CAPE NEWS

Newsletter of the Indian Society for Pediatric and Adolescent Endocrinology (ISPAE) *www.ispae.org.in*

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Contents

From the Editor's Desk

Dear members,
Wishing you all a very happy and prosperous new year 2020 on behalf of the Editorial team!

Last quarter of 2019 has been very eventful and happening for ISPAE and its members. Apart from a grand 6th Biennial meeting at Kolkata, ISPAE members organised various activities in different parts of the country. A summary of all these events with pictures is included in this edition of CAPE NEWS. Clinical pearls from ISPAE 2019 and ISPAE PET 2019 are included in this edition which should be interesting for the younger members. Apart from usual sections we have included experience of 2 ISPAE Fellows who completed the fellowship in 2019. A mini-review on Type 2 diabetes in children should be useful as T2DM is of late being reported among children and adolescents. A brief summary of International Society for Clinical Densitometry (ISCD) 2019 guidelines on use of DXA amongst children is presented.

With fast growing membership of ISPAE we expect more and more submissions for CAPE NEWS.

With warm regards,
Rakesh Kumar and team CAPE NEWS

Message from the ISPAE Office Bearers

Dear friends,

Happy New Year!

2019 had been an amazing year for ISPAE. The recently concluded biennial meeting of our Society at Kolkata was a grand success. ISPAE 2019 was well organised by Dr Subrata Dey and his team, at a great location, with a wonderful ambience and special Bengal cuisine. The main meeting was well attended, with an outstanding academic program, and an amazing amount of new research work from around the country highlighted. PET 2019 for the Fellows at the Vedic Village at Kolkata under the supervision of Dr Sudha Rao was a resounding success with the Fellows gaining enormously from a galaxy of international and national experts. All this indicates a great future for ISPAE.

The ISPAE 2020 Midterm Meeting is scheduled to happen at Chandigarh on 8-9 November, under the able guidance of Prof Devi Dayal. ISPAE 2021 will be held in Thiruvanathapuram. The venue and other details for these meetings would be available in the near future.

Our Society is growing vigorously, with the addition of 28 Life members and 14 Associate members in 2019. Our current membership stands at 584. I am sure we are going to see fabulous growth in our Society with the addition of more members in 2020.

Looking forward to a great year at ISPAE!!!

With regards
Preeti Dabadghao, Ahila Ayyavoo and Leena Priyambada

Hearty Welcome to New ISPAE Members

S.No	Name	Affiliation
1	Nandhini Lakshmana Perumal	Assistant Professor, Dept of Endocrinology, St Johns Medical College, Bengaluru
2	Saba Samad Memon	Senior Resident Endocrinology, Seth GS Medical College, Mumbai
3	Manjiri Karlekar	DM Endocrinology, KEM Hospital, Mumbai
4	Hriday De	Pediatric Endocrinology Fellow, Sir Ganga Ram Hospital, New Delhi
5	Suraj S Kubihal	DM Endocrinology, AIIMS, New Delhi
6	Sarah Alam	DM Endocrinology, AIIMS, New Delhi
7	Ramdas Bharat Barure	DM Endocrinology, Vydehi Institute Of Medical Sciences And Research Center, Bengaluru
8	Sumeet Arora	Associate Consultant, Ped Endo, Artemis Hospital, Gurugram
9	Pavan Kumar Reddy	DM Endo, Medanta Hospital, Gurugram
10	Manoj J Mahajan	Pediatrician, Ambernath, Maharashtra
11	Supreetha Shetty	Fellow, Ped Endo, Rainbow Children's Hospital, Bengaluru
12	Vikrant Gosavi	DM Endo, KEM Hospital, Mumbai
13	Anusha Priyanka	Pediatrician, Gurugram
14	Abhamani Baro	DM Endocrinology, Resident Physician, Dept of Endocrinology, Guwahati Medical College
15	Rathinavel C	Pediatrician, District Early Intervention Center, Salem, Tamil Nadu
16	Rahul Reddy Chintala	Pediatric Endocrinologist, Ankura Hospital for Women and Children, Hyderabad
17	Moosakutty Chettiyarammel TP	Consultant Pediatrician

ISPAE OBSERVERSHIP AWARDS 2019

Dr Anjali, Assistant Professor, Pediatrics, PGIMS, **Rohtak** completed her observership at Division of Pediatric Endocrinology at AIIMS, New Delhi.

"My Experience of ISPAE Observership at AIIMS"

I have recently completed observership of one month in Pediatric Endocrinology at AIIMS, New Delhi. It was a great learning experience under the guidance of my mentors, Dr Vandana Jain (In-charge, Pediatric Endocrinology, AIIMS) and Dr Rajni Sharma (Associate Professor, Pediatric Endocrinology, AIIMS).

I got an opportunity to see a variety of endocrine cases like CAH, Cushing/ Addison disease, DSD, T1D, panhypopituitarism, Grave's disease, refractory rickets, Turner syndrome, precocious/ delayed puberty etc. as well as a few interesting cases like adrenocortical carcinoma, LMBB, Noonan, Silver Russel syndrome, Albright osteodystrophy, agenesis of the corpus callosum with SIADH. I learned the diagnostic approach, management and follow up of such cases. The Pediatric Endocrinology clinic consists of a multidisciplinary team, including physician, dietician, clinical psychologist, staff nurse, diabetic educator and residents. Meticulous record keeping of the new as well as follow-up patients is done in structured proformas in the Clinic. As part of multidisciplinary management of T1D, I attended counselling sessions on diabetes as well as obesity, and was given hands-on training on carbohydrate counting and functioning of insulin pump in the Department.

I learned about day care tests, including growth hormone stimulation test, water deprivation test and other dynamic endocrine tests e.g. ACTH stimulation, HCG stimulation, GnRH stimulation tests, ODST etc. I was shown hormonal assays being done in pediatric endocrinology lab, and Body composition analysis by PEA POD for infant body composition and Body Composition Analyser (BCA) in older children. I presented clinical cases of short stature, refractory rickets and precocious puberty during my training period.

I had the privilege of attending an AIIMS workshop and Brainstorming Meeting on improving diagnosis and management of disorders of sex development by Dr Jain and Dr Sharma, and a workshop on Grant Writing by Dr Nikhil Tandon (Head, Endocrinology, AIIMS). Along with the clinical aspects, I got an overview of various research projects and theses of post graduate residents at AIIMS.

This training has definitely increased my interest and knowledge in Pediatric Endocrinology. It will enable me to start a speciality clinic at my institute Pt. BD Sharma PGIMS, Rohtak and help me in training and teaching postgraduates and undergraduates. Lastly, I am very grateful to my Institute for permitting me to attend this training, and to my mentors for their continuous guidance and support. I would also like to thank ISPAE for giving me the ISPAE Observership Award 2019 for training in the premier institute. Such awards are really a boost for the young interested faculty members who want to start clinics in their institutions.

Dr Aaradhana, Associate Professor, Department of Pediatrics, University College of Medical Sciences & Guru Teg Bahadur Hospital (UCMS & GTBH), Delhi completed her ISPAE observership at Division of Pediatric Endocrinology at AIIMS, New Delhi.

Report of completion of short-term observership at Division of Pediatrics Endocrinology, AIIMS, New Delhi

I completed a 3 month Observership (9th Jan- 8th Feb 2019 & 12th June -10th August 2019) in Pediatric Endocrinology at AIIMS, New Delhi. I attended the Pediatric Endocrinology clinic 3 days per week and the clinical ward rounds. I learned a lot during this period. I got an opportunity to see and manage a variety of endocrinology cases like type 1 diabetes mellitus, CAH, panhypopituitarism, DSD, pubertal disorders, etc. I learned dynamic hormonal testing like GH stimulation testing, GnRHa stimulation test, ACTH stimulation test etc. I got a wonderful opportunity to attend a lecture on hypophosphatemic rickets and pseudohypoparathyroidism by Dr Olaf Hiort, an eminent endocrinologist from Germany. During my training I made five presentations on DSD, lipid disorders, panhypopituitarism, approach to rickets, and delayed puberty.

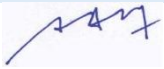
The observership has definitely increased my knowledge, and is helping me a lot in running the newly started Pediatric Endocrinology OPD at UCMS & GTB hospital, Delhi. I am thankful to Dr Vandana Jain (Professor and Head, Division of Pediatric Endocrinology, AIIMS) and Dr Rajni Sharma (Associate Professor, AIIMS) for their support and guidance. I am grateful to the ISPAE Committee for approving my observership. The procedure of application of ISPAE is smooth and easy with prompt responses from committee members. One suggestion I have is that there should be a well-defined curriculum for Observership too. This will help to maintain uniformity in observership at all places and will facilitate the learning process during training.

ISPAE 2019: Report by Organising Chairperson

The 6th Biennial ISPAE Meeting was held in Kolkata, the City of Joy, from 29th November to 1st December 2019 at ITC Sonar, a destination hotel. It was organized and delivered by the Organizing Chair, with renowned international and national Faculty delivering lectures, participating in panel discussions, and deliberating on original research work and clinical advances. There were over a hundred abstracts presented here, over the first 2 days. The third day of the conference, titled "Practical Pediatric Endocrinology for Pediatricians", was well attended, with over 300 registrations. There was also an amazing response from our colleagues In Bangladesh, with over 25 registrations for the 3 day program. This meeting was the first of its kind in Kolkata. Many prominent national Faculty discussed the entire range of Pediatric Endocrinology topics and provided algorithmic solutions. There were extraordinary international Faculty who gave a joint press conference with incisive messages for treatment of T1DM, congenital hypothyroidism, rickets, and growth hormone deficiency. This was an all-inclusive meeting, which embraced both senior and junior Faculty, with the theme "We Shall Grow Together". Inclusivity of all Pediatric Endocrine practitioners in the panel of speakers was the hallmark.

There were many enchanting moments. During the inaugural function, the Chief Guest Dr Bakul Parekh, IAP President Elect, was felicitated - he promised to establish strong ties with ISPAE in the coming year. Dr P Raghupathy, the Guest of Honor, was felicitated as the doyen of Pediatric Endocrinology for being awarded the *Outstanding Clinician of the Year* by ESPE in 2018. The Inaugural Cultural program presented by Kalasangam Nityashetra was sublime. The Gala Dinner on 30th night had the nationally acclaimed gazal singer Dhruvajit Bhattacharya performing for us at Spring Club, enthralling us for the entire evening.

This conference was a resounding success, setting a benchmark for future ISPAE meetings. It could not have been executed without the support of Marundeshwara Enterprises, the national event organizer, and Qubix, the local event manager, the National Organizing Secretary, and our Local Organizing team from Apollo Hospitals and beyond, who ensured timeliness which was the hallmark of the program. I am proud to say that this conference was on par with any International Conference of this stature. ISPAE 2019 at Kolkata was truly an academic gourmet and cultural feast.



