CAPE NEWS

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Contents

From the Editor's desk

Dear members,

This new issue of CAPENEWS, covers interesting current issues. Dr Supriya Phanse and Dr Vaman Khadilkar discuss in detail long acting growth hormone (GH) preparations which offer a convenient regimen and increase compliance in children receiving GH therapy. In another interesting article, Dr Anjana Hulse and Dr Prasanna Kumar KM share their experience with ambulatory glucose monitoring, which is a new, convenient, and cost-effective mode of glucose monitoring, for which additional data on accuracy and safety is still needed. Also included are summaries of recommendations from two major guidelines regarding two important, often debated topics: prevention and management of nutritional rickets, and diagnosis of polycystic ovary syndrome during adolescence. There is a report of a rare case of neonatal diabetes due to interleukin 2 receptor alpha (IL2α).

I am sure all those interested in pediatric endocrinology will find this issue useful. I thank all my team members, Dr Rajni Sharma, Dr Sachin Mittal, Dr Ravindra Kumar, and Dr Reetha Gopinath for their active participation in designing this issue and for their valuable contributions. My special thanks to Dr Anju Virmani, for her whole hearted efforts to make this issue a fantastic one.

Editor, CAPENEWS

ISPAE Biennial Meeting 2017: Coimbatore, Tamil Nadu, Nov- Dec 2017

Organizing Chairperson: Dr P Raghupathy, drp.raghupathy@gmail.com
Organizing Secretary: Dr Ahila Ayyavoo, ahila.ayyavoo@gmail.com

We are proud to announce that the 44th annual ISPAD meeting, **ISPAD 2018,** will be held in **Hyderabad, India from 11-14 Oct 2018**, in association with ISPAE.
This is the best time to become an **ISPAD member** (membership runs from 1st July to 30th June)! Click ispad.org. The discounted 3y membership for us in India (LMIC) is just $ 80/ year. Membership will allow discounted rates for attending the **42nd Annual ISPAD Conference,** in Valencia, Spain; **ISPAD 2017** in Innsbruck, Austria (18-21 October), and of course **ISPAD 2018.**

Mid-Term ISPAE Meet: Nashik, Maharashtra, 15-16 Oct 2016

in association with International Society for Pediatric and Adolescent Diabetes (ISPAD)
The theme of this meeting is **"Sugars & Beyond".**

Organizing Chair: Dr Sudha Rao, Organising Secretary: Dr Tushar Godbole
Scientific Chair: Dr Preeti Dabadghao
For registrations, please contact: **Dr. Tushar Godbole www.ispae2016.com, [+91-7774082834], Email: ispae2016@gmail.com**

Dear ISPAE members,

Dr Vijayasarathi and his team have come out with another excellent issue of CAPE NEWS. Congratulations to the whole team for their hard work!

This quarter of the ISPAE year has witnessed a few brilliant academic programs conducted under its banner. ISPAE –SSPHPGTI pediatric endocrinology CME at Noida was such an event organized by our Joint Secretary Dr Bhanu Bhakhri. Many renowned faculty from India and abroad shared their experiences with the delegates in this conference. Our members Drs Vandana Jain, Rajni Sharma and Anju Seth conducted a PG teaching program in Lady Hardinge Medical College in July 2016, as did Dr Sudha Rao at Wadia Children's with team members Drs Aparna Limaye and Rajesh Joshi.

The ISPAE National Midterm meet is on October 15th and 16th at Nashik. The scientific program is finalized and the brochure has been released. A new innovation is the workshop for diabetes educators and pediatricians, "Nuts and Bolts of Diabetes Management", to be held for a half day just prior to the main conference. The whole organizing team is working really hard to make this conference a landmark event in ISPAE history. Best wishes to Dr Tushar Godbole and his team. Our members Drs P Raghupathy and Shaila Bhattacharya will organize a pre-conference workshop during Bangalore Pedicon 2017.

ISPAE is very active in formulating guidelines on various topics related to pediatric endocrinology, tailor made for Indian patients and their care givers. Our Practice Guidelines on Type 1 Diabetes was released in 2011 and was well appreciated by both pediatricians and pediatric endocrinologists all over India. The second revised edition is in process. Kudos to the entire team involved in this great work which is headed by Dr Aspi Irani. Dr Anju Seth has been permitted to make an ISPAE guideline for the treatment and prevention of vitamin D and calcium deficiency in children.

ISPAE is not a pure academic organization. Our members are actively participating in various charity activities. This year's Charity Awards were given to Drs Reetha Gopinath, Veena Nair, Deepa Anirudhan and Ranjani Harish. Do read their detailed reports below. Congratulations to the recipients: their contribution to patient welfare and education is appreciated! Hope many more such charity activities will be there in the coming years also.

Patient education booklets are being prepared in Hindi, English and various regional languages. Many of these booklets and pamphlets (on Obesity, Type 1 Diabetes, Turner Syndrome, among others) have already been uploaded on the website. They will be of great use to our children (with various endocrine problems) and their parents. I urge all members to visit the site; the links to Consensus Practice Guidelines have also been updated and will be useful to professionals.

The ISPAE 2017 and the APPES-ISPAE Fellows' School (to be held in India in 2017) teams are getting geared up. We also look forward to ISPAD 2018, which is to be held in Hyderabad, India. The International Consortium of Pediatric Endocrine Societies held a teleconference with all member countries. Our office bearers were invited to attend and Dr V Bhatia represented us. A logo has been finalized for the Consortium, after consultation with all, and plans for a website are under way. As communicated in CAPE NEWS earlier, the Consortium will undertake the task of organising the Pediatric Endocrinology Joint Meeting from the year 2021 onwards.

Regards
Dr M Vijayakumar, Secretary ISPAE

Hearty Welcome to New ISPAE Members

1. Manpreet Sethi
2. Nihar Ranjan Mishra
3. Angadi Kudiappa
4. Sumana Kundagrami
5. Asha Mukherjee
6. Sadhna Sha
7. Phanishree P V

Long Acting Growth Hormone - Current Perspective

Vaman Khadilkar, Pediatric Endocrinologist, Jehangir Hospital, Pune and Bombay Hospital, Mumbai; Supriya Phanse, Pediatric Endocrinologist, Deenanath Mangeshkar Hospital, Pune

Background

For the past many years, growth hormone (GH) has been used to treat short stature secondary to GH deficiency, SGA sequelae, Turner syndrome, Prader-Willi syndrome, chronic renal failure and recently idiopathic short stature. Newer indications are continuously added with upcoming evidence from research studies.

Daily GH preparations have been used for over 25 years, with a well-established safety and efficacy profile. The prohibitive cost of therapy and the cumbersome administration schedule are the major obstacles for GH therapy. GH being a polypeptide with a short half-life, has to be administered subcutaneously daily at bedtime. Treatment entails daily injections from an early age for a period of many years, improving growth velocity and final adult height. Thus long term compliance proves to be difficult.

NEED FOR LONG ACTING GH FORMULATIONS:

Due to cumbersome daily administration of GH, compliance remains an issue with GH therapy in children and adolescents. To overcome this problem, numerous depot GH preparations are being developed. However, most are still in the research stage, being tested for their efficacy and safety. With a robust safety and efficacy profile of daily rhGH preparations, a cautious approach is being adopted in developing long acting GH preparations to ensure similar safety and efficacy.

Generally, there are two methods for creating long-acting preparations. The first method involves formation of reversible complexes which stabilize hGH, such as zinc-hGH complex. In the second approach, sustained-release preparations are fabricated, entrapping hGH into matrixes, like microspheres and hydrogels.

LONG ACTING GH FORMULATIONS:

NUTROPIN DEPOT: It was a recombinant GH encapsulated in biocompatible, biodegradable, poly lactide co-glycolide acid (PLGA) microspheres. Post subcutaneous injection, GH was released slowly over a 1 month period. Monthly 1.5 mg/kg or twice a month 0.75 mg/kg in prepubertal children did produce improvement in height and skeletal maturation. The downside of this preparation was early peak of GH (within 2 days) and significant local reactions. Though being the only approved formulation, it was withdrawn due to poor feasibility of its manufacture, and is no longer marketed.

LB03002: It is a sustained release rhGH suspension of microparticles, wherein GH is incorporated into sodium hyaluronate and dispersed in an oil base of medium chain

triglycerides. Trials of this weekly depot in a dose of 0.5 mg/kg/week in children showed improvement in growth similar to daily injections, and it was found to be safe. A trial in adults, with an average weekly dose of 4 mg/week, showed a reduction in fat mass and increase in lean body mass. However, injection site reactions, though mild, were common with this preparation.

Table 1: Sustained release preparations of Growth Hormone:

Sustained-release	**Advantages**	**Disadvantages**
Zinc-complex	Easily performed; can be adopted in other studies	Prolonging release not much improved
Microsphere	Easily prepared; commercially available	Acidic degradation of PLGA denaturation of rhGH
Hydrogel	Long and adjustable sustained-release; easily prepared	Adverse effect at injection site; shorter sustained-release time than microspheres
Prolonged half-life		
PEGylation	Reduced clearance; adjustable half-life based on PEGylated site	Initial burst (some studies have addressed this) Storage problem in the solution state
Albumin conjugation	13–15 h half-life in monkeys	Possible adverse events such as lipoatrophy
XTEN amino sequence fusion	110 h half-life in monkeys	May alter the potency of rhGH
Hybrid Fc fusion	High bioavailability	
Carboxy-terminal peptide fusion	No adverse effect observed	Low bio-availability
Extracellular receptor of hGH fusion	1 week efficacy has been demonstrated in a phase II trial	Further study in animal model required

h, hour; hGH, human growth hormone; rhGH, recombinant human growth hormone; PLGA, poly(lactic-co-glycolic acid); PEG, polyethylene glycol.

NNC126-0083: It is a pegylated rhGH with a 43-kDA PEG residue attached to glutamine 14 of rhGH, being developed as a weekly administered depot. Currently, it is in phase II clinical trial of development.

Prodrug ACP-001: It is designed to be administered weekly wherein the long acting pro-drug releases unmodified human GH. It is still in the phase II clinical trial stage.

Numerous GH fusion proteins (Albutropin, MOD-4023, VRS-317) are being developed to reduce the clearance of GH and thus increase its duration of action. However, all are in clinical trial phase I stage.

Depot GH in India:

Until now, LB03002 (Depot preparation of long acting GH by LG Life Sciences) is the only preparation tested in India as a part of phase III clinical trial. A large number of Indian children were recruited in the study, and hence conclusions from this study at least partly reflect the response seen in Indian children.

