JUNE 2023
Volume 27 - Issue 2

CAPE News

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

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Next issue: Puberty and Endocrine Disorders in Systemic/Chronic Diseases

https://ispae.org.in/cape-news/

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EDITOR'S MESSAGE

Dear ISPAE members,

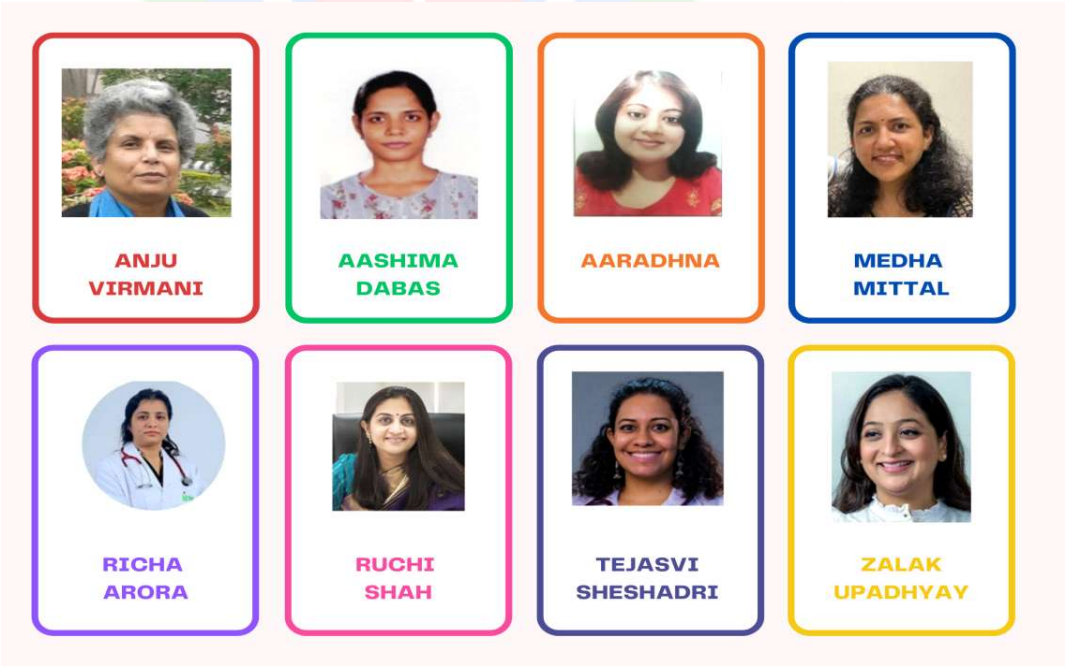
I take this opportunity to present the next edition of CAPE News, themed on thyroid disorders. The Editorial Board has tried to compile an interesting issue, with a minireview on updated Guidelines for Graves disease and Thyroid Hormone Resistance. Dr Theodor Kocher comes 'alive' through a breezy History section, and leads us to the future with a newer drugs and AI. The Patient Education section and Pedsendoscan will be useful and informative, as will the learning pearls from the March ISPAE-ACES meeting. Be ready for another challenging Trainees' section this time! Congratulations to the winners of the Trainees' Challenge in the last issue!

It is heartening to compile the case reports, achievements and activities by our members, which display their hard work and momentum to provide better patient care. The IDEAL report proves the advocacy and zeal of ISPAE in handholding healthcare workers and community to improve the quality of life of persons with T1D.The IDEALCore Committee is happy to announce IDEAL batch 6 and BEST batch 5. We eagerly look forward to the upcoming 8th biennial ISPAE Conference at Bengaluru (17-19 Nov 2023) - please do not forget to submit your abstracts soon!

The next CAPE News issue (September 2023) will focus on Puberty and Endocrine disorders in systemic diseases. We anticipate more participation and contributions from our dear members. Let us keep learning and shining!

Best wishes,

Aashima Dabas



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ISPAE Office Bearers

President	Secretary	Jt. Secretary
		
Ahila Ayyavoo	Rakesh Kumar	Sirisha Kusuma

Dear friends,

Greetings!

It's been a busy quarter for ISPAE!

The recent ISPAE Academic and Education Series (ISPAE-ACES) had two interesting lectures on pediatric bone disorders by Prof Zulf Mughal, Manchester, UK and Prof Rajesh Khadgawat, AIIMS, New Delhi, accompanied by two interesting case presentations.

The preparation for the next biennial meeting at Bengaluru from 17th-19th November, 2023 is in full swing. We hope to meet you all there for the fabulously organized academic program. This will be preceded by ISPAE-PET Fellows School from 14th-17th November, 2023 with brilliant faculty from around the world sharing their experience with Fellows.

We have seen several programs, including the IDEAL and BEST courses, continue their successful journeys under the focused organisation of Drs Anju Virmani, Shaila Bhattacharya, Santosh Olety and Team. The awareness about type 1 diabetes and the dedicated care for these children in India have improved over the last few years with these training programs.

Information modules for parents and teachers have been created and uploaded by several dedicated ISPAE members. Kudos for their efforts!

Several other programs are under preparation and would be unveiled soon. These include teaching modules for Pediatricians on common endocrine topics, creation of a type 1 diabetes registry etc.

We are deeply thankful to the CAPE News Team under the stewardship of Dr Aashima Dabas for their untiring efforts to make the current version interesting and useful.

Kind regards,

Ahila Ayyavoo - on behalf of Team ISPAE EC 2023-24.

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Welcome New ISPAE Members

Life members	
1. Dr Nimisha Dange, Maharashtra	
2. Dr Meghana N, Karnataka	
3. Dr Amrita Mehta, Maharashtra	
4. Dr Sushil Yewale, Maharashtra	
5. Dr Swati Dokania, West Bengal	
6. Dr Preeti Rose, Haryana	
7. Dr Yogesh Phirke, Uttar Pradesh	
8. Dr Kavya D R, Karnataka	
9. Dr Shagun Walia, Maharashtra	
10. Dr Alapan Mahapatra, West Bengal	
11. Dr Harshitha Jayaraj, Tamil Nadu	
12. Dr Pragati Sisodia, Uttar Pradesh	
13. Dr Amruta Phatak, Mumbai, Maharashtra	
Associate members	
1. Ms Bhavna Parmar, Gujarat	17. Ms Rachana Deo, Bihar
2. Mr Sam Gulati, New Delhi	18. Ms Nani Shova Shakya, Nepal
3. Ms Deepali Sharma, Jharkhand	19. Ms Leena Markose, Kerela
4. Ms Rajani Sawant, Maharashtra	20. Ms Divya Prabha, Karnataka
5. Ms Gunjan Sahani, Uttar Pradesh	21. Ms Shruti Arora, Haryana
6. Ms Swati Radadiya, Gujarat	22. Ms Deeptha Jayakar, Karnataka
7. Ms Arti Yadav, Rajasthan	23. Ms Lubna Dhalani, Maharashtra
8. Ms Vidhyadhari L, Telangana	24. Ms Narmada Nangadda, Andhra Pradesh
9. Ms Shilpa Parihar, Karnataka	25. Ms Rupali Panda, Odisha
10. Ms Kamyaba Sarvaiya, Gujarat	26. Ms Sabhpreet Kaur, Punjab
11. Ms Jyothi Karnam, Andhra Pradesh	27. Ms Nandini Nanda, New Delhi
12. Ms Treesita Tancouri, Mauritius	28. Mr Nithin Somasunder, Karnataka
13. Mr Sameer Shinde, Mumbai	29. Ms Divya Ragate, Karnataka
14. Ms Asreena N, Tamil Nadu	30. Ms Ketki Ambulkar, Maharashtra
15. Ms Hetashvi Gondaliya, Gujarat	31. Mr Sandeep Mittal, Haryana
16. Ms Rashmi Rathore, Rajasthan	32. Ms Varsha Kachroo, Uttar Pradesh

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An update on the ISPAE website

www.ispae.org.in

Sirisha Kusuma Boddu, Joint Secretary, ISPAE (2023-24)

We are happy to announce that new content and features are available for the benefit of all members on the ISPAE official website.

- As ISPAE endorsed ISPAD 2022 Low Resource Setting Guidelines for pediatric diabetes, we provided a direct link to the same on the homepage itself for easy access to all our members.
- The members can now purchase orchidometers at a reasonable price by sending their order request to the ISPAE office. The details can be found at www.ispae.org.in/orchidometer
- A new page 'School Resources' is being created as part of ISPAE's school awareness initiative, bringing awareness of childhood hormonal disorders to schools. It has downloadable content, in an easy-to-understand format, on conditions like pediatric diabetes, thyroid, and growth disorders in children. The diabetes care section of the school resources page has downloadable information brochures and posters on pediatric diabetes care at schools.
- The ISPAE website gives a direct link to the European Society of Pediatric Endocrinology (ESPE) e-learning modules in the 'Professionals' section, providing easy access to this useful educational content.
- A reminder to all members that in the 'Patient Resources – Diabetes' section, a link to the ISPAD-LFAC carbohydrate counting book link is provided. Please make use of this to download the carbohydrate counting book for Indian diet.
- Another reminder that all members who are in the online database can find other practicing pediatric endocrinologists in the areas they are searching for by utilizing the 'Member Search' option. This facility requires you to log in to access the information.

