DECEMBER 2022
Volume 26, Issue 4

CAPE News

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

CONTENTS

Theme: Calcium Disorders

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

From the Editorial Board

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Advisor

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Editorial board

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Dear ISPAE members,

It gives our team great pleasure to connect with ISPAE members through this December 2022 issue of CAPE News, themed on Calcium Disorders. We have many interesting articles, mini reviews, journal scan, and case reports, pertaining to childhood calcium disorders. There are reports of members' activities, useful information pertaining to pediatric endocrinology, Diabetes Educators' corner, and reports and learning pearls from our mid-term meeting, ISPAE 2022, from ISPAD 2022 and other meetings. In addition, of course, are reports of the numerous activities on the occasion of World Diabetes Day from across the country. Hope you have a good reading experience.

This is the last issue prepared by our team. We profoundly thank all ISPAE members for enthusiastically contributing to all the issues and enriching the content; all the trainees who participated in the quizzes that appeared in every issue; and the ISPAE executive council 2021-22 for their constant support and motivation.

We congratulate the new ISPAE team of Dr Ahila Ayyavoo, Dr Rakesh Kumar, Dr Sirisha Kusuma B, and the EC members, Drs Aayush Gupta, Amarnath Kulkarni, Chetankumar Dave, Jaivinder Yadav, Mahesh Maheshwari, Ravindra Kumar, and Zalak Upadhyay. Best wishes also to the new CAPE News team which we are sure will take CAPE News to greater heights.

Feedback is welcome at: *editor.capenews@gmail.com*

Thank You and Regards,
Team CAPE News 2021-22

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Office Bearers' Message

Dear ISPAE members,

Greetings from Team ISPAE 2021-22!

On behalf of the executive council of ISPAE, we wish all the members a very happy Xmas and an auspicious new year 2023! We thank God for almost an end to the difficult COVID pandemic for nearly two years and pray for no further COVID waves/pandemics! We congratulate the organizing team at Chandigarh for a very successful ISPAE-ISPAD Midterm meeting held on 19-20 Nov 2022! It was wonderful to attend the academic feast and meet & greet ISPAE members physically at Chandigarh.

The tenure for the current Executive council of ISPAE is completing this December. We congratulate the newly elected executive of ISPAE led by Dr Ahila Ayyavoo. We wish them all the best for their tenure 2023-24. We thank the Returning Officer for ISPAE elections 2022, Dr Vijaya Sarathi, for the smooth conduct of elections procedures.

Dr Shaila Bhattacharyya
President
ISPAE 2021-22

Dr Ganesh Jevalikar
Secretary cum Treasurer
ISPAE 2021-22

Dr Rakesh Kumar
Joint Secretary
ISPAE 2021-22

It gives us immense pleasure to humbly count the work done by the current EC over the last two years, even though most of our tenure was marked by the COVID pandemic. We initiated and ran our very successful monthly academic programme, ISPAE-ACES. We also started a much-needed training course for Diabetes Educators, the "ISPAE Diabetes Education and Learning" (IDEAL) program. the IDEAL program is a huge success and is being appreciated in various forums, including ISPAD 2022, where we had an oral presentation on its feasibility and cost-effectiveness. We thank all the faculty (more than 50 experts) who contributed to three IDEAL courses already completed, and the fourth ongoing course.

After the success of the first course of IDEAL, we started "Basic Education Series in Type 1 Diabetes" (BEST) for children with Type 1 Diabetes mellitus and their caregivers.

The ISPAE EC has also developed school education modules on common endocrine conditions including normal/abnormal Growth, Thyroid problems, Obesity, Diabetes, and Puberty. The modules are intended to be used by all ISPAE members as part of advocacy for children with endocrine disorders. The modules will soon be uploaded on the ISPAE website for free use.

To commemorate 'World Diabetes Day' on 14 Nov 2022, the ISPAE EC, under the leadership and guidance of Dr. Shaila Bhattacharyya, organized an awareness and education program addressing people with Type 1 Diabetes (T1D) and their parents/caregivers.

Other vital achievements (during 2021-22) worth mentioning include the online ISPAE membership application system, revamping the ISPAE website, changes in the ISPAE bylaws to smoothen the accounts for ISPAE conferences, enabling online transactions for the ISPAE bank account, and the start of ISPAE's YouTube channel.

We wish to put on record the immense guidance and support of our Advisors, including Prof Raghupathy P and Prof PSN Menon. Their wisdom and timely advice have helped us perform our job with more conviction over the last 2 years.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Office Bearers' Message

We must congratulate editorial team of the ISPAE's official journal, the Journal of Pediatric Endocrinology and Diabetes (JPED), for successfully launching the journal and completing one year with three issues. It has received excellent responses from India and abroad. We earnestly thank the ISPAE members who are already contributing manuscripts, and we appeal to all other members to contribute and spread its awareness among colleagues in their respective areas.

CAPE NEWS has seen a complete revamp with a very hard-working team under the leadership of Dr Hemchand K Prasad. It is very informative and a genuine reflection of our vibrant and dynamic Society.

The unified pediatric endocrinology fellowship training program under the ISPAE banner has been successful with Dr Anurag Bajpai as the coordinator. This initiative will bring the desired uniformity among all the Pediatric Endocrine training fellowships running at various places across India.

ISPAE membership has also seen swift growth over the last two years, with a total of 757 members at present.

We thank all ISPAE members for posing faith in us to serve and steer ISPAE in 2021 & 2022.

We are confident that the upcoming executive committee will take our ISPAE to newer heights.....!
Long live ISPAE!

Jai Hind!

Best Wishes,
Drs Shaila Bhattacharyya, Ganesh Jevalikar, Rakesh Kumar,
Team ISPAE 2021-22

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Welcome to new ISPAE members

- Dr Sibi KR, Pediatrician, Valluvanad Hospital, Palakkad
- Dr Arpita, Associate Professor, King George Medical University, Lucknow, UP
- Dr Nanda N, Yashoda Hospitals, Secunderabad
- Dr Mohammed Avais, Bijinor, Uttar Pradesh
- Dr Bifina Beegum, Government Medical College, Ernakulam
- Dr Abhishek Kothari, Saurashtra University, Bikaner, Rajasthan
- Dr Shruti Mondkar, Hirabai Cowasji Jehangir Medical Research Institute, Pune
- Dr Konpal Paharia, Senior Resident, AIIMS, Rishikesh
- Dr Deepa T Unnikrishnan, MOSC Medical College, Ernakulam
- Dr Ramya OM, Indira Gandhi Institute of Child Health, Bangalore
- Dr Sajad Ul Islam Mir, Sher-i-Kashmir Institute of Medical Sciences, Srinagar
- Dr Kamran Faisal, Chief Medical Officer, VMMC and Safdarjung Hospital, Delhi
- Dr Mughda T, Senior Resident, AIIMS, Bhopal
- Dr Rajeshwari K, Marvel Hospital, Bangalore
- Dr Archana Kumari, PDCC Fellow, SGPGI, Lucknow
- Ms Manju Panda, Senior Diabetes Educator and Nutritionist, Max Hospital, Saket, Delhi
- Ms Piridi Raga Deepthi, Hyderabad
- Dr. Guruprasad Udupi, Mallige Hospital, Bengalore
- Ms Sirisha Mantha, Diabetes Educator, Hyderabad, Telangana
- Ms Nilam Jani, Diabetes Educator, Jalgaon, Maharashtra
- Ms Sharanya Shetty, Dietician, Karnataka Institute of Endocrinology and Research, Bangalore
- Ms Harshita Agarwal, Dietician, Rainbow Hospital, Hyderabad
- Mr Jitheesh Mathew, T1D Society, Wayanad
- Ms Kudupudi Ooha, Clinical Dietician, Hyderabad
- Mr Aravind Madhi, Capgemini, Bangalore
- Ms Utpala Daryapurkar, Diabetes Educator, Jalgaon
- Ms Sreedivya Akula, Sweet Souls, Hyderabad, Telangana
- Ms Nazreen S, Thiruvananthapuram, Kerala
- Ms Pragya Verma, Pune, Maharashtra
- Ms Suma Reddy, Nutritionist and Diabetes Educator, Bangalore
- Ms Komal Nayyar, Gurgaon, Haryana
- Ms Hafzah Hameed, Homeopathic physician
- Ms Zeal Doshi, Clinical Dietician, Nurture Health Solutions, Mumbai
- Ms Rachitha Avinash, Nutritionist, Bangalore
- Ms Savita Agarwal, Trustee, JDPF, Ahmedabad

A warm welcome to the ISPAE family!

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Guidelines: Calcium Disorders

Dr Pragya Mangla, Pediatric Endocrinologist, Dept. of Endocrinology
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Evaluation and Management of Hypoparathyroidism

Diagnosis of Hypoparathyroidism (HypoPT) – Low serum calcium (S Ca) (low ionized serum calcium or total serum calcium adjusted for albumin), in the presence of undetectable, low or inappropriately normal intact PTH (utilizing either a second- or third-generation assay), on two occasions at least 2 weeks apart, confirms the diagnosis. Additionally, elevation in serum phosphorus, reductions in 1,25-dihydroxyvitamin D (1,25(OH)D) and elevations in the urinary fractional excretion of calcium are seen. Hypocalcemia due to Vitamin D deficiency and pseudohypoparathyroidism are the differential diagnosis.

Genetic testing in the diagnosis and evaluation of nonsurgical HypoPT:

Causes of Nonsurgical HypoPT may be genetic [DiGeorge Syndrome, an activating mutation of the extracellular calcium-sensing receptor (CASR) gene, Kearns-Sayre syndrome or MELAS syndrome etc.], autoimmune (APS-1 aka APECED syndrome and others), metabolic (mainly magnesium deficiency or excess), or rarely due to deposition of copper (Wilson disease), iron (congenital or acquired hemosiderosis), or aluminium, in parathyroid tissue or the invasion of the parathyroid glands by neoplastic diseases or granulomatous or inflammatory cells or by amyloid protein. In neonates with HypoPT, maternal hyperparathyroidism is frequently seen.

Genetic testing should be done in patients with nonsurgical HypoPT who have a positive family history of nonsurgical HypoPT, present with syndromic features, or are younger than 40 years. If other clinical features of autoimmune polyendocrinopathy– candidiasis–ectodermal dystrophy syndrome (APECED) are present, genetic testing for autoimmune regulator (AIRE) gene variants should be undertaken.

Avoid the designation of "autoimmune HypoPT" for patients who do not have APECED, because there are no definitive diagnostic tests for polygenic autoimmune HypoPT.

Postsurgical (PostSx) HypoPT: This is frequently seen in adults. It is considered permanent if postsurgery, the HypoPT persists even more than 12 months. Risk factors include patient factors (i.e., vitamin D deficiency), the underlying disease (malignancy, thyrotoxicosis, size of the parathyroid glands identified during thyroidectomy), and operative factors (reoperation, extent of operation, surgeon's practice volume).

Efforts should be made to avoid accidental parathyroidectomy. Intraoperative parathyroid auto-transplantation should be done only in cases of inadvertent parathyroidectomy (and not as a routine).

If PTH values are >10 pg/mL 12–24 hours after surgery, the development of permanent HypoPT is unlikely, and there is no long-term need for treatment with active vitamin D and calcium supplements in doses above the recommended daily allowance (RDA). Many patients with PTH values <10 pg/mL 12–24 hours postop may still recover from temporary HypoPT.

Most common symptoms and complications of HypoPT

In children: Mild symptoms include numbness and tingling of the extremities and perioral region, muscle cramps, and fatigue. Physical examination often reveals hyperreflexia and positive Trousseau sign. In severe cases, overt tetany, seizure, altered mental status, cardiac rhythm disturbances, refractory congestive heart failure, and laryngospasm can be observed.

In adults: Most common complications include cataract (17%), infection (11%), nephrocalcinosis/ nephrolithiasis (15%), renal insufficiency (12%), seizures (11%), depression (12%), ischemic heart disease (7%), and arrhythmias (7%).

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Optimal monitoring strategy for chronic HypoPT

Baseline assessment of serum Calcium, Magnesium, Phosphorus, Creatinine, eGFR, 25OH vitamin D and 24 hr Urine calcium-creatinine ratio is needed. Complete the baseline assessment for the presence of renal calcification or stones, with renal imaging.

Monitor serum calcium (ionized or albumin-adjusted) once or twice weekly during the initial dose adjustment period, and then 3 monthly when serum levels are stable. Stable patients are monitored with repetition of other laboratory profiles every 6–12 months. Unstable patients are followed more closely to ensure that serum calcium does not fluctuate widely and to avoid the symptoms and the long-term complications of HypoPT. Regular ophthalmic evaluation for cataract is needed.

Management of patients with HypoPT:

The primary goals of chronic management are to maintain an acceptable range of the following indices: (a) serum total calcium (usually in the low normal range: 8-8.5 mg/dl); (b) serum phosphorus (in the high normal range); (c) 24-h urine calcium excretion (< 300 mg/ 24 hrs or <4 mg/kg/24 hours) and (d) calcium-phosphate product under 55 mg2/dl2.

Conventional therapy as first-line therapy: Treat with elemental calcium [children and adolescents: 30-75 mg of elemental calcium/kg/day in divided doses, preferably with meals; adults: 0.5-3 g/day] and an active vitamin D analogue (calcitriol 0.25-3 mcg/day in adults and 20-60 ng/kg/day in children and adolescents or alpha-calcidol 0.5-6 mcg/day in adults) with the goal of raising serum calcium to the target range. High dose ergocalciferol (50.000 to 100,000 IU/day) is also used with calcitriol therapy – it is given initially for 3 weeks, then the dose of calcitriol is gradually tapered once ergocalciferol becomes effective. Cholecalciferol or ergocalciferol is also often required to maintain the 25(OH)D level within the normal range.

Hypercalciuria (> 4 mg/kg/24 hours) may be associated with a higher risk of renal stones in patients with HypoPT and thus should be avoided. Consider treating hypercalciuria with thiazide diuretics in conjunction with a low-sodium diet with careful monitoring of blood pressure (BP), serum magnesium, potassium, and renal function. Thiazide diuretics are not advised in the presence of adrenal insufficiency; they should be used carefully in the presence of autosomal dominant hypocalcemia, as the urinary magnesium losses are further enhanced with thiazide diuretics.

Avoid hyperphosphatemia. Prescribing calcium supplements with meals help to provide phosphate binding. Implement a low-phosphate diet if needed, and judiciously use active vitamin D analog therapy. Treat to normalize plasma magnesium levels.

Hypercalcemia management: Different modalities for managing associated hypercalcemia are hydration, saline diuresis, furosemide after rehydration, glucocorticoids and bisphosphonate; all to be to be used as per accepted guidelines.

In case of severe acute hypocalcemia, emergency management is advised in the presence of carpal or pedal spasm, seizures, broncho- or laryngospasm, or if the albumin-adjusted calcium <7.0 mg/dL. Intravenous (iv) calcium bolus administration is given slowly not greater than 2 ml of Inj. Calcium Gluconate/kg over 10 minutes, diluted in 100 ml 5% dextrose/ 0.25 normal saline in children and adolescents and 90–180 mg elemental calcium over 10–20 minutes in adults and requires closed monitoring of pulse rate and QT interval. This is followed by a slower iv calcium infusion 10-11 ampoules of calcium gluconate in 1 L of 5% dextrose water or normal saline and initiate infusion at 50-100 mL/hour and titrate to serum calcium) and initiation of oral therapy with calcium and calcitriol/alphacalcidiol. A typical infusion rate is 0.5 to 1.5 mg/kg of elemental calcium per hour. An elemental calcium iv dose of 15 mg/kg over the course of 4–6 hours is expected to elevate serum calcium by approximately 2-3mg/dl. Vitamin D deficiency or hypomagnesaemia should be treated appropriately. Calcium bolus or infusion might be needed to be continued for a week.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

PTH Replacement Therapy

The majority of cases of paediatric HPT are well controlled on conventional treatment with calcium and vitamin D analogues. However, this treatment may be inefficient, especially in patients with APECED syndrome and with activating mutations in the calcium sensing receptor (CaSR). Thus PTH replacement therapy can be considered in patients who are not adequately controlled on conventional therapy. Inadequate control is considered to be any one of the following: (i) symptomatic hypocalcemia (ii) hyperphosphatemia, (iii) renal insufficiency, (iv) hypercalciuria, or (v) poor quality of life. Individuals with poor compliance or malabsorption or who are on or intolerant of large doses of calcium and active vitamin D may also benefit from PTH therapy.

Studies have demonstrated beneficial role of rhPTH (1-34) in pediatric population in short term but pediatric data regarding rhPTH (1-84) and long term use of rhPTH (1-34) is lacking.

References:

1. Khan AA, Bilezikian JP, Brandi ML, Clarke BL, et al. Evaluation and Management of Hypoparathyroidism Summary Statement and Guidelines from the Second International Workshop. J Bone Miner Res. 2022 Aug 28. doi: 10.1002/jbmr.4691.

2. Di Maio S, Soliman AT, De Sanctis V, Kattamis CC. Current treatment of hypoparathyroidism: Theory versus reality waiting guidelines for children and adolescents. Acta Biomed. 2018 Mar 27;89(1):122-131. doi: 10.23750/abm.v89i1.7118.

Knowing the Calcium sensing receptor: A mini review

Aashima Dabas, Associate Professor, Dept of Pediatrics
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The calcium sensing receptor (CaSR) is a classic 7-transmembrane domain G-protein-coupled receptor, that regulates the calcium homeostasis in response to ionized calcium levels in the blood. CaSR structurally resembles a disulphide-linked homodimer. The CaSR gene is present on chromosome 3 that comprises of 8 exons (mapped at 3q13.3-21). The expression of CaSR is quite ubiquitous, but the main organs that express it include the parathyroid glands and the kidneys (thick ascending loop of Henle, distal tubules and collecting ducts).

The mechanism of action of CaSR in regulating serum calcium levels is shown in the figure 1 below. The levels of ionized calcium are primarily sensed in the blood by the CaSR present in the parathyroid glands, bone and kidneys. The activation of CaSR stimulates G proteins (notably Gi/o and Gq/11), with resultant activation of intracellular pathways, to cause a reduction in PTH secretion. This prevents mobilization of calcium from the bones, leading to a reduction in serum calcium levels. A gain-of-function mutation of CaSR is associated with abnormal channel activation that causes hypocalcemia, while a loss-of-function mutation causes hypercalcemia. The Gi/o protein predominantly controls the cAMP-mediated PTH secretion, while the Gq/11 regulates the endogenous regulated PTH secretion. CaSR also inhibits cell proliferation and inhibits PTH gene transcription. It increases the local production of 1,25 (OH) D3, that inhibits further PTH secretion. As a checkpoint, the CaSR in parathyroid glands is resistant to desensitization and remains activated and functional in mutated states.