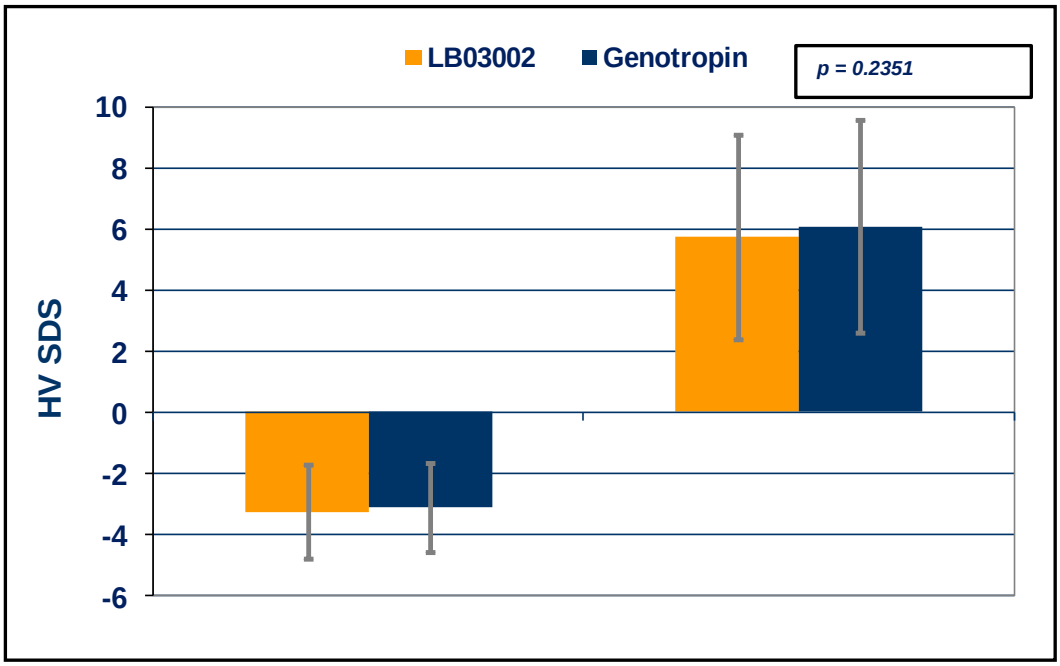

Figure 1: Comparative Efficacy of Depot vs. Daily injections of GH in improving Height Velocity over a 2 year period.

A phase III multinational, randomized, open label, comparator controlled, clinical trial was conducted to study the efficacy and safety of LB03002. Prepubertal GH deficient, treatment naïve children (mean age 7.8 years) were administered either LBO3002 (n=91) or daily GH (n=87) for 12 months. Following this, all were administered LB03002 for the next 12 months (LB03002 throughout n=87, switched to LB03002 from daily GH n=80).

There was comparable catch up growth in the first year among both the groups, with similar mean and SD height velocity in the first year (11.63 ± 2.60 cm/yr in the LB03002 group vs. 11.97 ± 3.09 cm/yr in the daily GH group). Mean height velocity remained high in the second year as well (8.33 ± 1.92 cm/year in the LB03002 throughout group vs 7.28 ± 2.34 cm/yr in the switched to LB03002 group). Bone maturation and height progressed parallel in both the groups. IGF-1 (IGF-1 SDS: -1.07 ± 1.86 in the LB03002 group vs. -1.47 ± 2.05 in the daily GH group) and IGFBP-3 (IGFBP-3 SDS: -0.51 ± 1.35 in the LB03002 group vs. -1.09 ± 1.97 in the daily GH group) responses at the end of 12 months were also similar in both the groups.

Safety profile of LB03002: There was higher incidence of injection site reactions, namely pain, redness, erythema and discoloration in the first 12 months in the LB03002 group.

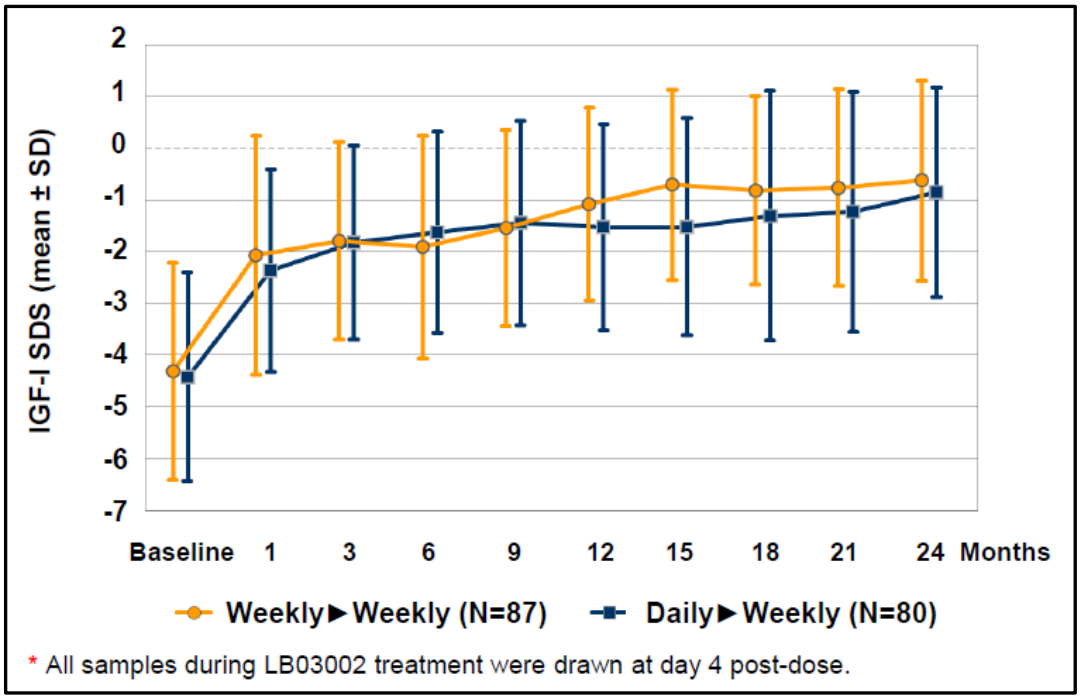

Figure 2: IGF-1 Z-score comparison between daily and weekly growth hormone

However, they were mild to moderate in degree, the commonest being swelling at the injection site and pain. This could be attributed to the larger volume of the depot preparation, its ingredients and the technique of injection. These settled in the following 6 months, and none progressed to nodule formation. There was no difference in the occurrence of serious adverse events between both the groups (2.2% in the LB03002 vs. 2.3% in the daily GH group). Glucose homeostasis was comparable in both the groups as well. GH antibody formation was significantly higher in the LB03002 group. Thirty-four of 91 patients (37.4%) receiving LB03002 tested positive for GH antibodies at least once during the first year, compared with 4 of 87 patients (4.6%) receiving daily GH. Although in the short term this did not affect the clinical response to GH, long term data is needed to understand the implications of this observation.

Thus, once a week administration of LB03002 had an acceptable efficacy and safety profile at least in the short term, making it ideal for long term GH replacement therapy in GH deficient children.

Conclusions

Long acting GH preparations are a major development in treating GH deficiency. Current evidence suggests that at least some preparations such as LB03002 have acceptable safety and efficacy profile in the short term; clinical experience will add to data on its long term safety and efficacy. We hope that these exciting developments in the sustained release / depot GH will bring about major improvements in long term compliance and thus response to treatment in children needing GH therapy.

Further Reading:

1. Khadilkar V, Radjuk KV, Bolshova E et al. 24-Month Use of Once-Weekly GH, LB03002, in Prepubertal Children with GH Deficiency. J Clin Endocrinol Metab. 2014;99:126-32.

2. Kang J, Wu F, Cai Y, Xu M, Yuan W. Development of recombinant human growth hormone (rhGH) sustained-release microspheres by a novel low temperature aqueous phase/aqueous phase emulsion method. Eur J Pharm Sci. 2014;62:141-147.

3. Webster R, Xie R, Didier E, et al. PEGylation of somatropin (recombinant human growth hormone): impact on its clearance in humans. Xenobiotica. 2008;38:1340-1351.

4. Cawley P, Wilkinson I, Ross RJ. Developing long-acting growth hormone formulations. Clin Endocrinol (Oxf). 2013;79:305-309.

Accuracy of Ambulatory Glucose Profile: a Pilot Study

Dr Santosh Olety, Karnataka Institute of Diabetes, Bangalore

The goal of diabetes management is to control glucose levels to reduce the risk of serious short and long term complications. Self-monitoring of blood glucose (SMBG) and glycosylated hemoglobin (A1C) may not provide a complete picture of the changes in the patient's glucose levels since they do not account for all the glycemic variability.

While CGMS are very useful tools looking at trends and patterns, one has to remember their limitations in terms of accuracy when compared to laboratory analysis. The manufacturer's data claims a mean absolute relative difference (MARD) of 11.1%, but their comparison was with glucometer readings rather than standard lab analyses. Here we share a small study at our institute comparing the Abbott Freestyle Libre CGMS with our laboratory analysis (hexokinase method). A total of 57 readings (fasting, random, postprandial) from 9 subjects: 3 T1DM children, 3 T1DM adults, 2 T2DM adults and 1 nondiabetic adult) were studied during Aug-Sep 2015.

Table 1: Sensor performance compared to lab analysis at different glucose levels

Glucose mg/dl	MARD
51-80 (n=1)	21.3%
81-120 (n=9)	23 %
121- 200 (n= 25)	19.7 %
201- 300 (n= 14)	14.25 %
301-400 (n=5)	8.6%
> 400 (n= 2)	5.3% *(one reading 661, sensor showed > 500)*

MARD across the range of glucose levels is summarized in Table 1.

When compared against venous plasma glucose analyzed by the hexokinase method, overall MARD for 57 readings was 14.2% (range: 0-46%).

Overall, 59.6% (n=34), 68.4% (n=39) and 84.2% (n=48) of sensor readings were within 15%, 20% and 30% of the corresponding venous plasma glucose analyzed by the hexokinase method.

According to our study, results showed the best acceptable MARD (< 15%) using the Abbott CGMS was when the glucose levels were above 200 mg/dl. Since our study number were very small, a larger number would be required to support or refute these findings to guide us in making the best use of CGMS

Use of Ambulatory Glucose Profile in Children with Diabetes

Anjana Hulse, Pediatric Endocrinologist, Apollo Hospital, Bannerghatta, KM Prasanna Kumar, Consultant Endocrinologist, CDiC, Bangalore

Glycemic control in children with diabetes is routinely assessed using self-monitoring of blood glucose (SMBG) and glycosylated haemoglobin (A1C). SMBG recording, though very useful to adjust daily insulin doses, may miss nocturnal hypoglycemia and post prandial hyperglycemia, which may be picked up by continuous glucose monitoring (CGM). Moreover, it has been demonstrated that glycemic variability is an independent risk factor for developing long term complications even when A1C is in the normal range.[1] CGM is being used to study glycemic patterns in children for many years. Recently, Ambulatory Glucose Profile (AGP) using a flash glucose monitoring (FGM) system is being used in adults; its use in children is yet to be explored.

AGP provides a standardised visualisation of glucose data. AGP differs from the existing CGM systems because it is factory calibrated and does not require calibration using SMBG measured by glucometer. This eliminates potential errors in the accuracy of the device, which could occur because of differences in glucometer readings and venous glucose values. The AGP system (FreeStyle Libre flash glucose monitoring system, Abbott Diabetes Care, Alameda, CA) includes a sensor (which can be used for 2 weeks after application) and a reader which when flashed against the sensor provides a record of glucose values every 15 minutes. Data from the reader is downloaded to a computer; the inbuilt software summarizes the data and provides visual and numerical display of glucose patterns. The percentage of glucose values in the target range, patterns of hypoglycemia, the shape of the median curve, and the width of the Interquartile range (IQR), can all be obtained at a glance.

