk by Dr Shaila Bhattacharyya (Bangalore)

- Every newborn must undergo thyroid screening after birth. Diagnosis **cannot** be made by clinical examination, as only 10-15% of newborns may be symptomatic.
- Screening can be done with cord blood/ DBS (dried blood spot) or venous sample for TSH at 48-72 hours of life.
- Thyroxine can be started (after confirming in repeat sample) if
  - Elevated TSH i.e.> 20 in <2 wk or >10 mIU/L beyond 2 wk, and FT4 < 1.17 ng/dl or T4 < 10 mcg/dl
  - Low FT4 < 1.1ng/dl or T4 < 8 mcg/dl (irrespective of TSH)
  - Persistent TSH elevation > 10 mIU/L beyond 3 wk with normal T4/FT4.
- Start with an appropriate dose and titrate accordingly with free T4 and TSH levels on follow up.
- Checking compliance is very important
- Also monitor growth and development of baby on thyroxine.

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Rickets: where Vitamin D fails to work. Talk by Dr Chetan Dave (Rajkot)

Referring to IAP guidelines (2021) on prevention and treatment of Vitamin D deficiency (VDD) and Rickets.

- Definition based on serum 25-hydroxy vitamin D3 levels: Deficiency <12ng/mL, Insufficiency 12-20 ng/mL, Sufficiency > 20 ng/mL, Toxicity> 100 mg/mL with hypercalcemia or hypercalciuria.
- Daily doses preferable to bolus doses: For Deficiency: Age <1y: 2000 IU/day x 12 wk; > 1y: 3000 IU/day x 12 wk. Treat with calcium also for 12 wk.
- Though Vitamin D is available from sunlight on bare skin, it depends on host and environment factors.
- Anti-epileptic drugs and malabsorption can lead to VDD and rickets.
- Rickets is a radiological diagnosis, biochemical evaluation is needed to confirm and find the etiology.
- Clinical improvement within few days, radiological changes seen 4-6 weeks after therapy.
- Consider Vitamin D Resistant Rickets if failure of 2 rounds of therapy (adequate doses of Vitamin D3 + calcium over 12 wk, given twice). Or positive family history; liver disease/ kidney disorders; polyuria/ acidosis/ alopecia suggestive of non-nutritional rickets.
- Biochemical tests to be ordered Calcium, Phosphorus, ALP. Special tests like PTH, vitamin D3, creatinine, albumin, ABG, urine protein and sugar; 1,25(OH)D3 levels on case-case basis.

Can humankind stay healthy unless boys learn to cook? Talk by Dr Anju Virmani (Delhi)

- Unsafe and unhealthy food options directly cause obesity & one third of all diseases
- Increasing non-communicable disease burden, including type 2 diabetes, in poor nations; presently an 18y discrepancy in life expectancy between rich and poor nations.
- Rapidly rising pediatric obesity worsened by Covid, fueled by increasing global consumption of hyperpalatable, ultra-processed foods and beverages, higher screen time, inadequate physical activity.
- Home cooking can reduce burden by improving physical, emotional health; dietary quality; BMI.
- However, share of home-cooked food in developed countries declining from the 1980s, because shadow price of home-cooked food rising (Market value of time of secondary earners increased, household size reduced).
- In developing countries: cooking time is still the most time-intensive part of home production, primary cooking almost 100% by women spending an average 23h/wk in cooking-related activities

Advantages of Boys learning to Cook		
Valuable life skill	Improved physical, emotional, and social well-being	Better nutrition
Less obesity, hypertension, violence	Improved gender roles	Better finances for entire family

LEARNING PEARLS_ PEP 15 March



ISPAE PEP (Pediatric Endocrinology for postgraduates)
Meeting 15Th March 2023 **Hypothyroidism**

Compiled by P Raghupathy, Jaivinder Yadav, and *Amarnath Kulkarni*

Congenital hypothyroidism

1. Congenital hypothyroidism is the most common cause of preventable mental retardation.
2. Thyroid gland dysgenesis (ectopic, aplasia, hemiagenesis or hypoplasia) and dyshormogenesis cause permanent hypothyroidism. Iodine deficiency, prematurity and maternal anti thyroid drug therapy are risk factors for the transient hypothyroidism in infants.
3. As most affected babies with congenital hypothyroidism manifest no clinical symptoms or signs at birth, newborn screening (on Day 3) is the best strategy for early diagnosis. Cord blood TSH may also be used. The TSH-based screening approach is most commonly used but may miss rare causes like central hypothyroidism.