The CaSR present in the kidneys and collecting system mediate calcium reabsorption coupled with paracellular movement of sodium chloride (NaCl) across the tubules. Apart from this paracellular pathway, filtered calcium and magnesium ions also get reabsorbed with the help of junctional proteins. The activation of renal CaSR receptors reduces the renal absorption of calcium (indirect PTH mediated action) to cause a reduction in serum calcium levels by inhibition of NaCl reabsorption and reducing expression of these junctional proteins.

The secretion of anti-diuretic hormone in hypovolemic states mediates increased water absorption through aquaporin-2 channels. This results in saturating the urinary calcium concentration. The CaSR on the luminal surface senses the increased calcium level and inhibits the tubular response to vasopressin (ADH) to limit further urine concentration (additional mechanism).

CaSR is also expressed in the bone (osteoblasts, chondrocytes, osteocytes, osteoclasts) to affect the bone development and maintenance. Homozygous CaSR gene knockout mice showed reduction in bone volume and size, reduced local bone growth factors and higher apoptotic and bone resorption factors, and higher levels of proteins that inhibited bone mineralization. Expression of CaSR in the nervous system modulates the release of neurotransmitters and polarization and depolarization of neurons. Additional role of the CaSR is in the gastrointestinal tract where it affects the gut barrier in inflammation and the respiratory system where it affects airway hyper-responsiveness and inflammation. CaSR is also expressed in pancreatic acinar cells and thus affects the metabolism of carbohydrates and fat.

Few disorders in CaSR are mentioned below:

- Gain-of-function mutations in CaSR result in autosomal dominant hypocalcemia type 1 (ADH1, OMIM# 601198). These patients have hypocalcemia with hypoparathyroidism and resultant hyperphosphatemia. However, with the defective renal calcium handling, these patients also have hypercalciuria. Few patients may have more severe presentation mimicking Bartter-like syndrome accompanied with metabolic alkalosis.
- Loss-of function/ inactivating mutations of CaSR cause decreased sensitivity to ionized calcium levels leading to hypercalcemia. Heterozygous mutations cause benign disease like familial hypocalciuric hypercalcemia (FHH) while homozygous states cause severe hypercalcemia, usually presenting in the neonatal period (neonatal severe hyperparathyroidism- NSHPT).
- Acquired antibodies to CaSR also results in inactivation of CaSR through allosteric modulation. The presentation is with hypercalcemia and variable severity of the disease.
- The expression of CaSR on thyroidal C-cells also affects the calcitonin release. This mechanism is less active in humans than rodents.

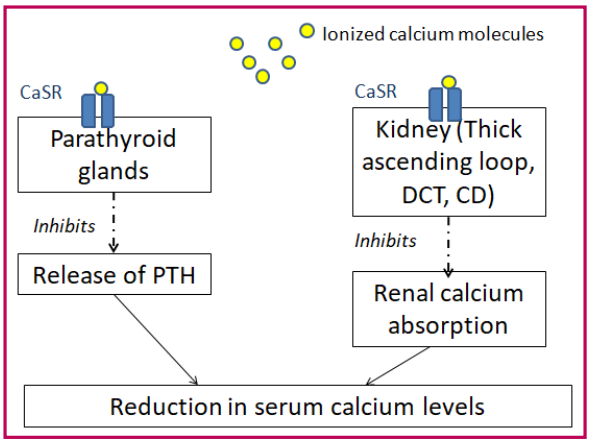

Figure 1: Calcium homeostasis maintained with activation of Calcium sensing receptor

The activity of CaSR is also affected by other polypeptides, antibiotics etc., thus diversifying the pathophysiological role of CaSR in other metabolic pathways. The expression of CaSR on hematopoietic cells and vascular endothelium has established its role with cardiovascular diseases. CaSR is involved in upregulation of cellular proliferation, release of inflammatory cytokines, vascular calcification, modulating vasoconstriction and vasorelaxation thus affecting hypertension and hypertrophy of cardiomyocytes, thereby having consequences on cardiovascular diseases. CaSR through its ubiquitous expression is a target for drugs like cinacalcet that decrease the calcium levels.

Additional reading:

1. Sundararaman SS, van der Vorst EPC. Calcium-Sensing Receptor (CaSR), Its Impact on Inflammation and the Consequences on Cardiovascular Health. Int J Mol Sci. 2021; 22: 2478.

2. Makita N, Ando T, Sato J, et al. Cinacalcet corrects biased allosteric modulation of CaSR by AHH autoantibody. JCI Insight. 2019;4(8):e126449.

3. Katie L, Fadil MH, Tracy MJ, et al. International Union of Basic and Clinical Pharmacology XXX: Calcium-sensing receptor Nomenclature, Pharmacology, and Function. Pharmacol Rev. 2020 July 01; 72(3): 558–604.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Diagnosis and management of pseudohypoparathyroidism and related disorders: first international Consensus Statement

Dr Aaradhana Singh, Associate Professor, Department of Pediatrics,
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Pseudohypoparathyroidism (PHP) and related disorders are associated with a spectrum of abnormal physical characteristics as well as neurocognitive and endocrine abnormalities that are caused primarily by the molecular defects that impair hormonal signalling via receptors that are coupled, through the α-subunit of the stimulatory G protein (Gs α), to activation of adenyl cyclase. Types of PHP include PHP1A, PHP1B, PHP1C and PHP 2. PHP 1A and 1C have similar clinical features with different molecular defects. PHP 2 is believed to occur in severe, long standing vitamin D deficiency. PHP related disorders are: pseudo pseudo-hypoparathyroidism (PPHP), progressive osseous heteroplasia (POH), acrodysostosis 1 and 2. Table 1 shows the features of PHP and related disorders. Table 2 shows the management and follow up of these patients.

Table 1: Clinical features of PHP and PHP related disorders

Feature	PHP1A	PHP1B	PPHP	POH	ACRDYS1	ACRDYS2
Growth	Growth velocity progressively decreasing Adult short stature	Macrosomia Average adult stature	SGA Growth velocity decreasing Adult short stature	SGA	SGA Adult short stature	SGA Adult short stature
Obesity	Early onset	Early onset	Normal weight or lean	Normal weight or lean	Present	Present
Brachydactyly	70-80%	15-33%	< 30%	Rare	97 %	92 %
Advanced bone age	70-80%	15-33%	Unknown	Unknown	100 %	100 %
Ectopic ossification	30-60%	0-40%	18-100%	100 %	0 %	0 %
PTH resistance	100 %	100 %	Rare & mild	absent	100 %	29 %
TSH resistance	100 %	30-100 %	Rare & mild	absent	100 %	16 %
Neurological symptoms	Cognitive impairment, Cerebral calcification	Cerebral calcification	Unknown	Unknown	Unknown	Cognitive impairment
Gonads	Gonadotropin resistance	Normal	Normal	Unknown	anatomical dysfunction	Unknown
Molecular defect	Maternal loss of function mutation at GNAS coding sequence	Methylation defect at GNAS coding sequence	Paternal loss of function mutation at GNAS sequence	Paternal loss of function mutation at GNAS sequence	Mutation in PRKAR1A	Mutation in PDE4D

Table 2: Management and follow up of PHP and PHP related disorders

Clinical features and Investigations	Treatment	Follow up
PTH resistance: Raised PTH, low calcium, raised phosphorus and calcidol.		
Hypocalcemia- - Tetany and seizures. - Failure of tooth eruption, short blunted roots, dental pulp alterations, hypodontia and enamel hypoplasia	- Active vitamin D metabolites or analogues (calcitriol/calcidol) - Calcium supplements - Phosphate binders rarely indicated in severe and long-term persistent hyper-phosphatemia	- Measurement of PTH, calcium and phosphorus every 6 months - Maintenance of serum calcium and phosphorus within normal range while avoiding hypercalciuria and lowering PTH levels as permitted by serum and urinary levels of calcium - Renal imaging for nephrocalcinosis - Dental reviews every 6–12 months
Ectopic calcium deposition- - Intracranial deposition of calcium (Fahr syndrome) - Ectopic depositions of calcium and phosphorus in eyes lead to cataracts, corneal opacities, macular degeneration, nystagmus, anisocoria, papilledema, tortuosity of retinal vessels and microphthalmia - Osteitis fibrosa cystica and slipped capital femoral epiphysis	- Physical therapy and meticulous skin care - Due to a high risk of recurrence, surgical excision limited to well-delineated, superficial lesions causing pain and/or movement impairment - In ossifications involving joints, immobilization should be avoided to prevent ankyloses. - No evidence supports use of nonsteroidal anti-inflammatory drugs, bisphosphonates, or steroids	- Cutaneous bony plaques should be examined at each visit - CT or MRI of ossifications should be performed in case of painful or symptomatic lesions, if joint or organ function is being jeopardized, or when considering surgical excision
TSH resistance: Raised serum levels of TSH and thyroid hormone levels that are normal or slightly reduced. Evaluation of thyroid for early detection of TSH resistance and early intervention is recommended in all patients with PHP and related disorders at diagnosis.		
Growth and Growth hormone deficiency - Majority of PHP1A and PPHP patients display adult short stature, 2.5 SD below the mean in average, despite having a normal length/ height during childhood. - Short stature is more pronounced in acrodysostosis, with final height being on average –3.5 SD	- Patients born SGA who do not demonstrate appropriate catch-up growth or patients showing GHD should be considered for treatment with rhGH - Higher doses of rhGH should be used.	Regular monitoring of growth, skeletal maturation and GH secretion advised in all affected children, starting around 3–6 years of age
Obesity		
Patients with PHP1A or PHP1B develop early-onset obesity,	Patients should be provided with psychological support and educational	All patients be screened for restless sleep, snoring, inattentiveness, and

usually within the first 2 years of life Sleep apnea, a well-known complication of obesity, has been reported to be more frequent in patients affected with PHP1A	programs, as early as possible, even in the presence of a normal BMI as a preventive strategy,	daytime somnolence and, if present, polysomnography is recommended Blood pressure, Lipid and glucose metabolism should be monitored on a regular basis
Gonadal function and puberty. Resistance to gonadotrophins is more subtle than resistance to other hormones such as PTH and TSH.		
Patients may present with menstrual irregularities in girls, cryptorchidism in boys, and blunted or absent pubertal growth spurt in adolescents	Cryptorchidism and/ or hypogonadism, when present, should be corrected and managed according to standard recommendations	- SMR staging and testicular descent should be regularly assessed. - Bone age should be determined. - Conversely, biochemical assessment of gonadal status is not recommended unless clinically indicated.
Fertility and pregnancy - Unassisted and uneventful pregnancies have been reported in patients with PHP1A1 and autosomal dominant PHP1B, and are more often seen in women with PPHP, who give birth to offspring with PHP1A.		
Osteoporosis - Patients with PHP and related disorders have several potential risk factors for osteoporosis (hypogonadism, chronic elevation of PTH and GHD). Routine dual-energy X-ray absorptiometry (DXA) measurements are not recommended. If osteoporosis is diagnosed, treatment of underlying secondary cause for bone loss (hypogonadism, postmenopausal status or related to sustained elevation of PTH levels and GHD) should be done.		
Cognitive impairment - Patients should be referred to a neuropsychologist for neurocognitive and/ or behavioral assessment at diagnosis or at preschool age, especially patients with PHP1A and acrodysostosis. Most patients will require specialized educational assistance.		
Brachydactyly and orthopaedic issues- Brachydactyly might contribute to difficulty with fine motor skills, such as handwriting, leading to need for occupational therapy services in early childhood. A high incidence of carpal tunnel syndrome has been observed in patients with PHP1A and PPHP.		

PHP and related disorders are primarily clinical diagnoses. Assessment of Gsα bioactivity is usually not required for the clinical diagnosis of PHP and related disorders. Molecular testing should be performed to confirm the clinical diagnosis and to identify the subtype of the disease. Genetic testing should be based on the clinical characteristics, local access to genetic testing and the most likely causes of the disease. Administration of exogenous PTH is not recommended.

Additional reading:

1. Mantovani G, Bastepe M, Monk D, et al. Diagnosis and management of pseudohypoparathyroidism and related disorders: first international Consensus Statement. Nat Rev Endocrinol. 2018;14(8):476-500.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Drug Corner - Recombinant PTH

Dr Hemchand K Prasad, Consultant, Department of Pediatric Endocrinology
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Hypoparathyroidism is conventionally treated with oral calcium and Vitamin D analogs (1,2). The problems with this treatment include poor metabolic control, hypercalciuria, renal dysfunction and ectopic calcification (2). Additional useful therapeutic agents in specific clinical indications include phosphate binders and thiazides. Indications for recombinant PTH 1-34 (rPTH) are well described in adults. A recent narrative has described a review of 70 children in 15 studies on the utility of rPTH in children (2).

Short term benefits of rPTH in the Indian setting in acute situations have been described (3). The authors described the use of a short course of rPTH in a dose of 20 mcg once a day and twice a day in two cases of severe hypocalcemia and hyperphosphatemia. The severe hypoparathyroidism was due to autoimmune polyendocrine syndrome -1 in one child, secondary to surgery for Graves' disease in the other child. Normalization of biochemical parameters helped in shortening the duration of stay in the intensive care unit.

A tertiary care center from North India reported a 10 year experience of rPTH in a single case of partial Jacobsen syndrome and hypoparathyroidism (4). The authors started rPTH because of the presence of hypercalciuria, which regressed with treatment, so oral calcium could be withdrawn after 8 years of therapy.

In a 3 year randomized parallel trial from NIH Maryland comparing conventional treatment with rPTH treatment in 12 children with chronic hypoparathyroidism, it was observed that rPTH allowed normal skeletal development with normal bone mineral accrual, growth and weight gain (5).

A long-term study on 14 children with hypoparathyroidism attributable to APS-1 (n=5) and CaSR (n=9) for 6.9 ± 3.1 years reported that rPTH therapy resulted in improved growth velocity and bone accretion rates (whole body, lumbar spine and femoral neck) (6).

rPTH is given subcutaneously in the dose of 0.5-1 mcg/kg/day in two divided doses. It may be considered if there is hypercalciuria, renal dysfunction, and/ or poor metabolic control. Monitoring of serum calcium and phosphorous, urine calcium excretion, and ultrasound abdomen are needed to adjust doses and withdraw conventional medications (oral calcium and vitamin D analogs). The primary concern with using rPTH in children with open epiphyses of the risk of osteosarcoma (7,8), arises from animal studies using high doses of rPTH. The relatively small doses used in children, and the absence of any reports of osteosarcoma with long term pediatric use are encouraging. However, aggressive surveillance for development of osteosarcoma should be done.

To summarize, rPTH 1-34 is an emerging modality of therapy for childhood hypoparathyroidism in appropriate clinical settings. Long term prospective Indian studies with appropriate sample size are needed to properly establish its utility and efficacy in pediatric endocrine practice.

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NEWSLETTER
DECEMBER 2022
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CAPE News | ISPAE

Parathyroid adenoma masquerading as acute kidney injury – a case report

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A 12-year old boy presented with nausea, vomiting, pain abdomen and loss of appetite for the past four months. The vomiting was 6-7 times daily, non-bilious, non-projectile, with no particular diurnal variation. The abdominal pain was generalized, dull aching but becoming more intense sometimes, and relieved with some medication taken from a local practitioner. The child had very poor appetite and was lying in bed most of the day. He had no fever, headache, yellowness of skin, cough, alteration in bowel habits or urine output. There was no significant past illness or family history. He was evaluated at another health facility, and found to have deranged renal function: blood urea 67 mg/dl, serum creatinine 2.6 mg/dl. Serum calcium was 12.9mg/dL, sodium and potassium were normal. An ultrasound showed mild left sided hydroureteronephrosis with bilateral renal concretions. He was referred to our hospital for dialysis and pediatric surgery consultation. Work up revealed Hb 11.8 g/dl, platelets 273,000/cu.mm, urea 48 mg/dL, creatinine 1.2 mg/dL, total calcium 14.6 mg/dl, ionic calcium 1.55 mmol/L, phosphorus 3.2 mg/dl, alkaline phosphatase 273 U/L, and iPTH (intact parathormone) 228 pg/mL. There was hypercalciuria: 12 mg/kg/day. Diethylenetriamine pentaacetate (DTPA) scan documented good bilateral cortical function and subrenal drainage. Computed tomography (CT) scan of the abdomen done on advice of the pediatric surgeons showed bilateral 2-4 mm concretions in lower renal poles.

The child was then referred to the pediatric endocrine clinic for hypercalcemia. He was admitted and given fluids for rehydration. For hypercalcemia, he was given injection calcitonin for 2 days, injection pamidronate over 3 days, and injection furosemide. Serum calcium gradually reduced to 11 mg/dl. A Tc99 Sestamibi scan showed increased radiotracer uptake in the postero-superior aspect of the right lobe of the thyroid gland, persisting in the sequential images taken after wash out of the tracer from the thyroid gland (Fig.1), consistent with a parathyroid adenoma. CT scan of the neck showed an intensely enhancing lesion 10mm x10mm x6mm at the same site. The parathyroid adenoma was excised under general anesthesia. Histopathological examination confirmed the presence of parathyroid adenoma. Post-surgery, his calcium dropped to 7.7 mg/dl and then 6.7 mg/dL (ionic calcium 0.98 mmol/L). This got corrected to 8.7 mg/dl with oral calcium, which could be withdrawn after 2 days. The child was discharged in a stable condition, and on OPD visits thereafter has remained well.

Discussion

Hypercalcemia is defined as serum calcium exceeding + 2 standard deviations above the normal mean. In children 4-18 years of age, the cut off values are: total calcium > 10.7 mg/dL and ionized calcium > 1.38 mmol/L. The underlying etiology could be PTH dependent (with overproduction of PTH) or PTH independent. PTH dependent causes include primary and tertiary hyperparathyroidism. PTH independent causes include vitamin D intoxication, drugs like thiazides, endocrinopathies (hyperthyroidism, Addison's disease, pheochromocytoma, severe congenital hypothyroidism), immobilisation, congenital syndromes like Williams syndrome, malignancy and granulomatous diseases. Primary hyperparathyroidism (PHPT) is rare in children, occurring in 2–5/100,000 children. CASR mutations with hyperplasia of all four glands is the commonest etiology in neonates, and parathyroid adenomas in adolescents. Other causes include familial hyperparathyroidism, either isolated or associated with multiple endocrine neoplasia. [1] Tertiary hyperparathyroidism is overproduction of PTH in response to hypocalcemia that results in long standing kidney disease with hyperphosphatemia.