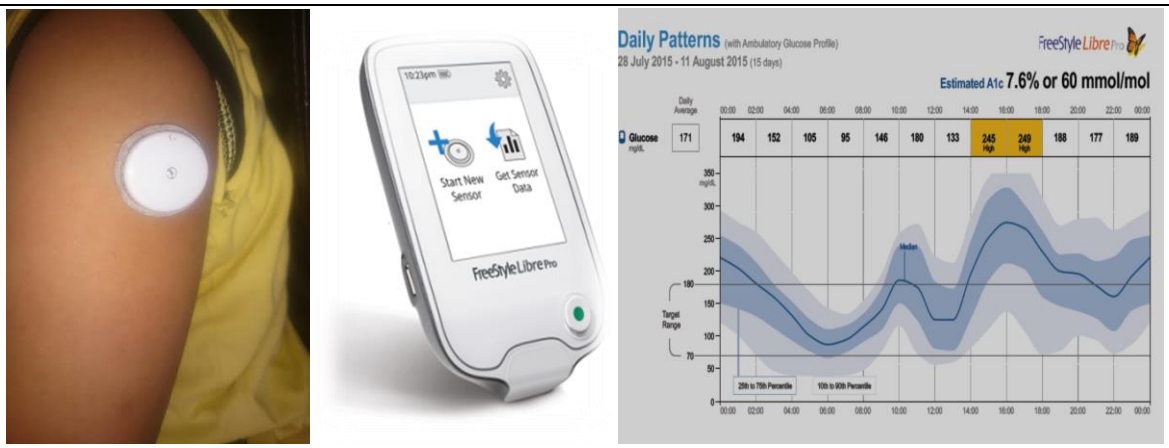

Figure1. Flash Pro Libre sensor, reader and glycemic profile of a patient

Accuracy of AGP has been studied in adults. However, the feasibility, acceptability, and accuracy of AGP in children are yet to be analysed. We looked at feasibility and acceptability of AGP in 46 children (22 girls and 24 boys) with diabetes with a mean age of 10.07 (range 1

to 18) years.[2] In 30 (65.21%) subjects the sensor remained in situ for complete duration of 14 days. Average duration of sensor wear for the cohort was 9.3 days. It was well accepted by most of the children. Only 5 children in the cohort complained of mild discomfort and pain.

We looked at the accuracy of AGP in 51 children (including the children in the feasibility study mentioned above).[3] Paired venous blood glucose (RBG), capillary blood glucose (CBG) and AGP data were analysed for these subjects. Seventy paired RBG, CBG and AGP data and 362 paired home monitored SMBG and AGP data were available. The linear regression coefficient of AGP over RBG was 0.93 and that of AGP over CBG was 0.89 (p<0.001). Average MARD of AGP over RBG was 9.6% and that of AGP over CBG was 15.07%. Dr Santhosh Olety has reported (in this newsletter) a MARD (AGP vs. RBS) of 14.2% in a small study involving 9 patients (57 paired samples). We also looked at the difference between AGP and home monitored SMBG values across different SMBG ranges. When SMBG was less than 75 mg/dl, only 65% of the AGP readings were within 20% of SMBG readings; whereas when SMBG was more than 200 mg/dl, more than 77% of the AGP readings were within 20% of SMBG readings (71% of the data were within 20% of SMBG when AGP readings were 75-200 mg/dl).[3] Our data is in favour of using AGP in children. However, since our study involved a small number, larger studies are needed to confirm the reproducibility of these findings.

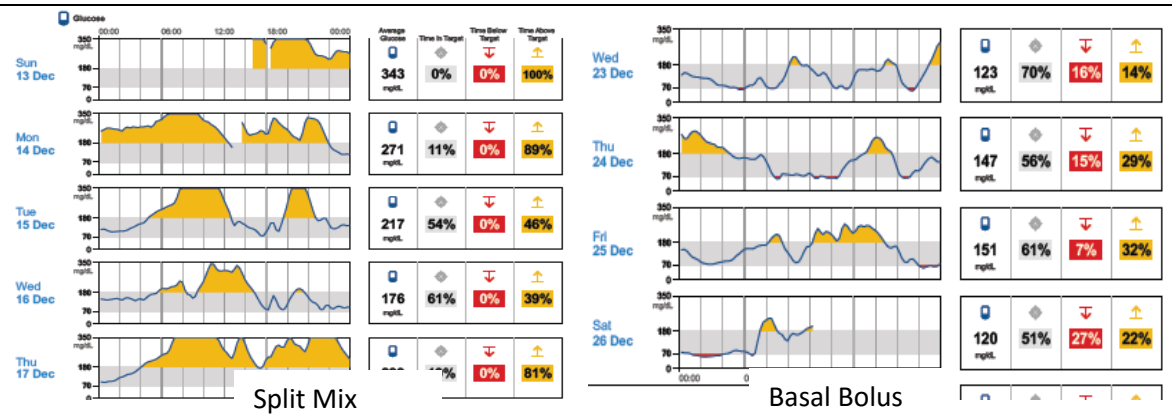

Figure 2 Glycemic variability in a patient while on split mix and basal bolus regimen

Scope for using AGP in children

- AGP shows glycemic variability over a period of 14 days which is a long enough time interval to reveal the glycemic profile of a patient. Glycemic variability in relation to food, exercise and insulin dosing can be identified. Glycemic variability in a patient when changed from split mix regimen to basal bolus regimen is illustrated in figure 2.
- It can be used to titrate insulin doses when a new patient is started on insulin or when a patient is started on continuous subcutaneous insulin infusion (CSII).
- AGP is useful in identifing nocturnal hypoglycemia, which may not be identified by SMBG.
- AGP helps in minimising pricks to the child during the sensor wear period.

- A Flash Pro Libre sensor would cost Rs. 2000 and the reader Rs. 5000. Therefore, it may not be economical to be used regularly for all patients. However, it could be used intermittently in children with diabetes to optimise glycemic control.
- In children with poorly controlled glycemic status, AGP can be used to detect persistent factors contributing to hyperglycemia. Visual display of their glycemic profile will be useful in convincing some of these patients to comply with stricter diabetes management.

Limitations of using AGP

- Flash Pro Libre AGP monitoring system does not record glucose levels below 40 mg/dl and above 500 mg/dl. Therefore, when glucose readings are very high or very low or if the patient is symptomatic, a glucometer should be used to confirm the glycemic status of the patient.
- In our study, only a few children reported mild discomfort, foreign body sensation and pain. However, with regular use, chances of skin reaction to the adhesive and infections cannot be ruled out.
- The manufacturers recommend applying the sensor over the upper arm. Efficacy and durability of the sensor when used elsewhere is yet to be established.
- Accuracy of AGP has been reported in the literature in some studies, but large data to support these findings are awaited.[4]

Potentially, AGP could be a very useful tool for optimising management of diabetes in children. However, much more data is needed addressing the feasibility and accuracy of AGP in children, before it becomes an integral part of 'an optimal diabetes management plan' in children.

References

1. Nalysnyk L, Hernandez-Medina M, Krishnarajah G. Glycaemic variability and complications in patients with diabetes mellitus: evidence from a systematic review of the literature. Diabetes Obes Metab 2010; 12:288–298.
2. Rai S, Hulse A, Prasanna Kumar KM. Feasibility and Acceptability of Ambulatory Glucose Profile in Children with Type1 Diabetes Mellitus: A Pilot Study. Indian J Endocr Metab, Accepted for September-October 2016 issue.
3. Hulse A, Rai S, Prasanna Kumar KM. Evaluation of Accuracy of Ambulatory Glucose Profile in an Outpatient Setting in Children with Type 1 Diabetes. Indian J Endocr Metab, Accepted for September-October 2016 issue.
4. Bailey T, Bode BW, Christiansen MP, Klaff LJ, Alva S. The performance and usability of a factory-calibrated flash glucose monitoring system. Diabetes Technol Ther 2015;17:787-94.

Summary of Global Consensus Recommendations on Prevention and Management of Nutritional Rickets

Horm Res Paediatr 2016;85:83-106

	Defining Nutritional Rickets and the Interplay between Vitamin D Status and Calcium Intake
1.1	**Definition and Diagnosis of Nutritional Rickets** • Nutritional rickets (NR), a disorder of defective chondrocyte differentiation and mineralization of the growth plate and defective osteoid mineralization, is caused by vitamin D deficiency and/or low calcium intake in children. (1⊕⊕⊕) • The diagnosis of NR is made on the basis of history, physical examination, and biochemical testing, and is confirmed by radiographs. (1⊕⊕⊕)
1.2	**Vitamin D Status** • The panel recommends the following classification of vitamin D status, based on serum 25-hydroxyvitamin D (25OHD) levels: (1⊕⊕⊕) - Sufficiency, >50 nmol/l, - Insufficiency, 30-50 nmol/l, - Deficiency, <30 nmol/l
1.3	**Vitamin D Toxicity** • Toxicity is defined as hypercalcemia and serum 25OHD >250 nmol/l, with hypercalciuria and suppressed parathyroid hormone (PTH). (1⊕⊕⊕)
1.4	**Dietary Calcium Intake to Prevent Rickets** • For infants 0-6 and 6-12 months of age, adequate calcium intake is 200 and 260 mg/day, respectively. (1⊕⊕⊕) • For children over 12 months of age, dietary calcium intake of <300 mg/day increases the risk of rickets, independently of serum 25OHD levels. (1⊕⊕○) • For children over 12 months of age, the panel recommends the following classification of dietary calcium intake: (1⊕⊕○) - Sufficiency, >500 mg/day, - Insufficiency, 300-500 mg/day, - Deficiency, <300 mg/day
1.5	**Vitamin D Deficiency and Fractures** • Children with radiographically confirmed rickets have an increased risk of fracture. (1⊕⊕○) • Children with simple vitamin D deficiency are not at increased risk of fracture. (1⊕⊕○)

2	**Prevention and Treatment of Nutritional Rickets and Osteomalacia**
2.1	**Vitamin D Supplementation for the Prevention of Rickets and Osteomalacia** • 400 IU/day is adequate to prevent rickets and is recommended for all infants from birth to 12 months of age, independent of their mode of feeding. (1⊕⊕⊕) • Beyond 12 months of age, all children and adults need to meet their nutritional requirement for vitamin D through diet and/or supplementation, which is at least 600 IU/day (15 µg), as recommended by the Institute of Medicine (IOM). (1⊕⊕⊕)
2.2	**Target for Vitamin D Supplementation** • In healthy children, routine 25OHD screening is not recommended, and consequently, no specific 25OHD threshold for vitamin D supplementation is targeted in this population. (1⊕⊕⊕)
2.3	**Candidates for Preventative Vitamin D Supplementation beyond 12 Months of Age** In the absence of food fortification, vitamin D supplementation should be given to: • Children with a history of symptomatic vitamin D deficiency requiring treatment (1⊕⊕⊕) • Children and adults at high risk of vitamin D deficiency, with factors or conditions that reduce synthesis or intake of vitamin D (1⊕⊕⊕) • Pregnant women
2.4	**Dose of Vitamin D and Calcium for the Treatment of Nutritional Rickets** • For the treatment of NR, the minimal recommended dose of vitamin D is 2,000 IU/day (50 µg) for a minimum of 3 months. (1⊕⊕⊕) • Oral calcium, 500 mg/day, either as dietary intake or supplement, should be routinely used in conjunction with vitamin D in the treatment regardless of age or weight. (1⊕⊕⊕)
2.5	**Appropriate Route of Administration and Duration of Therapy** • We recommend oral treatment, which more rapidly restores 25OHD levels than intramuscular treatment. (1⊕⊕⊕) • For daily treatment, both D_2 and D_3 are equally effective. (1⊕⊕⊕) • When single large doses are used, D_3 appears to be preferable compared to D_2 because the former has a longer half-life. (1⊕⊕⊕) • Vitamin D treatment is recommended for a minimum of 12 weeks, recognizing that some children may require a longer treatment duration. (1⊕⊕⊕)