Subrata Dey
Organizing Chairman
ISPAE 2019

ISPAE 2019: Pictures





Links to conference photos: Day 1 - https://photos.app.goo.gl/Z1xctoXzSjaAnjEXA
Day 2 - https://photos.app.goo.gl/y2QLn3x7hc3SYqvu9
Day 3 - https://photos.app.goo.gl/bk86SFGLKTN4zBMu7

REFLECTIONS OF AN ISPAE-PET 2019 FELLOW

Rejuvenation of the mind, body and soul

Dr Sarah Alam (ISPAE/PET Fellow 2019), DM Endocrinology Trainee, AIIMS, New Delhi

The picturesque natural beauty of Vedic Village Resort, with the amazing hospitality of the City of Joy, Kolkata, provided an idyllic setting where one could rejuvenate completely. We all reached a bit tired, but the immense energy of Dr Sarah Mathai and Dr Sudha Rao infused us with a new zeal to learn. It amazed me how wonderfully even little things were planned to perfection. All it took was an ice breaking session before we shed our inhibitions and started dancing. It all began when the genius minds of our organizers divided us randomly into teams, and we had the enjoyable task of describing the unknown partner. It was a great introductory method and there itself was the beginning of new friendships and embarkment of a new journey – the stage was set. Then there was this innovative modification of Musical Chairs - 'Anatomical Musical Chair' where one had to keep the announced body part on the chair first, which proved to be great fun. So our first day ended, and we went to our rooms to rest. Having a great room partner was just the icing on the cake.

Running on a tight schedule every day, we began at 6 in the morning with invigorating games. There was also yoga to alleviate the stress and keep one relaxed. After that, began our study sessions with group discussions – where in small groups, we had a face-to-face interaction with the stalwarts in Endocrinology. They brought their cases and tested us and we presented our difficult ones and got brilliant inputs from them. We learned not only from our teachers but also from other enthusiastic fellows.

"Marathon study sessions are too taxing on the mind"- I ask you to think again as ISPAE PET clearly proved otherwise. Case presentations by Fellows, explained in a remarkably simple fashion how decisions were made, and post-case discussions scrutinized every aspect to make concepts clearer and enrich our minds. The impeccably amazing Faculty presentations were so lucid, they made difficult-to-grasp concepts a cake-walk. They just reiterated the fact that to learn complex concepts one has to relearn the basics. The international faculty members were also extremely friendly, and interactions with them humbled us in more ways than one. What impressed us the most was not just the sheer brilliance of all faculty members, but their extreme humility, down-to-earth nature and the patience with which they answered all our questions. At one point, my emotions were echoed by this quote of Sir Isaac Newton, "I am only a child playing on the beach, while vast oceans of truth lie undiscovered before me." This process just stimulated an unquenchable thirst for knowledge and the need to learn and grow constantly.

And if the mind got a little tired after this superb academic feast, there were facilities to energize one, and what adds more fun to a gathering than Karaoke. Post-dinner was the time to test our vocal skills, and who knows, one of us may very well turn out to be the next singing sensation!

Sessions and group discussions were held in a similar fashion the next day and our learning continued. Another day accomplished under the expert tutelage of the giants in endocrinology, followed by a Gala Dinner at Bhoomi Restaurant. Scrumptious dinner followed by a walk in the woods refreshed us and forged new bonds of friendship.

The last day seemed short and too much left to do with too little time. There was a group photograph which captured the moment, and many candid photographs were also taken. Then there was a quiz by the superb Quizmaster, Dr Anurag Bajpai - the difficult questions racked our brains and we mentally revised everything. This was followed by a prize distribution and to our surprise, there were thoughtful prizes for almost everyone which literally made our day.

As the saying goes, “Give a man a fish, and you'll feed him for a day. Teach a man to fish, and you have fed him for a lifetime”, so here at ISPAE PET, we were taught the principles of problem solving and best practices to follow, which was like feeding us for a lifetime.

Last but not the least, the visit to Eco Park was simply mesmerizing. Who would have thought one could click a picture of Taj Mahal from the Great Wall of China, with Eiffel Tower in the background! So, as we were being transported back to our vehicle and feeling the gentle touch of a cool breeze on our faces, there was a sense of peace and calm of a job well done. There was a satisfaction of rediscovering old friends, meeting new ones, and countless memories etched in our minds forever, thinking about a wonderful future ahead – Kolkata, you will be definitely missed!

Pearls from ISPAE 2019

Dr Vikrant Gosavi, Dr Vijaya Sarathi

Diabetes Mellitus

1. Hippocampal volume and white matter volume are related to hypoglycemia in T1DM.
2. Hyperglycemia in T1DM is associated with neurocognitive decline.
3. Changes in the ISPAD 2018 Guidelines
    a. Goal changed to HbA1c of < 7%
    b. Criteria for SGLT2i use: age >18 years
    c. Strict adherence to insulin
    d. Use of CGMS (grade A recommendation)
    e. Use of CSII (grade B recommendation)
    f. Addition of a Chapter on 'Management of diabetes at school'.
4. Teplizumab (humanised anti-CD3 monoclonal antibody) reduces the risk of T1DM in antibody positive relatives of T1DM patients.
5. Effective measures for prolonging the honeymoon phase: continue insulin; prevent further episodes of DKA; promote exercise; Tepilizumab may be considered.
6. SMBG misses ~60% of hypoglycemias.
7. CGMS sensors without need for glucometer calibration can minimize the need for SMBG if used in selected patients.
8. CGMS sensors without need for glucometer calibration are cheaper and useful for glycemic control, despite having poor performance at low glucose levels.
9. Ambulatory blood glucose profile (ABGP) simplifies the trends of glucose monitoring for better interpretation and clinical applicability than CGMS.
10. It is necessary to keep a record of diet and physical activity and timing and dose of insulin stringently while CGMS is being recorded.
11. For proper CGMS interpretation, at least 70% data of at least 10 days is required.
12. A Time in range (TIR) of 70% corresponds to an HbA1c of 7%. Up to TIR of 70%, intima media thickness remains normal.
13. In healthy volunteers, TIR is > 90%. There may be few readings below 70 mg/dL, but never below 54 mg/dL.
14. TIR ideally should be 70-180 mg/dL for at least 80%, whereas guidelines recommend TIR of 70- 180 mg/dL at least 70%.
15. Hypoglycemia
    a. Level 1 (mild): 54-70 mg/dL
    b. Level 2 (moderate): < 54 mg/dL
    c. Level 3 (severe): Need help from another person (BG often < 40 mg/dL).
16. CGMS: BG <70 mg/dL and < 54 mg/dL should not exceed 1 hour and 15 min respectively.
17. CSII in carefully selected Indian children lead to significant improvement in HbA1c as compared to a closely monitored basal bolus regimen.
18. CSII with CGMS has better results in children than in adults, when applied properly.

19. CSII may be more cost effective for the hearth care system in the long run – a consideration for the future.
20. Sequence of introduction of technology in T1DM care: CGMS → CSII → Both.
21. Options other than insulin in T1DM
    a. Metformin - may be useful in patients with obesity and insulin resistance
    b. GLP1 analogues
    c. SGLT2 inhibitors- EMEA approved dapagliflozin and sotagliflozin for T1D adults with BMI ≥ 27 kg/$m^{2.}$
22. Genetic testing of choice for MODY: targeted NGS

Growth

23. Proportionate tall stature: Soto syndrome, Weaver syndrome, Fragile X syndrome.
24. Disproportionate tall stature: Klinefelter, Marfan, Beckwith-Wiedemann syndromes.
25. To correct for secular trend in India, 3 cm may be added to the target height derived from Tanner's formula.
26. In estimation of bone age, TW 3 system is more relevant for Indian children as Asian children were included in its derivation.
27. All methods for bone age estimation are formulated using average-height children; therefore, for short stature subjects, the value will be overestimated.
28. In syndromic short stature, molecular diagnosis is not beneficial in majority because of:
    a. Single variants
    b. VUS
    c. Gene environment interaction cannot be accounted for.
29. Presently there is no criteria for selecting short stature cases for molecular testing.
30. Molecular testing may be considered in short children with
    a. Microcephaly
    b. Syndromic features
    c. MPHD, severe IGHD
    d. Skeletal dysplasia
    e. SGA not showing catch up growth
    f. Girls with short stature.
31. Genetic testing is not indicated in patients with suspected CDGP or when both parents are short (Both have height SDS < -2).
32. Whole genome sequencing is preferred over clinical exome sequencing for the molecular testing of short children.
33. SAGhE study (2018): GH does not increase the risk for relapse in ALL. However, there has been minimal increase in risk for carcinoma of bone and bladder.
34. Vosoritide (long acting CNP analogue): blocks FGFR3 signalling by activating CNP signalling; provides sustained increase in growth velocity in children with achondroplasia.

Childhood Cancer Survivors

35. Weight gain is a known complication after cranial RT for ALL, and is treated with dexamphetamine.
36. Gonadal evaluation should not be done till the age of 10 years in cancer survivors.
37. Cranial irradiation can cause cerebral arteritis; in such girls transdermal estradiol should be preferred over oral estradiol.

Bone Health

38. At least 30% of bone loss is required for osteopenia to be apparent on X-ray.
39. Measurement of BMD at femur by DXA is included after 10 years of age.
40. 5-30% of patients on chronic glucocorticoid treatment may have asymptomatic vertebral fractures and vertebral fracture assessment (VFA) is the best diagnostic tool to detect them.
41. pQCT offers the advantage of rapid assessment along with 3D assessment of bone dimensions.
42. The most common cause of primary osteoporosis in childhood is osteogenesis imperfecta (OI), followed by idiopathic juvenile osteoporosis (IJO).
43. Vitamin D deficiency may have normal or elevated serum phosphorus level due to tubular resistance to PTH.

Neonatal Endocrinology

44. Transitional hypoglycemia is common in neonates; plasma glucose < 50 mg/dl is observed in up to 30% normal neonates in the first 24 hours of life.
45. Persistent hypoglycemia: GIR >8 mg/kg/min required beyond 72 hrs of life.
46. Low ketone level does not necessarily rule out ketotic forms of hypoglycemia in neonates, as they use ketones as alternative fuel in presence of hypoglycemia.
47. Definition of hypocalcemia in neonates:
    a. Term neonates: Serum total calcium < 8 mg/dl or serum ionic calcium <4.4 mg/dl
    b. Preterm neonates: Serum total calcium < 7 mg/dl or serum ionic calcium <4.0 mg/dl.
48. Persistent hypocalcemia: Hypocalcemia persisting beyond 48 hrs of life - requires further evaluation.
49. Even sick neonates must be screened for congenital hypothyroidism (CH) within 7 days of life; those sick neonates who are at high risk of hypothyroidism (preterm, LBW, same sex twins) must have a second screen for CH at 4 weeks of age.
50. Perinatal prevalence of skeletal dysplasia is 9.1/1000 perinatal deaths.

PEARLS FROM ISPAE PET 2019

Dr Manjari Karlekar, Dr Vijaya Sarathi

Neonatal Endocrinology

1. No role of GH in intrauterine growth; Insulin, IGF1 and IGF2 play a major role in intrauterine fetal growth.
2. Fetal to maternal total calcium ratio 1.4:1 as calcium is actively transported across the placenta.
3. Presence of testosterone during the critical period (8-12 weeks of gestation) is essential for appropriate virilisation of a male fetus.
4. There will be no ambiguity in males with hypo-hypo as placental hCG stimulates Leydig cells to produce testosterone.
5. FSH, LH and sex steroids are low at birth; start rising after 2 weeks of life, and peak at about 2 months (mini-puberty). The mini-puberty lasts up to 6 months in boys and 2-3y in girls.
6. In newborns with CAH, immunoassays may provide falsely elevated levels of steroids; hence, specific assays such as LC MS/MS should be preferred.
7. The placenta contains 11β-hydroxysteroid dehydrogenase 1, which inactivates cortisol and prednisolone but not dexamethasone and betamethasone.
8. Hyponatremia can be seen in patients with isolated glucocorticoid deficiency whereas hyperkalemia indicates concomitant mineralocorticoid deficiency.