Hypercalcemia has protean clinical manifestations in children, including anorexia, nausea, vomiting, constipation, polydipsia, polyuria, abdominal or flank pain, lethargy, hypotonia, irritability, seizures and long bone fractures. Chronic hypercalcemia may lead to nephrocalcinosis, nephrolithiasis and renal failure. Our case presented with

A systematic review of PHPT in India, collated the data reported by various tertiary care institutes (344 cases) across the country and reported 36% prevalence of renal disease. [2] Gopal et al., reported renal calculi, including nephrocalcinosis, in 40.5% of PHPT patients and as a presenting complaint in 15.1%. [3] Bhansali et al. reported renal calculi in 70% PHPT patients, with recurrent renal calculi as the presenting complaint in 21% the patients. [4]
Single parathyroid adenoma is the commonest cause (~80%) of pediatric PHPT. Ultrasonography, magnetic resonance imaging, CT, and radionuclide scans (Tc99 labeled sestamibi-single photon scan) have been used to localize the abnormal parathyroid gland(s) before surgical excision. Evaluation for associated endocrine tumors is necessary, if the family history suggests the possibility of MEN I or MEN IIA or if there are clinical findings suggestive of a prolactinoma, somatotropinoma, or pheochromocytoma (galactorrhea, excessive growth, or hypertension).
Severe hypercalcemia is managed by
(1) hydration with 0.9% saline (twice the maintenance volume over 24– 48 hours),
(2) calciuresis with the loop diuretic furosemide,
(3) inhibition of bone resorption using bisphosphonates like pamidronate and zoledronic acid; calcitonin and rarely the monoclonal antibody denosumab,
(4) hemodialysis in cases resistant to conventional therapy.
Surgical management of patients presenting with hyperparathyroid crisis secondary to adenomatous disease is effective, with a reported success rate of 92%. Complications of surgery include (1) transient hypocalcemia, usually managed with oral calcium, though occasionally "hungry bone syndrome" occurs, requiring intensive management; (2) permanent hypoparathyroidism, requiring calcitriol and calcium; (3) vocal cord dysfunction; (4) rarely, need for further surgery if a second adenoma develops.

Our case presents a rare endocrine disease (parathyroid adenoma) with atypical presentation (acute kidney injury) in a child, posing a diagnostic dilemma. Although hypercalcemia had been detected, it took several days to be recognized as the primary concern. It also highlights two facets of management: the preoperative management of a parathyroid crisis; and the management of transient hypocalcemia postoperatively.

Message:

Primary hyperparathyroidism in children has protean clinical manifestations, which may lead to false diagnosis, and requires a high index of suspicion for timely diagnosis.
Single sporadic parathyroid adenoma is the commonest cause of pediatric PHPT.
Evaluation of associated endocrine tumors is necessary as parathyroid adenoma may be a part of MEN syndromes.
Surgical excision of adenoma is effective but may be associated with complications like hypocalcaemia.

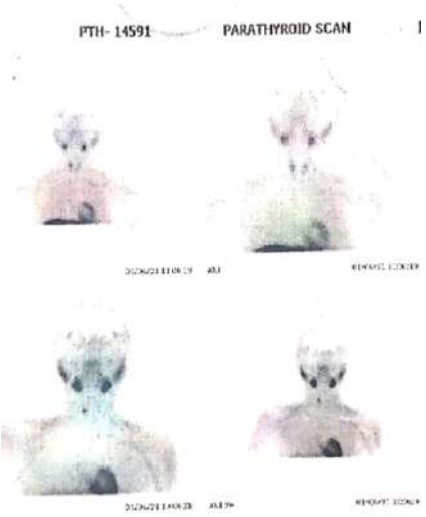

Figure 1. Image of Tc99 Sestamibi scan showing increased radiotracer uptake in the postero superior aspect of the right lobe of thyroid gland and its persistence in the sequential images (lower two images) taken after wash out of the tracer from the thyroid gland.

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NEWSLETTER
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Patient Corner

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Joseph Hubertus Pilates

The father of "Pilates", a form of muscle toning and strengthening exercise which is a multi-million-pound industry today, was born in 1883 to a gymnast father and a naturopath mother. They always inspired the frail child to work out to maintain good health and fitness. Suffering from asthma, rickets and rheumatic fever, he was bullied by his classmates to the extent that he lost vision in one eye due to a stone hit by one of them. Joseph felt the need of changing his skinny-sickly habitus, for which he re-educated his body through many forms of exercise, transforming himself to look like the Greek god Adonis. He worked as a circus performer and a professional boxer, teaching self-defence to policemen during World war I. He taught the world his theory of body building by Contrology and published two books on the principles of fitness. Even 50 years after his death, 'Pilates' is one of the popular forms of exercises with classes all over the world, depicting the revolutionary change Joseph Pilates brought about, despite, or perhaps because of his bony deformities and physical deficits.

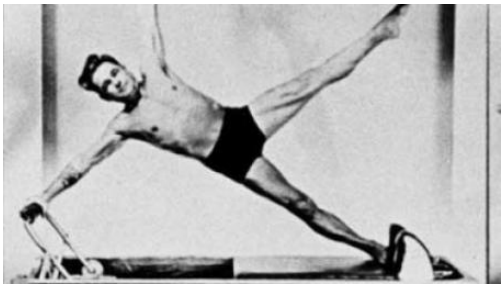

Image: ngelaroutledgepilates.com/blog-posts/2017/2/21/the-history-of-joseph-pilates

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Pedendoscan

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Lin TH, Lu HJ, Lin CH et al. Nephrocalcinosis in children who received high-dose vitamin D. Pediatr Nephrol.2022;37:2471–2478. https://doi.org/10.1007/s00467-022-05512-6

The ready availability of Vitamin D supplements as over-the-counter preparations, can result in cases of vitamin D overdose, causing nephrocalcinosis and life-threatening hypercalcemia. Errors in manufacturing of nutritional supplements may be a cause of vitamin D intoxication in children. This study was aimed at identifying factors associated with vitamin D overdose-related nephrocalcinosis in children. The authors conducted a retrospective study reviewed medical charts of pediatric patients with non-registered supplement-related vitamin D overdose at a tertiary referral hospital between 2006 and 2011. All clinical and laboratory characteristics of patients with or without nephrocalcinosis were evaluated. Receiver operating characteristics curve and area under the receiver operating characteristics curve were used to determine the most predictive value of each characteristic. The results of a total of 44 patients (males: 29; age: 7–62 months) were included. Age $\leqslant$ 16.5 months, body weight $\leqslant$ 10.25 kg, body height $\leqslant$ 78.5 cm, body surface area (BSA) $\leqslant$ 0.475 m2, 25-OHD3 $\geqslant$ 143 ng/mL, and calcium $\geqslant$ 10.65 mg/dL were predictive of developing nephrocalcinosis with a sensitivity and specificity of > 60%. Univariant analysis revealed that BSA was the most significant anthropometric prognostic factor (odds ratio: 12.09; 95% confidence interval: 2.61–55.72; P = 0.001). The authors concluded that **children with smaller BSAs were more vulnerable to high-dose vitamin D3-related nephrocalcinosis.** Physicians and parents should be aware of the potential adverse effects of vitamin D overdose in children.

Spinell C, Ghionzoli M, Bertocchini A et al. Factors associated with post-operative hypocalcemia following thyroidectomy in childhood. Pediatr Blood Cancer. 2022;69:e29576.https://doi.org/10.1002/pbc.29576

Postoperative hypocalcemia is a frequent complication of thyroidectomy. Hypoparathyroidism may be transient (TtHP), with normalization within six months of surgery, or permanent (PtHP) if the patient continues to require replacement therapy. The authors looked for factors associated with the development of hypoparathyroidism following thyroid surgery in a pediatric population. It was a retrospective multi-center study analyzing 326 patients. Gender, age, tumor size, thyroiditis, extrathyroidal extension, lymph node dissection (central/ lateral compartment, unilateral/ bilateral), parathyroid auto-transplantation, and histology, as well as postoperative calcium levels were recorded. They divided patients into 2 age groups (⩽15 or 15-18y). Mean follow-up was 5.8y (1-11y). Postop hypoparathyroidism occurred in 36 (11.0%): 20 cases (6.13%) developed PtHP. Postop hypoparathyroidism was more frequent in younger patients (P = 0.014), in larger tumors (P < 0.001), in case of extrathyroidal extension (P = 0.037), and in central compartment (P = 0.020) and bilateral lymph node dissection (P = 0.030). PtHP was more frequent in older patients (P = 0.014), in case of thyroiditis (P < 0.001), and extrathyroidal extension (P < 0.001). The first postop calcium level in the PtHP group was 8.17 mg/dL, with a 14% pre/postop decrease (ΔCa), whereas in the PtHP group calcium was 7.91 mg/dL with 16.7% ΔCa. The conclusions drawn were that **the risk of postoperative hypoparathyroidism is more with younger age, larger tumor, central compartment and bilateral lymph node dissection, and extrathyroidal extension.** The risk of PtHP is more with older age, thyroiditis, extrathyroidal extension, and greater decrease in postop calcium.

Del Pino M, Viterbo GL, Arenas MA et al. Growth in height and body proportion from birth to adulthood in hereditary hypophosphatemic rickets: a retrospective cohort study. J Endocrinol Invest. 2022 Jul; 45(7):1349-58. PMID: 35226335

Patients with hereditary hypophosphatemic rickets are short and disproportionate. Very little information is available on segmental growth, but the body disproportion at adulthood leads us to think that the growth velocity of legs is slower. The authors studied 96 children, plotting individual growth records of height and sitting height/height using Argentine reference data. Growth curves were estimated by fitting Preece-Baines Model 1 in 19 of them. Molecular testing was done in 42, and showed deleterious alterations or large deletions in 36. Those who had reached adult height (AH) were classified into two groups according to their compliance to conventional treatment (phosphate supplement and calcitriol). During childhood, 76% children grew below − 1.88 standard deviation score (SDS) and 97% had body disproportion. During adolescence, the mean peak height velocity for the good and poor compliance to treatment groups was 7.8 (0.6) and 5.4 (0.4) cm/year in boys and 7.0 (0.7) and 5.2 (0.8) cm/year in girls, respectively. At adulthood, the median sitting height/height ratio was 2.32 and 6.21 SDS for the good and poor compliance groups, respectively. The mean pubertal growth spurt of the trunk was –0.8 (1.4) SDS, with a short pubertal growth spurt of − 1.8 (0.4) SDS for limbs in the good compliance group. Median AH in 13/29 males and 30/67 females was –4.56 and –3.16 SDS, respectively. The authors concluded that **for all patients the growth spurt was slower, secondary to a short growth spurt of limbs, reaching a short AH with body disproportion that was more prominent in the poor compliance group.**

Paloian NJ, Nemeth B, Sharafinski M, et al. Real-world effectiveness of burosumab in children with X-linked hypophosphatemic rickets. Pediatr Nephrol. 2022;37: 2667–2677. https://doi.org/10.1007/s00467-022-05484-7

X-linked hypophosphatemic rickets (XLH) is the most common cause of inherited rickets. Historically, XLH has been treated with oral phosphate and calcitriol (conventional treatment). Burosumab, a fibroblast growth factor 23 (FGF-23) monoclonal antibody, was approved by the United States Food and Drug Administration (USFDA) in 2018 for XLH treatment. Nevertheless, conventional treatment of XLH continues to be recommended by some specialists due to lack of published experience with burosumab in the clinical setting. The authors studied 12 XLH patients aged 1–18 years old, comparing laboratory values and radiologic rickets severity scores observed during the period

they were on conventional therapy with those following transition to burosumab as part of routine care. It was a retrospective single-center study. All laboratory values improved following 1 month of burosumab treatment: the improvements were sustained over the 2-year study period. Rickets severity scores and height z-scores also improved with burosumab. Overall adverse events with burosumab were very infrequent and mild, with no serious adverse events. One patient developed asymptomatic mild elevation of serum phosphate, resulting in a temporary pause in therapy. **It was concluded that burosumab is safe and effective in treatment of XLH, yielding statistically significant improvement in height, lab and radiographic markers of rickets compared to conventional therapy.**

Khadilkar A, Kajale N, Oza C. et al. Vitamin D status and determinants in Indian children and adolescents: a multicentre study. Sci Rep 12, 16790 (2022). https://doi.org/10.1038/s41598-022-21279-0

Studies in Indian children to assess vitamin D status have been on small sample sizes, limited to specific geographical locations and using non-standard methods to measure 25(OH)D3. This multicentre study assessed 25(OH)D3 concentrations from dried blood spots (DBS) in 5-18 year old Indian children and adolescents using a standardized protocol, and identified factors contributing towards vitamin D deficiency. The authors conducted a cross-sectional, observational school-based study using multi-stage stratified random sampling. A city and nearby village were selected from 6 randomly selected Indian states (Maharashtra, Gujarat, Chhattisgarh, Assam, Tamil Nadu and Punjab), covering wide geographical areas. Demography, anthropometry, body composition, dietary intakes and DBS samples were collected. 25(OH)D3 was assessed from DBS using Liquid Chromatography with tandem-mass spectrometry. Vitamin D status was assessed in 2500 children (50% boys, 52.7% urban), with additional data collected on a subset (n = 669) to assess predictors. Mean vitamin D concentration was 45.8 ± 23.9 nmol/L, with 36.8% of subjects having sufficient vitamin-D (> 50 nmol/L); rural subjects and boys had higher concentrations ($p < 0.05$). On regression analysis, younger age, female gender, overweight and urban residence significantly contributed to deficiency. More than half the Indian children/ adolescents were vitamin-D deficient or insufficient. **The study reinforces vitamin D deficiency as a major public health problem across India, and the need for supplementation, food fortification and educating the population about measures to improve sufficiency status.**

UPDATE ON JOURNAL OF PEDIATRIC ENDOCRINOLOGY AND DIABETES

The Journal of Pediatric Endocrinology and Diabetes (JPED) is an open-access peer-reviewed journal committed to publishing high-quality articles and reviewing the latest developments in the field of Pediatric Endocrinology, Metabolism and Diabetes. It is ISPAE's official journal (www.ispae.org.in), run by an erudite panel of experts. The editorial board consists of Prof PSN Menon (Editor-in-Chief), Prof Rakesh Kumar (Executive Editor), Dr Rajni Sharma (Associate Editor), 13 international advisors, 10 national advisors, and 14 national editorial board members.

It is published by Scientific Scholar, in English, as an online-only version with 3 issues annually. The first issue was released in April 2021. It has a print and online ISSN, and so far has been registered with Scopus, Google Scholar, ProQuest, ReadCube, CrossRef, Portico, and EBSCO; the process to register on other indexing sites is ongoing.

As a new journal, JPED has received a very good response from authors and readers, evident from the number of manuscript submissions and viewership/ manuscript downloads on the journal website. A total of 65 manuscripts have been submitted till date, with an acceptance rate of ~ 65%. We are grateful to our reviewers (>50) and contributors of editorials/ invited reviews, and all the authors for submitting high quality research articles, case reports and clinical images etc.

The major highlights of the journal are its robust and user-friendly website interface and online manuscript submission system, it's wide visibility through open access without article processing charges for authors, and prompt reviewing. The broader visibility results in high impact.

For more details, the journal's website is reachable at www.ispae-jped.com. The latest issue of the journal can be accessed at https://ispae-jped.com/current-issue/.
PSN Menon , Rakesh Kumar, Rajni Sharma
(Editors)

Some interesting articles in JPED in year 2022 are:
Volume 2 issue 1 – January to April 2022

- Editorial on Bone health assessment in children with type 1 diabetes using dual-energy X-ray absorptiometry scans: What is known and the way forward by Nandhini Lakshmana Perumal & Raja Padidela
- Editorial on Bone health in children with type 1 diabetes mellitus by Anuradha V. Khadilkar & Shruti A. Mondkar
- Original Article on Evaluation of bone mineral density in children with type 1 diabetes: A cross-sectional case–control study by R. Akshay Kumar, CG Delhi Kumar, Jayaprakash Sahoo
- Editorial on Maternal hypothyroidism and mildly elevated thyroid-stimulating hormone levels during newborn screening – Is it clinically important? By Susan R. Rose
- Editorial on Diagnosis of hypothyroidism in pregnancy and screening of babies born to hypothyroid mothers by Sarah Mathai
- Original Article on Prevalence of congenital hypothyroidism and transient neonatal hyperthyrotropinemia in babies born to hypothyroid mothers at a tertiary care hospital by Kumar Sanjeev, Ruchi Mishra, Jasmine Kaur, Anand Prakash Dubey, Jyoti Bagla, Sarika Arora
- Invited Review Genetics for the pediatric endocrinologists – 1 by Radha Venkatesan, V. Mohan, Rakesh Kumar
- Case Report on Congenital aromatase deficiency – A virilizing masquerade! By Abhishek J. Kulkarni, Poorvi Chandraprakash Agrawal
- Clinical Images by Short child with hypermobility of shoulder joint: A rare case of skeletal dysplasia by T. N. Keerthana, H. N. Vani, Palany Raghupathy

Volume 2 issue 2 – May to August 2022

- Editorial on Type 1 diabetes in limited resource settings: Where are we and where do we need to go? By Leena Priyambada
- Editorial on Hypothyroxinemia of prematurity – Is it really transient and benign? By KG Ravikumar
- Original Article by A study on normalization of hypothyroxinemia in neonates below 34 weeks of gestation by Seema Gaonkar, Arvind Shenoi, Santhosh Olety Sathyanarayana, Arun Kumar Namachivayam, D. Malathi Raja, Nilesh Rao
- Original Article on Turkish children with new-onset type 1 diabetes mellitus had more severe clinical presentation during COVID-19 pandemic by Irmak Dicle Sargin, Heves Kirmizibekmez, Gulcan Seymen, Esra Kutlu, Fatma Dursun
- Invited Review on Genetics for the pediatric endocrinologists – 2 Primordial short stature in children and adolescents by Amit Kumar Gupta, Neerja Gupta
- Case Report by Allan-Herndon-Dudley syndrome: Report of a novel pathogenic variant in MCT8 gene by Abhishek Kulkarni, Devika Ramakant Desai, Pankhuri Nakul Kothari
- Case Report of A case of McCune–Albright syndrome hiding in the bones. By Gabrielle Doré-Brabant, Isabelle Rousseau-Nepton
- Case Report of Neonatal diabetes mellitus with congenital hypothyroidism (NDH) syndrome caused by GLIS3 mutation: A case report and review of literature by Shaila Sanjay Pachapure, Shriharsha Badiger, Satish Tadakanahalli, Elisa De Franco, Aishwarya Manthale, Vijay Kulkarni
- Clinical Images/Spotters by A child with hypocalcemia – Looking for the bedside clues! By Nithya Thuruthiyath, T. M. Sanjeev Kumar

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Diabetes Educator Corner
Skin problems in Type 1 Diabetes Mellitus


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Introduction

The skin, being the largest organ of the human body, is packed with nerves and blood vessels that allow us to sense touch, temperature, pain, and pressure. Diabetes mellitus (DM) is a common condition that might affect various organs including the skin. However, skin disorders are usually neglected and frequently under-diagnosed among people with diabetes (PwD). Uncontrolled diabetes can affect nerves and blood vessels, and individuals with peripheral neuropathy should be very careful to prevent injuries. A broad spectrum of skin disorders can occur in Type 1 diabetes (T1D). It is important to be aware of the conditions, and inspect skin regularly for prevention and early detection of problems. A common myth that wounds do not heal in PwD, can make parents needlessly stop children and adolescents from participating in sports. Healing is no different if diabetes is well controlled, which is helped by physical activities. At the same time, unnecessary injuries should be avoided, e.g. playing barefoot, especially outdoors.