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4. Premature or LBW newborns, sick babies, Down Syndrome babies and those with doubtful initial values require a second screening (TSH, free T4) at 2-3 weeks.
5. TSH cut-off > 20 mIU/ml (34 at 24-48 Hr in serum units) is a suspicious positive screen, and the baby should be called for confirmatory second testing and treatment if required.
6. Early treatment with appropriate dose of thyroxine replacement therapy (10-15ug/kg/day commenced within 2 weeks) ensures normal neurodevelopment.
7. The treatment targets are early normalisation of T4 within two weeks and to maintain T4 in the upper half of the normal range (10-16ug/dl) during follow-up.
8. The family should be adequately counselled for drug compliance, more often, lifelong and regular follow-up for optimal outcomes.
9. All TSH cut-offs are based on serum units, and most labs report it in the same. If a lab reports TSH value in whole blood units, it should be converted into serum units by multiplying it with 2.2 before interpreting it.

Acquired Hypothyroidism-

1. Autoimmune thyroiditis is the most common cause of acquired hypothyroidism, especially in girls.
2. Growth failure, constipation, dry skin, and increased sleepiness are common symptoms, but prolonged untreated cases may present with calf hypertrophy, pleural effusion, pericardial effusion and precocious or delayed puberty.
3. Children with type 1 diabetes, celiac disease, Down Syndrome, Turner Syndrome, and Noonan Syndrome are more prone to develop hypothyroidism.
4. Obese children frequently present with subclinical hypothyroidism (TSH between 5-10mIU/ml, T4 normal) which does not need treatment.
5. The diagnosis requires a thyroid function test (total or free T4/TSH) and bone age; autoantibodies (anti-TPO, anti-TG) may be done..
6. The treatment is started (in chronic and prolonged hypothyroidism) with a smaller dose (1-2µg/kg) and gradually increased to target T4 in the mid normal range. A higher dose may cause hyperactivity and faster bone maturation.
7. Subclinical hypothyroidism does not require treatment but warrants close clinical and lab monitoring.
8. Regular monitoring on IAP growth charts can help in early diagnosis of acquired hypothyroidism.
9. Prevent mental retardation & short stature by diagnosing and screening hypothyroidism in the community. Untreated hypothyroidism early in life, at birth or during infancy, leads to mental retardation but onset later affects physical growth by way of short stature.
10. Look for other associated autoimmune conditions such as like ptosis for hypopigmented patches for vitiligo, alopecia & polyuria/polydipsia for Type 1 Diabetes on follow-up visits.

ACHIEVEMENT:

Dr. Shantilal C Sheth Oration conferred upon Dr Vaman Khadilkar

The prestigious Dr. Shantilal C. Sheth Oration was delivered by Dr. Vaman Khadilkar on 21 February, 2023 at the 30th International Pediatric Association Congress & 60th PEDICON 2023 conference held at Gandhinagar, India. Dr. Shantilal C. Sheth was one of the pioneers in Pediatrics: the oration in acknowledgement of his work was initiated by the Indian Academy of Paediatrics in 1967. Dr Vaman Khadilkar delivered the oration on “IAP Growth charts and Indian Anthropometry - A powerful diagnostic tool for the Indian Pediatrician”. The

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session was chaired by the IAP President Dr. Upendra Kinjawadekar and IAP Secretary Dr. Vineet Saxena. Dr. Khadilkar's personal passion in anthropometry developed In United Kingdom where he worked at Great Ormond Street Hospital in London in the great Prof. JM Tanner's unit. He has been instrumental in producing the Revised IAP Growth charts, 2015, as part of the IAP growth chart committee and has continued his work on Indian anthropometry norms, touching every aspect with extensive data published in prestigious journals.

(Compiled by Dr Chirantap Oza)

ISPAE OBSERVERSHIP AWARD

Dr Namita Mishra from AIIMS Raebareli completed Observership in Pediatric Endocrinology from Dec 2022 to Jan 2023at the Dept of Pediatric Endocrinology, SGPGI, Lucknow. She found the course an extremely useful learning experience. The efforts of her mentors, Dr Vijaylakshmi Bhatia, Dr Preeti Dabadghao and Dr Siddnath Sudhanshu were reported as praise worthy. She was especially thankful to ISPAE for the opportunity.

ACTIVITIES BY ISPAE MEMBERS

CIAP-IAP Pediatric Endocrinology TOT-Workshop & World Obesity Day.