9. UTI is a cause of transient pseudohypoaldosteronism in neonates.
10. Serum uric acid and hematocrit levels in newborns can be used to differentiate hypovolemic hyponatremia from hypervolemic hyponatremia.
11. Pseudohypoaldosteronism (autosomal recessive form) can cause recurrent respiratory infection.
12. Vitamin D deficiency usually does not manifest with hypocalcemia during the first 2 weeks of life.
13. The fetus gets 80% of glucose from the mother passively.
14. Ketogenesis is ineffective in first 24 hours of life; so do not advise laboratory investigations for same.
15. Any detectable level of insulin in a newborn with hypoglycemia suggests hyperinsulinemia.
16. T3, T4 and particularly, TSH rise at birth; therefore, screening for CH is preferably at least 48 hrs after birth. However, if sample is taken from cord blood, it is appropriate and easy, as it is difficult to get 48 hours sample - most babies are discharged by then.

Disorders of Sex Development (DSD)

1. Isolated hypospadias with descended testes does not merit evaluation as DSD, whereas bilateral undescended testes do need evaluation as DSD.
2. Maternal ingestion of progestin should be asked for in 46XX DSD.
3. QFPCR and FISH provide rapid results within 2 days when compared with conventional karyotype, which takes 10-14 days.
4. Denys-Drash syndrome, Frasier syndrome and WAGR syndrome are associated with DSD and renal abnormalities.
5. In premature infants there can be clitoral enlargement due to true temporary virilisation, which regresses as age advances.
6. HCG-stimulated T/DHT ratio > 30 is a specific indicator of 5α-reductase deficiency.
7. ApoD, an androgen regulated transcript produced in genital fibroblasts, is used as a marker of androgen sensitivity in patients with suspected androgen insensitivity syndrome.
8. Prenatal treatment of CAH – the risks outweigh benefits.

Bone

1. The most important parameter to improve bone strength is to improve muscle strength with physical exercise.
2. BMD of fractured vertebrae may be falsely high.
3. Bones with larger diameter are stronger.
4. OI classification is not helpful in their management.
5. Zoledronic acid offers the advantage of less frequent doses (q 6 months) over pamidronate (q 3 months).

Growth and Puberty

1. IGF1 levels do not always correlate with the growth response.
2. Most of the GHST can have false positive results.
3. CDGP is the most common cause of delayed puberty in boys.
4. Testicular volume ≥ 4 ml, baseline testosterone of ≥ 25 ng/dl, hCG stimulated total testosterone ≥ 230 ng/dl, GnRH stimulated LH ≥ 14 mIU/ml favor the diagnosis of CDGP in a boy with delayed puberty; however, none of these tests have good accuracy to differentiate CDGP from congenital hypogonadotropic hypogonadism.
5. Hypothyroidism is a unique cause of precocity, with short stature and delayed bone age.
6. Paternally inherited inactivating *MKRN3* mutation is the most common cause of familial GnRH dependent precocious puberty.

Adrenal

1. Childhood Cushing syndrome most often presents with obesity and growth deceleration but no catabolic signs.

2. Adrenocortical carcinoma is the most common cause of Cushing syndrome in infants or toddlers.
3. Look for skin signs such as lentigines (Carney's complex) and café-au-lait spots (McCune Albright syndrome) in children and infants with Cushing syndrome respectively.
4. Inferior petrosal sinus sampling to differentiate Cushing disease from ectopic ACTH syndrome should be performed with CRH stimulation.
5. AAA (Allgrove) syndrome is a progressive disorder with manifestations evolving over time; it can have mineralocorticoid deficiency in 8-10% patients.
6. Patients with glucocorticoid deficiency may have modestly elevated TSH which normalises after glucocorticoid replacement.
7. Alacrimia is the earliest manifestation and is present in almost all patients of AAA syndrome in literature.
8. Pheochromocytoma enhances avidly on arterial phase (20 seconds) of contrast-enhanced CT which helps to differentiate pheochromocytoma from other adrenal tumours.
9. In paraganglioma, functional imaging is a must to look for metastasis and multiple lesions.
10. Genetic testing should be performed in all children with pheochromocytoma, and family members should be screened for pheochromocytoma.

Others

1. Ovaries are susceptible even to low dose local radiation.
2. Carbamazepine, cyclophosphamide and vincristine can cause hyponatremia.
3. Copeptin, a hormone co-secreted with vasopressin, is a useful test in the evaluation of children with diabetes insipidus.

Excerpts from recent Guidelines

Compiled by Nikhil N Lohiya, ESPE Fellow, Alder Hey Children's Hospital, Liverpool, UK

The Utility of DXA Assessment at the Forearm, Proximal Femur, and Lateral Distal Femur, and Vertebral Fracture Assessment in the Pediatric Population: The 2019 Official Pediatric Positions of the ISCD. Weber DR et al. J Clin Densitom. 2019 Oct-Dec;22(4):567-589. doi:10.1016/j.jocd.2019.07.002.

Utility of DXA Forearm Measurements (Grade: Fair, B,W)

DXA measurements at the 33% radius (also called 1/3 distal radius) may be used clinically in ambulatory children who cannot be scanned at other skeletal sites, provided adequate reference data are available. (Grade: Fair, B,W)

Utility of DXA Proximal Femur Measurements (Grade: Fair, B,W)

Proximal femur DXA measurements may be used, if reference data are available, for assessing children with reduced weight bearing and mechanical loading of the lower extremities or in children at-risk for bone fragility who would benefit from continuity of DXA measurements through the transition into adulthood. (Grade: Fair, B,W)

Utility of DXA LDF Measurements (Grade: Fair, B,W)

Official Position - LDF DXA measurements correlate well with increased lower extremity fragility fracture risk in non-ambulatory children. LDF DXA may be used, if reference data are available, to:

a. Assess BMD in children when the presence of nonremovable artifacts (orthopedic hardware, tubes), positioning difficulties, abnormal skeletal morphometry, or severe scoliosis with torsion interfere with DXA acquisition at other anatomical sites.
b. Monitor the effects of changes of weight-bearing in non-ambulatory children.

Utility of VFA in Children (Grade: Fair, B,W)

DXA VFA may be used as a substitute for spine radiography in the identification of symptomatic and asymptomatic VF, provided the evaluator has experience in the assessment of pediatric VF.

Following VFA, additional spine imaging should be considered in the following circumstances:

a. Vertebrae that are technically unevaluable by VFA (i.e. not sufficiently visible), provided the detection of a VF would change clinical management.
b. Assessment of a single, Genant Grade 1 VF, if confirmation of a Grade 1 VF alone would change clinical management.

c. Radiographic findings that are not typical for an osteoporotic VF (e.g. suspected destructive inflammatory or malignant processes, congenital malformations, acquired misalignments, or dislocations).

The Genant semi-quantitative method should be used for VFA in children.

The characteristics of each measurement parameter are summarised in the adjoining table.

Utility	Rationale	Adequate Reference data?	Precision	Future fracture prediction or other proxy outomes?	Can be used in all children or restricted to special groups?	Future Directions
DXA Forearm Measurements	Most common site of fracture in children. Also those who cannot be scanned at standard sites this is a useful site	Available. BMDCS reference data are accompanied by a method that allows for size adjustment of BMC and aBMD Z scores by height Z score	Reasonable for clinical use	Not known	Conflicting results. may be measured under circumstances when other skeletal sites cannot be measured safely, accurately, or without artifact interference	Studies needed on reference data<5y, predicting fractures, monitoring bone accrual, response to medical interventions
Proximal Femur Measurements	Clinically significant deficits in weight-bearing bones may be masked by normal upper extremity bone mass while reposting total body Z score.	Available	Few studies. But reported to be similar to those of spine and total hip.	Hip fractures rare in children hence association is difficult to assess.	May yield additional clinical relevant information.	Studies are Needed to predict future fracture risk.
LDF Measurements	Easily accessible, weight bearing site, clinically relevant fracture site	Available	Precision is 3% better for aBMD than BMC	aBMD has utility to monitor the effects of disease or treatment	Can be used both in healthy and disease affecting skeletal morphometry	Improvement in reference data needed. Longitudinal studies needed in healthy children. Larger studies for needed for prediction in diseased children

Utility	Rationale	Can be used as a substitute for Spine radiography	If abnormal when to repeat	VFA Method That Should be Used to Detect an Osteoporotic VF?	Technical and Biological Factors Limiting Accuracy?	Future Directions
VFA	High-risk pediatric populations have high risk of low trauma VFs. Pediatric VFs are frequently asymptomatic.	VFA assessments by expert readers is important	Incident Genant Grade 1 VF in patients with minimal or equivocal risk factors for osteoporotic VF and without previous fractures, needs follow-up radiology	Genant semi-quantitative method	Co-operation needed for minimize motion artifact. Technical factors has not been evaluated in different models and manufacturers	Research needed fo rhte spectrum of diseases that will be benefitted from routine use and monitoring use. Utility of VFA is not well known.

MINI-REVIEW

Type 2 Diabetes Mellitus in Children and Adolescents

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Definition

It is a heterogeneous syndrome of hyperglycemia caused by progressive insulin resistance, characterized by inadequate supply of insulin than demand (relative deficiency). It progresses from impaired glucose tolerance (IGT) to impaired fasting glycemia (IFG), before reaching the stage of T2DM. However, most patients are diagnosed at the stage of diabetes.

Prevalence and Incidence of T2DM

The prevalence of T2DM has been increasing world over for the last few decades. The exact numbers of T2DM in children and adolescent are not available as per IDF 2017. Although population-based surveys/data is not available from India, the incidence of T2DM in children has been increasing, as per small clinic-based data from different parts of India. It has been attributed to lifestyle changes and the obesity epidemic amongst children and youth. One of the earlier reports (2003) of T2DM came from South India of 18 children with slowly progressive diabetes with preserved C-peptide, negative GAD antibodies and response to metformin. Contribution of T2DM among children and youth has been reported to be 10-20% from tertiary referral centres in India. It is less than many Asian countries (Hong Kong, Japan) where T2DM comprises more than half of children and adolescents with diabetes. As per the SEARCH study in USA, the proportion of T2DM among youth with diabetes (10-19 years) varies from 6% to 76% among various ethnic groups, with the highest prevalence in Native American Indians.

Etiology and risk factors for T2DM

No specific etiological mechanism is elucidated for T2DM, but there is no immune-mediated beta cell destruction as seen in T1DM.

Risk factors for T2DM

1. Epigenetic mechanisms are known to play an important role in the development of T2DM. There is increased risk of T2DM among babies born with LBW and IUGR. Also, LBW "Thrifty Phenotype" is a risk factor, as suggested by the Barker Hypothesis.
2. Genetic risk – the genetic component in causation is suggested by family history of T2DM in 80-90% patients. Further, it has been seen that there is 60-90% concordance among identical twins. GWAS studies have shown that <20% of cases have specific genetic defects to account for T2DM. Common genetic defects identified by these GWAS studies to cause T2DM are Transcription factor 7 like-2 gene (TCF7L2), PPARG and KCNJ11.
3. Race/Ethnicity is identified as a major risk factor, with Asians, Native Americans, African-Americans known to have the highest risk for development of T2DM.
4. Family history of T2DM and GDM in the mother

5. Environmental risk factors
6. Obesity
7. Maternal smoking
8. Smoking in the Adolescents
9. Sleep deprivation
10. Psychosocial stress.