3.0	**Prevention of Nutritional Rickets/Osteomalacia: Identification of Risk Factors**
3.1	**Dietary Practices and Nutrient Intakes among Mothers Associated with Nutritional Rickets in Infants** • Maternal vitamin D deficiency should be avoided by ensuring that women of childbearing age meet intakes of 600 IU/day recommended by the IOM. (1⊕⊕⊕) • Pregnant women should receive 600 IU/day of vitamin D, preferably as a combined preparation with other recommended micronutrients such as iron and folic acid. (2⊕⊕○)
3.2	**Early Feeding, Supplementation, Complementary Feeding, and Nutrient Intake Associated with Rickets in Infants** • In addition to an intake of 400 IU/day of vitamin D, complementary foods introduced no later than 26 weeks should include sources rich in calcium. (1⊕⊕⊕) • An intake of at least 500 mg/day of elemental calcium must be ensured during childhood and adolescence. (1⊕⊕⊕)
3.3	**Association of Sunlight Exposure with Nutritional Rickets** • Because ultraviolet B (UVB) rays trigger epidermal synthesis of previtamin D_3, restricted exposure to sun increases the risk of vitamin D deficiency and NR. (1⊕⊕⊕) • Environmental factors, such as latitude, season, time of day, cloud cover, and pollution, affect the availability of UVB, whereas personal factors, such as time spent outdoors, skin pigmentation, skin coverage, age, body composition, and genetics, affect the dose response of UVB exposure and circulating 25OHD. (2⊕⊕○) • No safe threshold of UV exposure allows for sufficient vitamin D synthesis across the population without increasing skin cancer risk. (2⊕⊕○)
4	**Prevention of Osteomalacia during Pregnancy and Lactation and Congenital Rickets**
4.1	**The Relationship between Vitamin D during Pregnancy and Infant Growth and Bone Mass** • Pregnant women should receive 600 IU/day of supplemental vitamin D. This will ensure adequacy of maternal 25OHD, especially in women at risk of deficiency, to prevent elevated cord blood alkaline phosphatase (ALP), increased fontanelle size, neonatal hypocalcemia and congenital rickets, and to improve dental enamel formation. (2⊕⊕○) • There is little evidence that maternal supplementation with vitamin D will protect or improve birth anthropometry (2⊕○○) and no evidence that supplementation with

	vitamin D will protect or improve growth or bone mass accretion. (2⊕⊕○)
4.2	**The Effect of Calcium Supplementation during Pregnancy on Infant Bone Mass** • Pregnant women do not need calcium intakes above recommended non-pregnant intakes to improve neonatal bone. (1⊕⊕⊕)
4.3	**Influence of Calcium or Vitamin D Supplementation in Pregnancy or Lactation on Breast Milk Calcium or Vitamin D** • Lactating women should ensure they meet the dietary recommendations for vitamin D (600 IU/day) for their own needs, but not for the needs of their infant. (1⊕⊕⊕) • Lactating women should not take high amounts of vitamin D as a means of supplementing their infant. (2⊕⊕○) • Pregnant and lactating women should meet the recommended intakes of calcium. Maternal calcium intake during pregnancy or lactation is not associated with breast milk calcium concentrations. (1⊕⊕⊕)
4.4	**Causes and Therapy of Congenital Rickets** • Supplementing mothers with 600 IU/day of vitamin D and ensuring they receive recommended calcium intakes, or appropriate therapy of maternal conditions predisposing to hypocalcemia or vitamin D deficiency, prevent congenital rickets. (2⊕○○)
5	**Assessing the Burden of Nutritional Rickets and Public Health Strategies for Prevention**
5.1	**Assessment of Disease Burden** • The prevalence of rickets should be determined by population-based samples, by case reports from sentinel centers, or by mandatory reporting. (1⊕⊕⊕) • Screening for NR should be based on clinical features, followed by radiographic confirmation of suspected cases. (1⊕⊕⊕) • Population-based screening with serum 25OHD, serum ALP, or radiographs is not indicated. (1⊕⊕⊕)
5.2	**Public Health Strategies for Rickets Prevention** • Universally supplement all infants with vitamin D from birth to 12 months of age, independently of their mode of feeding. Beyond 12 months, supplement all groups at risk and pregnant women. Vitamin D supplements should be incorporated into childhood primary health care programs along with other essential micronutrients and immunizations (1⊕⊕⊕), and into antenatal care programs along with other

	recommended micronutrients. (2⊕⊕○) • Recognize NR, osteomalacia, and vitamin D and calcium deficiencies as preventable global public health problems in infants, children, and adolescents. (1⊕⊕⊕) • Implement rickets prevention programs in populations with a high prevalence of vitamin D deficiency and limited vitamin D and/or calcium intakes, and in groups of infants and children at risk of rickets. (1⊕⊕⊕) • Monitor adherence to recommended vitamin D and calcium intakes and implement surveillance for NR. (1⊕⊕⊕) • Fortify staple foods with vitamin D and calcium, as appropriate, based on dietary patterns. Food fortification can prevent rickets and improve vitamin D status of infants, children, and adolescents if appropriate foods are used and sufficient fortification is provided, if fortification is supported by relevant legislation, and if the process is adequately monitored. Indigenous food sources of calcium should be promoted or subsidized in children. (1⊕⊕⊕) • Promote addressing the public health impact of vitamin D deficiency as both a clinical and a public health issue. (1⊕⊕⊕)
5.3	**Economic Cost/Benefits of Prevention Programs** • The cost-effectiveness of supplementation and food fortification programs needs further study. (1⊕⊕○)

Summary of Recommendations from The Diagnosis of Polycystic Ovary Syndrome during Adolescence Group.

Horm Res Paediatr 2015:83:376–389

1	**What Are the Criteria for Clinical Evidence of Clinical Hyperandrogenism in the Adolescent Girl?** (1) Isolated mild hirsutism should not be considered clinical evidence of hyperandrogenism in the early post-menarcheal years when it may be in a developmental phase (Level C). (2) Moderate to severe hirsutism constitutes clinical evidence of hyperandrogenism (Level B). (3) Girls with acne that is persistent and poorly responsive to topical dermatologic therapy should be evaluated for the presence of hyperandrogenemia before initiation of any medical therapies (Level C).

2	**What Are the Criteria for Evidence of Biochemical Hyperandrogenism in the Adolescent Girl?** (1)Hyperandrogenemia needs to be defined, based on the detailed characteristics of the testosterone assay used (Level A). (2) Biochemical evidence of hyperandrogenism, as indicated by persistent elevation of serum total and/or free testosterone levels and determined in a reliable reference laboratory, provides the clearest support for the presence of hyperandrogenism in an adolescent girl with symptoms of PCOS (Level B). (3) A single androgen level >2 SD above the mean for the specific assay should not be considered to be evidence of hyperandrogenism in an otherwise asymptomatic adolescent girl (Level C).
3	**What Are the Criteria for Evidence of Oligo-Anovulation in Adolescents?** (1) The majority of adolescents establish a menstrual interval of 20–45 days within the first 2 years after menarche. Menstrual intervals persistently shorter than 20 days or greater than 45 days in individuals 2 or more years after menarche are evidence of oligo-anovulation (Level B). (2) A menstrual interval greater than 90 days is unusual even in the first year after menarche. As such, consecutive menstrual intervals greater than 90 days are rare and require further investigation regardless of years after menarche (Level B). (3) Lack of onset of menses by age 15 years or by more than 2–3 years after thelarche, regardless of chronologic age, is statistically uncommon and warrants evaluation and consideration of diagnoses such as PCOS (Level B).
4	**What Are the Criteria for PCO Morphology in an Adolescent Girl?** (1) No compelling criteria to define PCOM have been established for adolescents. Until further research establishes definitive criteria, an ovarian volume >12.0 cm^3 (by formula for a prolate ellipsoid) can be considered enlarged. Follicle counts should not be utilized to define PCOM in adolescents (Level B). (2) Further, a multifollicular pattern, which is defined by the presence of large follicles distributed throughout the ovary, does not have a relationship with hyperandrogenism, is more common in adolescents, and should not be considered a pathological finding (Level C).

	(3) Additionally, in healthy girls with regular menstrual cycles and without hyperandrogenism, PCOM does not indicate a diagnosis of PCOS (Level B). (4) Abdominal ultrasound in adolescents, particularly obese girls, may yield inadequate information (Level C). (5) AMH concentrations should not be used to characterize PCOM (Level B). (6) Until better quality-consistent data are available, ovarian imaging can be deferred during the diagnostic evaluation for PCOS (Level C).
5	**What Diagnostic Procedures Are Appropriate in Adolescents to Exclude Other Causes of Hyperandrogenism and Amenorrhea?** (1) A thorough medical history, physical examination, and appropriate laboratory assessment are essential to provide the information necessary to exclude other disorders associated with androgen excess (Level A).
6	**What Is the Role of Insulin Resistance/Hyperinsulinemia in the Diagnosis of PCOS in Adolescents?** (1) Although prevalent among adolescents at risk for PCOS, insulin resistance and hyperinsulinemia should not be utilized as diagnostic criteria (Level B). (2) Insulin resistance and hyperinsulinemia can be considered as indications to investigate and treat potential comorbidities (Level B).
7	**Does a Diagnosis of PCOS during Adolescence Provide an Opportunity for Meaningful Intervention? What Are the Risks of Overdiagnosis?** (1) A timely diagnosis of PCOS in symptomatic adolescent girls is important for the initiation of appropriate screening and treatment (Level A). (2) Validated diagnostic criteria supported by robust clinical and hormonal findings are needed to avoid overdiagnosis and unnecessary treatment in otherwise healthy normal girls without hyperandrogenism (Level C). (3) Research evaluating long-term interventions using high-quality RCTs and lifelong follow-up of girls with PCOS diagnosed during adolescence would be ideal (Level C).

IL2RA mutation causing Neonatal Diabetes and Hypothyroidism

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Case Report

A 16-day-old female was admitted in our NICU with rapid breathing, dehydration, excessive crying, fever and refusal of feeds. She is the first child of her parents, born of 3rd degree consanguineous marriage. She was born at term by caesarean section with a birth weight of 3.1 kg. She was on exclusive breast feeding and was well till the 15th day of life. Parents noted refusal of feeds on the 16th day of life, associated with excessive crying, fever and rapid breathing.

On examination, the neonate was dehydrated, irritable and tachypneic. The heart rate was 120/min, respiratory rate 92/min, and oxygen saturation low at 80%. She had decreased urine output; weight had decreased to 2720 g. She was started on intravenous (IV) fluids and oxygen. Oxygen saturation normalised and she was taken off oxygen by the next day, but she continued to be tachypnoeic. Arterial blood gas analysis showed severe metabolic acidosis with a pH of 6.8. Her serum sodium was 144 mEq/L, potassium 5.5 mEq/L, serum creatinine 1.7 mg/dl and blood urea 46 mg/dl. Complete blood picture showed a hemoglobin of 16 g/dl and elevated leucocyte count. Sepsis screen was negative. Blood glucose (BG) repeated multiple times was more than 400 mg/dl, glycated haemoglobin was 10%, T4 was 0.3 µg/dl and TSH more than 150 µU/ml. A provisional diagnosis of diabetic ketoacidosis was made and the neonate was started on insulin infusion. Oral levothyroxine (25 µg) was also started. Three days after initiation of insulin infusion, ketosis resolved. She was started on SC Insulin aspart in 30:70 ratio of rapid acting and intermediate acting components, 2 units in morning and 1 unit at night pre-feed and BG monitored for 48 hours. She was discharged on request. At home, the baby developed hypoglycaemia and insulin dose was lowered to ½ unit twice a day but she continued to have episodes of hypoglycaemia, which persisted despite changing to glargine 1 unit at bedtime and then to 0.5 unit. Hence, insulin was stopped but BG increased to 400 mg/dl. She was restarted on 0.5 units glargine but blood glucose decreased to 24 mg/dl. She was then started on glargine in 1:10 dilution, 0.1 unit at bedtime and dose gradually titrated to 0.2 units in morning and 0.1 unit at night. Repeat TSH after 15 days was still > 150 µU/ml with T4 of 8.4 µg/dl and parents confirmed compliance. The dose was increased to 50 µg/day. Ultrasound neck showed normal position, size and echotexture of the thyroid gland.