Common skin issues in persons with DM can be categorized as:

1. Cutaneous infections
2. Cutaneous complications of therapy
3. Other skin conditions.

Cutaneous infections:

Fungal infections:

Fungal infections create itchy rashes surrounded by tiny red blisters and scales. Commonly seen in children with T1D are Candida and Dermatophytosis.

a) Candida: Lesions may occur in the corners of mouth, axilla, infra-mammary region, vagina, vulva, groin, abdomen, or any kind of skin fold. It may present as white, curd-like patches on the buccal mucosa, tongue or other areas, or white vaginal discharge.

b) Dermatophytosis: Clinical presentation will be ringworm eruptions.

Anti-fungal medications are used to treat; prevention includes normalization of blood glucose (BG) levels.

Bacterial infections:

Bacterial infections cause inflamed, hot, swollen, red, and painful areas, and can occur anywhere, including on the eyelids, hair follicles, and fingernails, as well as injection sites if good hygiene is not maintained. They are treated with antibiotics, alongside good glycemic control.

Dry, itchy skin:

This can occur in anyone, but is more likely in people with uncontrolled diabetes, who can have poor circulation. Good glycemic control, adequate physical activity, ensuring skin does not stay wet for long periods, using mild soaps, and applying moisturizing lotions after bathing is recommended.

Cutaneous complications of insulin therapy/ injection technique:

Lipoatrophy, defined as a loss of subcutaneous fat around the site of repeated insulin injections, is a rare complication of insulin therapy, and causes erratic insulin absorption.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Lipohypertrophy is a result of giving repeated insulin injections at the same site. Lipohypertrophy makes insulin absorption slower and more erratic, thus affecting glucose control. It is very important to rotate injection sites to avoid it.
If lipohypertrophy or lipoatrophy is present, the PwD must be educated about injection site rotation and avoiding injecting into affected areas for 1-2 months.

Insulin Hypersensitivity: This is rare; it may be seen somewhat more often with conventional insulins when compared to analogs. It usually presents with aseptic inflammatory nodular lesions at injection sites, and necessitates a change to a different type of insulin molecule.

Device-related skin problems, causes, and prevention:
Skin complications that may result from CGM and insulin pump use range from mild itching and redness to severe hypersensitivity responses causing tissue damage and scarring, lipodystrophy, infection, and complex wounds.
Visible Tissue Abnormalities:

1. Scarring: Scarring may occur if site rotation is not done, and the devices are frequently inserted in the same places without giving time to the skin to recover. Scarring makes it harder to insert the devices and also affect insulin absorption/ accurate glucose measurements. Areas with heavy scarring should be avoided when inserting a pump patch/ CGM sensor.
2. Tearing: Tearing of the skin and underlying tissues can be caused by the repeated insertion in the same place, and stripping the tape or other adhesive materials roughly. Tearing can cause visible changes like redness, bleeding, bruising, and even discharge. Gentle handling and careful removal of adhesives are important to avoid this.
3. Hypersensitivity/Allergic Reactions: Hypersensitivity can occur with the contact of allergens found in adhesives of pump patches/ CGM devices. This can lead to hives, eczema, and skin reddening. Mild-to-moderate allergies can usually be treated with anti-histamine and/or anti-inflammatory creams and topical ointments. Use of barriers films like Tegaderm between the skin and adhesive can minimize the risk of hypersensitivity.

Suggestions for avoiding skin infections at insertion sites are:

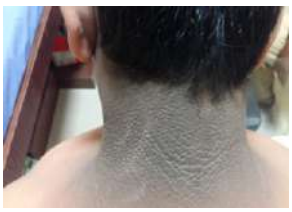
· Good hygiene and changing the infusion sites every 2-3 days, after a bath or shower, after drying the skin help.
· Adequate site rotation is a must.
· It is important to remove an infusion set at the first sign of unusual discomfort at the insertion site and place a new infusion set in a fresh site well away from the original area.

If any of these signs are present, one has to seek medical help:

· Warmth/ tenderness/ soreness/ redness/ harness around the site
· Oozing from the cannula site.
· Unexpected high BG levels.

Other skin conditions

Acanthosis Nigricans



This is a sign of insulin resistance, presenting as a dark patch or band of velvety skin in body creases (especially back of neck, armpits, or groin). Sometimes the patches can also appear on knuckles, elbows, or knees. It is common in people who have obesity and can be a sign of pre-diabetes and type 2 diabetes. The most effective treatment is to address the root cause, i.e. obesity/ insulin resistance through lifestyle modification.

Digital sclerosis

This condition also called limited joint mobility or Prayer sign, starts with tight, thick, waxy skin on fingers and can cause finger joints to become stiff and hard to move. This condition is more common in people with uncontrolled T1D. Optimal glycemic control and physiotherapy may help improve the range of motion of affected joints.

NEWSLETTER
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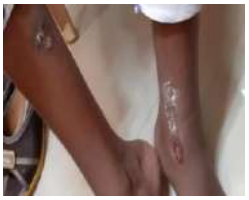
CAPE News | ISPAE

Bullosis Diabeticorum



Also known as diabetic bullae or bullous eruption of diabetes mellitus presenting as recurrent spontaneous blisters occurring on the extremities in those having a long-standing disease with peripheral neuropathy. The lesions are asymptomatic and heal slowly without scarring in 2-6 weeks. The pathophysiology is not completely clear and appears to be multifactorial. Generally, the application of topical antiseptics or antibiotics to reduce discomfort and prevent secondary infections is sufficient.

Calluses and corns

Callus is an area of thickened and hardened skin that gets formed as a result of repeated friction, pressure, or irritation. It can be painful or painless. Avoiding triggers would help in resolving but in rare cases surgical intervention would be needed.

Diabetic Dermopathy, Scleroderma-like skin changes are other skin diseases commonly seen in uncontrolled diabetes.

Summary:

A spectrum of cutaneous manifestations in diabetes is noticeable in PwD due to multiple factors like insulin therapy and incorrect technique, chronic degenerative changes, and metabolic disturbances. These manifestations may reflect suboptimal glycemic status, insulin hypersensitivity, and may also help in unmasking the new onset of Diabetes.

Many of these conditions are preventable with regular examination, good glycemic control, hygiene, and educating about the right technique of insulin injection therapy.

(Authors have obtained patient consent to present these images)

Learning Pearls : ISPAE mid-term meet 2022, Chandigarh

Dr Arun George, DM Senior Resident
PGIMER, Chandigarh

Type 1 Diabetes (T1D):

Progress on Semi and Non-Invasive Glucose Monitoring

1. We have moved from the era of urine glucose monitoring (Benedict solution, then urine dipsticks), to fingerstick capillary blood glucose monitoring and now continuous glucose monitoring using interstitial fluid.
2. A 2017 study assessing the accuracy of point-of-care glucose meters showed the MARD (Mean Absolute Relative Difference) was > 10% in 9 out of 17 devices. So meter accuracy should be regularly checked.
3. CGM accuracy has improved with each generation. The latest 6th generation has MARD values of less than 10%.
4. Diabetes technologies, especially CGM, have improved glycemic control, decreased hypoglycemia, reduced glycemic variability and improved quality of life.
5. Attempts at non-invasive glucose monitoring have not been so successful, but efforts continue.

Closing the closed loop- Far or Close?

1. CGM disadvantages include lag time, on-body presence, technology failure, the learning curve, and being overwhelmed by data.
2. Threshold suspends (insulin switches off during very low glucose), predictive low glucose suspend (cessation of insulin before glucose becomes low), and hybrid close loop with hypoglycemia and hyperglycemia minimiser (an added feature of insulin dosing above high threshold) belong to the first generation of pumps.

3. Automated basal/ hybrid closed loop (closed loop at all times with manual-assist bolusing) and fully automated insulin close loop (manual meal time bolus eliminated) belong to the second generation.
4. A fully automated multihormone closed loop is the third generation of automated insulin devices.
5. In AID pumps, ultra-rapid lispro was noted to have lesser postprandial hyperglycemia and overall hypoglycemia. However, it was associated with more infusion site problems.
6. In the bionic pancreas, there was no difference in glycemia between lispro/ aspart and fast-acting aspart.
7. Among youth using hybrid closed loop systems, there was no difference in mean glucose 6 hours post meal between those who bolused pre-meal and those who did not give boluses. However, time in range was 67% in those who bolused compared to 46% in those who did not.
8. Further advances in insulin (more physiological, faster onset of action and shorter duration) and other factors impacting glycemia, such as multi-hormone systems (glucagon, pramlintide and GLP-1 agonists) and activity detection sensors are required to fully close the loop.

Towards T1D cure

1. ATG preserves endogenous insulin secretion and improves HbA1c in Stage 3 (new-onset) diabetes.
2. Teplizumab is an anti-CD3 monoclonal antibody that has successfully delayed the onset of T1D. This is the first immunotherapy drug to be FDA approved for at-risk individuals with T1D.
3. Stem cell-derived islet cell therapies are promising and relatively safe. Recipients remain insulin independent for > 5 years, with reduced hypoglycemic episodes and improved quality of life.
4. Screening for T1D decreased DKA in antibody-positive individuals in the TEDDY study, and prevention trials are promising. However, screening with antibodies is recommended only in research settings.

Basics of Diabetes

1. Maturity Onset Diabetes of the Young (MODY) has to be suspected when there is mild fasting hyperglycemia [100-150 mg/dL] in non-obese, asymptomatic patients.
2. Prolonged honeymoon of > 1 year or low insulin requirement $\leqslant$ 0.5 U/kg/day after 1 year of diabetes is also a clue towards MODY or T2D.
3. Steroids, growth hormones, atypical anti-psychotics, tacrolimus, protease inhibitors, statins and L-asparaginase are drugs which can precipitate diabetes.
4. A mixed diet with at least 150 g of carbohydrates for three days should be ensured before performing OGTT.
5. OGTT is not needed and should not be performed if diabetes can be diagnosed using fasting, random, or postprandial criteria (can precipitate ketosis/ DKA).
6. In the absence of overt symptoms, the diagnosis of diabetes requires two abnormal test results from the same sample or two separate test samples.
7. Annual screening for CFRD from 10 years of age is recommended in all patients with cystic fibrosis.

Day-to-Day Management of Diabetes

1. The dietary management of T1D is based on healthy eating principles suitable for all. Dietary management aims to maintain ideal body weight, optimal growth and development.
2. Meal planning should comprise 40-50% carbohydrates, <35% fat (saturated <10%), and 15-25 % protein.
3. Sick day rules like frequent monitoring, hydration, and top-up doses of insulin should be taught to the family.
4. School setting: staff should be aware that the child has diabetes, allow self-care activities like BG testing and insulin dosing. and know what care has to be taken in case of hypoglycemia and hyperglycemia.

Management of DKA- changing paradigms

1. Venous pH and bicarbonate have a reasonable correlation in DKA.
2. Using a bicarbonate cut-off of 18 improves the sensitivity in diagnosing DKA while reasonably retaining the specificity.

3. Plasma β-hydroxybutyrate above 3 mmol/L is the cut off for defining DKA. However, a cut off of 5.3 mmol/L improves the specificity and positive predictive value in diagnosing DKA.
4. According to the PECARN trial, neurologic outcomes were not significantly influenced by the rate of delivery (24 hours vs. 48 hours) or the sodium chloride concentration (0.9% NaCl or 0.45%NaCl) of intravenous fluids in pediatric DKA.
5. Changes in corrected sodium depend on initial sodium and type of fluids. A fall in corrected sodium does not increase the risk of cerebral edema.
6. Acute kidney injury (AKI) is found in almost 1/3rd of all patients with DKA. Elevated chloride levels at 24 hours predicted the development of AKI.
7. For children who are volume depleted but not in shock, volume expansion should begin immediately with 0.9% saline, 10-20 ml/kg infused over 20–30 min to restore peripheral circulation. If tissue perfusion is poor, the initial fluid bolus volume should be 20 ml/kg.
8. Low-dose insulin infusion (0.05 U/Kg/hour) is non-inferior to standard dose therapy (0.1 U/Kg/hour) in the rate of BG decrease and resolution of acidosis, while helping to avoid hypokalemia and hypoglycemia in children with malnutrition.
9. In children with uncomplicated mild to moderate DKA, subcutaneous (SC) insulin: rapid-acting insulin analog (insulin lispro or insulin aspart) 2 hourly or Regular insulin 4 hourly, is safe and may be as effective as IV Regular insulin infusion.
10. Brain hypoperfusion, neuroinflammation and blood-brain barrier disruption are the possible causes of cerebral edema in DKA.
11. Severe acidosis at presentation, elevated urea (>20 mg/dL), hypocarbia (pCO2<20 mm Hg), and treatment with bicarbonate are risk factors for cerebral edema. Large volume fluids, rapid fluid correction and attenuated rise in sodium are not.

Monogenic Diabetes and Congenital Hyperinsulinism: From Genetics to Precision Medicine

1. Monogenic diabetes is categorized into MODY, Neonatal Diabetes Mellitus (NDM) and Syndromes of diabetes.
2. The MODY subtypes are caused by single gene defects with autosomal dominant inheritance, family history of diabetes in multiple generations, early age at onset (< age 35 years), no evidence of β-cell autoimmunity, and controllable without insulin for at least the first 2 years after diagnosis. However, they can have progressive β-cell dysfunction or loss and eventually require insulin.
3. NDM is diagnosed within 6-12 months of life, is autoantibody negative and have insulin-sensitive hyperglycemia.
4. Gain of Function missense variants in ABCC8 and KCNJ11 cause a spectrum of disorders from NDM and DEND (Developmental Delay, Epilepsy, and Neonatal Diabetes), to adult-onset type 2 diabetes (T2D). Loss of Function mutations in ABCC8 and KCNJ11 genes cause Congenital Hyperinsulinism (CHI).
5. Not all variants are pathogenic; not all are clinically actionable. ACMG guidelines classify variants into pathogenic, likely pathogenic, variant of uncertain significance, likely benign and benign.
6. HNF4A and HNF1A types of MODY lead to progressive severe hyperglycemia and are sensitive to low-dose sulfonylureas.
7. GCK subtype is associated with stable mild hyperglycemia, which responds to diet and exercise.
8. HNF1B causes severe progressive hyperglycemia and renal cysts and requires insulin for treatment.
9. Activating/ Gain of function mutations in Kir6.2 or SUR1 promotes the open state of the KATP channel to cause membrane hyperpolarisation and the lack of insulin release characteristic of NDM. More than 80% of patients respond to high-dose sulfonylureas.
10. Inactivation /Loss of function mutations in Kir6.2 or SUR1 result in constant membrane depolarisation and closure of the KATP channel leading to the excess insulin release characteristic of CHI.
11. NDM patients with ABCC8 and KCNJ11 mutations showed significant improvement in glycemic control after a change in treatment to sulfonylureas.

12. In CHI, type 1 mutations in the KATP channel gene lead to impaired trafficking of the KATP channel complex to the plasma membrane and are diazoxide unresponsive. Type 2 mutations are gating defects and are responsive to diazoxide.

Adjuvants to Insulin therapy

1. Despite advances in insulin therapies, patients with T1D have a shorter life span due to hyperglycemia-induced vascular disease and hypoglycemia.
2. Adjuvant therapies have a modest effect on HbA1c reduction.
3. Metformin may be added in patients with "Double diabetes". It reduces HbA1c initially, but this effect does not appear to be sustained.
4. SGLT2 inhibitors and GLP1 RA have the added advantage of reducing weight in obese T1D patients.
5. Euglycemic DKA is a concern with SGLT2 inhibitors.

COVID-19 Pandemic and T1D

1. COVID-19 pandemic has had a multi-pronged effect on T1D. COVID-19 could have acted as a trigger for autoimmunity towards β-cells and could have led to T1D.
2. There has been an increased incidence of T1D, with more children presenting with DKA.
3. According to CDC data, diabetes incidence was significantly higher among those with COVID-19 vs. patients without a COVID-19 diagnosis, and those with a pre-pandemic non-COVID-19 ARI.
4. Clinical presentation of COVID-19 in T1D was similar to non-diabetes patients.
5. MISC and mucormycosis are morbidities associated with COVID-19 infection.
6. Telemedicine use during the COVID-19 pandemic improved glycemic metrics, which can replace or integrate into routine practice.
7. Safe vaccines are available, and there were no significant differences in TIR, time in different glucose ranges, or mean BG levels in those who received Moderna or Pfizer vaccines.

