CAPE NEWS

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

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Contents

From the Editor's desk

Dear members,

Endocrine disturbances are common consequences of many chronic systemic diseases. In this issue, we have made a sincere effort to address the endocrinopathies in common chronic systemic diseases.

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

Editor, CAPENEWS

Dr Meena Desai Honored as ESPE International Outstanding Clinician for 2015 at ESPE Barcelona Meeting: Dr PSN Menon

Every year the European Society of Pediatric Endocrinology (ESPE) honors selected eminent pediatric endocrinologists around the world in recognition of contributions towards patient care, education and research in the field of pediatric endocrinology.

The International Outstanding Clinician Award for 2015 was accorded to Dr Meena Desai during ESPE 2015 at Barcelona. A citation about the various contributions by Dr Desai to the pioneering work for development of pediatric endocrinology in India and APPES region was read out by Dr Lars Sävendahl, President ESPE. Dr Desai could not attend the award ceremony due to health problems and it was accepted on her behalf by her son, Dr Neil Desai.

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

Organizing Chairperson: Dr P Raghupathy, drp.raghupathy@gmail.com

Organizing Secretary: Dr Ahila Ayyavoo, ahila.ayyavoo@gmail.com

Welcome to beautiful Coimbatore!!

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

in association with International Society for Pediatric and Adolescent Diabetes (ISPAD)

The theme of this meeting is **"Pediatric Diabetes".**

Organizing Team: Dr. Sudha Rao, Dr. Preeti Dabadghao, Dr. Tushar Godbole

Early bid registration has started. For enquiry and registrations, please contact:

Dr. Tushar Godbole [+91-7774082834], tusgod@gmail.com

Secretary's Report

Dear members of ISPAE,

Membership

As of today, our total membership is 412 with 248 life members, 162 associate members and 4 honorary members.

ISPAE Charity Awards

ISPAE is committed to provide assistance to various charity activities of its members. This time the Executive council decided to award Dr Ganesh Jevalikar and Dr Shafi Kuchay for their charity activities for flood victims in Kashmir, and Dr Hemchand Prasad for charity activities for children with diabetes in Chennai.

ISPAE Observership Awards

This year two members were given the Observership Awards: Dr Sanjay Kumar at Bharathi Vidyapith Pune under Dr Vaman Khadilkar, and Dr Deepty Kumar at SGPGI Lucknow under Dr Vijayalakshmi Bhatia and Dr Preeti Dabadghao. In 2014, these awards went to Dr Abraham Paulose (SGPGI Lucknow), and Dr Vishnu Agarwal (BJ Wadia Mumbai under Dr Sudha Rao). Dr Paulose has started a pediatric endocrinology clinic at his hospital in Cochin and is also undergoing a formal pediatric endocrinology fellowship at Bangalore.

Patient Education

Hindi and Malayalam diabetes education books are available in hard copy and soft copy is also freely available on our website. Serono patient education booklets on Turner Syndrome and CAH, translated in Hindi and customized for the Indian patient readership, made possible by Dr Margaret Zacharin, are free to read on the ISPAE website and also in hard copy for members to distribute to their patients.

Felicitation of the Recipients of International and National Awards

Every year ESPE presents 6 important and prestigious awards in recognition of outstanding teaching, research and contribution to pediatric endocrinology. The International Outstanding Clinician Award for 2015 was accorded to none other than our own Dr Meena Desai during ESPE 2015 at Barcelona. It was accepted on her behalf by her son, Dr Neil Desai.

Further, we congratulate our members Dr Ambrish Mithal and Dr Nikhil Tandon for being conferred with Padma Awards this year by the President of India for their distinguished services in the field of medicine.

Participation in International Fora and Working Groups

ISPAE, along with other major regional pediatric endocrine societies and country societies, is a member of the International Consortium of Pediatric Endocrinology, formed in 2015.

Our members Dr Vijayalakshmi Bhatia, Dr Anju Seth and Dr Rajesh Khadgawat, were nominated by ISPAE as part of the ESPE worldwide consensus on prevention and management of rickets. The meeting, convened in Birmingham in May 2015, has swiftly culminated into a guideline accepted for publication in JCEM and Hormone Research in Pediatrics.

Dr Preeti Dabadghao was nominated as APPES representative for a consensus group of all pediatric endocrine societies to set guidelines for diagnosis of PCOS in adolescents. The guidelines are freely available online (Witchel SF et al. The diagnosis of polycystic ovary syndrome during adolescence. Horm Res Paediatr 2015).