Dr Amarnath Kulkarni, National Joint Coordinator, CIAP Pediatric Endocrinology TOT Workshop

This TOT, conducted at Lotus Children Hospital, Hyderabad, on 5 March 2023, had 80 delegates participating. The prestigious faculty included Drs Leenatha Reddy, Sirisha Kusuma, Leena Priyambada, Kavita Sakamuri, Kishore Baske, Amarnath Kulkarni & Srikrishna RSV. The topics covered included precocious puberty, DKA, Ambulatory management of T1D, Growth & short stature, Hypothyroidism & Obesity. There were workstations on growth charts, insulin pens, carbohydrate counting, CGM, ketone meter, glucagon injection, and insulin pump. The CME also saw a poster release on the theme of World Obesity Day:*"Changing Perspectives: Let's talk about obesity"*.

Support group meeting for families with Type 1 diabetes, specifically pump users

Dr Meena Kumari Mohan, PSG Super Speciality Hospitals, Coimbatore

A parent support group meeting for type 1 diabetes was held on 11.02.23, exclusively for current and potential pump users at Zone Hotel in Coimbatore. Around 15 families (45 members) attended the session, including diabetes educators and well-wishers supporting the charity.

Various topics including questions on pumps, current and day-to-day challenges and difficulties faced, 'unmet needs with different models of pumps', 'different pumps in the market - their prices and features', the important role of CGMS in pump users, and

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'managing exercise and body building in pump users' were discussed. The issues around data protection in Libre and Librepro were discussed. The high point was the attendance of a teacher looking after siblings with T1D. It was interesting to hear from her the challenges that she sees these children facing around chocolates and birthday parties, sharing of food during snack and lunch time, management of hypoglycemia and the unwell child in a school setting, etc. Expansion of the charity "PEDENDOCARE" was discussed, and a 720G pump donated to a child with T1D with hemophilia.

The session was well received and appreciated by one and all. Parents welcomed such meetings with specific issues, as the issues could be discussed in more detail than in general T1D meetings.

Workshop on MNT in Diabetes Management and application of Carbohydrate counting

Ms Sharanya S Shetty and Ms Shruthi R, Karnataka Institute of Endocrinology and Research (KIER)

A workshop was conducted by the dietitians Sharanya S Shetty and Shruthi R of Nutrition Department for the Postgraduate students of Food & Nutrition on 11th January 2023 at Smt VHD Central Government Institute for Home Science, School of Home Science, Maharani Cluster University, Bengaluru. The workshop was a digital presentation and kicked off with a fun icebreaker question of the myths that they have heard about diabetes. This was displayed as a word cloud where the students had the exhilarating experience of viewing the live opinions of the board. The workshop was intended to educate, interact and share the overview about diabetes and different types of diabetes, Guidelines, risk factors, symptoms and management. Elaborate and special emphasis was laid on medical nutrition therapy, meal planning for persons with Type 2 and Gestational diabetes. It also taught practical aspects and detailed dietary analysis of children living with T1D, calculation of insulin sensitivity factor, insulin-carb ratio, tools and techniques for carbohydrate counting and planning of meals. Students were kept engaged throughout the session with live poll questions, activities and discussions of case scenarios, calculations and guessing of the carbohydrates of different Indian foods. Worksheets were shared with them as a part of take-home learning. The workshop ended with a live quiz that had leader board ratings where the students did exceptionally well.

Meeting for Type 1 Diabetes with the National Commission for Protection of Child Rights

Mr Harsh Kohli, T1D representative, Blue Care Pharmacy

NCPCR
NATIONAL COMMISSION FOR PROTECTION OF CHILD RIGHTS

NCPCR, a Government of India body, taking cognizance of the several issues faced by children, adolescents and adults with T1D, organized a meeting of all stakeholders to understand how to ensure the rights of affected children. It was held on 13/01/2023, in hybrid online + offline mode, and was well attended by Patient Representatives and leading Pediatric and Adult Endocrinologists and other specialists in the field, from across the country. Many issues related to T1D were discussed. Now that NCPCR is seized of the matter, we were looking forward to having some positive action in care of T1D children by the Government of India. 'It was very gratifying that action was indeed taken in the form of a directive to schools.'