Role of genetic analysis in Disorders of Sex Development (DSD)

1. DSD are broadly categorized based on etiology into sex chromosome aneuploidies (45, X or mosaic; 47, XXY or mosaic), genes or genomic regulators involved in gonadal development (gonadal dysgenesis, testicular or ovotesticular DSD), steroid hormone biosynthesis (with or without CAH), sex hormone responsiveness (e.g., CAIS/ PAIS) and HPG pathway defects (hypogonadotropic hypogonadism, LHCGR defects).
2. The bipotential gonad develops into the testis at 6-7 weeks, if the SRY gene is present, under the influence of various genes like SOX9, GATA4, WT1, and SF1 (NR5A1). If SRY is absent and the ovary-determining genes like FOXL2, RSPO1, WNT4, and DAX1 are present, then the ovaries develop.
3. P450 oxidoreductase (POR) is a co-factor used by 21-hydroxylase, 17-hydroxylase/ 17,20-lyase and aromatase and can lead to both 46XX DSD and 46XY DSD.
4. If an infant with ambiguous genitalia with no palpable gonads has biochemistry suggestive of CAH, molecular diagnosis is not necessary for diagnosis. However, it can still be helpful in antenatal counselling for subsequent pregnancies.
5. If a child with 46XY DSD has low testosterone, low AMH and a uterus, the most probable diagnosis is Gonadal Dysgenesis.
6. If a child with 46XY DSD has normal or increased testosterone (basal or post hCG), normal AMH and absent Mullerian structures, the diagnosis is probably PAIS or 5 alpha reductase deficiency (SRD5A2). These can be differentiated based on T/ DHT ratio. However, it is not a very specific test. DHT, if performed by LC/MS, might be more helpful.
7. If a child with 46XY DSD has low testosterone with absent uterus, testosterone biosynthetic defects should be considered.
8. Hypogonadotropic hypogonadism should be considered if the baby has micropenis with undescended testis and no ambiguity (no bifid scrotum, hypospadias).

9. In children with hypogonadotropic hypogonadism, evaluate for multiple pituitary hormone deficiencies.
10. Virilisation in puberty and primary amenorrhea (absent uterus) in a child raised as a girl- differentials to consider are SRD5A2, 17βHSD3 deficiency and NR5A1.
11. DAX-1 gene deletion presents with undescended testis, but the child can have adrenal insufficiency later. They can sometimes present first with adrenal insufficiency and later have hypogonadotropic hypogonadism. DAX-1 gene duplication leads to sex reversal.
12. If a child with 46 XY DSD presents with salt wasting, the differentials are 3βHSD, StAR, and CYP11A1.
13. Algorithmic approach to genetic testing can help cut costs. Hotspots have been identified in SRD5A2 and CYP21A2 genes.
14. CYP21A2 gene has an excellent genotype-phenotype correlation. 10 mutations account for more than 90% of all variations.
15. Newborn screening for CAH is based on 17OHprogesterone. It has low positive predictive value, so second-tier testing is a must. LC-MS/MS is the advised second-tier testing, but if that is unavailable, genotyping should be done.
16. Molecular analysis has a role in children identified by NBS to have CAH, particularly in boys with borderline but persistent elevation of 17OHP. It helps in avoiding unnecessarily treating NCCAH form.

Growth Hormone (GH): Conventional Versus Upcoming Regimens

1. Hypoplasia of labia minora is the female equivalent of micropenis in girls with GH deficiency (GHD).
2. Untreated GHD patients have a final adult height of -4 to -6 z score.
3. Children with isolated GHD are shorter than children with MPHD. In MPHD, due to delayed puberty, and later fusion of epiphyses, the time for growth is longer.
4. GH therapy is approved for achondroplasia in Japan and for short bowel syndrome, JCA, CF and VDRR in the UK.
5. Surface area is used rather than weight in calculating GH dose in obese children, e.g., Prader-Willi syndrome.
6. The response to GH therapy can be predicted through prediction models. These help to individualise GH dose.
7. Biosimilar GH was effective and safe in an Indian study. There was no difference in response to therapy in terms of growth velocity across indications. The adverse effects were mild and easily treated with symptomatic management.
8. Long-acting GH is prepared using methods like GH encapsulation, pegylation, conjugation, fusion proteins etc.
9. LB03002, a long-acting GH, was comparable to daily rhGH in 12-month height velocity. GH antibodies were seen in higher numbers in the LB3002 group than in the daily group. However, this did not affect the clinical response to GH. Long-acting GH was safe and well tolerated.
10. Somapacitan, a long-acting weekly GH, resulted in sustained efficacy over 3 years in children with GHD. The safety profile was similar to that observed for daily GH, with no new safety or tolerability issues identified. HRQoL (Health Related Quality of Life) data were favorable but were not statistically significant.

Delayed Puberty- CDGP vs. Hypogonadotropic Hypogonadism (HH)

1. Delayed puberty (DP) is defined as a lack of pubertal development by an age > 2-2.5 SD beyond the population mean: cutoff of 13y in girls and 14y in boys.
2. No progression of pubertal events for 2y or a delay of > 4y for completion of pubertal events are called arrested puberty.
3. CDGP is the most common cause of pubertal delay and is a diagnosis of exclusion.
4. When puberty has not started by age 18y, it is HH, never CDGP. Spontaneous entry into puberty by the age of 18y remains the gold standard for diagnosing CDGP.
5. In the presence of micropenis, cryptorchidism, midline/skeletal defects or anosmia/hyposmia in early childhood, congenital isolated HH should be suspected.

6. Family history of DP is not specific for CDGP, as familial clustering is common in congenital idiopathic HH.
7. Presence of pubarche helps in differentiating between CDGP and IHH. Pubarche will be delayed in CDGP while it may be present in IHH.
8. FSH-stimulated inhibin B is a novel dynamic test with 100% positive predictive value, negative predictive value, and diagnostic accuracy, for the prediction of pubertal onset.
9. Biochemical investigations (LH, Testosterone, Inhibin B, Triptorelin stimulated LH) done after testosterone withdrawal (2 months after the last dose of monthly testosterone injections for 3 months) help discriminate CDGP from IHH.
10. The management of CDGP involves short term sex hormone replacement, while patients with HH should be started on gonadotropin therapy at an age-appropriate time.

Hypothyroidism care: new solutions to old challenges of compliance and poor QoL

1. In children with congenital hypothyroidism (CH), QoL is affected in motor, cognitive and social functioning and autonomy. Lower IQ was the only parameter influencing QoL.
2. Children diagnosed before one month of age had better development quotient than those diagnosed late. Children diagnosed early have completely normal neurodevelopmental outcomes. This emphasises the importance of neonatal screening programs.
3. Earlier initiation of thyroxin treatment (<21 days) improves later IQ. Early high-dose thyroxine (10-15 mcg/kg/day) improves neurodevelopmental outcomes and could correct the delay in CNS maturation related to intrauterine hypothyroidism.
4. Thyroid function should be monitored once a month in infancy, every 3 months between 1-3 years, 4-6 monthly from 3 years to the peripubertal period, 3 monthly in the pubertal period and annually post-puberty.
5. Poor maternal education, low socioeconomic status, and the presence of symptoms at presentation are some of the factors associated with poor compliance.
6. Explaining the pathophysiology of the disease at the first visit, regular follow-up visits, use of pill boxes and patient counselling, education and support are associated with improved compliance.

Endocrine emergencies in newborns and infants

1. Persistent hypothermia, unexplained bradycardia, electrolyte disturbances, catecholamine-dependent shock, hypoglycemia (recurrent, refractory), hyperglycemia requiring insulin infusion > 5 days, hypercalcemia, late-onset hypocalcemia and atypical genitalia are the clinical features arousing suspicion of an endocrine disorder in a newborn.
2. Refractory hypoglycemia is defined as an increased glucose requirement- GIR of >/=8 mg/kg /min or persistent or recurrent hypoglycemia after 7 days of life.
3. CHI is the most common cause of refractory hypoglycemia.
4. Critical samples are indicated only in refractory or persistent hypoglycemia and not all babies with hypoglycemia.
5. The presence of ketones in the critical sample suggests ketotic hypoglycemia, but the absence of ketones does not necessarily mean it is a non-ketotic form of hypoglycemia.
6. A Ga DOTA-Exendin scan helps diagnose focal lesions in the pancreas in children with CHI. Radiolabelled exendin-4 specifically binds the glucagon-like peptide 1 receptor on pancreatic β-cells and hence identifies the lesions in the pancreas with greater sensitivity.
7. The goal of therapy in CHI is a pre-feed BG > 70 mg/dl and tolerate fasting as age appropriate.
8. Transient NND resolves by 18 months of age but can relapse later. Permanent NND (40-50%) does not resolve with age.
9. PTH sample should be taken in EDTA, and plasma should be separated within 24 hours and stored at 4o C until analysed. Inappropriate processing of PTH samples is the most common reason for low PTH in practice.
10. In any female looking neonate with adrenal insufficiency, perform an ultrasound to look for Mullerian structures. This will help us diagnose XY sex reversal in children with defects in the steroidogenic pathway, such as StAR deficiency.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

PCOS

1. Maturation of the HPG axis can take up to 5y after menarche.
2. Cycles lasting less than 21 days or longer than 45 days for 1-3y post-menarche is considered menstrual irregularity. Cycles <21 days and >35 days from 3y post menarche are also abnormal.
3. Lack of onset of menses by age 15y or more than 2–3y after thelarche, regardless of chronologic age, is considered abnormal.
4. Hirsutism is defined as terminal hair in a male-like distribution. It should be differentiated from hypertrichosis, which is in non-androgen-dependent areas.
5. Elevated androgens and testosterone are valuable markers of biochemical hyperandrogenism. A testosterone cutoff of 1.7 nmol/L is widely accepted.
6. The polycystic ovarian morphology guidelines have been laid down for transvaginal ultrasound, which is unsuitable for adolescents.
7. In the transabdominal ultrasound, an ovarian volume > 10-12cc and a follicular count greater than 20 are significant.
8. Ultrasound should not be done for at least 3 years post-menarche.
9. AMH correlates well with ovarian volume in ultrasound; however, it has not been accepted as a marker for diagnosing PCOS due to concerns with assay standardisation.
10. Insulin resistance (IR) has a significant role in the pathogenesis of PCOS, but testing for IR is not recommended.
11. NCCAH, hypothyroidism, hyperprolactinemia, Cushing syndrome and androgen-producing tumours must be excluded before diagnosing PCOS.
12. Menstrual irregularity must be treated to prevent endometrial hyperplasia and for psychosocial reasons. Progesterone withdrawal is the preferred treatment for menstrual irregularity.
13. Combined oral contraceptive pills (OCP) are helpful in mild hirsutism, mainly if associated with menstrual irregularity.
14. Anti-androgens are helpful in the treatment of hirsutism. They should always be combined with OCP because they can cause irregular cycles, and because of the risk of conception, which can lead to undervirilization if the fetus is male.
15. Metformin is useful in obese and overweight individuals and those who develop impaired glucose tolerance or diabetes mellitus. It doesn't help in the regularization of menstrual cycles or hirsutism.

Hypoparathyroidism

1. Pediatric hypoparathyroidism differs from adult hypoparathyroidism for its longer disease duration leading to more complications, the predominance of genetic causes, involvement of other systems in syndromic causes, extensive renal/ brain calcifications and more pronounced effect on bone health.
2. The goals of therapy in hypoparathyroidism are to prevent symptoms of hypocalcemia, maintain serum calcium in low normal range, Ca x PO4 product < 55, prevent hypercalciuria and avoid renal/ extra-skeletal calcifications.
3. Conventional therapy in hypoparathyroidism (activated vitamin D, calcium supplements, phosphate binders, thiazide diuretics etc.) has many disadvantages: substantial pill burden, increased risk of hypercalciuria, nephrocalcinosis, chronic kidney disease and overall poor QoL.
4. PTH replacement therapy is recommended in patients not adequately controlled by conventional treatment. PTH use has no significant safety concerns except hypercalcemia. Osteosarcoma was observed in rat studies using mega doses: this risk was not found in humans.

Childhood Obesity

1. Metabolic syndrome and IR occur very early in obese children.
2. Simple clinical and biochemical tests can diagnose metabolic syndrome and other comorbidities.

3. Obesity with hypertension, IR, dyslipidemia and diabetes mellitus are risk factors for developing cardiovascular diseases.
4. An increase in adipose tissue and in the sympathetic nervous system triggers increased left ventricular mass and reduced diastolic function.

Learning Pearls October 2022 ACES

Dr Jahnavi M, Fellow in Pediatric Endocrinology
Aster CMI hospital, Bangalore

Approach to Neonatal calcium disorders

(Case presentation by Dr Jahnavi M, moderated by Dr Santosh Olety, and mentored by Dr N Kavitha Bhat and Dr Namratha Upadhya; followed by a lecture by Dr Sudha Rao)

1. 99% of calcium is in the bone, only 1% is in the exchangeable form.
2. Every 1 g/ dl decrease in albumin reduces serum calcium by 0.8 mg/dl.
3. In fetal life, the placenta is the source of PTHrP, which is the principal regulator of calcium. Calcium accretion happens during the 2nd and 3rd trimester of pregnancy.
4. Hypocalcemia is defined as serum calcium < 7.5-8 mg/ dl or Ionic calcium less than 4.4 mg/ dl in term newborns and serum calcium < 7 mg/ dl or Ionic calcium less than 3.6 mg/ dl in preterm or VLBW newborns.
5. The conversion factor for mg/ dl to mmol/l is 1mg/ dl = 0.25 mmol/L.
6. In the newborn period, the urine calcium-creatinine-ratio cut off for normalcy is 0.8.
7. Hypercalcemia is defined as serum calcium level above the upper limit of normal for the laboratory reference range (8.5-10.8 mg/ dl). It is classified as mild (< 12mg/ dl), moderate (12- 14 mg/ dl) and severe (> 14 mg/ dl).
8. Subcutaneous fat necrosis of the newborn occurs in term and post-term infants with risk factors like hypoxia, perinatal stress and hypocalcemia. 50% develop hypercalcemia.

Approach to DSD in a neonate

(Case presentation by Dr Chirantap Oza, moderated by Dr Hemchand K. Prasad, and mentored by Dr Vaman Kadilkar; followed by a lecture by Dr Peter A. Lee)

1. DSDs are conditions characterized by abnormal chromosomal, gonadal or phenotypic sex.
2. The frequency of DSD is 1 in 4500 live births, with CAH constituting 80% of the DSDs.
3. Hormonal investigations in an infant with DSD should be delayed till 72 hours to avoid confounders leading to misdiagnosis.
4. External masculinization score is used for assessment in infants with 46 XY DSDs. The pointers taken are scrotal fusion, micropenis, position of urethral meatus and position of right and left gonads. A score of < 7 is considered ambiguous.
5. Prader scoring is used for assessment in infants with 46 XX DSDs.
6. Ovo-testicular DSD refers to the presence of functional ovarian and testicular tissue in one individual. The most common karyotype of ovo-testicular DSD is generally 46 XX.
7. The presence of 46 XY chromosome in an ovo-testicular DSD may be associated with risk of malignancy in the intraabdominal gonad.

Learning Pearls November 2022 ACES

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Insights and interpreting diabetes technology – now & the future

Expert speaker: Dr Martin de Bock

1. HbA1c does not detect hypo- or hyperglycemia and is unreliable in patients with anemia, hemoglobinopathies and during pregnancy. Moreover, racial and ethnic differences exist in glycation rates.
2. Intermittently scanned CGM (isCGM) improves QoL, but evidence to support it substantially improving glucose outcomes is limited.
3. Real time CGM (rtCGM) is cost effective, should be the standard of care, and should be started as soon as possible after diagnosis.
4. More than 70% TIR (BG 3.9-10 mmol/L) corresponds to an HbA1c level of <7%.
5. Early initiation of rtCGM (within a year of T1D diagnosis) is associated with significant HbA1c reduction, and fewer diabetes-related emergency visits. CGM users demonstrated sustained and significant improvements in HbA1c compared to non-CGM-users in a 7-year follow-up study.
6. No CGM sensor is truly calibration free, particularly in the hypoglycemic range. All hypoglycemia observed on CGM must be cross-checked with a finger-prick BG, unless symptomatic.
7. Overnight sensor glucose between 3.5-3.9 mmol/L, that are steady and not dropping should be considered normal.
8. When a Spaghetti plot is seen on CGM (i.e. non-uniform daily plots), insulin is not usually the problem.
9. A saw-tooth pattern on CGM is observed either due to over-treating low sugars with high GI foods or mismatch between meal and insulin timing.
10. A slow climb pattern is seen following a high fat diet.
11. A cliff rollercoaster pattern is seen following a bolus rage (i.e. initial insufficient boluses causing slight reduction in sugar but not to baseline, with a subsequent bolus having additive effect to the insulin on board to produce hypoglycemia, followed by rebound hyperglycemia.)
12. The future of CGM: smaller, cheaper, implantable or non-invasive devices, combining with smart pens for decision aids.
13. The latest closed-loop insulin delivery pumps give auto-correction boluses in case of a missed bolus dose of insulin. The timing of a bolus injection in relation to the meal is very important. A bolus given by the patient after a meal may coincide with the automated bolus, leading to hypoglycemia. Hence, patients on these pumps should take a full bolus 15 minutes before a meal. If taking it within 30 minutes after the meal, half the bolus based on ICR should be taken and after 30 minutes, no bolus must be taken manually.
14. Future of automated pumps: Better algorithms, faster insulin, longer life of infusion sets.
15. Association of Children's Diabetes Clinicians endorsed guidelines are available for counselling children and families on: http://a-c-d-c.org/endorsed-guidelines/

Panel discussion: Understanding common Indian foods and choice of insulin

Moderator: Dt. Sheryl Salis | Panelists: Dt. Natasha Vora, Dt. Chhavi Kohli, Dt. Deepthi S

Starting diet counselling for a family with a child with T1D:

1. Understanding the interaction of food and insulin.
2. No separate "diabetic diet" needs to be charted out for the child, instead a healthy diet for all family members for optimizing glycemic control, growth and development is the target.
3. Explaining the type of nutrients (carbohydrates, proteins, fats) in different foods and emphasis on when, how much and what combination of foods should be consumed to lower the glycemic index (GI) is imperative.

Rice – whether to eat or not?

1. Complete elimination of white rice from the diet is not necessary. Unpolished varieties (brown rice, red rice, black rice) can be regularly used.
2. Consuming rice in moderation, and combining it with other protein and fiber rich foods (vegetables especially green leafy vegetables, whole legumes, paneer, meat) or adding some fat (e.g. ghee) reduces the glycemic index.
3. Rice cooled and eaten the next day has resistant starch with lower GI.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Low carbohydrate diet plans – Recommended or not?

1. Parental desire to give their child a low carb diet (e.g. 20 gm/d carb diet) stems from the pressure to achieve a flat line on CGMS and reduce insulin doses.
2. Such low carb diets are not recommended in children as they can cause micronutrient deficiencies and hamper normal growth.
3. The family must see beyond just sugars. Apart from ensuring good glycemic control, they need to take into consideration normal growth and development, as well as psychological and emotional aspects.
4. Most low carb alternatives (e.g. almond flour) are expensive, and add needless financial burden on the family.
5. Carb intake is not always the reason for high sugars, when consumed in moderation. Unbalanced nutrient intake, with high protein and fat intake, can often cause high BG.
6. Locally available, traditional foods consumed by the family should be encouraged.