She was provisionally diagnosed as having neonatal diabetes, with a possible GLIS3[1] mutation, but Sanger sequencing was negative for GLIS3. On Day 52 of life, she was re-hospitalised with fever and loose stools for 5 days prior to admission. She had oral thrush, abdominal distension, bilateral lung crepitations, mental dullness, shock and sclerema. Investigations revealed hypoalbuminemia, elevated serum creatinine (1.5 mg/dl), elevated CRP (10 mg/L), severe metabolic acidosis (blood pH 6.8), left upper zone consolidation, sterile blood culture and **HbA1C of 6.4%**. She was treated with IV insulin, antibiotics, antifungals, albumin, fresh frozen plasma, dopamine and adrenaline infusion, nasal CPAP

and later mechanical ventilation. She was continued on thyroxine supplementation since TSH was 6.8 µU/ml. Her BG levels kept fluctuating. She gradually deteriorated, developed refractory hypoxemia, shock, and expired. Meanwhile targeted next generation sequencing for neonatal diabetes was ongoing, which identified a ***homozygous deletion of exons 2-8 of InterLeukin 2 Receptor Alpha (IL2RA) gene.*** Both parents are heterozygous for the same mutation. The risk of transmission of the disease to a next child is 1 in 4.

Discussion

The IL2RA gene encodes the alpha subunit of the cell surface receptor for the T-cell growth factor interleukin-2 (IL2). The IL2 receptor is a heterotrimer of IL2RA, IL2RB, and IL2RG, and plays a vital role in maintaining the immune system. IL2RA is constitutively expressed on regulatory T cells (Tregs) and is involved in both tolerance regulation and T-cell expansion. IL2RA mutations cause the disorder, immunodeficiency 41 with lympho-proliferation and autoimmunity (IMD 41). It is also called CD25 deficiency. It is an autosomal recessive complex disorder of immune dysregulation. Affected individuals present in infancy with recurrent viral, fungal, and bacterial infections, lymphadenopathy, and variable autoimmune features, such as autoimmune enteropathy and eczematous skin lesions. Immunologic studies show a defect in T-cell regulation.

IL2RA mutations have been strongly associated with Type 1 diabetes T1DM). In a study by Lowe et al.[2] IL2RA T1DM susceptibility genotypes were associated with lower circulating levels of soluble IL2RA, suggesting that an inherited lower immune responsiveness predisposes to T1DM. Another study by Vella et al.[3] recognized that the association might not be with CD25 itself, but rather with a causal variant in linkage disequilibrium with CD25. Only one other case with neonatal diabetes has been reported worldwide by Caudy et al.[4] An 8-year-old boy presented at age 6 weeks with diarrhea, **insulin-dependent diabetes mellitus**, and respiratory insufficiency due to CMV infection. During childhood, he developed autoimmune enteropathy with villous atrophy, eczema, lymphadenopathy, hepatosplenomegaly, **hypothyroidism**, autoimmune hemolytic anemia, and autoimmune granulocytopenia. Recurrent infections, including Epstein-Barr virus (EBV) infection were present. The clinical features were reminiscent of IPEX but FOXP3 expression was normal on patient CD4+ T lymphocytes. Compound heterozygous truncating mutations were identified in the IL2RA gene. Each unaffected parent was heterozygous for one of the mutations. A defective IL-10 expression from CD4 lymphocytes was postulated secondary to IL2 receptor mutation. He needed rescue with IL-15 and high concentrations of IL-2.

The present case is only the ***second reported case of IL2RA mutation with neonatal diabetes and hypothyroidism.*** Survival is difficult in view of recurrent severe infections and extremely limited availability of IL-15 and IL-2.

Would like to acknowledge and thank Profs Andrew Hattesrley & Sian Ellard and Drs Sarah Flanagan, Elisa De Franco and Jayne Houghton of University of Exeter - Medical School for their help with genetic studies and management

References

1. Barone JV., Tillman EM., Ferry RJ., Jr: Treatment of transient neonatal diabetes mellitus with subcutaneous insulin glargine in an extremely low birth weight neonate. J Pediatr Pharmacol Ther 2011;16:291–297

2. P Dimitri et al. Novel GLIS3 mutations demonstrate an extended multisystem phenotype. European Journal of Endocrinology (2011) 164 437–443.
3. Lowe CE, Cooper JD, Brusko T, Walker NM, Smyth DJ, Bailey R, Bourget K, Plagnol V, Field S, Atkinson M, Clayton DG, Wicker LS, Todd JA. Large-scale genetic fine mapping and genotype-phenotype associations implicate polymorphism in the IL2RA region in type 1 diabetes. Nature Genet. 39: 1074-1082, 2007.
4. Vella A, Cooper JD, Lowe CE, Walker N, Nutland S, Widmer B, Jones R, Ring SM, McArdle W, Pembrey ME, Strachan DP, Dunger DB, Twells RCJ, Clayton DG, Todd JA. Localization of a type 1 diabetes locus in the IL2RA/CD25 region by use of tag single-nucleotide polymorphisms. Am J Hum Genet. 76: 773-779, 2005.
5. Caudy AA, Reddy ST, Chatila T, Atkinson JP, Verbsky JW. CD25 deficiency causes an immune dysregulation, polyendocrinopathy, enteropathy, X-linked-like syndrome, and defective IL-10 expression from CD4 lymphocytes. J Allergy Clin Immun. 119: 482-487, 2007.

A midline neck swelling in a 16 year old girl - Case of thyroid ectopia!

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Case Summary:

A 16 y old girl presented to the hospital with a progressively enlarging neck swelling. The parents had noted this swelling when she was about 5 years of age and the swelling had gradually increased over the last 2-3 years to the current size (Figure 1). The patient did not complain of any symptoms of compression or any pain over the swelling. On examination there was a 4 X 4 cm soft globular midline neck swelling at the level of the thyroid cartilage. The swelling moved with deglutition but did not move with protrusion of tongue. Oral cavity examination was normal and there were no palpable lymph nodes. Ultrasound showed a 3.8 x 3.6 x 2.3 cm spongiform (honeycomb pattern) lesion just above the level of the thyroid cartilage (Figure 2). The lesion was not vascular and lacked features of a true cyst. Normal thyroid tissue was not visualized in the usual location. Thyroid functions revealed primary hypothyroidism with a TSH of 16 µU/mL and T4 of 4.5 µg/dl. The patient had normal growth and milestones and attained menarche at age 13 years. She had attained her mid-parental height, indicating that the hypothyroidism noted on the present investigations was likely to be of recent onset. A review of tests done at 5 years of age (when the parents first noted the neck swelling) indicated euthyroid status with TSH of 1.6 µU/mL and T4 of 12 µg/dl. A ^{131}I nuclear scan done at age 5 years showed tracer concentration at a level higher than normal anatomical location of thyroid gland (Figure 3). Given the development of frank hypothyroidism and the increasing size of the ectopic thyroid gland, patient underwent removal of the ectopic thyroid tissue. A part of the thyroid tissue attached to the hyoid bone was also shaved off sparing the hyoid bone. Histopathology (Figure 4) showed normal thyroid follicular cells with abundant colloid and no evidence of malignancy.

Discussion:

Thyroid ectopia is defined as functioning thyroid tissue found anywhere other than the usual anatomic location of thyroid gland. An ectopic thyroid is usually located along the normal path of thyroid gland descent, but rarely can also be found in the mediastinum, heart, esophagus, or diaphragm [1]. Ectopic thyroid tissue is derived from abnormalities in migration of the medial anlage, hence typically it does not contain C cells. Failure of thyroid gland descent occurs in approximately 1 in 200,000 normal subjects and 1 in 6000 patients with thyroid disease [2]. The true incidence of thyroid ectopia is not known due to the asymptomatic nature of some ectopic thyroid tissue. The most common site of ectopic thyroid is a lingual thyroid. The wall of a thyroglossal duct cyst (TGDC) is the second most common site for ectopic thyroid tissue [3]. The entire thyroid gland can fail to descend to its normal adult orthotopic site. If the descent is completely arrested at the level of the base of tongue, a lingual thyroid will result. Partial descent can result in an ectopic gland in a sublingual or prelaryngeal position as in the case described above. Excessive migration can result in a substernal ectopic gland [2,4,5].

Some ectopic thyroids function normally, but approximately one-third of patients present with hypothyroidism. If hypothyroidism develops, the mass may enlarge as a result of stimulation by thyrotropin (TSH). Ectopic thyroid tissue may enlarge during puberty or pregnancy. The detection of hypothyroidism in a patient with a midline neck mass increases the suspicion of ectopic thyroid [6]. Treatment with thyroid hormone supplementation is usually sufficient for suppression, but surgical excision may become necessary. Surgical removal of thyroid ectopia can result in severe hypothyroidism if the ectopic thyroid is the only source of thyroid hormone, and necessitates lifelong replacement with thyroxine. Nuclear scan with either Tc^{99} or I^{131} is mandatory before surgery to confirm the location of the ectopic thyroid, and look for any functioning thyroid tissue in the eutopic location.

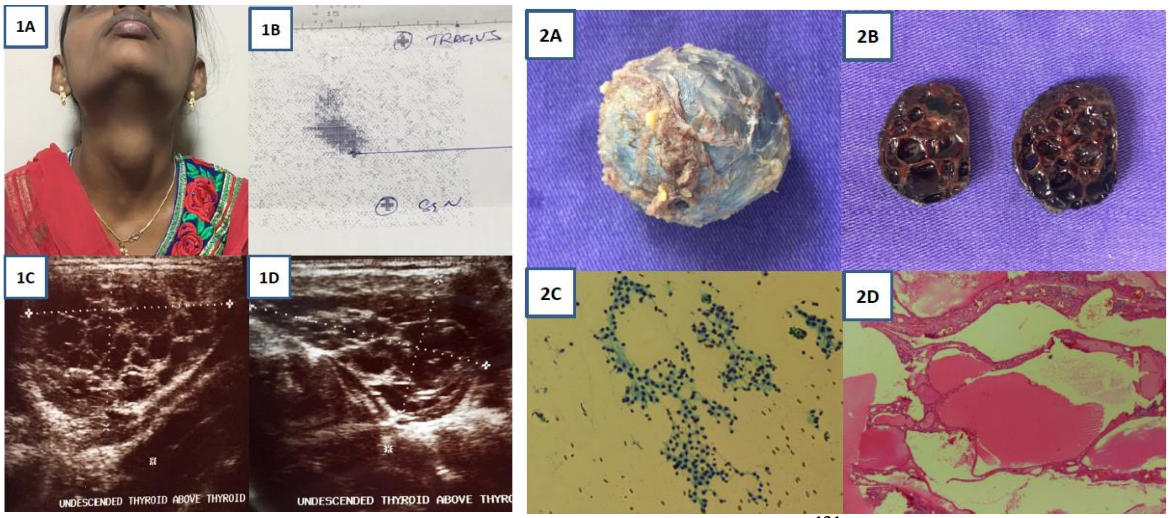


Figure 1: 1A: Clinical photograph of the mid-line neck swelling, 1B: I^{131} images done at 5 years of age (a) A-P view (b) Lateral view: Thyroid scan using I^{131} shows thyroid gland to be situated in the midline higher than the normal anatomical position of the thyroid gland; the gland appears as an oval area of radio-tracer concentration. The lateral view reveals the ectopic thyroid gland situated superior and posterior compared to the normal thyroid anatomical position. 1C and 1D: Ultrasound appearance (a) Sagittal (b) Transverse view of thyroid ectopia showing a well-defined spongiform lesion.