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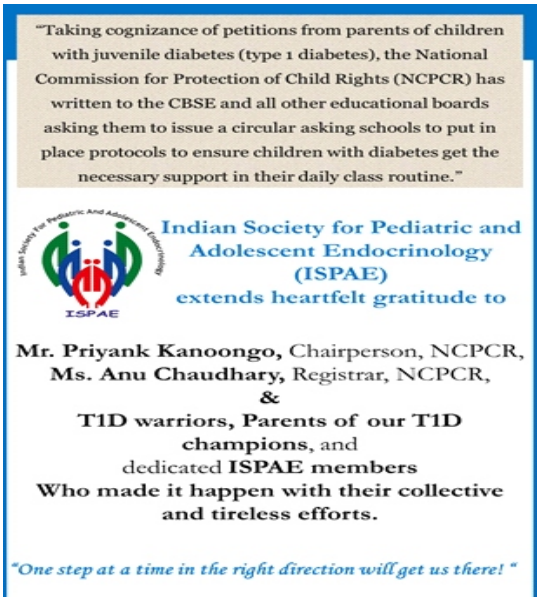
Message from NCPCR

'NCPCR had received several petitions from parents of children with T1D regarding difficulties faced in schools on a daily basis and especially during exams. Based on this, with guidance from ISPAE members, NCPCR has sent a directive to all education Boards across India, asking them to facilitate diabetes self-care during exams, and otherwise also. This was a welcome update of the CBSE directive of 2017, since Mr Kanoongo specifically directed that sensors and insulin pumps be permitted in school and examination halls.

ISPAE sincerely thanks NCPCR for this important step in the right direction, which will bring a big relief to all T1D families.

Please find NCPCR chairperson Mr. Priyank's message here: https://youtu.be/wYy-oUSCrJc (English)

https://youtu.be/RYH7s4cxo0I (Hindi)



Yog Dhyan Foundation (YDF) Activities

Dr Anil Vedwal, Chief functionary, YDF

YOG DHYAN FOUNDATION
Enriching Lives Holistically! Focused on Young With Type One Diabetes
www.yogdhyanfoundation.com

YDF Delhi, aims to empower children with T1DM, by providing physical resources, diabetes education, camaraderie and emotional support. Families not well off are given financial support, free glucostrips, insulin, syringes, pen needles, necessary tests; and on a special occasion, a thermos to transport insulin. There are twice-weekly online yoga classes, fortnightly physical camps, online education & discussion sessions with experts every second Sunday, monthly birthday celebrations every last Sunday, quarterly health checks, and other educational and social programs from time to time. YDF currently supports over 400 children, funded by Mr Rummy Chhabra, Ms Bindia Chhabra, numerous individual donations from T1D families and other well-wishers, and RSSDI-Sanofi. It is helping JDRF in its India activities. The successful online yoga classes started during the Covid lockdown are continuing as evening classes twice a week, conducted by Parent Volunteers Ms Ashu, Ms Renu and Ms Poonam; and Junior volunteers Kushal, Naman, Payal, Tanishka, and Akshita.

The monthly online meetings, initiated in June 2022, held on second Sundays from 12-1.30pm, are conducted by Mr Sam Gulati and Ms Chhavi Soni. YDF honors a "Diabetes Hero of the Month", who shares his/ her inspiring journey. Those honored so far have been Mr Lakshminarayan, Ms Shuchy Chugh, Ms Rekha Negi, Dr Sanjay Singh, Ms Bhumika Khurana, Ms Harleen Kaur, Mr Lokesh Chawla, Ms Mridula Bhargava, Mr Prashant Mani, and Mr Harsh Kohli. The Hero's address is followed by a talk and an extensive Q&A session dealing with the topic of the month, with a panel joining the Speaker and the Hero in answering the families' queries. Speakers have included Doctors Aashima Dabas, Anushree Mehta, Beena Bansal, Bhanu Kiran Bhakhri, Deepika Harit, Ganesh Jevalikar, Jyoti Kakkar, Medha Mittal, Meena Chhabra, Nupur, Pragya Mangla, Preeti Singh, Saurabh Srivastava, ShuchyChugh, Sumeet Arora, Sunita Manchanda, and Anju Virmani. Educators have been Ms Chhavi Soni, Mr Harsh Kohli, Ms Jasmine Ahuja, Ms Meenakshi Bajaj, Ms Mridula Bhargava, and Ms Rekha Negi. Themes covered were handling summer vacation, school reopening, why ketones are dangerous, preventing chronic complications, understanding types of insulins, hypoglycemia, improving adherence, nutritional management, celiac disease, and sick day rules. Recordings of all these sessions and other YDF activities are available on our YouTube channel, and our website yogdhyanfoundation.org. We are also available on Instagram and Facebook.