MUMBLE JUMBLE – Trainees' Section, March 2023 Issue - Answers

1. LEOPARD	10. DENOSUMAB
2. INSULIN	11. RATHKE POUCH
3. BLOOM	12. ACROMELIA
4. OXANDROLONE	13. KASPAR HAUSER
5. ACHONDROPLASIA	14. STAT5B
6. GHENT	15. RAS
7. HYPOPHOSPHATASIA	16. PHEX
8. LERI WEILL DYSCHONDROSTEOSIS	17. FENTON
9. BECKWITH WIEDEMANN SYNDROME	18. ASFOTASE ALFA

Clinical Case Diagnosis- **SEPTO OPTIC DYSPLASIA**

TOP THREE WINNERS-

* Dr TRISHYA REDDY- Fellow in Pediatric Endocrinology, Manipal Hospital, Bangalore
* Dr RESHMA M- DM Endocrinology Trainee, IMS BHU, Varanasi
- Dr JAYASHRI MN- Fellow in Pediatric Endocrinology, BCHI JJMMC, Davangere

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European Thyroid Association Guidelines 2022 - Management of Pediatric Graves Disease

Aaradhana, Associate Professor, Department of Pediatrics, UCMS & GTB Hospital, Delhi

Hyperthyroidism, characterized by increased synthesis and secretion of the thyroid hormones (TH) T4 and T3, is mostly caused by Graves disease (GD) in children, which may present with behavioral changes or poor school performance, apart from the classic symptoms and signs. Serum TSH receptor antibodies (TSHRAb) should be measured in the pediatric age group to guide diagnosis and management. Treatment should be prompt; the standard three options are medical treatment with antithyroid drugs (ATD), definitive treatment with radioactive iodine (RAI) thyroid ablation, or surgical thyroidectomy.

Medical treatment can be done by dose titration (DT) or (very rarely) block and replace (BR), using the thionamides: carbimazole (CBZ) or its active metabolite, methimazole (MMI). Propylthiouracil (PTU) has a higher risk of hepatic failure and is not preferred. Thionamides block TH production by blocking thyroid peroxidase enzyme, which blocks tyrosine iodination of thyroglobulin.

DT approach is the preferred method, starting with a single daily dose of CBZ (0.25-0.5mg/kg/day) or MMI (0.15-0.3 mg/kg/day), until TH normalize, and then reducing the dose by about 25% (or 50% if child becomes hypothyroid). If hyperthyroidism persists, the dose is increased by about 25%. In the first 4-6 months after diagnosis, dose titration should be guided by TH levels, not TSH. Beyond 4-6 months, doses should be guided by both TH and TSH levels.

BR approach may rarely be needed, with ATD started in a high dose of 0.5-0.75 mg/kg/day CBZ or 0.3-0.5 mg/kg/day MMI, which is likely to block endogenous TH in most patients. As TH normalize, levothyroxine (LT4) is started in a relatively low dose, and titrated by FT4, done every 4-6 weeks, until normal values are achieved.

Follow up and monitoring: Patients should be followed up 4 weekly for the first 3 months, then 2 and later 3 monthly, depending on the clinical course. TH normalize in most patients in the first 6 weeks. TSH can remain suppressed for several months. Minor, transient side-effects occur in 10-20% patients. Serious side-effects that warrant stopping ATD are rare (2-3 per 100,000). A white cell count, including neutrophil count, and liver function tests, should be checked at baseline because both can be affected by the underlying disease process and by ATD therapy. ATD should be stopped if sore throat or fever with agranulocytosis develop. Caregivers should be sensitized about the need for strict drug compliance, regular follow up, expected-side effects including susceptibility to excessive weight gain, while on ATD therapy.

Definitive therapy is needed if the patient has a large goiter, remains thyrotoxic in spite of high doses of ATD, develops neutropenia or liver dysfunction, or needs prolonged therapy (>5y).

When to stop drugs: ATD is normally administered for at least 3 years, and stopped only when TSHRAb levels have been low for several months. Remission rates after 2 years of ATD treatment are 20-30%,and may increase with continuous ATD therapy. Raised TSH despite a minimum dose of ATD (e.g. 2.5 mg of MMI or CBZ daily), together with normal TSHRAb, suggests the patient is in remission, and stoppage of ATD can be considered. After stopping ATD, follow-up should be every 3-4 months in the first year, every 6 months in the second year and annually thereafter, because of

the risk of relapse and autoimmune hypothyroidism. Definitive treatment (total thyroidectomy or RAI) is needed for some children (vide supra).

RAI with I-131 aims for complete thyroid ablation, to prevent relapse and future development of thyroid cancer. RAI is safe over age 10y, and may be considered in children aged 5-10 years if surgery is not a realistic option, but is best avoided if active orbitopathy is present. Before administering RAI, ATD is stopped for 3-7 days. Post-ablation lifelong LT4 is required.

Thyroidectomy: Total thyroidectomy is necessary, done after ensuring preop that the patient is euthyroid (with ATD, and if necessary, iodine, beta-blockers and/or glucocorticoids), and vitamin D replete. LT4 is started in the postoperative period.

Supportive management- GD patients should avoid excess iodine intake. Beta-blockers (e.g. propranolol or atenolol) attenuate peripheral adrenergic actions of TH, and are needed in moderate to severe TH excess, till levels and symptoms improve.

Thyroid storm- Occurs in untreated GD or is precipitated by infection, surgery or RAI therapy. The patient develops tachycardia, heart failure, hyperthermia, extreme anxiety, altered mental state and gastrointestinal upset. It is managed by administering iodine (e.g., potassium iodide solution) and a glucocorticoid (inhibits peripheral conversion of T4 to T3), in addition to ATD (an hour before iodine to stop release of preformed TH) and a beta-blocker.

Pediatric Graves orbitopathy (GO)- Mild GO symptoms can be followed expectantly or, if indicated, with selenium supplementation. Moderate to severe active GO cases can be treated with anti-inflammatory drugs (e.g., i.v. corticosteroids). Chronic inactive stable GO can be treated surgically by decompression surgery, but only after the facial skull has grown fully.

Management of increased thyroid cancer risk- Children with GD have a slightly higher risk of developing thyroid cancer, so if they develop a thyroid nodule/nodules, thyroid ultrasound and cytological evaluation is needed, and total thyroidectomy considered.

Reference: *Mooij CF, Cheetham TD, Verburg FA, et al. 2022 European Thyroid Association Guideline for the management of pediatric Graves' disease. Eur Thyroid J. 2022;11(1):e210073.*

THYROID HORMONE RESISTANCE- A MINI REVIEW

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

Thyroid hormone resistance (THR) is a rare syndrome of reduced end organ sensitivity, first recognized in 1967 by Refetoff, in two clinically euthyroid siblings with high circulating TH concentrations and several abnormalities, including deaf-mutism, dysmorphic facies, winging of the scapulae, pectus carinatum, short stature, delayed bone maturation, and stippled femoral epiphyses. This was called *Refetoff syndrome*. Since then, many patients and families have been identified, with a prevalence of THR of approximately 1 in 40,000.

*Thyroid hormone receptors***-** The effects of TH are mediated by receptor interaction with specific DNA response elements at TR (TREs), located in the promoter regions of target genes. There are two subtypes of TR: Alpha (TRα) and Beta (TRβ), encoded by genes on chromosomes 17 and 3, respectively; and three main isoforms: TRα1 (most abundant in the central nervous system, myocardium, and skeletal muscle), TRβ1 (predominant in liver and kidney), and TRβ2 (highly expressed in the pituitary and hypothalamus), generated by alternate splicing.

Pathogenesis-THR is usually dominantly inherited, though de novo mutations can also occur. *THRB* mutations have been strongly associated with THR. Genetic studies in 300 families with this syndrome showed 122 different point mutations or frame shift mutations within the hormone binding domain of the receptor. THR phenotype could also result from non-TRβ defects. They are clinically similar to subjects with *THRB* gene mutations but have a high female-to-male ratio and high prevalence of sporadic cases. Genetic and clinical studies have highlighted two novel non-TRβ defects giving rise to THR.

- Inactivating mutations of the TH transport protein, monocarboxylate transporter 8 (MCT8), resulting in Allan-Herndon-Dudley syndrome (AHDS).
- Intracellular metabolism SECIS binding protein 2 (*SECISBP2*) gene mutation, affecting synthesis of selenoproteins.

Classification- On the basis of tissue response to TH, THR has been classified as:

- *Generalized THR:* The patient is clinically euthyroid. The euthyroid state is maintained by a compensatory increase in TH levels. There may be low IQ without an effect on bone (normal stature), or vice versa, due to variable tissue resistance.
- *Pituitary THR:* The patient presents with hyperthyroidism. The inappropriately high pituitary TSH secretion causes overproduction of TH, establishing a new equilibrium. The presence of thyrotoxic features suggests that peripheral tissues are more sensitive to TH than the pituitary.
- *Peripheral THR:* The patient may present with clinical hypothyroidism, but normal TSH value. The sensitivity of peripheral tissues to TH is decreased relative to that of the pituitary, but the degree can be variable.

Clinical Features- The characteristic clinical feature is goiter (seen in 66-95%),without symptoms or metabolic consequences of TH excess. In some children, features of hypothyroidism, such as growth retardation, delayed dentition or bone age, can occur. Before the advent of sensitive TSH assays, a combination of goiter, palpitations and tachycardia (in 75% patients with pituitary THR) often led to a misdiagnosis of Graves disease. Approximately 33-60% patients have emotional disturbances, hyperactivity and learning disability. The presence or absence of thyrotoxic symptoms, suggesting either generalized THR or pituitary THR, is a useful guide to treatment.

THRα defects present with tissue-specific hypothyroidism (bone, gut, heart), and a characteristic broad facies with hypertelorism, macrocephaly, flattened nose, prominent tongue and thick lips. Growth retardation is often prominent and is predominantly of the lower segment. Radiological features of skeletal dysplasia may be present. Constipation is common and may be severe. Neuro-cognitive deficits including delayed milestones in childhood, dyspraxia, broad-based gait and slow speech can be found.