Figure 2: Gross pathology & histopathology: 2A: A well circumscribed tan-grey nodule measuring 4.5 cm in the greatest dimension was submitted for histopathological examination 2B: Cut surface shows a dark red multi-cystic nodule filled with brown fluid. 2C: 20X magnification image of FNAC of ectopic thyroid: Smear shows mono-layered sheets of benign appearing thyroid follicular cells and pigment laden macrophages in the background. 2D: 4X magnification of the ectopic gland: Sections show benign thyroid tissue. It is composed of varying sized thyroid follicles lined by benign follicular epithelium and containing abundant colloid.

References:

1. Pediatric Otolaryngology, 4, Saunders, Philadelphia 2002. p.1738.
2. Di Benedetto V. Ectopic thyroid gland in the submandibular region simulating a thyroglossal duct cyst: a case report. J Pediatr Surg 1997; 32:1745.
3. Lilley JS, Lomenick JP. Delayed diagnosis of hypothyroidism following excision of a thyroglossal duct cyst. J Pediatr 2013; 162:427.
4. Leung AK. Ectopic thyroid gland and thyroxine-binding globulin excess. Acta Paediatr Scand 1986; 75:872.
5. Leung AK, Wong AL, Robson WL. Ectopic thyroid gland simulating a thyroglossal duct cyst: a case report. Can J Surg 1995; 38:87
6. Radkowski D, Arnold J, Healy GB, et al. Thyroglossal duct remnants. Preoperative evaluation and management. Arch Otolaryngol Head Neck Surg 1991; 117:1378.

A report on Yog Dhyan Foundation

YDF, registered since 1985, works in Delhi/ NCR to provide support to children, adolescents and young adults with type 1 diabetes. Meetings are held on Sundays either at Saat Manzila Mandir, Tilak Nagar, near Tilak Nagar Metro Station gate no 2 (1st and 2nd Sundays), or Sant Nirankari Bhawan, Sector-19 B, Dwarka, near Nirankari Chowk and Sector 10 Metro Station, Dwarka (3rd Sunday). In a friendly environment, children and their parents share their problems and solutions. YDF provides ** free Yoga and Meditation classes, specially designed to maintain good health and normal sugars; ** free Diabetes Education, to understand how to manage fluctuations of sugar levels and complications, ** free Glucometer and 50 strips per month as well as financial assistance to families from low socio-economic status, so their children can manage diabetes well; ** picnics or trips from time to time, giving the children and their parents fun and liberty; ** free counselling and stress management classes. Please contact: Mr Anil Kumar Vedwal, Chief Functionary, Yog Dhyan Foundation, akvedwal@gmail.com, 919899548446.

A Report on ISPAE observership by Dr Deepty Kumar, Assistant Professor, Department of Pediatrics, Christian Medical College, Ludhiana, Punjab

I have undergone ISPAE observership program at SGPGI Lucknow, under the mentorship of Prof Vijayalakshmi Bhatia and Dr Preeti Dabadhgaho. After completing the course successfully, I am back at CMC, Ludhiana and have started a Pediatric Endocrine clinic here. I have special interest in endocrine work up of thalassemia children and have established a standard protocol to ensure regular endocrine evaluation of 60 patients with thalassemia who are registered at our center and are receiving regular blood transfusion and chelation therapy.

Pedendoscan

Dr Sachin Mittal, Consultant Endocrinologist, Fortis Hospital, Chandigarh

Diabetes Mellitus

Hemoglobin A1c (HbA1c) changes over time among adolescent and young adult participants in the T1D exchange clinic registry. Clements MA et al. Pediatr Diabetes. 2016;17:327-36

HbA1c lab results were collected from medical records at 67 T1D clinics. The pre-adolescent-to-adolescent cohort consisting of 85016 HbA1c measurements from 6574 participants, collected when the participants were 8-18y old; and the adolescent-to-young adult cohort, 2200 participants who were 16-26y old at the time of 17279 HbA1c measurements. HbA1c in the 8-18y cohort increased over time after age 10y until ages 16-17y; followed by a plateau. HbA1c levels in the 16-26y cohort remained steady from 16-18y, and then gradually declined. For the 8-18y cohort, insulin pump use, age of onset, and health insurance were significant in predicting individual HbA1c trajectory. The authors concluded that the glycemic control among patients 8-18y old worsens over time, through age 16y. Elevated HbA1c levels observed in 18y begin a steady improvement into early adulthood. Focused interventions to prevent deterioration in glucose control in pre-adolescence, adolescence, and early adulthood are needed.

Characteristics of maturity onset diabetes of the young in a large diabetes center. Chambers C et al. Pediatr Diabetes. 2016;17:360-7

To estimate the frequency and clinical characteristics of Maturity Onset Diabetes of the Young (MODY), a total of 97 subjects with diabetes onset before age 25y, a random C-peptide ≥ 0.1 ng/mL, and negative for all diabetes autoantibodies, were enrolled, and genetic testing for MODY 1-5 was done. A total of 22 subjects were found to have a mutation in hepatocyte nuclear factor 4A (n = 4), glucokinase (n = 8), or hepatocyte nuclear factor 1A (n = 10). Of these 22 subjects, 13 had mutations known to be pathogenic and 9 (41%) had novel mutations, predicted to be pathogenic. Only 1 of the 22 subjects had been given the appropriate MODY diagnosis prior to testing. Compared with MODY-negative subjects, the MODY-positive subjects had lower hemoglobin A1c level and no diabetic ketoacidosis at onset; however, these characteristics are not specific for MODY. In summary, this study found a high frequency of MODY mutations with the majority of subjects clinically misdiagnosed. Clinicians should have a high index of suspicion for MODY in youth with antibody-negative diabetes.

C-peptide levels in pediatric type 2 diabetes in the Pediatric Diabetes Consortium T2D Clinic Registry. Gregg B et al. Pediatr Diabetes. 2016 Jun;17(4):274-80

C-peptide levels were assessed in 331 youth with type 2 diabetes T2D T2D (mean age, 16.1 ± 2.5 yr; median T2D duration, 2.4 yr). Median C-peptide measurement was 3.5 ng/mL for for 90 fasted and 4.2 ng/mL for 241 random non-fasted samples. C-peptide levels were significantly lower with insulin therapy, lower body mass index, HbA1c ≥9%, and T2D duration ≥ 6 yr.

Diabetes Mellitus

Presentation of youth with type 2 diabetes in the Pediatric Diabetes Consortium. Klingensmith GJ et al. Pediatr Diabetes. 2016;17:266-73.

Clinical and laboratory characteristics at the time of diagnosis of 503 youth with T2D enrolled in The Pediatric Diabetes Consortium (PDC) T2D Clinic Registry from eight pediatric diabetes centers in the USA were analyzed. 67% presented with symptoms of diabetes and confirming laboratory data, but 33% were identified by testing at risk children, 11% presented with diabetic ketoacidosis (DKA), and 2% with hyperglycemic hyperosmolar state (HHS). The mean age was 13.1 ± 2.3y (range 4.6-19.8y) with 38 (8%) less than 10y of age at diagnosis. The majority was female (65%) and had a family history of T2D (92%). The median body mass index (BMI) z-score was 2.3. Fewer than half (46%) lived with both parents, only 30% had parents with education beyond high school, and 43% lived in a low income household. The authors concluded that T2D may occur at younger ages than previously thought and should be considered in all high-risk children presenting with diabetes.

PCOS

Circulating Anti-Müllerian Hormone Levels in Daughters of Women with and without Polycystic Ovary Syndrome. Olszanecka-Glinianowicz M et al. Horm Res Paediatr. 2016;85(6):372-8

Clinical, ultrasonographic and biochemical evaluation along with plasma AMH was assessed in 75 girls aged 13-18y (35 PCOSd and 40 daughters of healthy women) to assess whether circulating anti-Müllerian hormone (AMH) levels in daughters of women with polycystic ovary syndrome (PCOSd) correspond with clinical and biochemical features of hyperandrogenism, polycystic ovary morphology and menstrual cycle disturbances. A higher AMH level in PCOSd is associated with menstrual cycle disturbances and larger ovarian volume but not with clinical and biochemical features of hyperandrogenism.

Do the Anti-Müllerian Hormone Levels of Adolescents with Polycystic Ovary Syndrome, Those Who Are at Risk for Developing Polycystic Ovary Syndrome, and Those Who Exhibit Isolated Oligomenorrhea Differ from Those of Adolescents with Normal Menstrual Cycles? Savas-Erdeve S et al. Horm Res Paediatr. 2016;85(6):406-11

Anti-Müllerian hormone (AMH) levels were compared in adolescents with polycystic ovary syndrome (PCOS, meeting 3 diagnostic criteria, n = 21), PCOS risk (meeting 2 diagnostic criteria, n = 20), isolated oligomenorrhea (OM, n = 21) and with a normal/regular menstrual cycle (NMC, n= 30). The AMH levels in the PCOS group were similar to those in the PCOS risk group but significantly higher than those in the OM and NMC groups. The specificity for PCOS and PCOS risk with a cutoff value of 7.25 ng/ml for AMH was 72.5% and the sensitivity was 58%. The authors concluded that an AMH cutoff value of 7.25ng/ml can be used for the diagnosis of PCOS in the adolescent period.

Obesity

Cardiac Autonomic Function at Baseline and under Stress and Its Relationship to Circulatory Markers of Inflammation in Obese Compared to Nonobese Children: A Pilot Study. Hursh BE et al. Horm Res Paediatr. 2016;85(5):339-46.

To gain insight into cardiac autonomic dysfunction and inflammation in childhood obesity, 15 obese children and adolescents without metabolic complications and 15 non obese controls underwent heart rate variability and impedance cardiography testing during rest, mental stress, and physical stress. Inflammatory cytokines and immune reactivity were measured. There was no statistically significant difference between groups in cardiac ANS testing at rest or in response to stress. Median high-sensitivity C-reactive protein (hsCRP) was higher in the obese group while Interleukin-6 and tumour necrosis factor-α were similar between groups. The authors pointed out that obese children and adolescents without metabolic complications did not have cardiac ANS dysfunction.

Growth

Predictors of Insulin-Like Growth Factor-I Responses to Growth Hormone Replacement in Young Adults with Growth Hormone Deficiency. Thankamony A et al. Horm Res Paediatr. 2016;85(6):379-88.

IGF-I levels and predictors of IGF-I responses in young adults on GH replacement were evaluated in 310 young adults (age 15-26y) with severe GH deficiency related to childhood-onset disease and commenced on 'adult GH replacement'. 'IGF-I responses' were estimated from first-year increments in IGF-I standard deviation scores (SDS) and adjusted for GH dose. IGF-I levels increased markedly from baseline to 1 year of replacement but remained low compared to normative data despite dose titration. In multivariate models, IGF-I responses were positively associated with age and BMI SDS and inversely associated with female gender and baseline IGF-I SDS. Low IGF-I levels in young adults on treatment may reflect suboptimal GH replacement.