Annual General Body Meeting

The AGBM 2015 and a special GBM were held at Gurgaon during ISPAE 2015. A special GBM has been convened in Ahmedabad in December 2015.

Biennial Scientific Meeting of ISPAE 2017 and Midterm Meeting 2016

Invitations were called for conducting the Biennial Meeting of ISPAE in 2017 and the Midterm Meeting in 2016. It is decided that the next ISPAE midterm meeting for the year 2016 will be held at Nashik, Maharashtra, with Dr Tushar Godbole as the Organizing Secretary. ISPAE 2017, the biennial meeting, will be conducted at Coimbatore, with Dr Ahila Ayyavoo as the Organizing Secretary.

ISPAD 2018 to be held in India

The International Society for Pediatric and Adolescent Diabetes (ISPAD) has decided to hold their annual 2018 meeting in India, in collaboration with ISPAE.

CMEs and Workshops

CMEs and workshops were conducted in Coimbatore, Chennai, Mumbai, Bengaluru and Thiruvananthapuram under the banner of ISPAE or the IAP Subspecialty Chapter of Pediatric and Adolescent Endocrinology.

Secretary, ISPAE

Hearty Welcome to New ISPAE Members

Alla Kiranmay, Ped, Vijaywada
Anish Kolly, Med, Bangalore
Amarnath Kulkarni, Ped, Hyderabad
Fauzia Mohsin, Ped, Dhaka
Jaivender Yadav, Ped, Rohtak
Jean-Claude Carel, Paris, France
Kirti Vasudev Prabhu, Ped, Bangalore
Kumar Abhisheka, Med, Delhi
Madhura K Joshi, Ped, Mumbai
Medha Goel, Ped, Delhi
Mithun Bhartia, Med, Guwahati
Mohan T Shenoy, Ped, Kochi
Mounika Anitha Chintala, Med, Vizag
Nilesh Lomte, Med, Mumbai
Nishant Raizada, Med, Delhi
Om Jitender Lakhani, Med, New Delhi
Olaf Hiort, Lubeck, Germany
Pankaj M Patel, Med, Rajkot
Parvathy Lalitha, Ped, Kochi
Pragya Bajaj, Ped, Haryana
Pramila Dharmshaktu, Med, Delhi
Samarth Vohra, Ped, Kanpur
Shubana Thapa Karki, Ped, Kathmandu
Shobi Anandi Viswanathan, Ped,Bangalore
Smita Koppikar, Ped, Mumbai
Suhitha Chittamuri, Med, Kakinada
Suraiya Begum, Ped, Dhaka, Bangladesh
Tanveer Nawab, Ped, Bangalore
Tarannum Bano, Med, Gurgaon
Vani HN, Ped, Bangalore
Virendra Patil, Med, Aurangabad
Viveka Jyotsna, Med, Delhi
Yashpal Gogate, Med, Nashik

Growth patterns of HIV-infected children in India: Recent Trends

Dr Meghna Chawla* & Dr Girish Bhardwaj**
***Asst. Prof., Dept of Pediatrics, Smt Kashibai Navale Medical College, Pune; &**
****Dept of Pediatrics, Armed Forces Medical College, Pune, Maharashtra**

One of the most important challenges in global health is the pandemic of HIV/AIDS. The UNAIDS report in 2015 [1] estimated that 20.9 lakh people in India are living with HIV/AIDS, of which children < 15y account for 7% (1.45 lakh). However, with the effective intervention and preventive strategies of National AIDS Control Program (NACP), India has demonstrated an overall decrease of 57% in annual new HIV infections in the past decade [1]. With increased awareness and advent of Anti-Retroviral Therapy (ART), the spectrum of HIV has shifted from a rapidly fatal disease to a more chronic one, with more children reaching adolescence and adulthood. As with any other chronic disease, growth failure is a marker of disease progression, and HIV is no exception, thus the importance of regular growth monitoring cannot be overemphasized.

In perinatally acquired HIV, the birth weight is usually normal, as transmission of the virus occurs late in gestation or at delivery. Growth failure can be detected as early as 3mo of age. Failure to thrive eventually progresses to complete growth failure and wasting syndrome. Causes of growth failure are multifactorial - malnutrition, enteropathy leading to malabsorption, co-morbidities such as tuberculosis, and increased tissue catabolism. Contributing endocrine abnormalities include GH resistance, hypothyroidism and pubertal delay. It is important to note that measurement of IGF-1 and IGFBP-3 may be difficult to interpret due to malnutrition and increased proteolysis respectively. IGF-1 levels may increase with initiation of ART; however, this is due to increase in the muscle mass, and not due to increase in linear growth [2].