Allan-Herndon-Dudley Syndrome:

- A rare, X-linked recessive, intellectual disability syndrome caused by mutations in the *SLC16A2* gene (Xq13.2). This gene encodes for MCT8, which is a specific transporter of the thyroid hormone T3 into nerve cells.
- Patients have global developmental delay, profound intellectual disability, and severe neuromotor impairment. The disease manifestations appear in infancy.
- Hyperthyroidism manifests as poor weight gain, reduced muscle mass, and variable cold intolerance, sweating, elevated heart rate, and irritability.
- Abnormal transport function is reflected by elevated free T3 and decreased free T4 levels, along with typical clinical features.

- Tissues that largely depend on MCT8 for cellular entry of TH are relatively hypothyroid, whereas tissues that rely on other transporters are exposed to the high T3 levels in the circulation, resulting in a thyrotoxic state.

Table below summarizes the laboratory findings in THR syndromes.

- *Table: Classification of THR*

THR	***Gene***	***Thyroid hormones***	***TSH***
THR beta	*THRB* gene	High T4 and T3	High
THR alpha	*THRA* gene	Low/normal T4 & high/normal T3, subnormal T4/T3 ratio and variably reduced reverse T3 (if increased deiodinase 1 activity)	Normal
AHDS	*SLC16A2* gene	High T3 and low or normal T4 and decreased reverse T3	
SECIS-BP2	*SECISBP2* gene	Elevated T4, low/normal T3, high reverse T3	Normal/ high TSH

Other causes that may mimic the laboratory findings in THR should be considered in the differential diagnosis: drug effects (amiodarone, heparin), sick euthyroid illness, thyroiditis, analytical errors, TSHoma, or abnormal thyroid binding proteins. Serum Sex Hormone Binding Globulin (SHBG) is more likely to be decreased (though it may be normal)in THR, unlike in hyperthyroidism, where there is increased expression of SHBG from the liver.

Management

- Individuals with heterozygous TRβ-mediated THR do not usually require treatment, as the THR is compensated by elevated levels of TH. In these individuals, a genetic diagnosis of THRβ is important to prevent inappropriate treatment recommendations. A minority of patients exhibit thyrotoxic symptoms. The first line of treatment is symptomatic, consisting of β-blockade for tachycardia, and anxiolytics.
- Levothyroxine therapy has been beneficial in some childhood cases of THRα with predominant hypothyroid symptoms, in improving growth, alleviating constipation, and improving motor development and well-being.
- The management of patients with hyperthyroid symptoms is controversial. The administration of antithyroid medications will cause a rise in TSH production and increase goiter. There is a theoretical risk for pituitary thyrotropic cell adenomas. TH levels should not be normalized, but rather maintained above or at the upper end of the normal range.

Recent Advances- Treatment with triiodothyroacetic acid (**Triac**), a thyromimetic agent with a higher affinity for TRβ than TRα, may achieve lowering of TSH and serum TH concentrations, thus reducing clinical thyrotoxicity. Others have used liothyronine (LT3) successfully for similar reasons.

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- *Schwartz CE, Stevenson RE, The MCT8 thyroid hormone transporter and Allan-Herndon-Dudley syndrome, Best Pract Res Clin Endocrinol Metab, 2007;21:307–21.*

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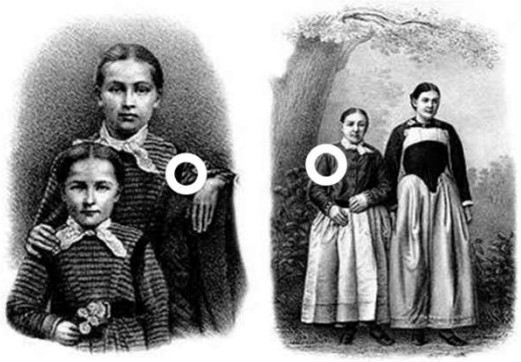
History Corner - Dr Theodor Kocher

Ruchi Shah, Pediatric Endocrinologist, Endokids Clinic, Ahmedabad.

It was a life-changing letter, written one evening of 1883, to 42 year old Emil Theodor Kocher, then Chair of his hospital in his hometown Berne, Switzerland, and widely acknowledged as one of the best surgeons of the world. It was sent by a physician in a nearby town, about a young woman named Maria, who had had her thyroid removed by Dr Kocher almost 10 years earlier, when she was 11. Since that surgery, Maria had experienced a substantial change in her character. Before the surgery, she was maturing normally. Now, while her younger sister had grown into a pretty lady, Maria remained "small and exhibited ugly looks of a semi-idiot" (picture, circle indicates Maria) (*Kocher, T. Arch KlinChir 29:254-337,1883*).



Some background: Kocher became a professor of surgery at the University of Bern at the age of 31 in 1872, a time when modern medicine and surgery were in their childhood. Famous for being very meticulous and for bloodless operative fields, he invented many surgical techniques. Till date, more things bear his name than any other person in medicine: Kocher-Debre-Semelaigne syndrome, Kocher sign in Graves disease, Kocher maneuver for shoulder reduction, Kocher incision for biliary tree exposure, Kocher artery forceps, Kocher's transverse incision for thyroid gland (earlier it used to be vertical), Kocher's point in the brain.

Iodine deficiency was widespread then, so goiter was common. The exact function of the thyroid gland was unclear, and it was very strange to find an organ not connected to anything obvious like lungs, heart, intestines, etc. However, its enlargement was found to cause problems, so removal would be planned, even though thyroid surgery was extremely difficult in the 1860s, with mortality as high as 75%. In Kocher's hands, mortality had come down to <0.5%, which is the same as today!

An ordinary surgeon would dismiss such a letter, considering it unrelated to the surgery. Kocher need not have been concerned about Maria's condition 10 years after surgery. It should have been enough that she was alive. However, not only did he decide to see her personally, after seeing her, he then, in early February 1883, sent invitations to 77 of the 102 patients whose thyroid he had operated on, excluding dead or recent patients. He was able to re-examine 34 patients and receive written reports from 26 (of whom 7 had died due to different reasons). Of the 53 living patients whom he knew to have had benign disease, 28 had undergone partial removal of the gland. They seemed to be doing well, were "very happy with and grateful for the success of the operation." (Kocher 1883a, p 275). Those who had total removal of the gland had entirely different outcomes. There had been slow physical and mental decay following surgery, with puffiness of the face, hands and body, decreased growth in height and noticeable pallor explained by anemia. He designated these and other physical signs as a new disease specific to the removal of the gland (instead of enlargement), naming it "cachexia strumipriva" (decay resulting from lack of goiter). (Kocher 1883a, p 285).

He presented detailed findings in a lecture to the German Society of Surgery on 4th April, 1883. Although he had made wrong assumptions regarding thyroid function and correlation of symptoms

of hypothyroidism, it was a REAL MILESTONE because it was the FIRST TIME EVER a surgeon decided to look retrospectively, audited and presented the research, including frank reporting of the mishaps because of surgery.

Kocher received the Nobel Prize in 1909 for his work on the physiology, pathology and surgery of the thyroid gland. Till then he had received almost all the highest prizes of Europe. Although thyroxine was discovered on Christmas Day 1914 by Kendall, long after his lecture in Berlin, he laid the foundation of endocrinology. He is considered the father of thyroid surgery. University of Bern initiated an annual Theodor Kocher Prize for outstanding young researcher in 1915.

[Images Source- *https://www.abebooks.co.uk/first-edition/Ueber-Kropfexstirpation-Folgen-pp.254-337-lith-Taf/988612611/bd and https://www.nobelprize.org/prizes/medicine/1909/kocher/biographical/]*

References

- *Tröhler, Ulrich. Towards endocrinology: Theodor Kocher's 1883 account of the unexpected effects of total ablation of the thyroid. J Royal SocMed. 2011; 104: 129-32.*
- *https://www.youtube.com/watch?v=XSEbsOscZQA. 'A Pioneer Surgeon's Bold Pursuit of Truth' by Laura Mazer*

Patient corner- Thyroxin Dosing

Richa Arora, Consultant Pediatric Endocrinologist, New Delhi

Hypothyroidism being a chronic condition, the clinician needs to counsel patients well, to ensure regular follow up and compliance with medication. Below are a few essential messages that need to be communicated to all patients on thyroxin therapy.

- The thyroxin dose does not impact TSH monitoring, but if T4 test is also planned, it may be best if the sample is taken before the morning dose. The target of therapy is to maintain TSH between 0.1-5 mIU/ml and T4/ FT4 in the upper range of normal.
- The dose of thyroxin is age dependent. In congenital hypothyroidism, the initial dosage varies from 10-15 mcg/kg/day, that reduces to 4-6 mcg/kg/day by age 2-5 years and is usually 1-3 mcg/kg/day in older children and adults.
- In following up children with hypothyroidism, along with regular thyroid function tests (TFT), monitoring should include anthropometry, and pubertal assessment in the peripubertal years.
- The minimum interval for TFT should be 4-8 weeks.
- Thyroxin should preferably be consumed on an empty stomach, at about the same time daily. Dosing can be associated with a daily morning routine to avoid missed doses.
- With thyroxin, avoid calcium and iron supplements for at least 4 hours. Any food item should be given after about half hour of medication. Thyroxin should be given with some water or in expressed breast milk (in congenital hypothyroidism).
- Thyroxin is available in tablet form with a wide variety of strengths. It is important to check if the prescribed dose matches the tablet dispensed. The brand should not be changed unless advised.
- The medicine should be stored in a cool and dry place, avoiding places of high humidity like the kitchen and bathroom, or direct exposure to sunlight. Discard discolored or expired medicines.
- If a dose of thyroxine is missed, it should be taken as soon as it is remembered, but preferably avoid food 0.5-1 hour before and after it's intake. Alternatively, double the dose can be taken the next day. Keeping a weekly pill count is useful to avoid missed doses.