National Workshop: Lifestyle &Metabolic diseases in children & adolescents: Role of Millets & Beyond.

Dr Anjali Verma, Associate Professor, PGIMS, Rohtak

A National Workshop on "Lifestyle and Metabolic diseases in children and adolescents: Role of Millets & Beyond" was organized by the Multi-Disciplinary Research Unit (MRU) of University of Health Sciences, Rohtak on 1st March

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2023. The United Nations General Assembly at its 75th session in March 2021 declared 2023 as the International Year of Millets (IYM 2023) for which the proposal was sponsored by the Government of India. Hence, IYM2023 will be an opportunity to raise awareness and to direct policy attention to the nutritional and health benefits of millets. Going with the theme, this workshop was an initiative to create awareness among doctors, students, and paramedical staff regarding beneficial use of millets in various lifestyle and metabolic diseases in children.

More than 250 doctors from various departments of colleges affiliated to PGIMS and UHSR, PG students, dieticians, and paramedical staff participated. The organizing chairperson was Dr SimmiKharb, Nodal Officer, MRU; the Organising Secretary was Dr Anjali. Dr Baljeet Singh Yadav (Professor, Department of Food Technology, MDU), Dr Rajni Sharma (Additional Professor, Pediatrics, AIIMS), Dr Medha Mittal (Associate Professor, Pediatrics, Chacha Nehru Bal Chikitsalya, New Delhi) and Dr Meenakshi Chauhan (Senior Professor and Unit Head, Obstetrics & Gynaecology, PGIMS) graced the program as the keynote speakers. The topics of discussion were 'Millets as key to Food and Health Security', 'Practical approach to a child with obesity', 'Pediatric Diabetes: what, when and how much to eat?' and 'Recent advances in management of PCOS'. The keynote speakers also answered the questions of the audience pertaining to the use of millets in the daily routine, for prevention and management of lifestyle diseases.

WORLD OBESITY DAY

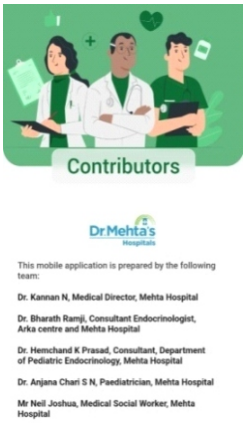
Dr Ravindra Kumar, Senior Consultant and Incharge Pediatric Endocrinology, Hindu Rao Hospital and North Delhi Medical College, New Delhi

World Obesity Day was organised by Dr Ravindra Kumar, I/ C Pediatric Endocrinology at North Delhi Medical College & Hindu Rao Hospital,Delhi in association with IAP North Delhi. In the morning session visiting pediatric OPD at Hindu Rao Hospital were briefed about healthy diet, healthy lifestyle, reducing screen time and avoiding junk food.Patient were provided with apples and bananas to sensitize them about healthy food. More than 100 patients visiting OPD were taught how to control Obesity. Dietician explained in detail about healthy food and harmful food. Our physiotherapist showed the correct way of daily exercise. In the afternoon session a CME was organised which was attended by close to 100 doctors and paramedical staff. A panel discussion was held on " How to manage Obesity" moderated by Dr. Ravindra Kumar with panelists being Dr. Nishant Raizada , HOD, Deptt Of Endocrinology, University College of Medical Sciences & GTB Hospital, Delhi and Dr. Richa Arora, Pediatric Endocrinologist, Fortis Hospital and Jaipur Golden Hospital Delhi, in which all delegates interacted with faculty actively.

Online App - Dr Hemchand Prasad

Childhood obesity is on the rise. To stem this tide of obesity, our team has developed a mobile application called as “Obeasigo”. This app aims to help families of children with obesity fight the pandemic of obesity. Its helps in identification of obesity and its metabolic complications in children. It provides valuable advice on how to tackle obesity using lifestyle measures. The app also helps to assess the response to the interventions. It is free to download, both on Google playstore and on Appstore. Please do share with relevant groups so that many children and adolescents with obesity are benefitted.