Problems in differentiating T1DM versus T2DM in Adolescents

1. Autoimmune markers for T1D may be positive in 1/3 of adolescents with T2DM.
2. In the present obesity epidemic, a significant proportion of children/ adolescents with T1DM may have obesity (population prevalence), leading to suspicion of T2DM.
3. DKA can occur even in T2DM, though rarely, due to severe infection, etc.
4. Some children with slowly progressive T1DM may be mislabelled as T2DM.
5. Prolonged remission in T1DM may be labelled as T2DM.
6. There is considerable overlap in insulin or C-peptide measurements between T1DM and T2DM at onset of diabetes and over the first year. Reasons are the honeymoon phase in T1DM, and glucotoxicity/ lipotoxicity on beta cells in T2DM. A cut-off of fasting C-peptide value of 0.8-0.9 ng/ml has been suggested to differentiate between T1DM and T2DM.

T2DM: Children versus Adults

Adults with symptoms of diabetes have 50% reduction in insulin secretion at the time of diagnosis, and may become insulin dependent within a few years. However, adolescents have nearly 85% reduction in insulin secretion, and require insulin earlier, with greater chances of complications, starting with shorter duration of T2DM, compared to adult onset T2DM.

T2DM versus T1DM in Children

1. Diabetes and obesity related comorbidities are more in T2DM at onset/ diagnosis and progress more rapidly. The majority of children with T1DM are below average weight and BMI. Obesity may be seen in T1DM with population prevalence.
2. Autoantibodies against the pancreatic antigens are seen in 10-20% children with T2DM versus 80-90% in T1DM.
3. The median age of onset of T2DM in children/adolescents is 13.5 years (median age of puberty) and 1 year later in boys. The median age of onset of T1DM is 7-8 years.
4. There are variable characteristics of T2DM among adolescents in different countries/ ethnicities. Nearly half of South Asian urban children with T2DM have normal weight (<120% ideal for height).
5. The proportion of T2DM among 10 to 19-year-olds vary greatly by ethnicity.
6. Youth onset T2DM has a male: female sex ratio that varies from 1:4 to 1:6 in native North Americans to 1:1 in Asians and Libyan Arabs. In some reports from China, the prevalence of T2DM in males is higher than in females.
7. In countries like China and India, more affluent children are more likely to develop T2DM. It is otherwise in the developed world, where poor and marginalised communities have more chances of developing T2DM.

Autoimmune T2DM
A phenomenon of autoimmune T2DM has been proposed. This is also sometimes referred to as T1.5DM, T3DM, or double diabetes. The phenotype of antibody-positive form of T2DM in youth has less overweight, lower BP, lower triglycerides, higher HDL-C, less likely to be female, and more likely to be nonminority than otherwise similar antibody-negative patients, with more rapid development of insulin dependence.

Clinical Features of T2DM children and adolescents
Almost all of the cases of T2DM diagnosed in children/ adolescents are between 12-19 years (median age 13.5y i.e. median age of puberty and 1y later in boys). The incidence of T2DM increases with increasing age. The majority (~ 50%) of adolescents are asymptomatic, and diagnosed on routine screening. Among those with symptoms, the majority (~50%) have mild polyuria/ polydipsia, and nearly 10% may have DKA at presentation. Family history of T2DM is present in >95% of children diagnosed with T2DM. On examination, most will have obesity, increased BP, acanthosis nigricans, striae and increased waist to hip ratio.

Diagnosis of T2DM
Diagnosis of IGT, IFG or DM can be made based on fasting plasma glucose (FPG), or 2-hour glucose concentration during an oral glucose tolerance test (OGTT) or hemoglobin A1c (HbA1c: normal is 5.7%-6.4% (40-46 mmol/mol)), using the ADA criteria below.

- **Impaired Fasting Glycaemia (IFG)**: FPG ≥5.6 to 6.9 mmol/L (≥100-125 mg/dL)
- **Impaired Glucose Tolerance (IGT)**: Post-challenge plasma glucose ≥7.8 to 11.1 mmol/L (≥140-199 mg/dL)
- **DM:** FPG> 6.9 mmol/L (>125 mg/dL); 2 hour post glucose challenge plasma glucose of >11.1 mmol (>200 mg/dl) OR a random plasma glucose >200mg/dl with osmotic symptoms.

In the absence of symptoms, testing should be confirmed with a repeat test on a different day. Clinicians should be aware of the limitations of each diagnostic test, especially in children. The various diagnostic cut-offs of blood sugars and HbA1c are not validated in children and are extrapolated from adult studies. IFG and IGT constitute pre-diabetes - about 40% adolescents with pre-diabetes go on to develop T2DM over the next 5-10y. The more the HbA1c in the range 5.7-6.5%, the more the chances of progression to T2DM.

Criteria for Screening for T2DM in children and adolescents
Overweight (body mass index >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height)

Plus

Any 2 of the following risk factors:

a. Family history of T2DM in a first or second degree relative
b. Race/ ethnicity (Native American, African-American, Hispanic, **Asian**, Pacific Islander)
c. Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome).

How and when to screen?

The age of initiation for screening is 10y, or at onset of puberty if puberty occurs at a younger age. Screening should be performed every 2y. FPG is preferred over HbA1c in children. OGTT should be performed if the FPG is borderline.

Treatment of youth onset T2DM

Management of T2DM in children is different from T1DM, due to the following patient-related factors specific to T2DM:

1. Older age at diagnosis.
2. Socio-economic status (usually lower in West and higher in developing world).
3. More family experience: there is almost always family history of T2DM.
4. Co-morbidities and complications at diagnosis are common.
5. Lifestyle education is more important.
6. The chances of hypoglycemia are low, so the target range of HbA1c advised is lower.

Objectives and goals of treatment

1. Education for diabetes self-management
2. Normalization of glycemia while minimizing hypoglycemia
3. Weight loss
4. Reduction in carbohydrate and total calorie intake
5. Increase in physical activity and exercise capacity
6. Control of comorbidities and complications, including hypertension, dyslipidemia, nephropathy, sleep disorders, and hepatic steatosis.

Components of treatment

1. Diet: Medical Nutrition therapy
2. Exercise
3. Family lifestyle modification
4. Drugs (Oral)
5. Insulin
6. Complications & Screening for them

Medical Nutrition Therapy

It is different from diet management for T1DM, and has to be tailored to individual needs. It should mainly focus on removing all simple sugars, sugary drinks, junk food, with restriction of calories, portion control, ensuring adequate protein intake, avoidance of eating out, encouraging home cooked foods, eating more fruits and vegetables and whole grain cereals, etc. The whole family approach is more likely to be successful.

Exercise

A minimum of 60 minutes of moderate to intensive exercise daily is recommended, which could be completed even in parts. Reduction in screen time is critical to achieve this goal. Again, a whole family approach is more likely to be successful.

Drug therapy

In contrast to a variety of groups of drugs available for adults, so far only two drugs were approved for use in adolescents i.e. metformin and insulin. On 17 June 2019, US FDA also approved liraglutide (GLP-1 analog) for use in children above 10y with T2DM. The ADA

now recommends that if glycemic targets are not met with metformin ± basal insulin, liraglutide should be considered in children 10y or older, if there is no history or family history of medullary thyroid carcinoma or MEN2.

Several Phase 2 and 3 trials are being conducted in adolescents for other oral drugs, including SGLT2 inhibitors.

The main goals of drug therapy are to improve glycemia, prevent metabolic decompensation, improve insulin sensitivity, prevent acute and chronic complications, improve endogenous insulin secretion if possible, restore glucagon and incretin physiology, and provide exogenous insulin as and when required.

Initial therapy

There is no role of only lifestyle management (LSM) for youth with new onset T2DM. If the patient is asymptomatic, has no ketosis, and A1c is ≤ 8.5%, metformin should be started along with LSM. The dose has to be slowly built up, starting with 500 mg once to twice daily, and increased 1-2 weekly to a maximum of 2500 mg/ day over 4-6 weeks, with titration as per sugar records. Some children may report GI intolerance with high doses of metformin at the outset.

In children with ketosis/ ketonuria/ ketoacidosis or A1c > 8.5%, insulin must be started at the outset. Once-a-day basal insulin (starting dose 0.25-0.5 U/kg/day) is recommended to attain metabolic control, adding metformin once ketosis has settled. Shifting to metformin alone can usually be achieved over 2-6 weeks by decreasing the insulin dose by 30-50% each time the metformin dose is increased, if glycemic control is maintained. In the majority of children started on insulin at the onset, it can be weaned off and shifted to metformin alone, by 3-6 months of diagnosis.

Subsequent therapy

The glycemic target should be A1c of <7.0%. If control is not achieved within 4 months of reaching the maximum dose of metformin, basal insulin should be added. If A1c of <7% is not achieved even on basal insulin of 1.5 U/kg/day, liraglutide should be added. Bolus/ prandial insulin should be added to this regimen if glycemic control is still not attained. Other OHAs are not yet approved for use in children below 18y.

Drugs for T2DM in children and Adolescents

a) Metformin

Dose: 1500-2500 mg/day in 2-3 divided doses

Mechanism of Action: Increases insulin sensitization through AMP kinase activity in liver, muscle, and fat.

Salient features: There is no significant risk of hypoglycemia with metformin monotherapy. GI intolerance in the form of transient abdominal pain, diarrhea and nausea is the commonest side effect, and can be ameliorated by taking it with food. It should be avoided during GI illnesses. It should not be given to patients in ketoacidosis, with renal impairment, cardiac or respiratory insufficiency.

Periodic monitoring of vitamin B12 should be considered, as B12 deficiency has been reported with metformin.

b) Glucagon-like peptide 1 (GLP-1) analogs

Liraglutide, a GLP-1 analog, has been recently approved by FDA for use in children above 10y not well controlled on metformin and basal insulin. Unfortunately, it is also an injectable drug given 1-2 times/day. GLP analogs stimulate insulin secretion and inhibits glucagon secretion, thereby lowering blood sugar.

c) Other drugs

Drugs which could be useful but are not approved in adolescents below 18y due to lack of safety and efficacy data, are listed in the Table below.

Monitoring and follow-up for glycemic control

During the initial phase of drug therapy to achieve target glycemia, self-monitoring of blood glucose (SMBG) may be required frequently, with fasting and prandial sugars done a few times every week. The frequency of SMBG may be individualised, based on fluctuations of blood sugars, patient motivation, financial condition etc. On a long-term basis, higher frequency of blood sugar testing is needed on regimens including insulin, and during acute illnesses. HbA1C should be performed every 3-6 months.

Table: List of potential useful drugs for children and adolescents with T2DM

Drug group	**Mechanism of action**	**Name**
Sulfonylureas	Promote insulin secretion binding to K/ATP channels on beta cell membrane	Chlorpropamide Tolbutamide Glipizide Glyburide Glimepiride
Glitinides	Promote insulin secretion binding to K/ATP channels on beta cell membrane	Repaglinide Nateglinide
α-Glucosidase inhibitors	Slow hydrolysis and absorption of complex carbohydrates	Acarbose Miglitol
Thiazolidinediones	Peripheral insulin sensitizers	Rosiglitazone Pioglitazone
Sodium-Glucose Co-transporter 2 (SGLT2) inhibitors	Inhibition of renal glucose reabsorption, causing renal glycosuria	Canagliflozin Dapagliflozin Empagliflozin
Gliptins	DPPV-4 inhibitors	Sitagliptin Linagliptin Saxagliptin

Monitoring and screening for co-morbidities and complications

Youth with T2DM are at high risk for co-morbidities and complications even at diagnosis, therefore they should be screened for the following at diagnosis, and at least annually thereafter, and adequately treated where needed:

1. Obesity
2. Hypertension
3. Nephropathy
4. Dyslipidemia
5. Atherosclerosis and vascular dysfunction
6. Polycystic ovary syndrome (PCOS)
7. Non-alcoholic fatty liver disease
8. Obstructive sleep apnea
9. Depression, anxiety, eating disorders, cognition.