- Thyroxin should not be missed on a sick day; it should preferably be taken as always.

Reference- *Kalra S, Unnikrishnan AG, Tiwaskar M, et al. Medication Counseling for Thyroxine. Indian J Endocrinol Metab. 2017;21(4):630-1.*

DRUG CORNER - Radioactive iodine

Ruchi Shah, Pediatric Endocrinologist, Endokids Clinic, Ahmedabad

Nuclear medicine uses trace amounts of radioactive substances for diagnosis and treatment of disorders. A radioisotope is most frequently attached to a drug/ligand that travels to a specific tissue, where it emits specific rays which can be captured by camera, thus providing greater details regarding functioning of the organ, compared to the morphological information provided by conventional radiological procedures. Radioisotopes produce 3 types of rays – α, β and γ. As α and β have shorter wavelengths, they are more penetrative and used for therapeutic purposes for Graves disease and thyroid cancer. Gamma (γ) rays are more useful for diagnostic purposes.

The three main radioisotopes used in thyroid disorders are Technetium-99m (Tc-99m), Iodine-131 (I-131) and Iodine-123 (I-123, not available in India). Although historically iodine was used most frequently, Tc-99m scans are increasingly used these days.

Substance	**Tc-99m**	**I-131**
Rays	Gamma (γ)	Beta (β) and Gamma (γ)
Half life	6 hours	8 days
Administration	Intravenous	Orally as capsule/syrup
Time to scan	15-20 minutes	48 hours after ingestion
Use	Best for diagnostic purpose in congenital hypothyroidism, thyrotoxicosis and well differentiated thyroid carcinoma	Rarely used for diagnostic purpose, as it is cumbersome, takes time and more radioactive
Dose	0.05-0.1 mCi/kg, not more than 2.5 mCi for children	Therapeutic dose decided based on ultrasound & diagnostic scan. Most guidelines suggest higher doses like 0.4 mCi/gram of thyroid tissue
Precautions	No therapeutic effect Should not be done if patient is taking thyroxin for more than 3-4 days	• Should be avoided in children <5 years and used cautiously in 5-10 years (if surgery not possible) • Anti thyroid medication should be stopped 3-7 days before and restarted in 1-2 days after RAI • Should be avoided with active Graves ophthalmopathy (consider course of steroids) • Pregnancy test should be done before RAI, pregnancy should be avoided for at least 6 months post treatment

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- *2022 European Thyroid Association Guideline for the management of pediatric Graves disease.*
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Drug Corner - Role of Triac (Triiodothyroacetic acid) in thyroid disorders

DhanyaSoodhana, Pediatric Endocrinologist, Aster MIMS, Calicut, Kerala

TSH controls the thyroid gland's production and secretion of thyroid hormones (TH): predominantly prohormone thyroxine (T4) and to a lesser extent, bioactivehormone 3,3′,5-triiodothyronine (T3) (Triac) [1]. Triac use (also known as Tiratricol) is a TH analog whose cellular entry is not dependent on monocarboxylate transporter 8 (MCT8). It inhibits TSH secretion, thereby lowering endogenous TH production, yet has relatively weak thyromimetic activity in peripheral tissues. Preclinical studies in animal models indicate that Triac restores abnormal neuronal development and myelination in MCT8 deficiency if administered in early postnatal life. Studies in mice showed that Triac was taken up by the brain and suppressed serum TSH levels, resulting in lowering of serum T3 and T4 levels.

Indications

- Triac has higher affinity than T3 for several TRβ mutants, and is the treatment of choice in patients with thyroid hormone resistance (THR) syndrome. Used in a few THRβ cases, it was able to partially alleviate goiter and thyrotoxic symptoms, including tachycardia, excessive perspiration, and attention deficit disorder [2].
- Triac has also been safely utilized for TSH suppression in patients with differentiated thyroid carcinoma, after thyroidectomy, with reported data up to 6 months.
- Triac treatment could result in normalization of the abnormal serum TH values in Allan-Herndon-Dudley syndrome (AHDS). Further more, Triac could replace the function of T3 in tissues that depend on MCT8 for TH uptake.

Dosage: Triac (Teatrois tablets, 350mcg, Rare Thyroid Therapeutics) has been tried in 46 patients with MCT8 deficiency, by individualized dose-escalation, following a pre-defined dose- escalation protocol in a multi-center, open-label clinical trial [3]. A daily starting dose based on body weight (175mcg Triac<10kg; 350mcg Triac ≥ 10kg) was administered without any dose-limiting toxicity. The dose was increased progressively, in 175mcg or 350mcg steps, to attain serum total T3 (TT3) levels within the target range of 1.4-2.5 nmol/L; at a median maintenance dose 38 mcg/kg/day.

Triacis available as an orphan drug [Emcitate] to be prescribed by registered specialists in Europe and USA for MCT8 deficiency and THR type beta (THR β). It is not effective in increasing metabolic rate for weight loss in people with normal thyroid function. The FDA has issued a warning against Triac use for weight loss.

Adverse effects: A retrospective long term (6 years) real life follow-up study on 67 children and adults with MCT8 deficiency treated with Triac, assessed for primary end points (T3 concentration) and 63 patients for secondary end points (body weight for age, and heart rate for age) did not show any severe adverse events. It can cause transient signs of increased thyrotoxicosis such as irritability, anxiety, reduced sleep, increased blood pressure (BP) and tachycardia [4]. Triac is better avoided in the elderly, during lactation, in individuals with heart disease, high BP, diabetes, liver disease, myxedema and bleeding problems; and has drug interactions (refer drug insert). Triac works similarly to TH, so taking Triac with TH might increase their side effects.

Conclusion- Ever since the report of Triac in 1953, the field has actively developed, with testing of other TH analogs. Triac Trial II, a Phase IIb clinical trial will evaluate the effects of Triac on neurodevelopment, when treatment is initiated early in life. Rational design with appropriate clinical studies, should pave the way for wider therapeutic usage of Triac in THR disorders, which have lacked effective treatment so far.

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Diagnosis Corner- Role of Artificial Intelligence in Thyroid disorders

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

Artificial intelligence (AI) is the new technology frontier that is evolving as an efficient, reliable and reproducible tool in healthcare. Machine-based learning and computer-assisted diagnosis have revolutionized diagnostics and therapeutics. The process involves data acquisition, data interpretation and data selection to train a machine-model, model development, model training and finally model testing/ retraining and cross-validation.

Recent reports document the advantages of AI in thyroid nodule characterization and prediction of malignancy. The art of using AI in radiodiagnosis is better termed as **radiomics,** using data extraction for analysis and diagnosis through high-throughput images with advanced analytical and machine-learning models/ tools. AI can assist in interpreting ultrasonographic images of thyroid modules for risk stratification for malignancy. This can be helpful for untrained observers and can avoid unnecessary invasive cytopathological tests. Second, deep-learning models can help in staging thyroid nodules based on radiography, cytology and molecular diagnosis with high accuracy. AI has also been found reliable for automation-based image analysis on cytopathology of thyroid samples. This has huge potential to transform clinical management decisions in suspicious thyroid nodules, establishing its role in adults and perhaps in children also, though, the risk of thyroid cancer is lower in children than in adults.

In addition to thyroid cancer risk prediction, AI has also been documented to influence interpretation of thyroid function tests. AI models have shown good potential in preanalytical, analytical and post-analytical stages for thyroid functions as shown in the **Table** below.

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Table: Artificial Intelligence in Thyroid Function Test (TFT) Analysis

Pre-Analytical stage	*Analytical stage*	*Post-analytical stage*
• Optimize selection of TFT for a patient • Suggest appropriate collection& transport methods	• In-silico modelling can improve performance & robustness of TSH and thyroid hormone assays • Aid in classification and sub-classification of thyroid disorders • Epitope mapping and prediction (Example: of the TSH receptor blocking antibodies) • Develop predictive statistical models for cytotoxic molecules, drugs	• Process large datasets for personalized reference intervals in different conditions and laboratories • Adjust biological variability to interpret thyroid reports • Predict progression to hypothyroidism • Guide clinical decision support systems in thyroid cancer &autoimmune thyroid disease

Though the approach using AI models seems exciting, it is important to know that it has its own challenges. Data safety and privacy need to be respected and implemented within an appropriate legal framework. These scientific advancements will carry some inherent costs, suggesting the need for comprehensive monitoring to ensure data reliability and quality.

At present, AI definitely seems to have exciting potential to use in thyroid disease prediction and management. We would be able to better gauge its true utility in the coming few years.

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Case report- Fetal Goiter in a Euthyroid Mother: an interesting manifestation

Meghana N, Clinical Fellow; Ramya OM, Clinical Fellow;
Vani HN, Consultant Pediatric Endocrinology;

P Raghupathy, Professor, Dept of Pediatric & Adolescent Endocrinology, Indira Gandhi Institute of Child Health, Bengaluru

Fetal goiter is rare, with a reported incidence of 1 in 40,000 live births. Causes can range from maternal (deficiency or excess iodine, autoimmune thyroid disorders, exposure to medications or goitrogens which can cross the placenta), to fetal (thyroid hormone production defects)[1]. We report a rare case of fetal goiter in a euthyroid mother.