Celiac disease in T1D:

1. Wheat can be replaced with millets (bajra, jowar, ragi), legumes, amaranth, chestnut flour, corn flour, raw plantain flour, and other gluten free foods.
2. Soyabean flour can be added for the binding effect while making rotis.
3. Washing, drying and then grinding of grains done at home avoids contamination with gluten-containing products and reduces costs.
4. In circumstances where home grinding is not possible, commercially available gluten-free flours can be used.
5. Inclusivity is important for compliance; changes in the entire family's diet should be tried, at least intermittently, for the child to feel included.

One size fits all – Is it true regarding diet plans for children with Diabetes?

1. It is untrue as each child's/family's meal preferences and approach to food can differ, routines and insulin regimens differ.
2. Planning of timing and content of meals should take the child's likes and daily routine into consideration.
3. The type of bolus insulins should also be prescribed accordingly, e.g. short acting (Regular) insulin can cover a meal and a small snack 2h later; rapid acting insulin generally covers one meal.
4. Provision of healthy snacks should be made prior to unexpected exercise or very vigorous activity.
5. Regular daily BG monitoring (either SMBG or CGM) is essential for titrating insulin doses, timing and carbohydrate content of meals.
6. Food sweeteners may be allowed in small amounts for table top use; use in large quantities is unsafe and best avoided.
7. For scenarios like outings or birthday parties, parents can try to find out the tentative schedule beforehand (activities, meal timing, menu) and discuss options with the child, i.e. choosing what to eat, proportions, insulin dosage etc. For children on insulin pumps, the bolus wave pattern can be changed if needed. BG should be checked during outing if possible (convenient with CGM) and after returning home.
8. Carbohydrate counting and giving higher doses occasionally at the time of festivals should be taught to the child / parents.
9. Encourage children and parents to read food content labels and teach them to avoid foods with refined carbohydrates, palm oil and transfats.

ISPAD 2022 meeting – October 2022 – Abu Dhabi
Theme: "From illness to wellness in childhood diabetes"

Dr Anju Virmani, Director, Pediatric Endocrinology
Max Smart Super Specialty Hospital, Saket & Madhukar Rainbow Children's Hospital, New Delhi

Report: The 2022 ISPAD meeting held in Abu Dhabi was a hybrid one after 2 years of virtual meetings due to the Covid pandemic. In spite of all constraints, it was well organized by Dr Asma Deeb, was well attended and much appreciated. There was a sizable Indian contingent, as speakers, oral and poster presenters, and delegates.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

It was the occasion for the release of the much-awaited ISPAD Clinical Practice Guidelines 2022, which come every four years (the last edition was released during ISPAD 2018 in Hyderabad). The 2022 Guidelines have been prepared under the able leadership of Dr Maria Craig as Editor-in-Chief, and include several ISPAE members as authors. As Project Officer, Dr Leena Priyambada was the key person helping Dr Craig in putting them all together. She is also an author of the DKA chapter. Other ISPAE member authors are Dr Preeti Dabadghao (Type 2 Diabetes), Dr Leenatha Reddy (technology in insulin delivery), Dr Ganesh Jevalikar (hypoglycemia), and Ms Sheryl Salis (nutritional management). Dr Anju Virmani is lead author of the chapter of diabetes management in Limited Resource settings. This topic has been given the status of a separate chapter for the first time in 2022.
The IDEAL course was given an oral presentation and a poster: both were much appreciated.
The results of the ISPAD elections were also announced during the meeting. It was indeed gratifying to find both the ISPAE members who had stood for the Advisory Council – Dr Leena Priyambada and Ms Sheryl Salis – were elected with a high number of votes.

Learning Pearls from ISPAD 2022

Dr Rachna Keshwani, Fellow in Pediatric Endocrinology
Bai Jerbai Wadia Hospital for Children, Parel, Mumbai.

1. The language used by health care professionals can have a profound impact on how people with diabetes and their caregivers and other family members experience their condition and feel about living with it day-to-day and how society at large perceives it. Hence the conscious use of neutral, non-judgemental, strengths-based, respectful, and person-centered language is important. For example, it would be preferable to use 'Persons with Diabetes (PwD)' instead of 'diabetics, patients, study subjects'; use 'have diabetes' instead of 'suffering from diabetes', use 'condition' instead of 'disease', use 'persons without diabetes' instead of 'normal persons', use 'glycemic targets' instead of 'glycemic control', and so on.

2. Stages of Type 1 Diabetes (T1D) are as follows:
   Stage 1- Euglycemia + 2 or more islet cell autoantibodies
   Stage 2- Dysglycemia + 2 or more islet cell autoantibodies
   Stage 3- Clinical diagnosis + 2 or more islet cell autoantibodies
   Stage 4- Long-standing T1DM

Because 80-90% of children with multiple islet autoantibodies progress to stage 3 within 15 years, there is greater hope of being able to prevent T1D in years to come. At present, routine testing of islet cell autoantibodies in a child with classical T1D or family members is not recommended.

3. T1D has a heritable component with a twin concordance rate of 70% and a sibling risk of 8%. The genetic risk is explained by variation at HLA class 2 DR-DQ loci, the HLA class 1 region and > 50 non HLA SNPs. This high genetic heritability explains the possible diagnostic potential of T1D genetic risk scores (T1D GRS). The T1D GRS converts the complex information of multiple T1D risk loci into number that has a potential role to provide improved discrimination between T1D and non T1D (MODY, T2D).

4. There are several advances in diabetes treatment to look forward to, including hope for diabetes cure with β-cell replacement by islet cell transplantation (stem cell therapy), antiviral treatment (Plecoranil, Ribavirin), and immunotherapy for T1D, but not without hurdles in clinical application.

5. The biochemical criteria for DKA diagnosis must have all three criteria:
   (i) BG > 200 mg/dl +
   (ii) Ketones ⩾ 3 mmol/L in blood OR moderate to large ketones in urine +
   (iii) Venous pH < 7.3 OR Bicarbonate <18 mmol/L. The cut-off for bicarbonate has been increased in ISPAD 2022 from 15 to 18 so as to not miss cases.

6. Diabetes self-management education (DSME), initial and ongoing, is an indispensable tool in diabetes management and must be tailored not only to be culture and age appropriate but also to match the education level (Basic, Comprehensive, Advanced).

7. Continuous glucose monitoring (CGM) and carb counting should be offered to all families of T1D at the time of diabetes onset. 'Provider bias' should be avoided.

(i) Routine use of CGM improves glycemic status (low and high BG can be anticipated as trends are visible), informs nutrition education practices (the impact of food can be well seen, including visual evidence, by the families), assesses dietary and activity behaviors, and aids personalized strategies to optimize BG profiles.

(ii) Carbohydrate counting, use of insulin to carbohydrate ratio, insulin dosing for fat and protein, opting for low glycemic index carbohydrates, structured meals, with adequate preprandial insulin: all contribute to achieving target postprandial glycemia.

(iii) High protein and high fat meals also contribute to the postprandial glycemic response, contributing to post-meal hyperglycemia at 3-5 hours vs. 1-2 hours with carbohydrates.

(iv) ISPAD 2022 recommends a dietary pattern providing carbohydrates amounting to 40-50% TDE (Total Energy Expenditure), proteins 15-25% TDE, fats 30-35% TDE, with saturated fat <10% TDE. Both a lower (<40%) and higher percentage of carbohydrate intake (>44%) reduced the probability of reaching the target TIR >70%.

8. Age and duration are confounders of diabetes complications. Older age increases risk for the same duration of diabetes. There is a non-uniform effect of prepubertal diabetes duration on relative risk of diabetes complications, with a lower risk further away from gonadarche.

9. LDL-C $\geqslant$ 100 mg/dL, BP $\geqslant$ 90 th centile, BMI $\geqslant$ 85 th centile, HbA1c $\geqslant$ 9 are risk factors for macrovascular disease in youth with T1D. A therapeutic inertia to risk factor minimization in pediatrics needs to be overcome.

10. For the adolescent who wishes to fast, a risk assessment needs to be done. Risk will be based on diabetes characteristics and fast characteristics.

(i) Diabetes characteristics - Type of diabetes, duration of diabetes, type of insulin regimen, frequency of SMBG, suboptimal glycemic control, comorbidities (hypoglycemia unawareness, recurrent hypoglycemia, other comorbidities).

(ii) Fast characteristics - Duration and timing of fast, what type of foods are allowed during the fast, number of times the person is allowed to eat, what interventions are permitted (SMBG, Insulin, oral drugs), associated practices (physical activity, feasting).

Strategies for a safe fasting involves the use of an individualized approach involving prefast counselling (to be started 6-8 weeks prior), risk stratification, glycemic optimization, advice on nutrition and activity, technology (CGM, insulin pumps etc) and telemedicine.

Written instructions about when to break the fast should be given: BG < 70 mg/dl, BG > 300 mg/dl, symptomatic, acute illness.

11. Objective neurologic assessment has shown that > 90% children with K-ATP channel mutations have some degree of neurologic dysfunction. Glibenclamide, the specific treatment of NDM due to K-ATP channel mutation and chromosome 6 linked diabetes, is a neuroprotective drug with a clear beneficial effect on neurodevelopmental outcomes in persons with K-ATP channel mutation proven in studies.

12. SLC25A36 and ADCY7 are new genes reported in hyperinsulinimic hypoglycemia. SLC25A36 deficiency causing impaired transport of guanine nucleosides causes a novel form of protein sensitive HH. The impairment of GTP which ensues, increases activity of GDH, leading to protein induced hypoglycemia. ADCY7 encodes a calcium sensitive adenylate cyclase expressed in β-cells that converts ATP to cAMP which has an important role in insulin secretion regulation. ADCY7 knockout studies have shown to cause hyperinsulinism.

13. The Edmonton Obesity Staging System for Pediatrics (EOSS-P) is a classification system for obesity looking at clinical aspects, based on obesity related co-morbidities and barriers to weight management, using 4 Ms - Metabolic, Mechanical, Mental health, Milieu, to stage obesity as stage 0, 1, 2, and 3. Comparison of the Edmonton classification with the WHO BMI classification found that 76% who were in class 1 of obesity as per WHO were in class 2/3 according to EOSS-P. The reason for this is 'mental health' as these issues are equally distributed across BMI classes while metabolic, mechanical and social issues are higher as BMI increases.

14. BMI has a high specificity but low sensitivity to detect excess adiposity. It fails to identify a quarter of children with excess body fat percentage. Waist circumference (WC) is one of the easiest and most readily available measures of adiposity and is shown to correlate with total and abdominal fat after controlling for BMI percentiles. WC explains a greater variance in abdominal fat and worse metabolic profile than the BMI percentile.

ISPAE activities

Report of ISPAE-ISPAD 2022 meeting – Chandigarh

Dr Devi Dayal, Dr Rakesh Kumar and Dr Jaivinder Yadav

ISPAE-ISPAD 2022, the mid-term meeting of the Indian Society for Pediatric and Adolescent Endocrinology, was conducted in Chandigarh on November 19-20, 2022. It was organized by the Endocrinology and Diabetes Unit of the Department of Pediatrics, PGIMER Chandigarh, in collaboration with ISPAE, ISPAD, and the Association of Pediatricians of Chandigarh. The meeting, with about 180 participants (including faculty), was inaugurated by the Director of PGIMER in the gracious presence of ISPAE President Dr Shaila Bhattacharyya.

The first day of the conference was devoted entirely to childhood diabetes; the second day to other endocrine topics. The first day began with four virtual sessions by ISPAD-designated faculty, which focussed on advancements in pediatric diabetes care and care of children living in conflict zones. All sessions generated enormous discussions. The meeting also included a diabetes workshop on Day 2 for allied healthcare professionals (HCPs), supervised by Dr Rakesh Kumar and Dr Soham Mukherjee and attended by about 20 HCPs.

Fifty-two abstracts were submitted, all presented as e-posters. The Award Committee consisting of Drs Sangeeta Yadav and Dhivyalakshmi, assisted by Drs Jaivinder Yadav, Arti Yadav, and Vinod Gupta assessed the deidentified e-posters, and declared the winners by consensus, as follows:

1st Prize: Drs Preetam Basak, Naresh Sachdeva, Sanjay Bhadada, Devi Dayal: PGIMER, Chandigarh. Title: Development of exosome-based immunomodulatory therapy for the remission of autoimmune responses in Type 1 diabetes

2nd Prize: Drs Ankita Tyagi, Priyanka Srivastava, Devi Dayal, Inusha Panigrahi, Anupriya Kaur: PGIMER, Chandigarh. Title: SHOX gene variations in Idiopathic Short Stature in North India and its overall prevalence in Asia.

Joint 3rd Prize:

Drs Shruti Mondkar, Nikhil Shah, Chirantap Oza, Vaman Khadilkar, Anuradha Khadilkar: Hirabai Cowasji Jehangir Medical Research Institute, Pune. Title: Effect of metformin adjunct therapy on glycemic and cardiometabolic parameters in Indian youth with Type 1 Diabetes: A randomized control trial.

Drs Payal Kubsad, Raghupathy Palany, Vani HN: Indira Gandhi Institute of Child Health, Bangalore. Title: Efficacy and safety of long-acting Octreotide in congenital hyperinsulinemic hypoglycemia.

In addition, the following presenters won consolation prizes:

Dr Vandana Jain (AIIMS, New Delhi),
Dr Moumita Saha (CMC, Vellore),
Dr Aashima Dabas (MAMC, New Delhi),
Dr Preeti Singh (LHMC, New Delhi),
Dr Pamali Nanda, Swaminathan K, Latika Rohilla, Arti Yadav, and Ashish Agarwal (PGIMER, Chandigarh).

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

The local organizing committee of Drs Jaivinder Yadav, Rakesh Kumar, and Devi Dayal of this successfully conducted meeting, received consistent support from ISPAE President Dr Shaila Bhattacharyya, Secretary-Treasurer Dr Ganesh Jevalikar, Executive Committee members and Advisors. It was sponsored by Novo Nordisk, Sun Pharma, Pfizer, Medtronics, Cipla, Ferring, Ypsomed, Trustcare, and Medgenome. The logistics were managed by Joy Enterprises, Chandigarh.

Information on upcoming Biennial meet in Bengaluru ISPAE 2023

Dear friends,
Greetings from the Organizing Committee of ISPAE 2023!!
It is indeed with great pleasure that we invite you to the 8th Biennial meeting of ISPAE to be held at Bengaluru, on 17 - 19th November 2023. Distinguished experts from international bodies, viz., European Society of Paediatric Endocrinology (ESPE), Asia Pacific Paediatric Endocrine Society (APPES), and International Society for Pediatric and Adolescent Diabetes (ISPAD) and reputed national speakers will be sharing their knowledge and expertise at this prestigious event. We do not need to remind you that this will also be the first physical conference after 4 years, hence we presume that you will be happy to attend this memorable event, and will grace it in large numbers.
The Pediatric Endocrinology for Trainees (PET) School will be organized as a residential 3 day Pre-Conference Academic Activity (14 - 16th November 2023), with Dr Ahila Ayyahoo as the Convener and Dr Shaila Bhattacharyya the Co-Convener. We shall be enrolling nearly 40 Clinical Fellows currently training in Paediatric Endocrinology in various centres in India and also the APPES region. Various topics related to growth, diabetes and other endocrine disorders will be covered during this training programme. This is being arranged amidst the green, sylvan surroundings of a natural resort close to Bangalore International Airport.
Details of both these meetings are available on our website www.ispae2023.com.
We extend a hearty welcome to you, one and all! Please do attend and enjoy the academic feast and our hospitality!
We are looking forward to your visit!
With best wishes,
Yours sincerely,

Dr Shaila Bhattacharyya	Dr Raghupathy P	Dr Vani HN
Organising Chairperson	Chief Patron	Organising Secretary

IDEAL – ISPAE Diabetes Education And Learning: a report

Dr Sirisha Kusuma Boddu, Rainbow Children's Hospital, Hyderabad.

We are extremely pleased to report that ISPAE's flagship Pediatric Diabetes Educator course IDEAL, launched in October 2021, continues its journey without any roadblocks. We trained 2 batches of diabetes educators, one of pediatricians, and are currently training our fourth batch, with 29 trainees – diabetes educators - eagerly pursuing this intensive and interactive course, which will be completed by January 2023. The success of IDEAL is not possible without the dedication and commitment of the Core Committee and our amazing team of faculty hailing from all over India, volunteering considerable time, effort, and expertise. They not only conduct their sessions, they also evaluate the trainees' submitted assignments and provide detailed feedback during the feedback sessions.
Being cognizant of the fact that learning is and should be a continuous process, with constant exchange of ideas and experiences, we had formed a WhatsApp group for those who are already IDEAL certified. This group, affectionately called 'IDEALITES', is serving as a platform for lively discussions on various practical aspects of managing type 1 diabetes. It is also providing a platform for networking and creating a feeling of community, generating mutual inspiration and motivation, so that the seeds are being sown for a ground force intent on working for the social and administrative reforms essential to improve the lives of our children and young people with type 1 diabetes.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

ISPAD 2022: At the recently held Annual ISPAD (International Society for Pediatric and Adolescent Diabetes) 2022 meeting, our work showcased in the form of an oral presentation and a poster, was highly appreciated and commended.

HOW TO APPLY: Applications are invited 1 month before the start of each batch via an online application form that must include a recommendation letter from the pediatrician/ pediatric endocrinologist/ endocrinologist the applicant is working/ associated with. Application procedure and links for registration and entry assessment can be found on the ISPAE website www.ispae.org.in/ideal. Or you can contact ispae.ideal@gmail.com

Feedback on ISPAE IDEAL course

Dr Dhruti Manish Pandya, Senior Resident, Department of Pediatrics
CU Shah Medical College, Surendranagar, Gujarat (IDEAL batch 3)

I follow the ISPAE page on Facebook and through it, I came to know about the ISPAE IDEAL program. The poster giving information about IDEAL program was up to the mark, and the qualifying entrance exam was also practical oriented. Encouraging emails were sent to us as selected candidates and fee submission was a hassle-free process.
The first session was very warm and inspiring, with all the faculty welcoming us wholeheartedly. All the teaching sessions were very informative and thorough. Apart from in- depth understanding of theoretical aspects, the highlight of the teaching was the very minute and detailed practical aspects regarding everything. Post-session discussion with faculty made us learn the nuances of practice, through sharing of our teachers' experiences. Concepts related to nutrition, insulin pump, CGMS and other latest technologies were taught very clearly. At every point, we were taught to have empathy towards our patients and their parents and to involve them in decision-making, so as to improve compliance and results. The psycho-social impact of T1D and its relevance in clinical practice was a very important topic discussed in one of the sessions. Pre-tests and post-tests were framed very intelligently. All the assignments given to us were scenarios we were likely to face in day-to-day practice; they made us understand the importance of counselling and explaining every detail to the patient. Gradings and comments of teachers for the assignments were very insightful. The exit exam was finely conducted and faculty was very supportive during the viva voce. The Whatsapp group created during the session was always active and all faculty responded to our doubts with thorough explanations.
All in all, my experience with IDEAL is one which I will cherish forever. I strongly recommend it for all practicing pediatricians, as it will empower us to manage our T1D patients in a much better way. I will be forever indebted to this program as it has enabled me to touch the lives of my T1D patients much more than before.