Suggested Reading

1. American Diabetes Association. 13. Children and adolescents: Standards of Medical Care in Diabetes 2019. Diabetes Care 2019;42(Suppl. 1):S148–S164
2. Youth-Onset Type 2 Diabetes Consensus Report: Current Status, Challenges, and Priorities Diabetes Care 2016;39:1635–1642 | DOI: 10.2337/dc16-1066
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Case Report

Infantile Cushing Syndrome and Hypothyroidism in a case of McCune Albright Syndrome.

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BACKGROUND:

McCune Albright syndrome (MAS) is a rare disease resulting from somatic mutation of *GNAS* gene, with an estimated prevalence between 1/ 1000000 and 1/100000. The classic triad of MAS includes precocious puberty (PP), fibrous dysplasia (FD) of bone, and cafe´-au-lait spots (CALS). The nonendocrine manifestations include renal phosphate wasting, hepatobiliary dysfunction, and heart disease. Hyperfunctioning endocrinopathies include GnRH-independent precocious puberty (GIPP), hyperthyroidism, GH excess, hyperprolactinemia, and hypercortisolism [1]. As FD is the most frequent component of MAS, a broader definition than the triad will be clinically more relevant. Hence, MAS may be defined as FD plus any one of the typical hyperfunctioning endocrinopathies and/or CALS, with almost any combination being possible.

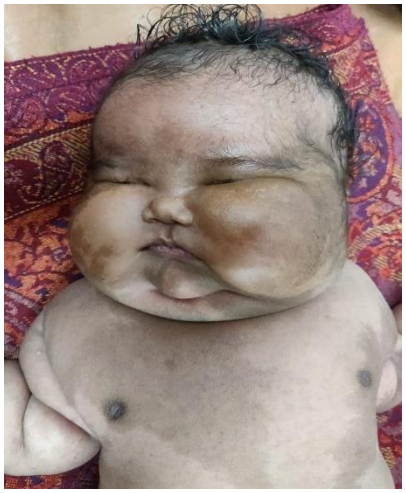
Most of the cases of MAS reported worldwide are associated with hyperthyroidism [2].

Here, we report a case of MAS with Cushing syndrome (CS) and central hypothyroidism.

CASE PRESENTATION:

A 3-month-old female infant presented with weight gain for the last 2 months. The baby was vaginally delivered with birth weight of 2.6 kg at term, and exclusively breastfed since

birth. She was not receiving any systemic or topical medications. Mother had noticed hyperpigmented patches all over her body from 1 month of age, which were not seen earlier. The child had weight of 4 kg, length of 47 cm, and head circumference of 33.5 cm. Child had moon facies, facial plethora, hypertrichosis and CALS characteristic of MAS (the coast-of-Maine-like-borders) (figure 1: Cushingoid facies, hypertrichosis and Café-au-lait spots with irregular margins).



Laboratory investigations are summarised in table 1.

	Observed value	Reference range
Serum free tri-iodothyronine (pg/mL)	0.26	1.95-6.04
Serum free thyroxine (ng/dL)	0.09	0.89-2.2
Serum TSH (µIU/ml)	0.253	0.72- 11.0
¶ Serum 8:00 am cortisol (µg/dL)	22.4	5-25
Serum evening cortisol (µg/dL)	26.2	< 50% of ¶
Overnight dexamethasone (15 µg/kg) suppressed serum cortisol (µg/dL)	21.6	< 1.8
Plasma 8:00 am adrenocorticotropic hormone (pg/ml)	< 5	< 5 indicates ACTH independent CS
Serum ionic calcium (mmol/L)	1.3	1.3-1.5
Serum phosphorus (mg/dl)	4.8	4.3-5.4
Serum alanine transaminase (U/L)	225	< 22
Serum sodium (mmol/L)	137	135-145
Serum potassium (mmol/L)	5.13	3.5-5.5
Serum chloride (mmol/L)	102	

The USG abdomen showed mild diffuse enlargement of both adrenal glands and bulky ovaries with multiple follicles. The 2D Echo revealed ostium secundum atrial septal defect. However, the infant succumbed to severe (suspected pneumocystis *jiroveci*) pneumonia during evaluation.

DISCUSSION:

CS in MAS most commonly manifests during infancy. It can present as early as the neonatal period, but has not been reported after the first year. CS occurs in up to 7.1% of MAS patients [3]. Hypercortisolism may be the first recognized manifestation of MAS in some cases (often appearing before the development of the CALS). Hence, MAS should be suspected in all infants with ACTH independent endogenous CS irrespective of the presence of CALS. In suspected cases, a rapid assessment for hypercortisolism, associated morbidities (hyperglycemia, hypertension and nephrocalcinosis) and MAS-associated significant comorbidities (hyperthyroidism, liver and cardiac diseases) should be performed.

Typical features of CS in MAS infants include moon facies with plethora, hypertrichosis, weight gain and reduced linear growth. However, exceptional cases of MAS with CS may present with no excessive weight gain or even failure to thrive, which may be due to concomitant hyperthyroidism [3]. CS is unique among MAS-related endocrinopathies in its tendency to remit spontaneously. This may reflect the fact that the Gsα-mutation is found within cells in the fetal zone of the adrenal cortex, which undergoes rapid apoptosis in the postnatal period. Hence, these patients are at risk for adrenal insufficiency as the hypercortisolism resolves and should be regularly evaluated for adrenal reserve. However, in few patients with apparent remission there may be continued autonomous cortisol secretion.

Presence of CS in MAS is associated with greater number of MAS-associated endocrinopathies as well as poor prognosis. This may be just a reflection of greater total body burden of Gsα-mutation in MAS patients with CS. Poor outcome in MAS patients with CS is also linked to the presence of comorbid diseases such as liver disease or particularly heart disease. Hence, early adrenalectomy should be considered in CS patients with these comorbidities when medically feasible. Recent studies have reported high incidence of developmental problems among survivors of CS which may be due to exposure to excess glucocorticoid during fetal or early postnatal life or this may also represent mutated Gsα in the central nervous system as part of greater total body mutation burden [3].

Hyperthyroidism (38%) is the most common thyroid dysfunction observed in MAS [4]. Initially MAS patients with hyperthyroidism are often clinically euthyroid despite biochemical derangement (suppressed TSH with raised T3). Later, some may progress to frank hyperthyroidism; hence, their TFT should be regularly monitored. Surprisingly, our patient had central hypothyroidism. To the best of our knowledge, this is the second case of MAS associated with central hypothyroidism. In a previous MAS case (12y old girl) with central hypothyroidism reported from India, it was associated with hypocortisolemia and a pituitary macroadenoma. Central hypothyroidism in this patient was attributed to the compressive effect of pituitary macroadenoma on the normal functioning pituitary tissue [2]. However, the cause of central hypothyroidism in our infant could not be sought as the imaging of the pituitary was not performed.

CONCLUSION:

We report a rare case of MAS associated with Cushing syndrome and central hypothyroidism.

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Pedendoscan

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1 MATERNAL THYROID FUNCTION DURING PREGNANCY AND CHILD BRAIN MORPHOLOGY: A TIME WINDOW-SPECIFIC ANALYSIS OF A PROSPECTIVE COHORT. Toyah A Jansen, Tim I M Korevaar, Tessa A Mulder, Tonya White, Ryan L Muetzel, Robin P Peeters, Henning Tiemeier. **Lancet Diabetes Endocrinol. 2019 Aug;7(8):629-637.**

ABSTRACT: Background: Adequate thyroid hormone availability during pregnancy is necessary for optimal fetal brain development. During the first 18–20 weeks of gestation, fetal thyroid hormone availability largely depends on the placental transfer of maternal thyroxin. Although various studies have shown that maternal thyroid dysfunction is associated with suboptimal child neurodevelopmental outcomes, the most vulnerable time window remains to be identified. The aim of this study is to examine the association of maternal thyroid function with child brain morphology and to study whether any association depends on the timing of thyroid assessment.

Methods: This prospective cohort study was part of the Generation R Study in Rotterdam, Netherlands, with a prospective population-based birth cohort. Pregnant women living in Rotterdam with an expected delivery date between April 1, 2002, and Jan 1, 2006, were eligible. Other inclusion criteria were maternal serum thyroid-stimulating hormone (TSH) and free thyroxine (FT4) measurement in early or mid-pregnancy (≤18 weeks) and available brain MRI data for child at age 10 years. Exclusion criteria were pre-existing thyroid disorder, thyroid disorder treatment, twin pregnancy, in-vitro fertilisation-induced pregnancy, and suboptimal-quality MRI data or major incidental finding on MRI. The main outcome was the association between maternal TSH and FT4 concentrations with brain MRI outcomes of children. Regression analyses accounted for gestational age at blood sampling, maternal age, ethnicity, education level, smoking, thyroid peroxidase antibody positivity, child sex, age at MRI, and total intracranial volume. Effect modification by gestational age at blood sampling was also investigated.

Findings: Between Dec 1, 2001, and June 30, 2005, 7069 women were enrolled during early or mid-pregnancy (≤18 weeks of gestation), of whom 5088 were not included because they did not have available data on maternal serum TSH or FT4 concentrations (n=1175), their child did not have brain MRI done (n=3377), or they met exclusion criteria (n=536). Thus, 1981 mother–child pairs were included in the study, with TSH and FT4 concentrations measured during pregnancy at a median of 13.1 weeks of gestation (IQR 12.1–14.5) and offspring brain morphology assessed by MRI at a median age of 9.9 years (9.7–10.2). Maternal TSH had an inverted U-shaped association with offspring total grey matter volume (p=0·007) and with cortical grey matter volume (p=0·022). The association of maternal TSH with child total grey matter volume (pinteraction=0·053) and cortical volume (pinteraction=0·086) differed by the duration of gestation. Analyses stratified for gestational age at blood sampling showed an inverted U-shaped association of maternal TSH with child total grey matter volume and cortical grey matter volume, which was most evident at 8 weeks gestation. After about 14 weeks of gestation, TSH was no longer associated with child brain morphology. Maternal FT4

concentrations were not associated with child's total grey matter volume after adjusting for total intracranial volume (p=0·75).
Interpretation: Here, we show that both low and high maternal thyroid function are associated with smaller child total grey matter and cortical volume. To the best of our knowledge, this study is the first to show that an association with a neurodevelopmental outcome is most evident when maternal thyroid function is measured early in pregnancy. These novel findings suggest that embryonic brain development is particularly vulnerable to altered maternal thyroid function.
ANALYSIS: Thyroid hormones play a fundamental role in regulating the in-utero neurodevelopmental process which includes the proliferation, migration, and differentiation of neuronal cells that ultimately develop into the grey matter of the brain. Neurogenesis begins at the fifth week of gestation and thyroid hormone receptors are present in the fetal brain from 8 weeks of gestation onwards. The production of fetal thyroid hormone begins around the 14th week, however the fetal thyroid gland is not completely matured until 10-20.5 weeks. Thus, fetal thyroid hormone availability during crucial phases of early brain development predominantly depends on the ***placental transfer of maternal thyroxine*.** This means adequate maternal thyroid function is required for optimal fetal brain development. Cortical and total grey matter volume can be taken as surrogates of fetal brain development. It has been found that the maternal TSH concentrations have an inverted U-shaped association with fetal total grey matter volume and cortical grey matter volume, which means both hyper- and hypothyroxinemia are detrimental to fetal neural development. Furthermore, this association is best evident before 14 weeks gestation, as subsequently the curve flattens, indicating that in the latter half of pregnancy, fetal grey matter volume is independent of maternal thyroid status. Maternal T4 levels did not show any significant association with the grey matter volume of the fetus. Also, there is no statistically significant association between maternal TSH or fT4 and fetal white matter volume. A possible explanation for this is that myelination begins in the latter half of pregnancy, by which time the fetal thyroid glands become functional. It has also been seen that the children's IQ shows a positive association with total grey matter volume. Thus, it can be concluded that both low and high maternal thyroid function are associated with smaller child total grey matter and cortical volume. These novel findings suggest that embryonic brain development is particularly vulnerable to altered maternal thyroid function, and these effects are more evident in early pregnancy, with a suggested effect threshold around the 14th week of pregnancy. Hence, it is important to test the maternal thyroid function either in early pregnancy or even before conception, so as to ensure normal maternal thyroid function in pregnancy.