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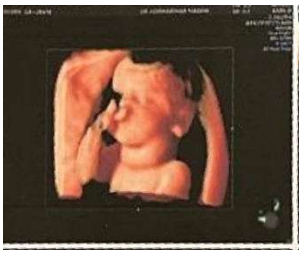

Case: Baby of T, first-born male baby to consanguineous parents, was transferred to us from the Neonatal intensive Care Unit (NICU) of another hospital, on day 24 of life, with history of a neck swelling, for further management. The mother gave a history of regular antenatal checkups, with normal antenatal ultrasonography (USG) in the first and second trimesters, and normal thyroid function tests (TFT) during routine investigations. At 27 weeks of gestation, USG revealed a diffusely enlarged fetal thyroid gland measuring 23*48*42 mm, with predominantly peripheral vascularity, and causing mild compression of the trachea and esophagus **(figure)**, suggestive of a hypothyroid goiter, as per the scoring system described by Huel, et al. There was no associated fetal tachycardia or premature epiphyseal ossification, just mild polyhydramnios. Parents had been advised cordocentesis to assess the fetal thyroid function, but they refused due to the risk of fetal loss. Serial USG monitoring showed no increase in size of goiter or development of fetal complications. The mother started self-medication with levothyroxine (25 mcg daily), without consulting her doctor, for almost 2 weeks prior to delivery.

She went into spontaneous labor at 37 weeks gestation, and delivered per vaginum. Birth weight was 2200 grams (small for gestational age). He was treated in the NICU for respiratory distress, needing CPAP support for ~2 weeks. TFT done on day 8 of life was reported to be normal (Table).

Table: Baby's serial TFT

Age	*fT4 ng/dL*	*Total T4 mcg/dL*	*TSH IU/L*	*Thyroxin dose*
D8	0.95		13.28	
D24	1.43	12.9	13	5 mcg/kg/d
Wk6	1.4	11.2	4.3	5 mcg/kg/d (after 2 wk LT4)
Wk8	0.93	8.11	23.53	10 mcg/kg/d (after 4 wk LT4)

On day 24, when he reached us, he was alert, with mild respiratory distress, no tachycardia, and no features of hypothyroidism or hyperthyroidism. A diffuse firm goiter was present (~5*3cm, on both sides of trachea, extending superiorly till the mandible and inferiorly up to the clavicle). USG neck showed features both lobes of thyroid and isthmus enlarged (~6cc each) with normal vascularity. A Technetium-99m pertechnate uptake scan showed a mildly enlarged thyroid gland with increased uptake. Scintiscan with iodine-131 and perchlorate discharge test showed no significant washout of tracer (<10%). As fT4 & TT4 were in the normal range, but TSH was elevated (13 IU/L) at age 3 weeks, he was started on levothyroxine (LT4) in a low dose of 12.5 mcg daily, which was later increased. Serial thyroid functions of the neonate are shown in the **Table**. Now the infant is 4 months old, on regular follow up. Goiter size has reduced significantly, and TFT and milestones for age are normal.

***Discussion*:** The fetal thyroid gland can be assessed accurately by USG after 20 weeks of gestation, and scored on the basis of pattern of color Doppler, fetal heart rate, bone maturation, and fetal mobility[2]. A score of <2 suggests hypothyroidism, while ≥2 suggests hyperthyroid goiter[1]. However, this is non-specific; the gold standard for diagnosis is fetal TSH measurement by cordocentesis. Fetal therapy requires intra-amniotic instillation of LT4, as the transplacental transfer of thyroxin is limited by the presence of placental deiodinase type 3 enzyme. The rationale for prenatal treatment is to optimize fetal growth and development, and to reduce goiter size, thereby relieving obstruction. Although most studies have documented a reduction in the size of fetal goiter following intraamniotic instillation of LT4, the optimal dosing regimen and effect on neonatal thyroid function remain undefined, with risk of associated maternal complications[3]. In

view of these caveats, intraamniotic therapy is generally considered only when there is progressive hydramnios or likely tracheal occlusion, as conservative management in this context may be associated with preterm delivery and neonatal death. In the present case, the parents refused invasive prenatal testing and treatment; the LT4 tablets taken antenatally by the euthyroid mother would have had limited benefit to the fetus. Fortunately, there were no intrauterine complications, and the baby was euthyroid postnatally till 3 weeks of age.

Fetal goiter with hypothyroidism and dyshormonogenesis, in the setting of maternal euthyroidism, has been managed successfully with radiological surveillance, followed by elective delivery and neonatal LT4 treatment[4]. Sometimes, concerns regarding dystocia may necessitate Caesarean section, and intubation may be required at birth to tackle respiratory compromise.

In summary, slow-growing or stable fetal goiters can be managed conservatively, with serial USG, avoiding invasive intrauterine procedures, which have inherent risks.

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PedsEndoscan

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

Cattoni A, Molinari S, Capitoli G, et al. Thyroid Function Tests in Children and Adolescents with Trisomy 21: Definition of Syndrome-Specific Reference Ranges. J Clin Endocrinol Metab. 2023 Jun 3:dgad333.

Non-autoimmune subclinical hypothyroidism is arguably an over-diagnosed entity in Down Syndrome (DS), as the hypothalamic-pituitary-thyroid axis is reset at higher median TSH values. Another proposed reason has been late maturation of thyroid follicles because of over expression of Dyrk1a gene on chromosome 21.The authors outlined syndrome-specific nomogram ranges for thyroid function tests in a retrospective review of a population of 548 DS patients over an average follow up of 5.8 years, but not on thyroid specific treatment. They observed that of the total 3748 TSH measures, 20% were above the 97.5th centile of healthy controls. The 50th centile of TSH in syndromic patients for 0-1y, 1-6y, 6-11y and 11-18y, were 5.30, 4.38, 3.87 and 3.41 mIU/mL; i.e., higher than healthy controls ($p<0.001$). FT3 and FT4 were statistically lower than controls at specific ages (0-11y for FT3; 11-18y for FT4). The authors also noted considerable intra-individual variability in TSH over time, with over 50% values not in agreement with previous ones. TSH values higher than 75th centile predicted development of hypothyroidism with NPV of 0.9. **TSH values in DS are significantly higher than in healthy controls; syndrome-specific nomograms should be used for interpretation.**

Yu A, Alder N, Lain SJ, et al. Outcomes of lowered newborn screening thresholds for congenital hypothyroidism. J Paediatr Child Health. 2023 May 15.Epub ahead of print.

The threshold values of newborn screening blood spot TSH (b-TSH) for recall of babies suspected to have congenital hypothyroidism (CH) have been progressively lowered from 15 to 8mIU/L in Australia. To evaluate the impact of these changes, the data of 346,849 babies born between November 2016 and March 2020 was analyzed. With the changed protocol, those with values ≥8 mIU/mL (against old threshold of ≥15 mIU/mL) were called for a repeat b-TSH. The rest of the protocol remained unchanged, that is, those with repeat b-TSH of 7 or more were referred for evaluation of CH. Of the 346,849 newborns screened, 1668 were recalled (1462 had values 8-14.9mIU/mL and 206 had values ≥15mIU/mL) representing an eight-fold increase in recall rate from 0.06% to 0.48%. Preliminary diagnosis of CH was made in 212 and 62 (29.2%) of these had b-TSH values of 8-14.9mIU/L. The program achieved a 41% increase in diagnosis of CH. With the lower threshold, the PPV of the screening decreased from 74.3% to 12.8%.**Lowering the first screen b-TSH threshold from 15mIU/mL (99.9th percentile) to 8mIU/mL (99.5th percentile) could detect an additional 41% newborns who were commenced on thyroxin treatment.**

Darrat M, Kayes L, Woodside JV, Mullan K,Abid N. Congenital hypothyroidism in Northern Ireland: 40 years' experience of national screening programme. Clin Endocrinol (Oxf). 2023 Jun 6.

Northern Ireland has a uniform newborn screening program for congenital hypothyroidism (CH) since 1980, with a TSH cutoff value of >8mIU/mL. The authors present a retrospective review of the database of 800,404 newborns screened between January 1981 and March 2020. They noted a steady and significant increase in incidence of CH over time. While there were 26 cases per 100,000 live births in 1981, there were 71 cases per 100,000 in 2019, a nearly trebled incidence. Twice as many females were affected as males. Though 16% of the cohort were preterm, more in the later years, the median gestational age of the affected babies was similar - 40 weeks in 1988 and 39 weeks in 2010s. The ethnicity of the population did not vary over the decades. A total of 471 cases were diagnosed, of which 62% had permanent hypothyroidism, while the rest had transient CH. Diagnostic imaging performed in 143 cases revealed 70% had thyroid dysgenesis; the rest had dyshormonogenesis. Extrathyroidal abnormalities were diagnosed in 185/471, with 8.4% having congenital heart disease, an incidence similar to that reported in literature. The increased incidence could not be explained by increased survival of preterm newborns/ change in ethnicity of the population or any other clear reason. **The incidence of CH has been steadily increasing in Northern Ireland over the past four decades as has been reported from other parts of the world**.

Satapathy S, Majeed AK, Ballal S, Bal C. Differentiated thyroid cancers in young adults versus children: Clinical characteristics and ten-year follow-up outcomes [published online ahead of print, 2023 Jun 7]. J Clin Endocrinol Metab. 2023;dgad343.