We review a few recent Indian studies which have looked at the dynamic interplay of HIV, nutrition, co-morbidities, immune response, ART, and their collective effect on growth in children. The recent 2013 WHO guidelines [3] recommend starting ART for all children below 5y of age. The benefits of sustained catch-up growth in Indian children following early initiation of ART has been shown by Parchure et al in 2015 [4]. They studied the growth patterns of 302 HIV infected children in response to ART. Median weight and height z-scores increased from -2.14 to -1.34 and -2.42 to -1.94 respectively post ART. They concluded that improved catch-up growth is dependent on baseline factors including age, WHO clinical stage, HIV associated immunodeficiencies, and nutrition status at start of ART; as well as response to treatment.

Devi NP et al (2011) at the Tuberculosis Research Centre, Madurai, studied 102 HIV infected children, of which 49 were started on ART after assessment at the ART centre [5]. More than 60% of the cohort was between 5-10 years. All children were provided with nutritional supplements and counselling, along with cotrimoxazole prophylaxis. The change in nutritional status at 1yr was compared. While weight for age z-scores (WAZ) improved significantly from -2.84 to -2.18 in the ART group, they worsened in the non-ART group from -1.85 to -2.12. Change in WAZ correlated highly with baseline immune status and CD4%

increase. However the height for age z-score (HAZ) did not improve (-2.02 to -2.27 in ART group; -1.76 to -1.80 in non-ART group). The authors concluded that the effect of chronic malnutrition on height may be irreversible and suggested that early ART and adequate nutritional supplementation may be beneficial.

A more descriptive study on the effect of micronutrients on growth in HIV infected children was published by Shweta KG and colleagues at the National Institution of Nutrition (ICMR) at Hyderabad this year [6]. They studied 77 HIV infected children in two orphanages, both on ART and not on ART. They observed that more than half the children were stunted and underweight, with micronutrient deficiencies, especially vitamin D, vitamin A, iron and folic acid, being more prevalent in the non-ART group, supporting the fact that ART improves the nutritional outcome of children with HIV.

Kessler et al in 2013 [7] showed that the final adult height of persons with HIV is less than that of controls (Ht SDS: -0.78±1.1 vs -0.05±0.78) despite normal timing and magnitude of pubertal growth spurt, and concluded that the greatest impact on height occurs before puberty.

Growth monitoring is of utmost importance: disordered growth could be a marker of unresponsiveness or non-compliance to ART or development of comorbidities. There is a paucity of Indian data on growth in HIV infected children. Well-designed longitudinal studies are needed, especially in adolescents, to understand growth patterns and trajectories of Indian children till they attain final adult height.

References:

1. National AIDS Control Organization. Narrative Country Progress Report of India. Ministry of Health and Family Welfare, Government of India; 2015.

2. Loomba-Albrecht LA, Bregman T, Chantry CJ. Endocrinopathies in Children Infected with Human Immunodeficiency Virus. Endocrinol Metab Clin N Am 2014; 43:807-28.

3. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva; WHO 2013.

4. Parchure RS, Kulkarni VV, Darak TS, Mhaskar R, Miladinovic B, Emmanuel PJ. Growth Patterns of HIV Infected Indian children in response to ART: A Clinic Based Cohort Study. Indian J Pediatr 2015;82:519-24.

5. Devi NP, Chandrasekaran K, Bhavani AK, Thiruvalluvan C, Swaminathan S. Persistence of stunting after highly active antiretroviral therapy in HIV-infected children in South India. Indian Pediatr 2011;48:333-34.

6. Swetha GK, Hemalatha R, Prasad UV, Murali V, Damyanti K, Bhaskar V. Health and nutritional status of HIV infected children in Hyderabad, India. Indian J Med Res 2015;141:46-54.

7. Kessler M, Kaul A, Santos-Malava C. Growth patterns in pubertal HIV-infected adolescents and their correlation with cytokines, IGF-1, IGFBP-1 and IGFBP-3. J Pediatr Endocrinol Metab 2013;26:639-44.