2. AN ANTI-CD3 ANTIBODY, TEPLIZUMAB, IN RELATIVES AT RISK FOR TYPE 1 DIABETES. Kevan C. Herold, et al., for the Type 1 Diabetes TrialNet Study Group*. **N Engl J Med. 2019 Aug 15;381(7):603-613.**

ABSTRACT: Background: Type 1 diabetes (T1D) is a chronic autoimmune disease that leads to destruction of insulin producing beta cells and dependence on exogenous insulin for survival. Some interventions have delayed the loss of insulin production in patients with T1D, but interventions that might affect clinical progression before diagnosis are needed.
Methods: We conducted a phase 2, randomized, placebo-controlled, double-blind trial of teplizumab (an Fc receptor–nonbinding anti-CD3 monoclonal antibody) involving relatives of patients with T1D who did not have diabetes but were at high risk for development of clinical disease. Patients were randomly assigned to a single 14-day course of teplizumab or placebo, and follow-up for progression to clinical T1D was performed with the use of oral glucose-tolerance tests at 6-month intervals.
Results: A total of 76 participants (55 [72%] of whom were ≤18 years of age) underwent randomization — 44 to the teplizumab group and 32 to the placebo group. The median time to the diagnosis of T1D was 48.4 months in the teplizumab group and 24.4 months in the placebo group; the disease was diagnosed in 19 (43%) of the participants who received teplizumab and in 23 (72%) of those who received placebo. The hazard ratio for the diagnosis of T1D (teplizumab vs. placebo) was 0.41 (95% confidence interval, 0.22 to 0.78; P = 0.006 by adjusted Cox proportional-hazards model).

The annualized rates of diagnosis of diabetes were 14.9% per year in the teplizumab group and 35.9% per year in the placebo group. There were expected adverse events of rash and transient lymphopenia. TIGIT+KLRG1+CD8+ T cells were more common in the teplizumab group than in the placebo group. Among the participants who were HLA-DR3–negative, HLA-DR4– positive, or anti–zinc transporter 8 antibody–negative, fewer participants in the teplizumab group than in the placebo group had diabetes diagnosed.
Conclusion: Teplizumab delayed progression to clinical T1D in high-risk participants.
ANALYSIS: T1D is caused by autoimmune destruction of insulin-producing beta cells**,** and several immune interventions have been tried in the past to delay the decline of beta-cell function mostly in newly diagnosed T1D. These include immunosuppressive drugs like azathioprine, abatacept, cyclosporine and steroids. Though some of these agents had shown promising results in delaying the progression of disease by either decreasing or the insulin requirement or producing significant difference in HbA1c, they had poor risk benefit ratio. Teplizumab studied in trial, is an Fc receptor–nonbinding anti-CD3 monoclonal antibodies. This modifies the action of CD8+ T lymphocytes, which are thought to be the important effector cells that kill beta cells. This placebo controlled multicentric trial studied the ability of Teblizumab to delay the onset of T1D in high risk individuals (relatives of individuals with T1D with an abnormal oral glucose tolerance test and at least two diabetes related autoantibodies positive). They found the hazard ratio of teplizumab vs. placebo to be 0.41, with no major side effect, and postulate that Teplizumab can be a promising drug in the near future for delaying the onset of T1D in high risk persons.

3. **EARLY HIGH-DOSE VITAMIN D3 FOR CRITICALLY ILL, VITAMIN D–DEFICIENT PATIENTS.** The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network*. **N Engl J Med. 2019 Dec 11.** doi: 10.1056/NEJMoa1911124. [Epub ahead of print]

ABSTRACT: Background: Vitamin D deficiency (VDD) is a common, potentially reversible contributor to morbidity and mortality among critically ill patients. The potential benefits of vitamin D supplementation in acute critical illness require further study.
Methods: We conducted a randomized, double-blind, placebo-controlled, phase 3 trial of early vitamin D3 supplementation in critically ill, VDD patients who were at high risk for death. Randomization occurred within 12 hours after the decision to admit the patient to an intensive care unit. Eligible patients received a single enteral dose of 540,000 IU of vitamin D3 or matched placebo. The primary end point was 90-day all-cause, all-location mortality.
Results: A total of 1360 patients were found to be VDD during point-of-care screening and underwent randomization. Of these patients, 1078 had baseline VDD (25-OHD level <20 ng/ mL [50 nmol/L]) confirmed by subsequent testing and were included in the primary analysis population. The mean day 3 level of 25OHD was 23.2 ng/mL (58 nmol/L) in the vitamin D group and 5.6 ng/mL (14 nmol/L) in the placebo group (difference, 35.5 ng/mL; 95% confidence interval [CI], 31.5-39.6). The 90-day mortality was 23.5% in the vitamin D group (125 of 531 patients) and 20.6% in the placebo group (109 of 528 patients) (difference, 2.9 percentage points; 95% CI, −2.1 to 7.9; P = 0.26). There were no clinically important differences between the groups with respect to secondary clinical, physiological, or safety end points. The severity of VDD at baseline did not affect the association between the treatment assignment and mortality.
Conclusions: Early administration of high-dose enteral vitamin D3 did not provide an advantage over placebo with respect to 90-day mortality or other, nonfatal outcomes among critically ill VDD patients.
ANALYSIS: Vitamin D is a potent immunomodulatory agent that is essential for lung development and function. VDD is common among critically ill patients and constitutes a potentially modifiable risk factor associated with longer lengths of stay in the hospital and intensive care unit, lung and other organ injury, prolonged mechanical ventilation, and death. Studies in past have shown that Vitamin D supplementation to VDD, critically ill patients was associated with lower observed mortality than placebo; however, those trials were underpowered for analysis of the mortality end point. This along with meta analyses of several previous trials regarding benefit of vitamin D treatment in critical illness

raised the need for a larger, phase 3 trial to evaluate the effect of short-term vitamin D supplementation on mortality among critically ill patients. This randomized, double-blind, placebo-controlled, phase 3 trial in 1078 critically ill, VDD patients at high risk for death, found no significant difference in 90-day mortality with early D3 supplementation. This trial efficiently enrolled, early during their critical illness, a large, diverse, and representative population of patients. Also, it achieved strong separation between the groups, with rapid correction of VDD. With all these advantages, this study's conclusion that early correction of VDD gives no advantage with respect to mortality or other, nonfatal outcomes, which differs from the previously held belief, is important in clinical practice.

4. PROSPECTIVE EVALUATION OF INSULIN-TO-CARBOHYDRATE RATIO IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES USING MULTIPLE DAILY INJECTION THERAPY. Ahmed M. Hegab, Pediatrics Department, Faculty of Medicine, Sohag University, Egypt. **Pediatr Diabetes. 2019 Dec;20(8):1087-1093.**

ABSTRACT: Aim: Assessment of insulin-to-carbohydrate ratio (ICR) in children and adolescents with type 1 diabetes mellitus (T1DM) using multiple daily injection (MDI) therapy.
Methods: This prospective observational study was conducted over a 2-year period at Sohag University Hospital, Egypt. Children and adolescents aged 4-17y, diagnosed with T1DM for at least 1y, with fasting serum C-peptide levels <0.24 ng/dL and whose parents accepted to shift their management to flexible MDI using carbohydrate counting, were included. Participants were initially hospitalized for estimation of ICR and insulin doses, then followed-up monthly for further adjustments. Insulin doses, ICR, and glycemic control parameters were assessed after 3 months.
Results: The study included 201 participants, 110 (54.7%) males. The median age was 9.5y (interquartile range: 7-12.5y). Bolus insulin requirements estimated by the 500 rule were significantly lower than the actual doses used by the study participants for all meals ($P < .001$). Bolus insulin requirement for morning meal was significantly higher compared to other meals ($P < .001$). Linear regression analyses between ICR for different meals and the reciprocal of total daily dose (TDD) in 96 participants with optimum glycemic control revealed that ICR could be calculated as 301- 309/TDD for morning meal ($R2 = 0.97$, $P < .001$), 317-331/TDD for afternoon meal ($R2= 0.96$, $P < .001$), and 362-376/TDD for evening meal ($R2= 0.98$, $P < .001$).
Conclusions: The ICR for children and adolescents with T1DM using MDI therapy showed diurnal variation with higher bolus insulin requirements for morning meals compared to other meals. Using 301-309/TDD, 317-331/TDD, and 362-376/TDD formulas would be more appropriate than the 500 rule for initial estimation of ICR for morning, afternoon, and evening meals in children.

ANALYSIS: Estimation of the ICR with carbohydrate counting is essential for calculation of bolus insulin doses in T1DM. This gives the flexibility of eating different meal sizes with adjustment of insulin doses according to the carbohydrate content of their meals. This study demonstrated diurnal variation in bolus insulin requirements, with highest bolus needs for the morning meal. This was in line with the findings of the very few previous pediatric studies that reported increased insulin requirements in the morning. The higher morning insulin requirement is explained by the dawn phenomenon, which results from the increase in secretion of growth hormone and other counter-regulatory hormones around 3 am, leading to increased hepatic glucose output and decreased insulin sensitivity, which usually begins around 4 am, peaks at 8-10 am, and subsides by midday. Interestingly, this well-planned and thought-out study with important clinical implications, published in a reputed journal, has only one author.

Events/Activities organised by ISPAE members

Compiled by Nikhil N Lohiya, ESPE Fellow, Alder Hey Children's Hospital, Liverpool, UK.

ENDOCON- Crowne Plaza, Rohini - Dr Richa Arora, Jaipur Golden Hospital, Delhi.

A full day meeting on pediatric endocrinology for general pediatricians was organized in association with North Delhi IAP, on 6 October 2019. It was attended by over 120 pediatricians from Delhi, UP and Haryana. The faculty included Dr Ravindra from Hindu Rao, Dr Rajni Sharma from AIIMS, Dr Vijay Jaiswal from Meerut, Dr Kochar from Apollo and many others from various hospitals of Delhi NCR and UP. There were talks on neonatal endocrinology, diabetes, panel discussion on obesity, short stature, and pubertal disorders. There were three workshops: bone age made easy, growth charts, and insulin pump.

Activities at Sri Ramachandra Medical College and Research Institute, Chennai. Dr Dhivyalakshmi

Type 1 Diabetes Children Meet - On 12th August 2019, for the third consecutive year, a T1D Children's Meet was organized at Sri Ramachandra Medical College and Research Institute, attended by 20 children with their families. Sessions on diabetes education, carb counting, pump and CGMS were conducted, and free glucometer strips, insulin syringes, and pen needles were given to the children who attended the program. Medals were distributed to children with T1D of more than one year duration with HbA1C < 8%. Motivational talks by Mr Gopalakrishnan Damodaran (father of T1D child, from USA) and Mr Prashanth Mani (T1D himself) gave a positive vibration to all our patients, highlighting that the ultimate goal in T1D care is good quality of life.