The data on differentiated thyroid cancer (DTC) in young adults from 1971-2016 has been presented in this paper. A total of 1803 DTC patients (176 pediatric i.e., below 18y and 1627 older patients) were included. Pediatric patients had worse outcomes, like extra-thyroid extension, nodal and distant metastasis and high-risk disease ($p<0.05$); with higher rate of incomplete response (94/176 vs. 223/1627; $p<0.001$). Recurrent or persistent disease was present in 13.1% pediatric and 7.4% older patients ($p=0.012$), with 10-year disease-free survival of 88.7% and 93.5%, respectively. **In the pediatric age group, DTC had poorer prognosis, with important determinants being high-risk classification and response in initial two years.**

Cui Y, Chen J, Guo R, et al. Relapse of Graves' disease in Chinese children: a retrospective cohort study. Eur Thyroid J. 2023 Apr 19;12(3):e230018.

The authors present a retrospective review of 204 pediatric cases of Graves disease diagnosed between 2013 and 2019. All except 4 received initial treatment with methimazole. Remission rate was 38.7% (79/204): with therapy duration of 2y, 3y, 4y, and ≥5 years the rates were 9.1% (3/33), 23.9% (16/67), 32.1% (9/28), and 14.5% (11/76), respectively. Prepubertal children were more likely to achieve remission. Relapse after withdrawal of therapy was seen in 40/79(50.6%). After adjusting for age, gender and family history, a longer time for normalization of FT4 was associated with a higher risk of relapse (adjusted OR = 2.51, 95% CI: 1.56–4.03). Among lifestyle factors, longer sleep duration was also associated with decreased relapse rate (adjusted OR = 0.45, 95% CI: 0.23–0.88). **Children with Graves disease who took longer time for normalization of fT4 and those with reduced sleep duration had a higher risk of relapse.**

Learning Pearls

23rd ISPAE ACES meeting: Pediatric Pheochromocytoma and paraganglioma (25 March 2023)

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

- Pediatric PPGLs are rare, and account for 1% of hypertensive children, rarer under age 4y.
- PPGLs are very slow growing tumors. The manifestations are usually due to catecholamine excess; symptoms are paroxysmal. An adrenal mass may be discovered incidentally on imaging in asymptomatic cases.
- About 80% may have a germline mutation. Of those which are genetically positive, ~ 80% are Succinate dehydrogenase subunit B (SDHB)/ VonHippel-Lindau (VHL) positive.
- PPGLs can be categorized in three clusters based on pathogenesis of germline mutations: **Cluster 1** - hypoxic pathway, **Cluster 2** due to RAS/MAPK signaling issues, and **Cluster 3** with somatic mutations. Cluster 1 is the commonest.
- The **10-90% rule in PPGLs:** 10% are malignant, 20% synchronous bilateral, 30% are extra adrenal, 40% are familial, 50% recur by age 30y, 60% occur in boys, 70% have sustained hypertension, 80% have positive germline mutation, 90% are secretory.
- Of the 90% secretory, 10% are epinehprigenic, while 80% are nor-epinephrigenic. The head and neck PGL are non-secretory. Thoracoabdominal PPGL are nor-epinephrigenic. The adrenal pheochromocytoma-cluster 1 are nor-epinephrigenic; cluster 2 are epinephrigenic.
- The common sites of metastases are skeleton, liver, lung and lymph nodes.
- The **diagnosis** is confirmed with plasma free metanephrines or urinary fractionated metanephrines. A cutoff of >900 mcg for 24-hour urinary normetanephrines or >400 mcg for metanephrines has a high sensitivity and specificity. Likewise, plasma metanephrine levels of >57 pg/mL (0.5 nmol/L) or normetanephrine >148 pg/mL (0.9 nmol/L) have a high diagnostic performance when collected after overnight fasting with indwelling venous catheter. When metabolite levels are more than twice the upper normal range, imaging studies are advisable.

- The preference for **imaging studies** differs as per different institution's protocols. Either CT or high signal intensity T2W MRI can be used. On CT, intense arterial enhancement is suggestive of pheochromocytoma, and differentiates from adrenocortical carcinoma. The light bulb sign (marked hyperintensity) on T2W MRI is positive in 50% of patients with pheochromocytoma.
- **Functional imaging (^{68}G – DOTATEC PET CT** preferred) is advised when clear identification is not possible on imaging studies, or metastatic disease is suspected, or post-surgery when residual disease is suspected.
- **Treatment**: Alpha-blockers (prazosin/ phenoxybenzamine) are used pre-operatively. It is better to shift to prazosin (before surgery) as phenoxybenzamine has a longer half-life. A beta-blocker may be added if tachycardia persists, or a calcium-channel blocker if hypertension persists. Patients on alpha-blockers should be asked to consume more salt – 6-10 gm/day to avoid postural hypotension.
- Intra-operatively, sodium nitroprusside may be used and titrated. Post-operatively, blood pressure is a good parameter to look for cure, but may remain high for few weeks to months due to vascular remodeling. Antihypertensives may need to be continued in those cases. The measurement of post-operative plasma free metanephrines or urinary fractionated metanephrines are better indicators of cure and may be done annually.
- PPGLs with SDH-related mutations need serial imaging (MRI head, neck, thorax, abdomen) 2-3 yearly. For those with VHL-related gene, serial fundoscopy 6-12 monthly, audiometry annually, and MRI brain +spine and ultrasound/ CT abdomen are recommended 2 yearly.
- **Long term prognosis:** Those with metastases have lower survival outcome- Lowest survival rate for SDHB positive. The recurrence rate after 6y is around 20% (irrespective of genetic etiology), so long-term follow up is mandatory.

Next issue- Learning Pearls: ACES meeting on **Bone disorders**

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Update on IDEAL program (ISPAE Diabetes Education And Learning)

Preeti Singh, Associate Professor, Dept of Pediatrics, Lady Hardinge Medical College and Kalawati Saran Children's Hospital, New Delhi

The IDEAL program is continuing successfully, with Batch 5 rolled out on 1st April. With critical feedback from earlier batches, faculty and examiners, and with the new ISPAD 2022 guidelines, the need to upgrade content was felt. The course curriculum was revamped with regrouping topics, updating and simplifying the content, emphasizing the common gaps in knowledge, and adding more practical aspects. Our dynamic and excellent faculty and Core Committee accomplished this herculean task well. Two new topics were introduced - advances in the treatment and prevention of pediatric diabetes; and data collection/handling/protection, that have been much appreciated. IDEAL faculty was partly reshuffled to provide a chance to our young pediatric endocrinologists.

Thirty-one trainees from across the country, and three international trainees, were selected for Batch 5. Like earlier batches, women predominate (88%), nearly a third are themselves T1D or parents of T1D, the group is heterogeneous in their background, knowledge, skills, and ethnicity, but with the common goal of sharpening skills and knowledge for managing T1D. The trainees are mostly sincere, receptive, actively interactive, and regular (>80% attendance is the eligibility criterion for the Exit exam). Along with the concepts taught during sessions, the IDEAL faculty discussed real-life experiences and impromptu analytical case scenarios on the batch WhatsApp group, to brainstorm and improve the learning curve. The trainees enthusiastically responded with discussing and sharing their perspectives, thus enhancing learning, while helping the faculty understand their strengths and weaknesses.

We are proud to have Mr Harsh Kohli, a PwD, a T1D father, first batch IDEALite and mentor to many families, who joined the IDEAL team in place of Mr Lakshminaryana. Besides coordinating the IDEAL sessions, he contributes to teaching during sessions by sharing his vast experience. Language continues to be a challenge, but for the first time, significant hand holding and guidance have been voluntarily offered by senior IDEALites to trainees with language issues. As we approach the Exit exam, the examiners' preparations are in full swing. The Core Committee has begun attempts to assess outcomes, which we hope to share during ISPAE 2023 in November.

We are also gearing up for the upcoming batch 6, exclusively for physicians, starting on an auspicious day: 15th August 2023. Content is being upgraded, keeping in mind the different needs of physicians, and the ADA 2023 guidelines. We request all of you to encourage pediatricians already looking after T1D to join this batch.

Meanwhile, earlier batches have a platform to stay in touch with colleagues and faculty via the IDEALite WhatsApp group. There is ongoing information and experience sharing, including filing a complaint with NCPCR against a quack promoting "diabetes reversal" for the young. Another initiative is the first IDEALite **OPDE** (Ongoing Pediatric Diabetes Education) session on 9th July. This will be a series to connect and refresh knowledge, to keep pace with time and technology, conducted by the IDEALites. We hope to gradually reach out to the far corners of the country to improve the provision of good pediatric diabetes care.

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AWARDS/ ACHIEVEMENTS

Award- Dr Kavitha Bhat

Dr. N Kavitha Bhat, Senior Consultant Pediatric Endocrinologist at Aster Hospitals, Bengaluru, completed her "Master's in Clinical Service Operations" from the prestigious Harvard Medical School, Boston. She was one of 40 candidates chosen from over 300 applicants for the course. The graduation ceremony was held on 25th May 2023 at Harvard.

(Contributed by Dr Namrata Upadhya, Aster Hospital, Bengaluru)

Receipt of the International Prader Willi Syndrome Organization (IPWSO) 2023 Conference fund and Microgrant fund

Eleven countries received the International Prader Willi Syndrome Organization (IPWSO) 2023 microgrants, representing 13 projects, designed to improve the lives of people with Prader Willi syndrome (PWS). ***Dr Jahnavi Muralikrishnan***, Fellow Pediatric Endocrinology, Aster Hospitals, Bengaluru, has been the recipient of 2 microgrants:1500USD to develop patient education materials in English and local languages; and 2500USD to conduct a 2-day scientific conference and family conference.