Congenital Adrenal Hyperplasia

Carotid Intima-Media Thickness Is Associated with Increased Androgens in Adolescents and Young Adults with Classical Congenital Adrenal Hyperplasia. Kim MS et al. Horm Res Paediatr. 2016;85(4):242-9

Youth with congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency develop cardiovascular disease (CVD) risk factors of obesity and hypertension. Carotid intima-media thickness (CIMT), a marker of CVD risk and its relationship with androgens and obesity in adolescents/young adults with CAH was examined in 20 CAH subjects (age 16 ± 3.3 years, 50% female) and 20 matched controls in this cross-sectional study. Within the CAH group, CIMT correlated with 17-hydroxyprogesterone and androstenedione and was greater in obese subjects. CIMT is associated with increased androgens in CAH adolescents and young adults, with loss of sex differences in CAH females with excess androgen exposure thus highlighting the importance of hormonal control for CVD prevention in CAH.

Puberty

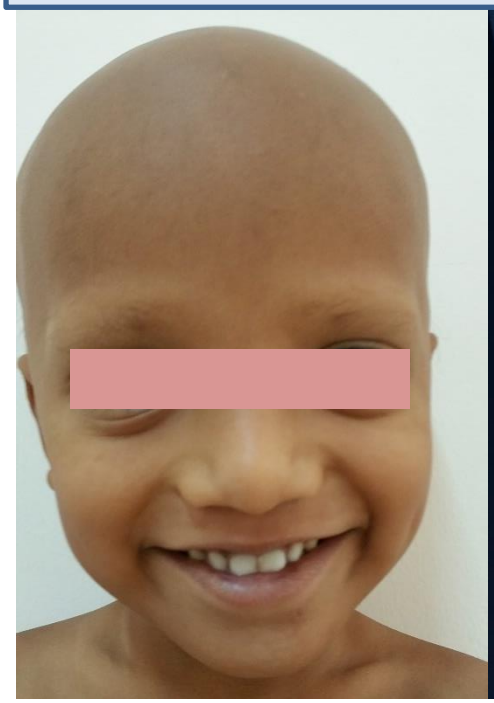
Pubertal Onset in Boys and Girls Is Influenced by Pubertal Timing of Both Parents. Wohlfahrt-Veje C et al. J Clin Endocrinol Metab. 2016 Jul;101 (7):2667-74

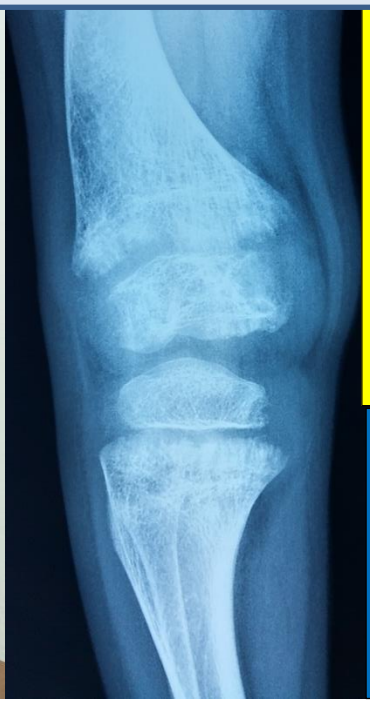
To estimate the impact of parental pubertal timing on the onset of puberty in boys and girls, annual pubertal examinations of 672 girls and 846 boys was done in a longitudinal cohort study. Information on parental timing of puberty was retrieved from questionnaires. In boys, PH2+ and TV3+ was earlier by 11.8 months and in girls, menarche was earlier by 10.5 months, if father/mother had early pubertal development. The authors concluded that maternal as well as paternal pubertal timing was a strong determinant of age at pubertal onset in both girls and boys. Age at breast and pubic hair development in girls seemed to be least dependent on heritability.

First Morning Voided Urinary Gonadotropin Measurements as an alternative to the GnRH Test. Demir A et al. Horm Res Paediatr. 2016;85(5):301-8

FMV (First Morning Voided) urinary gonadotropin concentrations were compared with basal and GnRH-stimulated serum gonadotropin levels in 274 children and adolescents (78 girls, 196 boys) aged 5-17y, to assess its use as a noninvasive alternative to the GnRH test in the assessment of the hypothalamic-pituitary-gonadal function in children. Receiver operating characteristic curve analyses using urinary and serum LH and FSH concentrations showed that FMV U-LH and U-LH/U-FSH performed equally well as the GnRH test in the differentiation of early puberty (Tanner stage 2) from prepuberty (Tanner stage 1) and equally well as basal serum LH in predicting a pubertal GnRH test result. FMV U-LH determination can be used for the evaluation of pubertal development and its disorders, reducing the need for invasive GnRH stimulation tests.

Photo Quiz





Serum biochemistry

Calcium: 8.2 mg/dl

Phosphorus: 3.3 mg/dl

Albumin: 3.93 g/dl

ALP: 827 IU/L

Intact PTH: 285.3 pg/ml

What is the diagnosis?

Activities by ISPAE Members

First West Zone Growth Hormone Research Society Symposium on Growth & Pediatric Endocrine Disorders

It was held at Bharati Vidyapeeth Univesity Medical College, Pune, on 16-17 April, 2016. Dr Vaman Khadilkar was the Organizing Chairman and Dr Rahul Jahagirdar, the Organizing Secretary. On the first day, hands on workshops were conducted, mainly for pediatric and adult endocrinology trainees and practitioners. Dr Raja Padidela, from Manchester, UK, and Dr Anuradha Khadilkar conducted a workshop on 'Interpretation of DEXA and Bone Health Parameters in children' followed by a workshop on 'Bone Age Assessment' conducted by Drs Vaman Khadilkar, Jahagirdar and Hemchand Prasad. The day concluded with an interesting workshop on 'Disorders of Sexual Development (DSD)' conducted by Drs Sudha Rao and Anurag Lila. The next day, there was a series of lectures on various topics in Pediatric Endocrinology, delivered by eminent national and international faculty: Dr Anna Simon, Dr Padidela, Dr Anurag Bajpai, Dr Shaila Bhattacharya, Dr Archana Arya-Dayal, Dr IPS Kocher, Dr Nikhil Phadke, Dr Ahila Ayyavoo and Dr Meena Mohan. The session concluded with a panel discussion on commonly seen pediatric endocrine disorders in day to day practice. The program was well appreciated. It was attended by about 350 delegates, including pediatric and adult endocrinologists from all over India, and pediatricians from in and around Pune.

2nd AIIMS-LHMC Pediatric Endocrinology CME

The departments of Pediatrics of AIIMS, New Delhi, and Kalawati Saran Children's Hospital (KSCH, Lady Hardinge Medical College), New Delhi, jointly organized a Pediatric Endocrinology CME for postgraduates on 23rd July 2016. The event was held at the KCSH Lecture Theatre, and accredited by the Delhi Medical Council for 6 hours and 45 minutes. The response to the CME was overwhelming: though, initially it was only planned for 60 participants, the final number exceeded 90, with a fully packed hall. The participants

consisted mainly of MD/DNB students, and Senior Residents of both Pediatrics and Endocrinology. The faculty included Prof Ram Menon (University of Michigan); Prof Anju Seth (KSCH); Prof Vijayalakshmi Bhatia (SGPGI, Lucknow); Dr Vandana Jain (AIIMS); Dr Rajni Sharma (AIIMS); Dr Preeti Singh (KSCH); and Dr Swati Dublish (KSCH). An array of topics covering the vast spectrum of Pediatric Endocrinology were discussed, including growth charts, short stature and Growth Hormone disturbances, persistent hypoglycemia in neonates, nutritional and refractory rickets, thyroid disorders, ambulatory management of type 1 diabetes, diabetic ketoacidosis, disorders of puberty, childhood obesity and disorders of sex development. The sessions were case-based and the faculty encouraged interaction with the participants. It was a pleasure for the faculty to have such an attentive audience who proactively took part in the discussions. The participants gave a very positive feedback, saying that the CME made them more confident about managing pediatric endocrine disorders, and many expressed their interest in pursuing the specialty in future.

Dr Bhanu Kiran Bhakri, SSPHPGTI- ISPAE Pediatric Endocrine Update, Noida

An update on pediatric endocrinology disorders, the SSPHPGTI- ISPAE Pediatric Endocrine Update, a collaborative effort of Super Specialty Pediatric Hospital and PG Teaching Institute, Noida (SSPHPGTI) and ISPAE, was held on 24th July 2016 at the Conference Hall, SSPHPGTI, Sector 30, Noida. This was the first major academic activity conducted by SSPHPGTI since its inception last year. The primary focus of the meeting was to update the practicing pediatricians and endocrinologists of the region with current evidence in approach towards disorders affecting growth, puberty, thyroid, glucose and bone metabolism. The update was attended by about a hundred delegates. The meeting was graced by the presence of eminent faculty members including Prof KN Aggarwal and Prof Ram Menon. Other faculty included Prof Vijayalakshmi Bhatia, Dr Rajni Sharma, Dr Ruchi Rai, Dr Rajesh Khadgawat, Dr Archana Arya, Dr Vandana Jain, Dr Ashish Prakash, Dr Anju Virmani, Dr Krishna Biswas, Dr Virendra Kumar, Dr Dheeraj Shah, Dr Bhanu Bhakhri, Dr DK Agarwal, Dr Ruchira Gupta, Dr Monashis Sahu, Prof Anju Seth, Dr NC Prajapati, Dr Alka Agarwal, Dr Vipin Singhal. Dr Ganesh Jevalikar conducted a panel discussion on 'growth hormone therapy' discussing all the common issues related with growth hormone therapy and presented simple yet important 'take home messages' for the audiences. A short picture quiz between the sessions was found to be useful in equally breaking the hesitation

of the participants as well as the monotony of the sequence. The participants discussed common problems encountered while managing children with endocrine disorders during the last interactive session. The meeting received considerable appreciation for scientific content, lay out and arrangements, and was well covered by regional media.

World Thyroid Day, Hindu Rao Hospital, Delhi

World Thyroid Day was celebrated on 02.06.2016 at Hindu Rao Hospital. Dr Ravindra Kumar spoke on 'Congenital Hypothyroidism: Update on Screening' and Dr Sangita Yadav delivered a lecture on 'Approach to Thyromegaly in children'.

Dr Hemchand K Prasad, Pediatric Endocrinologist, Dr Mehta Children's Hospital, Chennai

GROW DAY celebration

World Grow day was celebrated in MCH auditorium on May 1st 2016. 40 children with growth problems attended the program. The agenda included fun activities for children and education. This was followed by Q and A session.

CME on "World Thyroid Day"

IAP CCB and Mehta Children's Hospital jointly conducted a CME on "World Thyroid Day". The theme of the CME was Congenital Hypothyroidism. The speakers were Prof Anna Simon from CMC Vellore and Dr Trimurthi from MMM Hospital. The meeting was attended by 80 practicing pediatricians in Chennai.