Growth Symposium and Workshop - A Growth Symposium and Workshop was organised under the auspices of ISPAE, IAP- Chennai City Branch and IAP -Tamil Nadu State Chapter, at Ramada Inn, Chennai, allotted two credit hours by Tamil Nadu Medical Council. The first

session in the morning was an enlightening talk by Dr Vaman Khadilkar on **"Growth Charts in office practice - Concepts and what's new"**, followed by **"Assessment of growth and growth monitoring"** by Dr Dhivyalakshmi. The next session was an energetic presentation by Dr Ahila Ayyavoo on **"Approach to growth failure in a child"**, the highlight of the talk being the clinical pictures and case scenario puzzles which engendered a lot of interaction from the audience. Dr Hemchand Krishna Prasad (Pediatric Endocrinologist, Mehta's Children Hospital, Chennai) delivered a lecture on **"Bone age - what a pediatrician should know":** a mammoth task in simplified way. The last talk of the symposium was on **"Tanner Staging and its importance in growth monitoring and growth velocity in Indian Context"** by Dr Khadilkar. The post lunch **Workshop** had four case scenario based modules. **Under five years** by Dr Dhivyalakshmi, **Physiological and systemic illness** by Dr Rini Shah (Pediatric Endocrinologist, Chettinad Hospital, Chennai), **Bone age** by Dr Hemchand, **Disorders of weight gain** by Dr Karthik Balachandran (Consultant Endocrinologist, SRMC). Around 70 practicing physicians from all over Tamil Nadu attended this unique program conducted at the state level, to highlight the importance of monitoring growth in children. It was well appreciated by all the delegates, who were given a course booklet containing the proceedings.

Multidisciplinary CME on "Bone Health in Children" - This multidisciplinary CME was organized under the auspices of ISPAE on 19 October 2019, involving all specialties dealing with bone (Endocrinology, Nephrology, Neonatology, Orthopedics), awarded two credit hours by Tamil Nadu Medical Council. A competition of case presentations on "Interesting cases of bone pains in children" was conducted. Guest Speaker Prof. Vijaya Sarathi (Dept. of Endocrinology, Narayana Medical College, Nellore) delivered an excellent lecture on DXA

and approach to low bone mass in children. Other talks were given by Dr Dhivyalakshmi on "Vitamin D therapy in children - Myths and Facts", Dr G. Sangeetha (Pediatric Nephrologist, SRMC) on "Renal

Rickets", Dr Giri Raj (Associate Professor, Orthopedics, SRMC) on “Management of CTEV”, with a multidisciplinary panel discussion on "Metabolic bone disorders in children". Around 100 delegates attended the program.

Nurses Education Program on "Pediatric Diabetes" – This program was organized on 30th December 2019 as a full day session with workstations on insulin technique, glucometers and sick child management. Around 50 delegates in and around Chennai attended the program.

World Diabetes Day 2019, PeopleTree Hospitals, Bangalore. Dr Sharmila Nayak

A comprehensive educational program was arranged on the occasion of World Diabetes Day on 14 November 2019 at PeopleTree Hospitals, Yeshwanthpur, Bangalore. The Theme for this year was 'Family and Diabetes'. Talks were given by specialists on various aspects of how to support children with T1D at the family level, at school and the community as a whole. Education sessions on daily management of childhood diabetes were provided, and questions and problems were addressed in detail. There was enthusiastic participation from over 20 children and their parents, including in quiz competitions testing their knowledge of T1D. It was heartening to see young children answer all the questions with great clarity. This was followed by a drawing competition for the children to bring out their artistic abilities, for which prizes were given. The children brought out brilliant messages related to T1D in their drawings. After the program, healthy snacks were thoroughly enjoyed. Overall those who attended enjoyed the learning experiences and found the program useful.

UP PEDICON 2019 Aligarh

UP Pedicon 2019, organized at Aligarh, was attended by about 200 delegates. The program

was inaugurated by **Dr Digant Shastri,** National President IAP, with President-elect **Dr Piyush Gupta,** President UP IAP chapter **Dr Piyali,** and Secretary UP IAP **Dr Sanjeev Kumar.** The pediatric endocrinology session was fairly represented, with allotted time slot of 3 hours for various important topics. Dr Anurag Bajpai spoke on "Obesity, The New age Epidemic"**,** Dr Vijay Jaiswal discussed approach to short stature, Dr Vikas Mehrotra discussed diabetic ketoacidosis, and Dr IPS Kocher spoke on interpretation of thyroid function tests in office practice. In the **Expert Speak** session Dr A Bajpai moderated a session on "Pediatric Endocrinology Potpourri" with panelists Drs Ayesha Ahmad, Ravindra Rajput, Mahesh Maheshwari, and R Ahuja. Another highlight was the release by IAP President Dr Digant Shastri, a special issue of the official magazine of UP IAP on Pediatric Endocrinology (edited by Dr Anurag Bajpai and Dr Vijay Jaiswal).

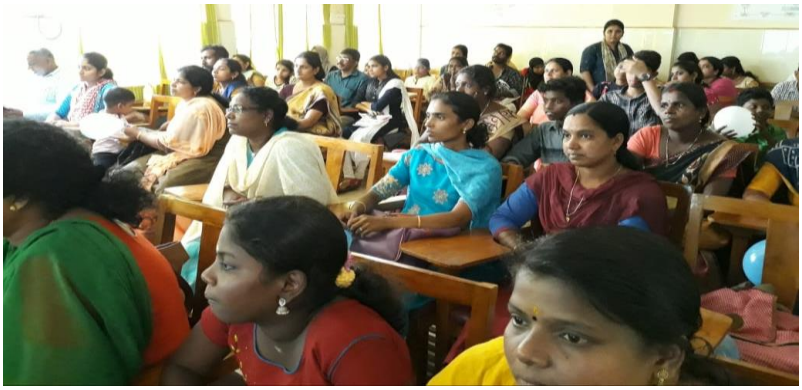
World Diabetes Day Celebration, Dept of Advanced Pediatrics, LLRM Medical College, Meerut. Dr Vijay Jaiswal

World Diabetes Day was celebrated at the auditorium, LLRM Medical College, Meerut, by the Dept. of Pediatrics along with the Depts. of Community Medicine and Internal Medicine on 24 November 2019. It was inaugurated by the honorable Principal Dr RC Gupta, HOD Pediatrics Dr Vijay Jaiswal, and HOD Internal Medicine Dr TVS Arya. This awareness program was attended by faculty and undergraduate students. A Debate was organized among UG students on Diabetes. The vote of thanks given by Dr Jaiswal had a special note to help children living with diabetes.

World Diabetes Day Celebration 2019 at Rainbow Children's Hospital, Bengaluru. Dr Kavitha Bhat.

World Diabetes Day 2019 was celebrated on 14 November, 2019 with full fervor at Rainbow Children's Hospital, Bengaluru, with children with Diabetes Mellitus and their families. There were interesting activities for children like Healthy Recipe Contest, and Talent Show, wherein children took part in poster making, singing, dancing and short speeches. An Interactive Panel Discussion was organized wherein parents and kids expressed the challenges in managing diabetes, and were guided by a panel of experts consisting of endocrinologists, nutritionists and a diabetes nurse educator. A unique Recipe Booklet was launched as an initiative of the Pediatric Diabetes Program. It has standardized recipes with raw and cooked weights and nutritional value, to serve as a ready reckoner for parents and children with diabetes to promote accuracy in carbohydrate counting and awareness on healthy eating. Also, 'Hypo Kit' was demonstrated by the nurse educator, to be used in a hypoglycemia emergency. A beautiful message was given in the event, stressing the importance of family support in managing diabetes in children. Families were motivated to handle the child's diabetes with confidence and create a positive atmosphere for the child to grow as a confident adult.

World Diabetes Day 2019 Celebrations, Govt Medical College, Thrissur, Kerala. Dr Deepa Anirudhan



WDD 2019 was celebrated at Govt Medical College, Thrissur, on 14 Nov 2019, inaugurated by HOD Dr Purushothaman, and attended by 63 children with T1d and their parents. A session on "Diet in diabetes" was taken by Dr Rose Mary, Senior Resident. After a painting competition for the children, a yoga session was conducted by Nandana, a patient with diabetes. There was a variety entertainment program by the children. Dr Keerthy, a PG student, conducted a quiz for children and their parents. Prizes were given to the winners.

SWEET CHILDREN MEET, Radhakishan Hospital, Kurukshetra (Haryana). Dr Mudita Dhingra

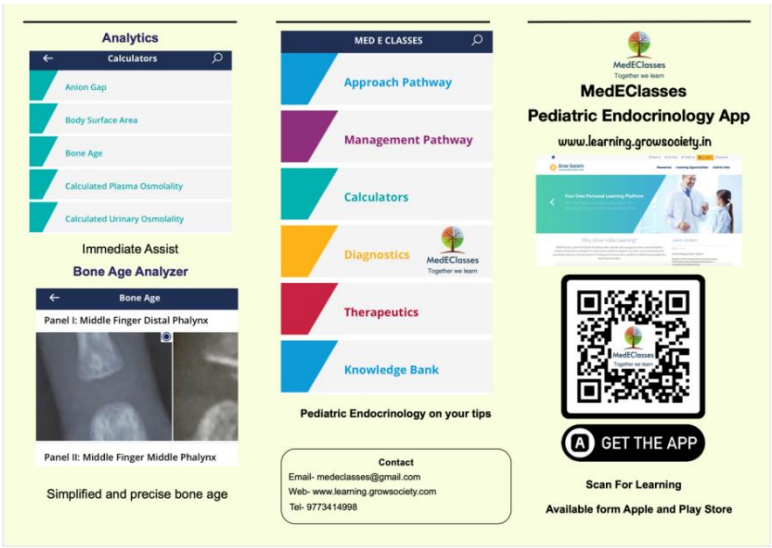
A "Sweet Children Meet" organised by the Division of Pediatric Endocrinology, Radhakishan Hospital, Kurukshetra, for children with T1D and their families on 16 Nov 2019, was attended

by 20 children and families. They were taught the basics of blood glucose monitoring, insulin therapy, dose adjustment and sick day management by Dr Mudita. They were also made aware of insulin pumps and recent advances in the technology of diabetes management. The nutritionist sensitized them about carbohydrate counting and distributed 5 healthy recipes; the child counselor and psychologist enlightened them on "Strong mind = Stable Blood Glucose" and discussed various psychological stress issues which the children and their families deal with on a day to day basis. It was an interactive session. Free blood glucose testing was done for all children before serving the evening snack. A poster competition was also held, won by 12y old Tanisha from Karnal (Haryana). All children were distributed plants in the end as a token of appreciation and motivated for better health and sustainable environment in the future.

World Diabetes Day, Kanpur. Dr Anurag Bajpai.

The Xth Grow India World Diabetes Day Program provided an opportunity to interact with over 100 children with diabetes and their families. The key highlights of the program included an awareness program, diabetes complication camp quiz and wonderful dances by children. The Grow India Interschool skit competition witnessed inspirational plays by school children on T1D.

MedEClasses Mobile Application – This mobile app provides 360-degree clinical assist in assessment and management of Pediatric Endocrine Disorders. The app uses a novel approach and management pathways to allow real-time decision making. It provides validated analytics with reliable estimates of bone age and growth inter-pretation; and management guides for treatment of diabetic ketoacidosis and electrolyte disorders, supplemented by exhaustive clinical resources related to diagnostics and therapeutics of pediatric endo-crine disorders. The application is recommended for Pediatricians, Intensivists, Pediatric Endocrinologists and Endocrinologists. The application is available at iOS and Play stores and can be accessed at https://learning.growsociety.in/mobile-app.