Android app Link: https://play.google.com/store/apps/details?id=io.phantom.obeasigo
iOS app Link: https://apps.apple.com/in/app/obeasigo/id1667199463+



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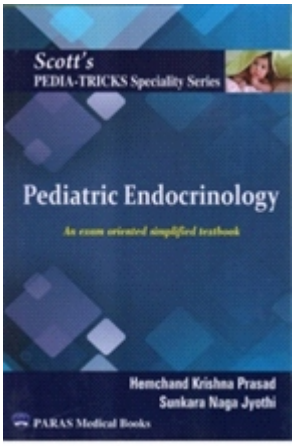
NEW BOOK REVIEW

Pediatric Endocrinology: Eds - Dr Hemchand K Prasad and Dr Sunkara N Jyoti



The Dept of Pediatric Endocrinology at Mehta hospital, Chennai, along with Paras Publishers, has come up with an exam-oriented simplified book on Pediatric Endocrinology. Exam-oriented discussions on important topics in pediatric endocrinology are presented in a question and answer format. The link to the purchase of the book is below:

https://parasredkart.com/product/scott-s-pediatricks-speciality-series-pediatric-endocrinology-1st-2022

SUPER SWEET HEROES - AN INITIATIVE BY FRENDOS GROUP

Sakthivel Sivasubramanian, Endocrinologist, Tiruchirappalli, Tamil Nadu

In order to impart completely scientific diabetes education, awareness material has been written by specialist doctors, for children with T1D. An endocrinologists' WhatsApp group called FRENDOS initiated a project. With 22+ endocrinologists volunteering to contribute chapters, a 3-volume booklet series called SUPER SWEET HEROES has been prepared.

Dr Sakthivel, the founder and co-ordinator of this group, informed that the books are informative and also easy for children to read. Each of the three volumes of the book can be shared with the child during monthly visits, so that the education can be done in a phased manner and is easy to assimilate. The first volume covers the basics, while the other two volumes deal with more intricate details. These exciting booklets can be obtained at a nominal price of Rs 300/-by contacting Dr Sakthivel by WhatsApp +917373728282 or by emailing to drsakthivel.endo@gmail.com.

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TRAINEES' SECTION

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

MUMBLE JUMBLE

Unjumble the letters to find the answers from the clues given related to Growth. Assemble the numbered letters in order to find the correct diagnosis for the case details given below.

1. Syndromic short stature with generalized multiple lentigines
2. Gold standard pharmacological stimulus of growth hormone
3. Short stature syndrome with increased predisposition for malignancies
4. An androgen which is used along with growth hormone in Turner syndrome for height gain
5. Most common cause of disproportionate short stature
6. Name of the diagnostic criteria for Marfan syndrome
7. Potentially lethal disease associated with short stature, bowing of legs, defective mineralization and tongue like projections on x ray
8. Skeletal dysplasia characterized by mesomelic dwarfism and Madelung deformity
9. Overgrowth syndrome associated with hyperinsulinism
10. Anti resorptive monoclonal antibody in trial for osteogenesis imperfecta
11. Embryological origin of adenohypophysis
12. Disproportionate shortening of hands and feet is known as
13. Name of the syndrome of psychosocial dwarfism
14. This mutation is associated with growth hormone insensitivity, eczema and immune dysfunction
15. Noonan syndrome is caused by defects in which pathway
16. X linked hypophosphatemic rickets is caused by which mutation
17. Growth chart used for preterm growth monitoring
18. Enzyme replacement therapy for hypophophatasia

ANSWERS

1. PROADEL

	2					

2. LIINUSN

		1				

3. OBOML

		5		

4. DONOEXNRALO

				8						

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5. AALAOCNDORSPIH

	7												

6. TNGEH

7. SPIHOPPAHAAOYTSH

		3												

8. ERIL LEIWL

			6

DYSNSDRTCOHEOOISS

9. TKBWEHIC

NMWAENDEI

DONYEMRS

	9					

10. BSODUNMEA

11. HRKATE

CUHOP

12. ACIROLMAE

11								

13. SKAPRA

SRHEUA

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14. AT5SBT

	4				

15. RSA

16. XEHP

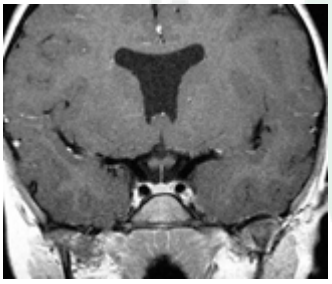
17. NETFON

18. OATFESSA

HPLAA

	10			

Diagnosis- A child with short stature, hypoglycemic convulsion and poor vision with below MRI picture



1	2	3	4	5

5	3	4	6	7

8	9	1	3	10	11	1	7	10

Please mail the correct answers to tejasviseshadri@gmail.com
(Answers will be communicated in the next issue of CAPE News).
The names of first three respondents with correct answers shall be acknowledged in the next edition

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UPCOMING EVENTS

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