Dr Bifina Begum M, Department of Pediatrics
Government Medical College, Ernakulam

I was lucky to be selected for the 3 month IDEAL Course in Batch 3. I was looking forward to learning basics of managing type 1 Diabetes, as I am in charge of a clinic with about 40 T1D on regular follow up. The faculty at IDEAL all have vast experience in the subject, and took us smoothly through two 2hr classes per week of a great learning experience for 3 months. There were pre- and post-class tests, and practical audio and video assignments at the end of each session, making sure that we were grasping what we heard in class. This was in simple terms aimed at making the student demonstrate what he /she learnt, to be doubly sure they learnt it correctly. The student-friendly faculty made sure we cleared our doubts during each class. I am greatly indebted to the faculty for the course, taken in such a responsible and detailed way, which instilled confidence among all of us to care better for our T1D children.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

World Diabetes Day – ISPAE (14th Nov 2022)

Dr Hari Mangtani, Pearl Endocrine Clinic
Ramdaspeth Nagpur

November 14th is marked as 'World Diabetes Day' worldwide to create awareness about this dreaded silent killer. To contribute to this cause, ISPAE, under the able leadership and guidance of Dr. Shaila Bhattacharyya organized an awareness and education program addressing, in particular, people with type 1 diabetes and their families.

Living with type-1 DM is associated with a lot of difficulties as the child's needs change with his age and thus the requirements of a toddler with diabetes are completely different from those of a adolescent with diabetes. To address this important point and to educate people with type 1 diabetes and their families, ISPAE organized a panel discussion on a public forum, with its president Dr. Shaila Bhattacharyya, as the moderator and the secretary Dr. Ganesh Jevalikar and the executive board members, as the panelists. This web meeting was attended by over 200 families. The panel discussed various issues about TIDM, including its definition, cause, and the basic pathophysiology of Insulin deficiency. The diagnosis and treatment were discussed in detail. The need for insulin and the management of hypoglycemia and hyperglycemia were also discussed. Useful tips were given by the experts about the management of DM at school and during sick days. The difficulties in managing adolescent DM were also addressed along with the myths associated with T1DM treatment.
Queries from .from the families were answered in detail at the end of the session. The well-moderated session was greatly appreciated.

WORLD DIABETES DAY CELEBRATIONS

WDD at AIIMS Bhopal - 4th November 2022 - Prof. Mahesh Maheshwari

The Dept of Pediatrics, in association with the Medicine and Adult Endocrinology departments at AIIMS Bhopal, organized various events for WDD. A Diabetic Education Gallery has been prepared for patients coming to the hospital, with an audio message in Hindi for each poster, depicting information about the cause, diet advice, physical education, various insulins and complications, with the help of a unique QR code. A Quiz competition for postgraduate students was organized on Kahoot platform online. A symposium was organized for the faculty and residents of the Institute and practitioners of Bhopal, during which Dr Mahesh Maheshwari and Dr VN Mishra gave talks. A camp for on-the-spot HbA1c testing and diabetes education was organized for patients with diabetes.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

WDD celebration at Indira Gandhi Institute of Child Health, Bengaluru – 26 Nov 2022 - Dr Vani HN

WDD is celebrated on 14th November every year. As a part of it, we conducted a comprehensive educational program at IGICH on 26 November, which had overwhelming participation from the children and their parents. Almost 120 children with diabetes, accompanied by their parents, attended the event, which was organized by Prof. P. Raghupathy and his team of doctors, including Dr Vani HN and endocrine Fellows. The program was inaugurated by Dr Sanjay KS, Director of IGICH, and started with a walkathon in the morning, followed by scientific talks given by eminent speakers. The topics discussed were 'Eating right for a better tomorrow' by nutritionist Ms Deepthi (dietician at KIER) and 'Psychological support for Type1 diabetes' by child psychiatrist Dr Eesha Sharma (Asst Prof. NIMHANS). Dr Raghupathy and Mr Dinakaran (Retired Senior Manager, Novo Nordisk) were felicitated.
The parents and children were educated about the usage of insulin pens, their advantages and ways to overcome the pitfalls. Parents had the opportunity to clear their doubts with regard to daily management of diabetes. Entertainment programs like a puppet show and dance events were thoroughly enjoyed by everyone. To make the occasion more memorable and lively, a drawing/ painting competition was held and prizes given. These sweet kids also showcased their talents by dancing, singing, and performing yog asanas. Prizes were distributed to children who had achieved good HbA1c control, or excelled in academics and sports. At the end of the event, all the children were provided with free monthly insulin, lancets, glucometers and gifts. Overall, it was a memorable day for children, parents and our endocrine team.



Sweet Little Stars Celebration - Apollo Children's Hospital, Chennai – Dr V Soundaram

As part of WDD celebration 2022, we organized an event in the Auditorium of our hospital. There were 3 academic sessions – 'Trouble-shooting high sugars', 'Mental health challenges in T1D', and 'Common mistakes in diet'. Miss Athira, a young playback singer, did mash-up for 15 mins. We had also organized games for the kids. The program was sponsored by Novo Insulin and Pulse Nutrition.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Sweet Souls Organization, Hyderabad - Sree Divya Akula, Lakshminarayana and Sirisha Mantha.

A fun themed Patient Awareness Program was organized on 13 Nov 2022 in association with CDiC (Changing Diabetes in Children) by Dr PV Rao. Many children with T1Diabetes from under- privileged sections from Telangana and Andhra Pradesh participated. There were tambola, a painting competition and dances. Many adult T1Ds shared their journeys and discussed multiple topics. The Chief Guests - Dr Kamalakar (Medical Director, Ramadev Rao Hospital) and Dr Sunitha Krishnan (Founder of Prajwala, and Padma Shree awardee) gave motivating talks. Dr PV Rao has been supporting diabetes treatment essentials like insulin, strips and tests for many years. Right diabetes education, right action, and access to right treatment play key roles in optimal management of Diabetes.

On 20 Nov 2022, in association with Dr Neelaveni, Sweet Souls organized a Parent Awareness Meet for Sweet Souls' adults to share their experiences, motivate and interact with T1D kids. Varied responses from acceptance to rebellion are observed. It was reinforced that a positive attitude, acceptance, learning and action in management, are the key to an optimal long term outcome.

On 27 Nov 2022, an informative and interactive Meet of kids, teens, adults, family members and certified diabetes educators was held at Sanjeeviah Park, Hyderabad. The aims of the meet included breaking myths, sharing experiences, learning newer developments and improving confidence levels.

WDD program - Karnataka Institute of Endocrinology and Research, Bengaluru - 12/11/2022.

A program was organized on 12 Nov, with this year's WDD theme: "Education to protect tomorrow", by Dr Santhosh Olety, and dietitians Sharanya S Shetty, Shilpa C Parihar, Deepthi S, and Shruthi R. Almost 80 kids with T1D delightedly took part, along with their family members. The program started with an invocation song by one of our T1D kids, followed by an exhilarating magic show conducted by a parent, and many fun games, uplifting team spirit and delivering messages on how sharing knowledge and awareness can create a platform for a better tomorrow. Rotary Clubs announced that 45 more kids will be adopted and supported with diabetes supplies like analog insulin, pen needles, glucose testing strips and glucometers. T1d heroes were introduced to kids and families - Dr Shuchy Chugh, Mr Anirudh S, Mr Nithin Somasundar, Mr Angad Chandhok, Mr Sahil Om Madan, Ms Geethanjali Rangaswamy and Ms Marielle Bostrom, conveying a strong message that uplifting people living with T1D with proper diabetes education and help, can enable them to achieve their dreams. The program ended with a talent show, gifts, and a healthy lunch.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Get Together for People with T1D - Nehru Park, New Delhi - Mr Harsh Kohli

A meet was organized by Mr Harsh Kohli (IDEAL batch 1) at Nehru Park, New Delhi and attended by 30 children/ adults (head count 70) living with T1D. Children enjoyed various activities like a Blue Balloon Challenge, Art & Craft activity, and Dumb Charades. In Blue Balloon Challenge, a big blue balloon, representing Diabetes as a whole, was handed over to persons with T1D. The idea of passing it around highlighted the importance of community and learning from each other. In the Art & Craft activity, the kids were asked to illustrate through drawings/ writing one thing they like about living with T1D, and one thing they dislike about it. Dumb Charades (T1D Style) consisted of handing over chits to people with T1D - they had to enact what was in the chit. For example, someone who got a chit with 'Site Rotation' written on it had to enact Site Rotation. After this was successfully done, the importance of Site Rotation was explained to everyone. The parents and adult T1Ds were asked to estimate their monthly expenses of living with T1D, the aim being to highlight the increasing cost of diabetes management and the rationale for uniting to reach out to policymakers to give tax exemptions so that the high costs can be partially subsidized. The event was enjoyable and thought provoking.

WDD 2022 celebration- PGIMS, Rohtak - Dr Anjali

A webinar on "Challenges and Solutions in the management of children with T1D" was organized by the Multi-Disciplinary Research Unit, of the University of Health Sciences, Rohtak, on 14 Nov 2022 on the occasion of WDD. More than 90 doctors from various departments of colleges affiliated with PGIMS and UHSR, PG students, and parents of T1D children, participated in the webinar. The organizing secretary was Dr Anjali, Coordinator of MRU and Assoc. Prof., Dept of Pediatrics. Pediatric Endocrinologist Dr Arundhatee Khare graced the program as the keynote speaker. All attendees were educated about T1D management, so that future complications can be prevented. Dr Khare also answered the questions of parents and children pertaining to their day-to-day problems in maintaining blood glucose levels in normal range.

Trek & Picnic That Healed Souls - JDF, Mumbai - Vaishali Vakil & Alex Fernandes

Picnics can heal the mind; at times, even the soul. Precisely what a day's outing did to a few people newly diagnosed with T1D. The Juvenile Diabetes Foundation, Maharashtra Chapter, organised a day-long trip to Yeoor Hill, about 24 km from Mumbai, on the eve of WDD. The group comprised a motley mix of 37 people of different age groups - the youngest was 3y and the oldest 50y old. The whole idea of organising the outing was to give the newly diagnosed the lesson that life can be a celebration despite diabetes. In fact, this has been the credo hammered out by our support group and its doctors over the past 40 years of its existence.

Out on the picnic, we indulged in the usual fun and frolic - singing and playing games up there - from a vantage point which gave us a picture postcard view of the beautiful world around.

There was some talk about diabetes, especially a barrage of queries from the younger lot and their caregivers. The senior pack of us, those living with the chronic medical condition for a long time, answered these patiently to the best of our ability. The focus of the discussion was more on how one can lead a good life, and diabetes won't be a hurdle.

This lesson among the peers - from the old-timers to the newly-diagnosed - was possible only because of the lessons that we have all learnt over the years at JDF. The support group has helped us grow together, learn not just the clinical aspects of diabetes but also the nitty-gritty of living well. And that is what the one-day picnic did to the newly diagnosed persons. It taught them the most important thing is that you can enjoy life and live well, with a little care and concern.

This lesson we could pass on was because a handful of doctors thought about the T1 community in the early 1980s, and formed this support group. Without that, it may not have been possible to face the challenges that life poses. Amazing how healthcare personnel - doctors, nutritionists, counselors - can come together and do their bit for people living with a chronic medical condition. A support group really helps. The picnic atop Yeoor hill has proven this yet again.

WDD 2022 Celebration - Govt Medical College, Ernakulam - Dr Bifina Begum

WDD was celebrated in the Dept of Pediatrics, Government Medical College, Ernakulam, Kerala, with support from the Kerala Social Security Mission. There was a get together of T1D children who are being followed up at the Mittayi Satellite Center in GMC, Ernakulam. Twenty children with parents attended the program, which began with an awareness class on day-to-day management of T1D. After this, there was an interactive discussion to clear the parents' doubts. This was followed by a drawing competition (for children above 10 years age) and coloring competition (for children between 4-10 years age), and many other fun activities. Prizes were awarded for winners of various events. There was a small exhibition-cum-sale of stuffed toys hand made by a 15 year old girl with diabetes: all the toys were sold out. Finally there was a sumptuous lunch for all attendees.

WDD 2022 – AHRI and IRIS, Thiruvananthapuram - Dr Veena V Nair

On the occasion of WDD 2022, Ananthapuri Hospitals and Research Institute arranged a one-day fun trip on 12 Nov for children with T1D to Magic Planet, Kazhakkoottaom, Thiruvanathapuram. Magic Planet is a mesmerising place founded by the great magician turned motivational speaker Prof. Gopinath Muthukad. It showcases magic shows, circuses, dramagic and heart-touching performances by differently-abled children in an exciting ambient environment. Nine T1D children with their parents and the hospital team, including doctors, dieticians and other support staff, joined the program. In addition to the routine attractions at the Center, we were lucky to have an opportunity to interact with Prof Gopinath Muthukad, the unique man behind this venture, who after voluntarily winding up his professional magic life, continues his magic of changing the life of children with disabilities like autism, learning disabilities, etc. through rehabilitation and empowerment. He addressed the group and filled our

hearts with positive hopes through his enchanting words. Apart from this, we used the occasion to educate the families on various aspects of day-to-day management of diabetes.

WDD 2022 Celebration - Endocare for Kids, Rajkot - Dr Zalak Upadhyay

Dr Zalak was able to spread awareness through Radio on 14 Nov, by giving an important message on diabetes in children and it's management.

Juvenile Diabetes Foundation, Rajkot celebrated WDD on 13 Nov 2022, Sunday, with almost 400 kids. All the important topics were covered by endocrinologists in this camp. Dr Zalak gave a talk on "Importance of blood glucose monitoring, HbA1c and screening of complications".

Dr Zalak's clinic, Endocare for Kids, celebrated WDD on 4th December 2022, Sunday at Rajkot. We invited all our T1D kids and their parents. We had 4 different tables for education on – Importance of glucose checking and CGM, Dietary management and carbohydrate counting, Insulin administration techniques and Insulin pump. Education was followed by tattoo making and interesting craft activity for kids, with special performances by our little stars, and lunch for all. The function was attended by almost 50 kids and their families.



WDD 2022 – "Education to Protect Tomorrow" - Rainbow Children's Hospital, Banjara Hills, Hyderabad

On the occasion of WDD 2022, the Pediatric Diabetes Team of Drs Leenatha Reddy, Leena Priyambada, Kavitha Sakamuri, and Sirisha Kusuma, at Rainbow Children's Hospital, Hyderabad, in collaboration with 'Sweet Souls' (an NGO support group consisting of families with T1D) invited a few school Principals and Telengana Government Officers involved in NCD programs, to raise awareness regarding T1D, the need for policies especially for schools, and "Diabetes Education for Caregivers in Schools". Families presented their experiences and challenges faced at school while the teachers enunciated their limitations. The 2022 ISPAD guidelines on the management of T1D in schools were presented, and plans for incorporating them in our schools discussed.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

There was active participation amongst the families (~70pax). The NCD officers received the discussions well, and gave very positive feedback. Children with T1D presented an interesting dance and skit. There were some delicious simple low-carb snacks and drinks. We hope that these small steps will evolve into helpful practices and policies to make T1D management a little easier and more successful.

WDD celebrations - Lady Hardinge Medical College, New Delhi – Dr Preeti Singh

On WDD, 14 Nov 2022, the Endocrine division of the Dept of Pediatrics, in collaboration with the Dept of Medicine, organized a program on T1D at LHMC, New Delhi, with the theme "Optimising health care in T1D". It had two components: a morning session for children with T1D and their caregivers; and an afternoon academic session for physicians/ resident doctors, postgraduates, dieticians and nurses from the Depts of Pediatrics and Medicine. Almost 60 T1D children with their families, dietitians, nurses, and senior members from Yog Dhyan Foundation and People to People Health Foundation, participated in the forenoon session. They were engaged in informative talks by Prof. Anju Seth (Head, Dept of Pediatrics, LHMC), Dr Anju Virmani (Senior Pediatric Endocrinologist at Max Smart Super Specialty Hospital, & Madhukar Rainbow Children's Hospitals, Delhi) and Dr Preeti Singh (Assoc. Prof., Pediatrics, LHMC) and a panel discussion by pediatric diabetes experts on ongoing care of children with diabetes, while addressing the families' concerns. Mr. Harsh Kohli, a certified diabetes educator, who is living with T1D for the past 30 years and father of a 10y old son with T1D, shared his experience of using CGM and insulin pump with the families, to sensitize them about technological advancements. Dr Smita Joshi, trustee, Dr Vasudev J Raval Charitable Trust, Gujrat, was kind enough to join this program to create an awareness drive in India about the needs of children with T1D. This program also provided a platform for children and their caregivers to develop bonds and gain support from each other. A stationery kit was gifted to the children, and healthy snacks - chhach, peanuts and apples - were distributed as refreshments to all present.

The afternoon session was preceded by an inaugural function attended by the Chief Guest Shri S Gopalakrishnan (Special Secretary, Health); Guest of Honor Dr Atul Goel (Director General Health Services); Dr Virendra Kumar (Director, LHMC and associated hospitals), and other dignitaries, senior faculty members from various departments; resident doctors, postgraduates, dietitians and nurses. Through this program, attention was drawn towards the needs of the children and adults with T1D and ways to facilitate providing optimum care to them.