"Eat Right, Be Bright, Stay Fit" - World Diabetes Day, Children's Day, IAP Child & Adolescent Health Care Week - Samrat Endocrine Institute of Diabetes, Obesity & Thyroid, Aurangabad. Dr Hemant Phatale & Dr Priti Phatale

Taking into consideration the rising trends of non-communicable diseases (NCDs) and their comorbidities, Samrat Endocrine Institute of Diabetes, Obesity and Thyroid in association with Aurangabad Academy of Pediatrics organised an activity keeping in mind that 1. Children are the future of our nation. 2. It is important to befriend teens for a better tomorrow. 3. Awareness about healthy lifestyle is the key for healthy adulthood. The activity started with interaction with secondary school students, seeking their views about healthy lifestyle and its benefits, the role and responsibilities of children in the family as well as in the development of the Nation. It was followed by a PowerPoint presentation on the theme by Dr Priti Phatale (childhood obesity specialist). The School Principal, teachers, school authorities and about 200 children were motivated by this session. Drs Hemant and Priti Phatale felt that a milestone of enrolment of a school in preventing the rising burden of NCDs was achieved.

World Diabetes Day 2019 - Department of Endocrinology, Diabetes & Metabolism, Narayana Hrudhalaya Hospitals. Dr Subramanian Kannan

The Department of Endocrinology, under Dr. Subramanian Kannan conducted its annual event marking WDD. The day started with a pledge to stay healthy and a 5K run for all hospital employ-ees, followed by a small CME session for house-staff and doctors on practical management of diabetes. About 45 children with T1D assembled at the Dept of Endocrinology and began their day with painting/ coloring on chart paper within a Blue Circle given to them, on the theme of "What Diabetes means to You". Dr Prasanna and Ms Manjula from Pediatric

Psychiatry/ Psychology services had a Q&A session with the parents and children about common conflicts at home between parents and children and how to handle them. The Diabetes Educators and nurses performed skits showcasing common mistakes/ mischiefs done by children and their parents and how to rectify them. Then the stage was set for a cultural program, where the children rocked, with dances and songs from latest Kollywood/ Tollywood numbers. Prizes were given to the best painting in various age groups, and for the cultural event, by the department faculty including Dr Shivaprasad KS, Dr Kranti Khadilkar, and Dr Basavaraj. School bags and Hypokits (Glucagon injection) were given to all children. The day concluded with a workshop for nurses and nurse educators on insulin techniques, hypoglycemia management, sick day rules and basics of dietary instructions for diabetes.

World Diabetes Day – Dept. of Pediatric Endocrinology, Indira Gandhi Institute of Child Health, Bengaluru. 23 November 2019.

A comprehensive educational program arranged along with observance of WDD, was

conducted in the spacious auditorium of IGICH, as an annual event on 23 November. There was enthusiastic participation from the children and their parents this year – **165 children** with diabetes attended the function. Professor P Raghupathy, with his team of doctors (Drs Vani, Namratha, Avani Hegde, Nabanita, Pooja, Soujanya, Shruti Appaji), dietitian (Ms Rachitha), nurses (Ms Neelamma and others) and volunteers (Ms Jamuna and others) from the Institute helped in conducting the program, which was well received by the children and their parents. In keeping with this year's theme of **Family & Diabetes**, parents and children were provided educational sessions in daily management of diabetes, and their questions and problems regarding low or high blood sugar values, sick day management, insulin action and adjustment of daily dose, self-monitoring of blood glucose at home, etc. addressed in detail. News about recent advances in diabetes was also discussed. Nutritious, healthy, well-balanced meal planning and carbohydrate counting was discussed by Ms Rachitha.

To make the occasion more memorable and lively, a drawing/painting competition and a diabetes quiz were held. The children and parents took active part and bagged prizes. They participated enthusiastically in singing and dancing too. Their talent was amazing. Entertainment was also provided by an NGO called **Little Dreams**, in the form of a magic show. This was a great hit with the younger children, who enjoyed it thoroughly with very active participation. All those who attended the function benefited from the learning experiences, while also relishing the opportunity to participate in singing, dancing, narration of stories, etc. The free 2-monthly regular supplies of insulins, syringes, glucostrips, lancets etc. were distributed as usual to all the children who attended.

Such annual events have helped the children to develop self-confidence in managing their diabetes; to be independent; complemented by help and support from their parents and family members. The function was held under the auspices of ISPAE and Growth Hormone Research Society, and supported by the CDiC program of Novo Nordisk Education Fund.

Childhood Diabetes Education Day. Dept of Pediatrics PGIMER, Chandigarh. Prof Devi Dayal, Prof Rakesh Kumar, Dr Jaivinder Yadav.

We organized a T1D Education Day for children and their caregivers to commemorate WDD on 14 Nov. Nearly 50 families with T1DM children attended the half-day education program. Prof Anil Bhansali graced the occasion as the Chief Guest. He shared his experience of nearly 40 years in managing patients with diabetes. The main topics covered were the importance and ways of managing diabetes at school, dietary management, and practical skills required for day-to-day management of T1DM. Representatives of six major pharma companies marketing T1D related medicines and equipment, discussed the services from their company for these children. Three adults with T1DM from early childhood shared their personal experiences and shared tips and tricks to improve sugar control. This was very heart warming and motivating for younger children and their parents.

The parents of children with T1DM taking treatment at Pediatrics dept. at PGIMER have registered a Society called ***A***ssociation for ***C***hildren with ***T***ype 1 diabetes (ACT for Diabetes). The Secretary of the Association, Mr Eish Bajaj, shared the main objectives of the ACT Society.

Support group for children and families with T1D. Dr Meena Kumari Mohan, Pediatric Endocrinologist, PSG Super Speciality Hospital, Peelamedu, Coimbatore.

A support group session was conducted for children and families with T1D at the Hospital Auditorium, PSG Super Speciality Hospital, Coimbatore. The emphasis was on exercise and extracurricular activities. Children had a session of yoga to kick off the day. Then they were given the option to perform on stage various extracurricular activities like dance, karate, singing, etc., to exhibit their talents. Both parents and children were encouraged to explain how easy/ hard it was to get on with life, to fit in exercise/ extracurricular activities, along with managing diabetes on an ongoing basis. A session on managing carb counting and exercise was well received. Diabetes educators were present and facilitated the sessions. About 40 children along with their parents attended the event. A total 130 people were benefitted from the day's happenings.

Yog Dhyan Foundation (YDF), Delhi. Anju Virmani, Senior Consultant Pediatric Endocrinologist, Max, Pentamed & Rainbow Hospital, Delhi

YDF has completed 10y of helping children and families with T1D who are not well off, providing free glucometers,glucostrips, diabetes education, subsidized lab tests, annual eye checks, financial support and Yoga classes, along with crucial psychological support. Starting with 2 children, they are now a thriving community of over 250 T1Ds, volunteers, physicians and paramedics. They have just launched a **10th Anniversary Special Newsletter** "**Thrive**", which will now be brought out every 6 months to showcase their achievements. This year, apart from weekly yoga classes, ongoing and special sessions for diabetes education (lipohypertrophy, healthy eating, safe disposal of sharps, dose adjustments), they organized a showing of the movie "**Mission Mangal**" followed by lunch, celebrated **International Yoga Day, Diwali, World Diabetes Day**, and now **Christmas**. They gave awards to "**Stars of the Quarter**" (those with A1c < 7.5% without much hypos), and to those who got married. YDF

collaborated with **Diabetes Fighters Trust** to provide Frio wallets, organized a diabetes awareness program at 10 Metro stations from 11-20 November with **Delhi Metro Rail Corporation**; and a National public program "**Act Now for Diabetes Rights**" on 26 November. YDF children have won **prizes** at an awareness quiz at AIIMS, and in a Sports Camp on November 3 at Jawaharlal Nehru Stadium, Delhi. Young T1D volunteers have represented YDF at the **World Diabetes Congress 2019** in Jaipur, and the **International Diabetes Conference** organized by Diacon at Ahmedabad. On 22 December, at a Christmas get-together, the **newsletter "Thrive"** was launched by Santa Claus, as a **10th year Anniversary Special.** Children enjoyed gifts and brought their own lunch boxes with them, with a session on how to have balanced meals and count carbs, while emphasizing the need for calculating and taking the pre-lunch insulin dose. Their latest and very heartening program is launching a **Parents Volunteer Group** of 10-20 parents, who have started helping poor, illiterate and recalcitrant parents to learn numeracy, basic Hindi and basics of diabetes, so they can improve management of their children's diabetes.

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2. Kumar R. Continuous vs. Intermittent Insulin Delivery in Children and Adolescents with Type 1 Diabetes Mellitus: Pediatric Endocrinologist's Viewpoint. Indian Pediatr. 2019 Jul 15;56(7):599-601. PubMed PMID: 31333216.

Awards and Fellowships

Dr GD Ramchandani (Sr. Physician & Consultant Diabetologist, Ramchandani Diabetes Care & Research Center (RDCRC); Professor & Head, Dept. of Internal Medicine, Daswani Dental College, Kota) was conferred with Fellowship of RSSDI (**FRSSDI**) at the 47th National Conference at Jaipur in November. He was also conferred with Fellowship of the Royal College of Physicians, Edinburgh (**FRCPE**), Fellowship of the Royal College of Physicians, Glasgow (**FRCPG**), and Fellowship of the American College of Endocrinology (**FACE**) in May 2019. He has also been nominated Member of the American Association of Clinical Endocrinologists (AACE) International Committee and Disease State Network for 2019-2020. He was awarded **Mentors' Certificate in Diabetes** at the DiaMet Summit in the Ireland-India Metabolic Medicine Summit 2019 organized by UCD Conway Institute, University College Dublin – Diabetes Complication Research Center (UCD-DCRC) School of Medicine at Dublin, Ireland on 19th July 2019. The RDCRC has been approved as an International Diabetes Federation – **IDF Center of Education** (valid until September 2020).

Dr Deep Dutta from Center for Endocrinology, Diabetes, Arthritis & Rheumatism Superspecialty Clinics, Sector-13, Dwarka, New Delhi, was awarded the Fellowship of Royal College of Physicians (FRCP) at the annual convocation held at the Royal College at Edinburgh, Scotland UK on 8th Nov 2019.

ISPAE 2019 Awards

Oral Papers: 1st - Dr Riddhi Patel, Regency CDER, Kanpur
2nd - Dr Rajni Sharma, AIIMS, New Delhi
3rd - Dr Rakesh Kumar, PGIMER, Chandigarh

E Poster Award: Day 1- Dr Sophie Karika, CMC Vellore
Day 2- Dr Kriti Joshi, SGPGI, Lucknow

Poster Award: Dr Riddhi Patel, Regency CDER, Kanpur;
Dr Hemang Mendapara, Regency CDER, Kanpur

Upcoming important Conferences

1. **PEDICON**, 6-9 February 2020, Indore, India.
2. **PES Annual Meeting** 24-27 April 2020, Texas, USA
3. **59th ESPE Meeting**. 10-12 September 2020, Liverpool, UK
4. **46th Annual ISPAD Conference** 14-17 October 2020, Abu Dhabi, UAE.
5. **54th Annual Meeting of the JSPE**. 22-24 October 2020, Yokohama, Japan.
6. **ISPAE-ISPAD Midterm Meeting**, 7-8 November 2020, Chandigarh, India.
7. **11th Biennial Scientific Meeting** of APPES. 18-21 Nov 2020, Kuala Lumpur, Malaysia.

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