Publications

Sirisha Kusuma Boddu, Ahila Ayyavoo, Vani Hebbal Nagarajappa, Kiran V Kalenahalli, Shantakumar Muruda, Raghupathy Palany. Van WykGrumbach Syndrome and Ovarian Hyperstimulation in Juvenile Primary Hypothyroidism: Lessons From a 30-Case Cohort, *J Endocrine Society*, June 2023, 7; 6, bvad042, https://doi.org/10.1210/jendso/bvad042

ACTIVITIES by ISPAE MEMBERS

pDKA App

Dr Kavitha Sakamuri, Pediatric and Adolescent Endocrinologist, Rainbow Children's Hospital, Hyderabad

Introducing a free mobile application (app) "pDKA": an easy-to-use mobile phone app for use in children/young people that helps doctors diagnose and manage Diabetic Ketoacidosis (DKA) has the potential to save lives by improving DKA management. Dr Kavitha Sakamuri announced the worldwide launch of the pDKA App on 23 March 2023 by Dr William Lamb (UK), who has been managing pediatric diabetes for four decades. During a Q&A session on DKA management as part of the launch, Dr Lamb said "DKA is life-threatening if not managed properly: this app could save

lives". The pDKA app is based on the 2021 BSPED guidelines, which are broadly similar to the ISPAD guidelines, and takes into account the updated NICE NG18 guidance. The required concepts (DKA protocols, calculations & flowcharts) were provided by Dr Sakamuri; Dr Vivek Shivhare, pediatric intensivist, wrote the software; Dr Satish Deopujari, pediatric intensivist, supported its free availability; and Dr Lamb oversaw the whole concept, from conception to completion. Apple iOS and Android users can download the app free of cost from App Store or Google Play.

Activities at Endokids

Dr Shalmi Mehta, Dr Ruchi Shah, Endokids Clinic, Ahmedabad

World Obesity Day was observed on 5th March, 2023, focusing on the importance of physical activity. We had a fun session of exercise with music, followed by a discussion about the importance of physical activity, in a child friendly manner.

The second activity was on the **importance of mental health** (child and family) in type 1 diabetes on 24th March, 2023. Dr Shuchy Chugh, well known diabetes educator living with T1D, and Dr Megha Desai, pediatric and adolescent psychiatrist, were co-faculty with Drs Shalmi and Ruchi. The event was attended by more than 40 families, where various coping mechanisms to deal with day-to-day life stresses and managing the different age-stages of a child with T1D were discussed.

An online event was organized by Drs Shalmi and Dr Ruchi on '**Revisiting basics of insulin therapy**' on Zoom and YouTube live. The basics of insulin therapy, different types, action, changing doses based on logbook data, etc. was discussed. This was attended live by more 35 families, with more views on YouTube later.

Webinar: Congenital Hyperinsulinism Consortium

Compiled by Dr Kavitha Sakamuri, Pediatric Endocrinologist, Hyderabad, Dr Jaikumar Contractor, Assistant Professor, Department of Anatomy, Pramukhswami Medical College, Gujarat, Dr Pratik Shah, Consultant Pediatric Endocrinologist, The Royal London Children's Hospital- Barts Health NHS Trust

The first online webinar by CHI India consortium in collaboration with Organization for Rare Diseases in India (ORDI) was held on 23 April 2023 via Zoom meeting platform. The webinar had over 400 registrations that included pediatricians, neonatologists, pediatric endocrinologists, geneticists, independent researchers in CHI. The webinar included interesting case

presentations, expert panel discussion, story of diazoxide in India as well as recent update on clinical trials. The webinar proceedings were duly acknowledged by the authorities of nationally reputed organizations like Indian Academy of Pediatrics (IAP), National Neonatology Forum (NNF) India and ISPAE. In further updates, CHI-India announced free availability of genetic testing for CHI in collaboration with Madras Diabetes Research Foundation, first National Professionals CHI Conference later this year and CHI parents' conference in 2024 (dates to be announced soon) as well as establishment of CHI parent support group.

T1D awareness session at Sancta Maria International School, Hyderabad

Ms Sirisha Mantha, Certified Diabetes Educator, Representative- Sweet Souls NGO, Hyderabad

A Type 1 Diabetes Awareness Session was conducted using the T1D School Resources (ISPAE), at Sancta Maria International School on 8th June 2023, made possible by the enthusiastic response we received from the school's Principal Ms. Ruchira Ghosh. The session was led by Dr Sirisha Kusuma Boddu, Dr Leena Priyamvada and Ms Sirisha Mantha, a T1D parent and representative of the NGO, Sweet Souls. It was attended by about 100 participants, including the academic and sports teachers, school nurses, and senior administration. The 90-minute program was extremely lively and interactive, imparting knowledge of the essentials of childhood diabetes and basics of day-to-day management, busting commonly held myths, and creating awareness of the latest directives from the National Commission for Protection of Child Rights (NCPCR). The program concluded with participants receiving a list of do's and don'ts, and T1D information brochures; while the infirmary was given a hypoglycemia treatment Guide Poster. The audience greatly appreciated the session.

Activities at Indira Gandhi Institute of Child Health, Bengaluru

Dr Vani HN, Associate Professor, Pediatric Endocrinology, IGICH

"Wish Bone Day" was celebrated at IGICH on 6thMay 2023, organised by the Indian Osteogenesis Imperfecta Foundation (IOIF) and IGICH. About 60 children receive free bisphosphonate injections and other physical assistance devices free from IOIF. The Depts of Pediatric &Adolescent Endocrinology, Pediatric Orthopedics Physiotherapy, and Pediatric Dentistry, provide ongoing multidisciplinary care to these children. A girl with OI who completed her MBBS was felicitated at the event. Cultural programmes were organised for these children.

An insulin pump was provided free of cost to a T1D child with the help of an NGO at IGICH on 23rdMay 2023, in the presence of the Director of the Institute, Ms Jayashree Murali (senior advocate from the NGO), Mr Deepak (from Medtronics), Dr P Raghupathy (senior Pediatric Endocrinologist) and Dr Vani HN.

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Scholarships of Rs 25,000 per child were provided on 26th May 2023, by Novo Nordisk, to fiveT1D children who have excelled in academics and have good glycemic control. The team from Novo Nordisk Education Foundation, Dr Sanjay KS (Director, IGICH), Dr Raghupathy P and Dr Vani HN were present at the felicitation.

Type 1 Diabetes meeting

Ms Beenu Singh, IDEAL- batch 2

A meet was organized for people living with Type 1 diabetes on 9th April, 2023, at Tilyar Lake, Rohtak, by IDEALite Ms Beenu Singh from Bangalore. Kids and care givers joined the first-of-its-kind meetup in Haryana, from Rohtak, Hisar and Gurgaon. Everyone shared their journey of diagnosis and management. The basics of T1D management, the challenges faced, and the strategies to overcome different situations, in achieving better control of T1D were discussed. Later, everyone enjoyed activities like boating and visiting the zoo, followed by lunch, where giving the bolus dose together was fun.

Yog Dhyan Foundation (YDF) activities

Dr Anil Vedwal, Chief Functionary, YDF, Delhi

YDF celebrated the completion of the first year of its "Look, One Virtual Event" on 11th June 2023. This successful monthly event, held every second Sunday, has enabled YDF to reach out to children and families with T1D everywhere, to educate on relevant topics, discuss important issues, resolve audience queries, and inspire with "Diabetes Heroes" (individuals and families). It is organized by Dr Anil Vedwal, Dr Anju Virmani, Ms Chhavi and Mr Sam Gulati. The Heroes in this quarter, since our last report, were T1D Mr Harsh Kohli; T1D Mr Naman Sharma and his parents; T1D brothers Mr Aditya and Harshit Johri, their parents and grandparents; and T1D Mr Angad Chandhok. Speakers and panelists have been Dr Bhanu Kiran Bhakhri (Sick Day Rules in T1D), Dr Beena Bansal and Dr Anju Virmani (Common Mistakes and Misunderstandings in Management of T1D) Dr Prateek Kakkar (Monitoring Eye Care in T1D), Dr Meena Chhabra, Prof Jyoti Kakkar, Dr Preeti Singh, Dr Anil Vedwal, Dr Arpita Prusty, Dr Srishti Puri, as well as Ms Chhavi, Ms Mridula Bhargava, and Ms Sanya Duggal. Meetings are moderated by Chhavi, Prerna, Amrita, Aruna and Sam.

YDF is tirelessly helping children with T1D by providing BG strips, insulin and syringes, and access to nutritious food; holding quarterly HbA1c camps and virtual weekly yoga sessions; and keeping track of health records. During recent fortnightly medical camps, we discussed CGM devices. While the concept of more information with hardly any finger pricks was met with smiles from children and parents alike, these devices are beyond the reach of most families. We

want to assess if intermittent use can help understanding and thereby improve glycemic control. To make a beginning, YDF has applied 10 CGM sensors (with readers loaned) free of cost to volunteers. On World Environment Day, we celebrated locally by having a "one person-plant-one tree" function in a nearby park.

We are overjoyed that we will soon be inaugurating a permanent office in Kailash Colony, to improve access to resources and support, and thereby the children's health and nutrition. We hope to continue to grow in scope and reach.