After lunch, there was a symposium on T1D, which included sessions on ambulatory care (Dr Preeti Singh), complications and comorbidities (Dr Aashima Dabas, Assoc. Prof., Pediatrics, Maulana Azad Medical College, New Delhi), challenges in managing adults with T1D (Prof. Shubhalaxmi, Dept of Medicine, LHMC) and sensitization on technological advancements like understanding and interpreting Continuous Glucose Monitoring (Dr Anju Virmani) and Insulin Pump (Dr Ganesh Jevalikar, Pediatric Endocrinologist, Max Super Specialty Hospital, Delhi & Gurgaon). The sessions were well attended and appreciated by the resident doctors and postgraduates from Depts of Pediatrics and Medicine. The aim of involving both departments jointly was to improve the process of transition for persons with T1D, once they outgrew Pediatrics.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Dr Meena kumari Mohan, PSG Super Speciality Hospitals, Coimbatore.

World Diabetes Day celebrations were conducted at PSG Super Speciality Hospitals on 13.11.2022. The day started with two simultaneous workshops for two groups of postgraduates from Medicine - one on Insulin pumps, and the other one on CGMS. It was well attended by 18 doctors. This was followed by Parent support group meeting for families with children with T1D. Free Hba1c was done for all the children who attended the meeting.
A case presentation of an adult who poorly managed T1D with complications was done, followed by a discussion by two adult endocrinologists on managing this with CGMS. Workshops as smaller group sessions on various topics including hypoglycaemia, sick day management, blood glucose monitoring, informing school about diabetes, carb counting, pumps, etc were conducted by diabetes educators and the dietician. Forty children and their families [total number 150] attended, with 25 children given free glucometers with 50 strips each on the occasion.

Yog Dhyan Foundation T1D Health Carnival – New Delhi – Dr Anil Vedwal

WDD was celebrated on 11 Dec 2022 Sunday by YDF with a Health Carnival, at Satbari Farmhouse, in south Delhi, for children, adolescents and young adults with T1D, many with celiac disease also. At entry, all the children and their family members were given free YDF volunteer T-shirts and Caps, and a BG check with snacks to make sure everyone could enjoy the fun without hypoglycemia. The Carnival had lots of games and dance activities, as well as booths for free Blood checkup, Eye checkup including fundus examination, Diet advice, and Diabetes Education. The monthly distribution of free diabetes supply to the children was done. YDF has commissioned an anthem and dance specially for T1D – this was performed for the first time on the huge stage. Later there were a Quiz contest, a dance competition and a Yoga performance, with lots of prizes for winners and participants. For the birthday celebration for T1D kids born in November, there were gluten free cakes: everyone got small portions so they could enjoy without any worry. YDF President Mr Rummy Chhabra and Vice President Ms Bindia Chhabra (Metro Tyres) announced support for YDF from Rotary Southend Next, BeatO, and Center for Sight, and continuing support from Ypsomed. They felicitated doctors, donors and partners who have been providing support to YDF for years, including Dr Anju Virmani, Dr Meena Chhabra, Dr Jyoti Kakkar, Dr Anil Vedwal, Dr Nikhil Tandon, Dr Praveen Pradeep, Dr Preeti Singh, Dr Beena Bansal, Mr Gautam Chopra (founder, BeatO), and members of Rotary Southend Next. There were dedicated counters for games, snacks and lunch. Almost 220 T1D children and their families (total 750 people) enjoyed themselves in the warm winter sun. The immense support and positive energy gives the motivation to continue to help these children lead healthy, productive lives.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

WDD celebration - LLRM Medical College, Meerut, UP

WDD was celebrated at LLRM Medical College with a half day CME by the Depts of Pediatrics, Medicine and Endocrinology. It was conducted in the presence of the honorable Principal Dr RC Gupta, SIC Dr KN Tiwari, and HOD Medicine Prof Abha Gupta; and attended by faculty and residents of the clinical departments. This year's theme Education to protect tomorrow for effective management of diabetes was discussed in detail. A Quiz on diabetes was conducted for under-graduates. The Vote of thanks to the audience and media persons was given by Dr Vijay Jaiswal.

Tamil Nadu Type 1 Diabetes Foundation awareness camp - organised by Aravind M, Mr Prashanth Mani, Mrs Beemajan Yussouf ,Tamil Nadu Type 1 Diabetes Foundation , Type 1 Diabetes Foundation of India

An awareness Camp for children with type 1 diabetes to help them learn how to manage their condition was conducted. The Program provided safe and supportive environment for children to learn about diabetes, nutrition, exercise and other important topics. The camp also provided an opportunity for children to connect with other children who have type 1 diabetes and to build relationships with Diabetes educator who can provide ongoing support. Self confidence and proper Diabetes management is pivotal to maintain glycemic control, academic and professional achievement.

WDD Celebration - Dr Ravindra Kumar, Hindu Rao Hospital, Delhi

Hindu Rao Hospital and IAP North Delhi organized a community free blood glucose testing camp at Japanese Park, Rohini, Delhi, on the occasion of WDD. More than 200 adolescents and adults were tested. In addition, a Diabetes Awareness Session was organized in the Pediatric OPD of Hindu Rao Hospital for children with T1D and their families. The importance of SMBG and carb counting was reinforced. In the afternoon, a CME organized for doctors and paramedical staff, was well attended by over 70 participants. Dr Ravindra Kumar discussed CGM and pumps, while Dr Medha Mittal spoke on current concepts in T1D.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Sweet Children Meet - Shree Guru Kripa Endocrine Clinic (SGKEC), Kurukshetra (Haryana)
Dr Mudita Dhingra, Consultant Paediatric & Adolescent Endocrinologist

A Sweet children meet was held at SGKEC, Kurukshetra on 30th October, 2022 for children and families living with Type 1 Diabetes. It was a half day event which emphasised on Diabetes Education (Revision of Basics) to sensitisation about latest technology and Insulin Pump use in current scenario. Nutritional counselling and carbohydrate counting was highlighted by Sheryl Salis (NHS, Mumbai) who joined virtually. Another aspect of Diabetes care which is usually ignored was covered Ms Naumita Rishi , Cognitive Behavioral Therapist , who emphasised on psychological aspects of Diabetes care . It was attended by nearly 30 families and was highly appreciated by all. In addition, children played games together and bonded at the same time. Prizes were given to children who actively answered the quiz questions and with best Time in Range/HbA1c.

Academic activities of ISPAE members

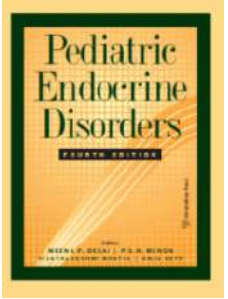
The Second Pediatric Pituitary Conference – Dr V Soundaram, Apollo Proton Cancer Center, Chennai.

Pituitary disorders are relatively rare in the pediatric age group, but need multi-disciplinary care. This meeting was organized to enhance the knowledge of pediatric endocrinologists, neurosurgeons and radiation oncologists handling such patients. It was conducted under the aegis of the Apollo Proton Cancer Center and ISPAE. Top experts from Indian and UK gave lectures to the approximately 70 doctors. There were no sponsors.

CME, Common Pediatric Endocrine issues - PGICH, NOIDA – Dr Bhanukiran Bhakhri

A CME on pediatric endocrinology in office practice was conducted on 17 Dec 2022, Saturday, at the Post Graduate Institute of Child Health (PGICH), Noida. It was organized by Dept of Pediatrics, PGICH in association with AOP Noida. The focus was kept on problems encountered commonly in pediatric practice like obesity, poor growth, and interpretation of abnormal thyroid reports. Practicing doctors and PG residents from institutions in NOIDA and Greater NOIDA region attended. The pediatric endocrine Quiz was jointly won by the teams from PGICH NOIDA and the Government Institute of Medical Sciences (GIMS), Greater NOIDA. The event was a step towards orientation of PG students to endocrinology as an important sub specialty of pediatric medicine.

New book release



The fourth edition of the basic Indian textbook on "Pediatric Endocrine Disorders" has just been released. Edited by Prof Meena P Desai, Prof PSN Menon, Prof Vijayalakshmi Bhatia and Prof Anju Seth, this well curated and well written book is a useful resource for pediatric endocrinologists, as well as pediatricians and adult endocrinologists with interest in pediatric endocrinology. Practical aspects of approach to pediatric endocrine disorders, including clinical presentation, investigations, and management, in developing countries like India, have been extensively dealt with.

Key features include:
A) Contributions from a vast galaxy of academicians and stalwarts in pediatric endocrinology, with several new authors,
B) Extensively revised chapters on: diabetes mellitus, thyroid disorders, obesity and adrenal disorders,
C) Coverage of novel topics, like Transition of care to adult endocrinology, and Community pediatric endocrinology,
D) Vibrant new look in an all-color format.

It can be purchased from Amazon or procured from the following contact persons:
Chennai: SJ Prem Kumar, premkumar.sj@orientblackswan.com, Mob: 9382321233.
Hyderabad: B Janardhan Reddy, janardhan.reddy@orientblackswan.com, Mob: 9346301635
Mumbai: Sachin Karad, sachin.karad@orientblackswan.com, Mob: 7710055164
Delhi: Sandeep Vashisth, sandeep.vashisth@orientblackswan.com, Mob: 9015167337
Kolkata: Govind Singh Yadav, govindsingh.yadav@orientblackswan.com, Mob: 7488033714

Achievements of ISPAE members

Dr Vaman Khadilkar has been nominated for the Hon. Surg Cmde Late Shantilal C. Sheth Oration for the year 2022, to be delivered during the 60th Pedicon being held with the 30th IPA Congress 2023. It is to recognize his contributions to the Indian Academy of Pediatrics, as well as to Child Welfare and Pediatric Education at large over the years. The oration is scheduled for 20th February 2023: 11 am to 12 pm: in the Main Hall, at the Mahatma Mandir Convention & Exhibition Center, Gandhinagar, Gujarat. It is a proud moment for ISPAE. Hearty congratulations from team ISPAE CAPE News 2021-22.

Dr Soundaram V presented "A case of thyrotropic pituitary adenoma unresponsive to Octreotide" along with neurosurgeon Dr.Roopesh Kumar and Dr.Vijayasarathi at The Pituitary Update Course 2022, at Estonia, Europe in October 2022.

Publications:
Dr Medha Mittal:Mittal M, Dhungel S, Bandarpalli H, Rai A. Walcott Rallison syndrome-beyond neonatal diabetes. Indian Pediatr CaseRep October-December 2022 vol 2, issue 4 p 212-216.

Trainees Section

Dr Diksha Shirodkar, Senior Clinical Fellow, Pediatric Endocrine and Diabetes
Bristol Royal Children's Hospital, Bristol, UK

Unjumble the letters to discover the answers from the clues given related to calcium metabolism. Assemble the special letters which are numbered below in an ascending order and discover the phrase at the end.

1. Parathyroid hormone acts indirectly via ..... to absorb calcium from the gut.
2. High levels of FGF 23 cause a ..... in serum phosphate concentrations.
3. PHEX, ENPP and DMP 1 are all ..... to FGF 23
4. Loss-of- function mutations in TRPM6 result in autosomal recessive ..... and secondary hypocalcaemia
5. Biallelic inactivating mutations in CLDN19 coding for ..... 19 result in hypomagnesemia (secondary to renal wasting of Mg), hypercalciuria, and nephrocalcinosis and decreased vision due to retinal malformation.
6. A drug found effective in decreasing secretion of PTH in patients with either primary or secondary hyperparathyroidism.

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

7. The multifunctional protein that serves as a coreceptor thereby converting FGFR into specific FGF23 receptors in the parathyroid glands and kidney.
8. a. Loss-of-function mutations in ALPL lead to infantile, childhood, and adult forms of which condition?
b. Name the drug approved for its treatment
9. Name the condition resulting from homozygous or compound heterozygous inactivating mutations in the parathyroid hormone receptor-1 gene.
10. In the syndrome CATCH-22 what does H stand for?
11. A radionuclide scanning technique using ..... can be used to localise a parathyroid adenoma
12. A condition arising in the immediate postoperative period following total parathyroidectomy in a new born with life threatening neonatal severe hyperparathyroidism.
13. In the management of Hypercalcemia apart from Hydration, ... and ..... could be potentially helpful.

1. TIARICOLCL
   1
2. ESRAEDEC
   20
3. YTBINIOHRI
   14
4. PMEYIHNGMOASAE
   2 19 4
5. DAILUNC
   5
6. TACNCIEACL
   18 16
7. HPAAL TKOLOH
   23
8a. OPASYPSAATOIPHHH
   7
8b. TSSFEOAA AHPLA
   22 15
9. BOMDASLNRT
   17 6
   PYSNHROOCSDAILAD
   21 12
10. CMHALOAIYEPC
    13
11. MTC99 BTEMSAIIS
    8
12. HGURYN OENB
    10
13. ASPHONPSTEOBHSI
    9 11
    YRTRINCDOSHEOO
    3

ANSWER

1 2 3

4 5 6 7 8 9 10 11 12 13 14 15 16

17 18 19 20 21 22 23

NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Trainees section : Quiz

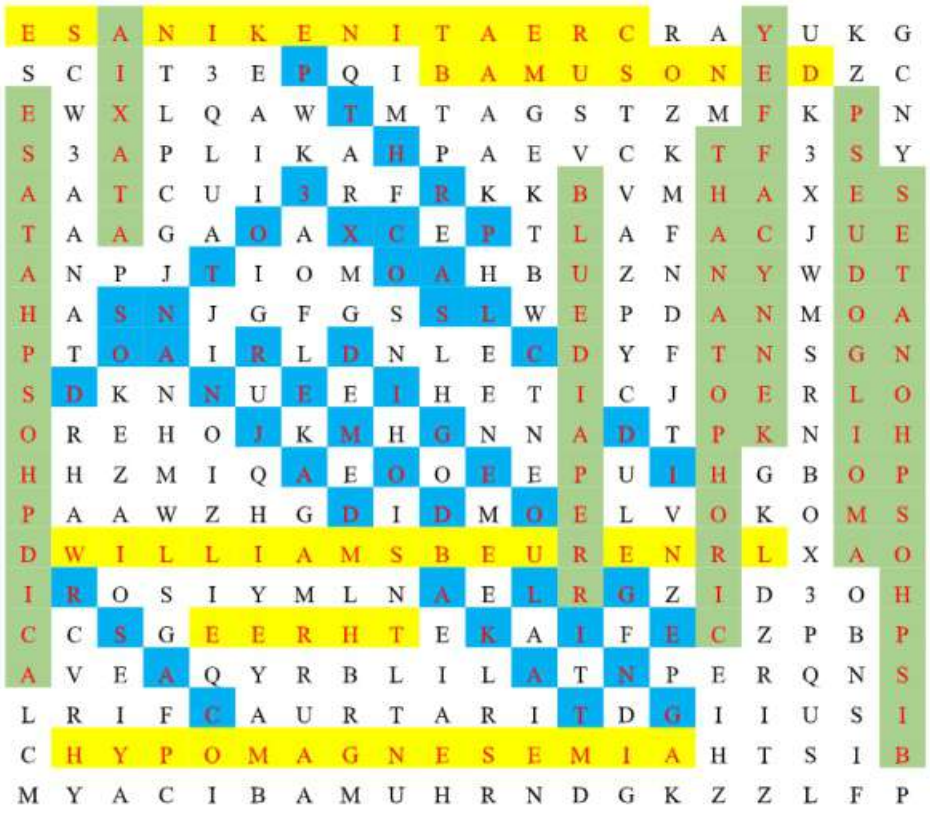
Solutions to Bone and mineral metabolism that appeared in October 2022 issue of CAPE News - Word Hunt on Bone disorders in children

Clues:

1. Familial isolated congenital hypoparathyroidism (autosomal recessive, autosomal dominant, or X-linked recessive trait) can be because of gain-of function mutations in ---------- gene
2. Hyperparathyroidism in an infant/neonate due to disturbances in the tryptophan metabolism is called ------- --------- syndrome.
3. Cardiovascular abnormalities, especially concerning the aorta, facial dysmorphism, behavioral abnormalities and hypercalcemia in a child are seen in --------- syndrome.
4. In SeSAME syndrome, along with hypomagnesemia, what does A stand in the acronym?
5. ----------hypophosphatasia involves premature shedding of teeth with periodontitis.
6. A major cause of humoral hypercalcemia of malignancy.
7. A continuous process in which portions of formed bone are periodically reabsorbed and replaced by new bone.
8. MODY 5 is associated with abnormality of which mineral metabolism?
9. The neurocristopathy caused mostly due to microdeletions of 22q11.2 is --------syndrome.
10. A syndrome with severe growth retardation, dysmorphic features, episodic hypocalcemia, hypoparathyroidism, seizures and medullary stenosis of long bones with thickened cortices.
11. X-linked hypoparathyroidism caused by mutation in ----- gene.
12. The type of Osteogenesis Imperfecta, in which extremities showing flared metaphyses ("popcorn-like calcifications"), bowing and thin cortices, most commonly seen.
13. Mutations in the gene LRP5 (Low density lipoprotein receptor-related protein 5) causing impaired Wnt signalling and osteoblast function causes osteoporosis --------- syndrome.
14. Atypical Femur Fractures are commonly an adverse effect of ----- therapy
15. Mutation in the tubulin co-factor E (TBCE) gene causing primary hypoparathyroidism and craniofacial abnormalities with occasion hyposplenism is ------- syndrome
16. Biomarkers for osteopetrosis are increased serum levels of ------ ------ and the brain isoform of ------ ------.
17. 25-Hydroxycholecalciferol is also called?
18. A lethal form of skeletal dysplasia with micromelia, bowed femurs and varying severity of craniosynostosis.
19. A human monoclonal antibody called as "pseudo-osteoprotegerin"

Answers

1. CaSR
2. Blue Diaper
3. Williams Beuren
4. Ataxia
5. Odonto
6. PTHrP
7. Remodeling
8. Hypomagnesemia
9. Di-George
10. Kenny Caffey
11. SOX3
12. Three
13. Pseudoglioma
14. Bisphosphonates
15. Sanjad-Sakati
16. Acid Phosphatase, Creatine K
17. Calcidiol
18. Thanatophoric
19. Denosumab



NEWSLETTER
DECEMBER 2022
Volume 26, Issue 4

CAPE News | ISPAE

Trainees section : Quiz

Solutions to Trainees section Word jumble quiz on Calciuum disorders that appeared in this December issue of CAPE News:

Answers

CALCITRIOL
DECREASE
INHIBITORY
HYPOMAGNESEMIA
CLAUDIN
CINACALCET
-KLOTHO
HYPOPHOSPHATASIA
ASFOTASE ALPHA
BLOMSTRAND CHONDRODYSPLASIA
HYPOCALCEMIA
99mTc SESTAMIBI
HUNGRY BONE
BISPHOSPHONATES
HYDROCORTISONE

Phrase:
THE INDISPENSABLE MINERAL