Lectures delivered by Dr Hemchand

- Talk on "New IAP growth charts and growth monitoring" – IAP Thanjavur meeting April 2016
- Talk on "New IAP growth charts and growth monitoring" – IAP Erode association May 2016
- Talk on "Management of metabolic syndrome" and "Congenital Hypothyroidism" – IAP Tirunelveli
- Talk on "Management of short stature" – IAP Madurai

Type 1 Diabetes Education Day for children with T1DM and their parents/caregivers

This program was organized by Pediatric Endocrinology Division, Department of Pediatrics, Advanced Pediatrics Centre (APC), PGIMER, Chandigarh on 24th April 2016 between 9:30 am to 1:00 pm at APC auditorium, PGIMER, Chandigarh. The program aimed to provide the latest information on management of T1D with regards to best insulin regimens, insulin pump therapy, experimental therapies and future hope, dietary planning and day to day management of sugar fluctuations, in a common platform for T1D children as well as for their caregivers. They conducted a session themselves, sharing their experiences and problems in managing these children at home. In addition, a few adult patients having T1D since childhood, who have done well in managing their disease, and are now successful in their life, shared their experiences and were a great source of motivation for them. Mr Sukhjinder Singh spoke on dietary management for children with T1D, Dr Devi Dayal on 'Day to day practical management of T1D', Dr Rakesh Kumar on 'Newer advances in management of T1D, and Mr Rajendra Singh on his experience of using an insulin pump.

Dr Sri Nagesh, Consultant Endocrinologist, CARE Hospital, Banjara Hills, Hyderabad.

- Delivered a lecture on "Management of Pediatric Endocrine Tumours" at the 3rd Midterm National Hematology and Oncology Conference on 9th July 2016 at Hyderabad.
- Delivered a Lecture on "Type 1 Diabetes-Difficulties and Delights" at TRENDO 2016, the 4th Annual Conference of the Tamil Nadu State Endocrine Society on July 10th 2016 at Coimbatore.

Answer to Photo Quiz: Vitamin D dependant rickets type 2

Charity Activities by ISPAE Members

Charity Activity Report by Dr Deepa Anirudhan

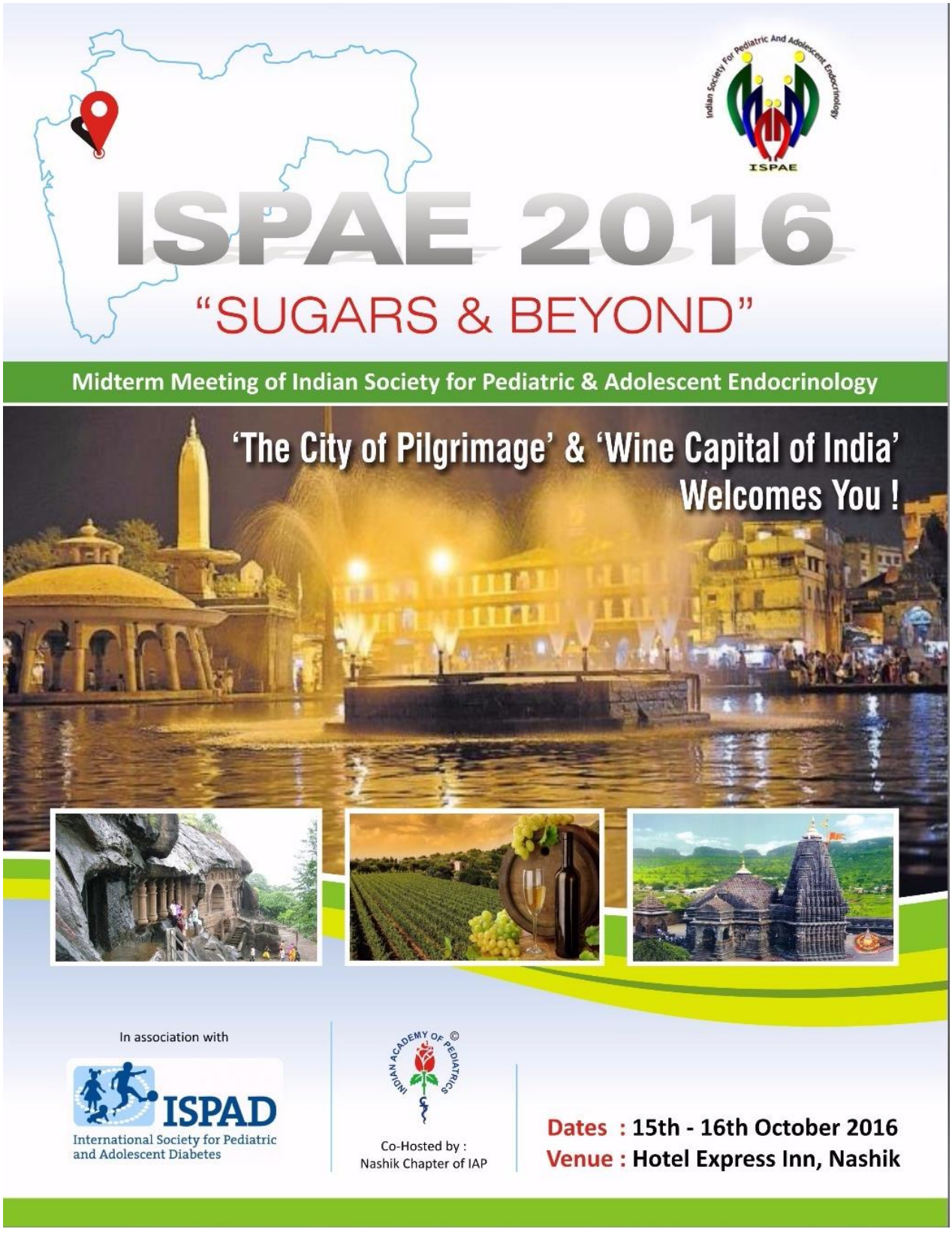
Department of Pediatrics, Govt. Medical College, Thrissur has 57 children with diabetes, of whom the majority have Type 1 diabetes, with one case each of Type 2 DM, DIDMOAD syndrome and secondary diabetes in thalassemia. The diabetes clinic is functioning every month on second Saturdays. Dr Deepa Anirudhan, Assistant Professor, is in charge of the clinic. Every year an awareness class is conducted for the patients and their parents. We have also had classes by a dietician and a clinical psychologist. A yoga class was conducted by two diabetic children a year back. Free insulin is being supplied by the hospital. Insulin syringes and glucometer strips are purchased by the eDpartment with the help of volunteers' and students' Charity Wing 'Pratheeksha".

Dr Deepa, Assistant Professor and Dr Anu, Senior Resident at Diabetic Clinic

Distribution of free syringes to a patient by Dr Parvathi, Additional Professor of Pediatrics and Social worker Ms Anugraha

Charity Activity Report by Dr Reetha Gopinath

A diabetes meeting was held on 14.11.2015 at Pariyaram Medical College, Kerala. Forty patients with type 1 diabetes and their families attended the meeting. We had education sessions and free insulin and insulin syringes were distributed to all the children.


ISPAE 2016
"SUGARS & BEYOND"
Midterm Meeting of Indian Society for Pediatric & Adolescent Endocrinology
'The City of Pilgrimage' & 'Wine Capital of India'
Welcomes You !
In association with
ISPAD
International Society for Pediatric and Adolescent Diabetes
Co-Hosted by :
Nashik Chapter of IAP
Dates : 15th - 16th October 2016
Venue : Hotel Express Inn, Nashik

ISPAE 2016

"SUGARS & BEYOND"

The Indian Society for Pediatric & Adolescent Endocrinology [ISPAE] announces its midterm conference, in collaboration with International Society for Pediatric & Adolescent Diabetes [ISPAD].

Recognizing the rising burden of diabetes in childhood, the theme for ISPAE 2016 conference is 'Sugars and Beyond'.

Dates : 15th - 16th October 2016 Venue : Hotel Express Inn, Nashik

Topics : Diabetes & Endocrinology

- Neonatal Diabetes
- Primary Prevention of Diabetes, Where Do We Stand ?
- Hypoglycemia Management
- Counting Beyond Carbs
- Newer Drugs In Diabetes
- Growth Hormone Therapy
- Hypothyroidism
- Childhood Obesity
- Insulin Resistance, Type2 DM
- Islet-Cell Transplant
- Secondary Diabetes
- Adolescent PCOD
- Newborn Screening
- Gadgets In Diabetes
- Pubertal Problems In Children

Faculty : International faculty **Dr. Carine De Beaufort** (Secretory General, ISPAD) & **Dr. Kim Donaghue** (Chief of Pediatric Diabetes, Westmead Children's Hospital (Sydney) National Faculty in the field of Pediatric & Adolescent Endocrinology.

"NUTS & BOLTS OF DIABETES MANAGEMENT"

ISPAE 2016 Pre-conference Workshop on Pediatric Diabetes **Saturday 15th October, 8.00 am-1.00 pm**

[For Pediatricians, Diabetologists, Nurses, Nutritionists & Educators]

Topics : Insulin Basics, Newer Insulins, Home Blood Glucose Monitoring, Insulin Pumps, Choosing A Glucometer, Diet In Diabetes, Sick Day Management, Diabetes In Resource Limited Setting, Glycemic Control, Survival Skills, Dose Adjustment.

Limited Entries, Registration Mandatory.

Organizing Team

Advisors :
Dr. PSN Menon
Dr. Nalini Shah
Dr. Subhash Kashyape
Organizing Chair :
Dr. Sudha Rao

Organizing Secretary :
Dr. Tushar Godbole
Scientific Chair :
Dr. Preeti Dabadghao
Workshop Convener :
Dr. Anju Virmani

Workshop Co-convener :
Dr. VIjayalakshmi Bhatia
Organizing Committee :
Dr. Yashpal Gogate
Dr. Ganesh Jevalikar
Dr. Rahul Jahagirdar
Dr. Abhishek Kulkarni
Dr. Samir Dalwai
Dr. Ruchi Parikh
Dr. Ravindra Sonawane
Dr. Sagar Sonawane

Visit our website www.ispae2016.com for further details.

ISPAE 2016

"SUGARS & BEYOND"

15th-16th October 2016 - Venue : Hotel Express Inn, Nashik

Registration Form

Conference Registration Number :

Name : ..... Sex : ..... Age : .....

Current Affiliation : .....

Address for Correspondence :

Phone Number : .....

Email ID : .....

Membership Numbers (If any) :

ISPAE / ISPAD : ..... CIAP : .....

Amount Paid :

Workshop : ..... Main Conference : .....

Mode of Payment : ☐ Online ☐ Cheque ..... ☐ DD ..... ☐ Cash

Secretariat Address : Dr. Tushar Godbole,

A104, Zion Herald, Rameshwar Nagar, Pipeline Road, Nashik - 422013. (M) +91-7774082834, email ispae2016@gmail.com

Registration Details for Main Conference

Registration Slot up to	ISPAE or ISPAD Members	Others
30th April 16	3000/-	3200/-
31st July 16	3500/-	3700/-
30th Sept. 16	4000/-	4200/-
Spot	4500/-	4500/-
PG Students / Nurse / Educator / Nutritionist (Letter from HOD required)		2500/-

ISPAD
International Society for Pediatric and Adolescent Diabetes

Registration fees for Workshop :

Practising Pediatricians	Post-Graduate Students	Nurse / Educator / Nutritionists
1500/-	750/-	500/-

Payment by cheque/online. Prior registration is compulsory.

75% refund for cancellations before 31st July, no refunds after that.

Block your dates & Register soon !

Online Payments : IDBI Bank
Account No. : 1991104000005456
IFSC Code : IBKL0001991
Cheque / DDs in favour of "ISPAE 2016"

ISPAE

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Dr. Ruchi Parikh
Dr. Ravindra Sonawane
Dr. Sagar Sonawane

Visit our website www.ispae2016.com for further details.