TRAINEES' SECTION

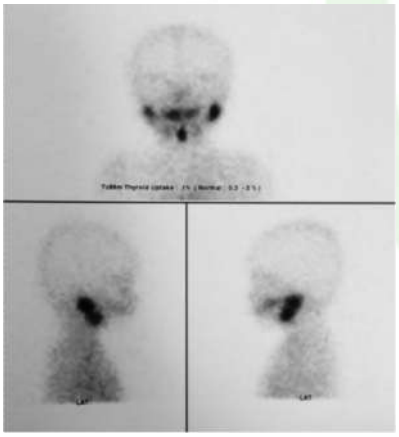
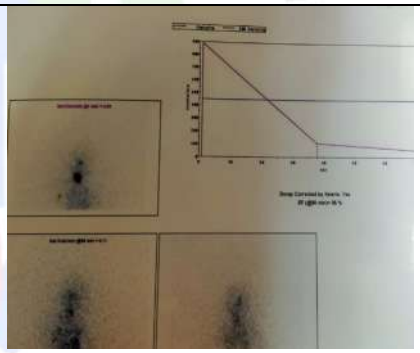
Tejasvi Sheshadri, Consultant Pediatric and Adolescent Endocrinologist,
Sparsh Super Speciality Hospital & Shishuka Children's Hospital, Bangalore

Please mail the answers to email: tejasviseshadri@gmail.com

Top three Winners (fastest responses) will be announced in the next issue

PART 1- The Pictorial Quiz:

Name the diagnosis based on the thyroid nuclear scan images given below

1	2
	

PART 2- THE CROSSWORD PUZZLE

Tease your brain, and complete the crossword puzzle based on ACROSS and DOWN clues related to the THYROID GLAND.

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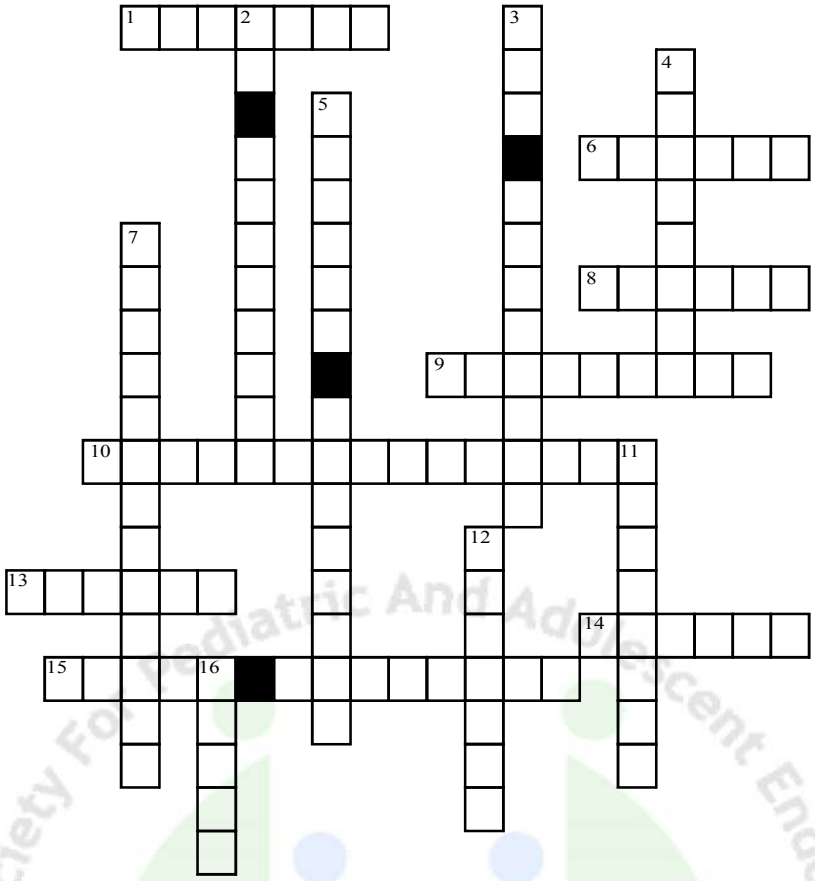

ACROSS	DOWN
1. Syndrome of diffuse goiter with sensorineural hearing loss 6. Most common cause of hyperthyroidism in children 8. Mutation causing mild transient congenital hypothyroidism with partial iodide organification defect 9. Most common type of thyroid cancer in children 10. Most serious complication of anti-thyroid medication is 13. Clinical scoring system for congenital hypothyroidism 14. Sodium iodide symporter is encoded by 15. Effect when excess iodide inhibits thyroid hormone synthesis	1. Gaint cell thyroiditis is also known as 2. Sporadic congenital non-autoimmune hyperthyroidism (SCNAH) is caused by which mutation 3. Round calcific collection characteristic of papillary thyroid carcinoma on FNA 4. Syndrome associated café-au lait spots, nodular goitre and thyroid hyperfunction 7. Measurement of this is cornerstone to post operative monitoring of thyroid carcinoma 10. Eye sign in Graves ophthalmopathy associated with infrequent and incomplete blinking 11. Most common thyroid dysgenesis 16. Mutation associated with congenital hypothyroidism and spiky hair

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June Activities by ISPAE

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IDEAL- "ISPAE Diabetes Education and Learning" Program
6th Batch exclusively for physicians (Aug 2023-Nov 2023)

IDEAL-CORE COMMITTEE

Program directors:
- Dr. Anju Virmani
- Dr. Aspi Irani
- Dr. Santhosh Olety
- Ms. Sheryl Salis
- Dr. Shaila Bhattacharyya
- Dr. Preeti Singh
- Dr. Sirisha Kusuma Boddu

ISPAE Office Bearers:
- Dr. Ahila Ayyavoo
- Dr. Rakesh Kumar

COURSE OBJECTIVE:
To develop a pool of certified Pediatric Diabetes Educators with expertise in ambulatory management of childhood and adolescent diabetes, by imparting theoretical and practical knowledge and skills, by experienced, learned faculty from ISPAE.

COURSE MODALITIES:
Structured online training course consisting of 17 teaching sessions, 6 feedback sessions, and an exit exam.

COURSE DURATION:
12 weeks, 2 hr. sessions, 2 days per week (Wednesday 7-9 PM and Sunday 3-5 PM)

LANGUAGE OF COMMUNICATION: English. Essential to have a laptop/ Desktop/ Tablet/ Smartphone; Chrome and Firefox (preferably latest versions); IOS 9 and above (all iPad & Android devices), with good connectivity.

ELIGIBILITY CRITERIA:
This course is intended for physicians already caring for children and adolescents with diabetes, and keen to learn comprehensive care.

COURSE FEE:
12000 INR/person (to be paid before start of course: non-refundable)

COURSE COMMENCEMENT DATE:
15th August 2023

CANDIDATE SELECTION:
Selection of the candidates will be through an online application and assessment exam.

APPLICATION:
To apply, fill in the registration form with the link given below. A maximum of 30 participants will be selected per course. Upon selection, candidates will be required to become members of ISPAE.
Links given below.

ONLINE REGISTRATION FORM LINK:
https://docs.google.com/forms/d/e/1FAIpQLSc XLpOUCF_EKdkAsVWuA3Ifl9FJm-HOu4LB9BXKVp_iEeYg/viewform

ONLINE ENTRANCE EXAM LINK:
https://docs.google.com/forms/d/e/1FAIpQLSeOJpH oxEjcpKxzxl3enHHh7qp31VSgtn0Vmc8Zq08R_Cg/viewform

LAST DATE FOR SUBMISSION OF APPLICATION: 24th July 2023

For queries and clarifications, contact ispae.ideal@gmail.com

ISPAE - BEST (Basic Education Series in Type 1 Diabetes) 5th Batch

BEST-CORE COMMITTEE

Program Directors
- Dr. Shaila Bhattacharyya
- Dr. Aspi Irani
- Dr. Santhosh Olety
- Ms. Sheryl Salis
- Dr. Preeti Singh
- Dr. Sirisha Kusuma B

ISPAE OFFICE BEARERS
- Dr. Ahila Ayyavoo
- Dr. Rakesh Kumar

For any queries:
Contact Mr. Ankit @ 9041493138
abukoushal@gmail.com

COURSE OBJECTIVE:
To provide basic education on the ambulatory management of children and adolescents with type 1 diabetes

COURSE MODALITIES:
Structured online training course consisting of 8 teaching sessions (each session one hour, two sessions/day)

COURSE DURATION:
4 weeks, (Tuesday 7-9 PM), two-hour duration

LANGUAGE OF COMMUNICATION:
English. Essential to have a laptop/ Desktop/ Tablet/ Smartphone; Chrome and Firefox (latest versions); IOS 9 and above (all iPad & Android devices), with good connectivity.

ELIGIBILITY CRITERIA:
This course is intended for trained nursing staff, physician assistant, assistive school personnel, parents/caregivers of children with T1D, or adults with T1D, to learn basics of type 1 diabetes and its ambulatory management

COURSE FEE:
1000 INR/person (to be paid before the start of the course: non-refundable)

COURSE COMMENCEMENT DATE:
18th July 2023

CANDIDATE SELECTION:
A maximum of 30 participants will be selected per course.

APPLICATION:
To apply, fill in the online registration form.
https://docs.google.com/forms/d/e/1FAIpQLSdUNupWTI9q-U6IzgM1yeekUG_dD5F8wpPSib5qNyZrTP7zOA/viewform

LAST DATE FOR SUBMISSION OF APPLICATION 8th July 2023

Contact us: editor.capenews@gmail.com


ISPAE 2023
Enhancing Paediatric Endocrine Care - Shaping the Future Together
14th - 19th November 2023
8th Biennial Meeting of
Indian Society for Pediatric and Adolescent Endocrinology (ISPAE)
Venue: Hilton Garden Inn, Embassy Manyata Business Park, Bengaluru
17th - 19th November, 2023
Abstract Submission is Now Open
ABSTRACT SUBMISSION CLOSES ON
31ST JULY, 2023
CLICK HERE TO SUBMIT YOUR ABSTRACT
www.ispae2023.com