Endocrinopathies in Acute Leukemia

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Introduction

Acute leukemia is the most common cancer diagnosed in children, constituting nearly 30% of all childhood cancers. Acute lymphoid leukemia (ALL) is the most common type of childhood leukemia accounting for nearly 78% of cases according to Cancer Research UK. In India the estimated incidence of ALL ranges between 40-85% of all childhood leukemias. The treatment of childhood ALL has improved over the last 4 decades, with a 5y survival approaching 90%. This improvement in outcomes is attributed to use of newer multi-agent chemotherapy regimens and radiotherapy. Unfortunately, along with increasing survival rates, there is an increased risk of morbidity and early mortality in survivors. It is said that around 70% of pediatric cancer survivors are likely to develop a medical complication within 30y following diagnosis, these complications being attributed and related to treatment of their primary cancer. The 4 types of standard treatment options for childhood leukemia are:

- Chemotherapy
- Radiotherapy
- Chemotherapy with stem cell transplant
- Targeted therapy

Endocrine complications can be broadly categorized as those occurring during the course of therapy, and those noted in survivors, as late effects following completion of therapy. Children exposed to radiotherapy and high doses of alkylating agents are particularly at risk of developing endocrinopathies. Treatment can cause direct damage to the hypothalamic-pituitary axis, thyroid gland or gonads, or result in altered body composition, abnormal glucose homeostasis and reduced bone mass. The nature and type of endocrine dysfunction depend on the combination of medications received, the age at which treatment was started, doses and duration of therapy and the patient's gender.

Endocrine dysfunction occurring DURING acute leukemia treatment

Children undergoing cranial radiotherapy, chemotherapy and corticosteroid treatment are at increased risk of developing:

Disordered growth: Growth velocity is reduced during all phases of chemotherapy, with glucocorticoids (GCs) especially contributing to poor growth. If the child has received only chemotherapy, catch up growth is often seen after completion of therapy.

Obesity: Excessive weight gain is often noted during ALL therapy, most often associated with GC use. Cranial radiotherapy is a major risk factor, though the exact mechanism is not clear. It may be related to damage to CNS control of appetite and eating patterns.

Adrenocortical Insufficiency: This can occur with GC therapy, the incidence varying with dose and duration of therapy. A high index of clinical suspicion is needed for diagnosis, as the clinical features are not always clear and can appear similar to side effects secondary to

chemotherapy. Treatment may not always be required, except during periods of metabolic stress. Replacement therapy is with parenteral/oral hydrocortisone.

Diabetes mellitus (DM): Glucose intolerance with hyperglycemia is seen in children receiving GCs (due to increased insulin resistance) or L-asparaginase (which reduces serum insulin levels). Combination therapy with both agents increases the risk of DM further. Once diagnosis is confirmed, a trial of diet modification and increased physical activity is initiated, followed by insulin therapy if the response is not satisfactory. The aim of treatment is just to reduce very high blood sugars; strict glycemic response is not needed as there is a high risk of hypoglycemia. Recent evidence that metformin can reduce proliferation and cause apoptosis of cancer cell lines through AMPK-dependent and independent mechanisms, while insulin and insulin analogs are associated with high proliferation rate and chemoresistance, may change approach to managing hyperglycemia in the future.

Syndrome of inappropriate anti-diuretic hormone (SIADH): This can occur in children receiving cyclophosphomide and vincristine therapy as a result of continued ADH release. Vincristine toxicity is increased by concomitant use of azole antifungals. Diagnosis is confirmed by noting serum hyponatremia and reduced serum osmolality along with inappropriately high urine osmolality and urinary sodium excretion. Fluid restriction is the treatment of choice.

Impaired bone mineralization: There is a significant risk of developing bone demineralization and osteoporosis during or after leukemia therapy, especially with GC use. Weight bearing activity is of benefit and should be advised. Calcium and vitamin D supplements are of limited value in GC-induced bone demineralization and can result in hypercalcemia and hypercalciuria.

LATE-ONSET Endocrine dysfunction in childhood leukemia survivors

The late onset endocrine complications are mainly due to the effects of cranial radiation therapy and chemotherapy, the severity depending on multiple factors including dose and duration of therapy, use of combination therapy, and host factors such as age and gender.

Late effects of chemotherapy: Endocrine dysfunction is most commonly associated with the use of alkylating agents (cyclophosphamide) and antimetabolites (methotrexate) and includes:

Gonadal effects: Agents like busulfan, procarbazine, mechlorethamine and cyclo-phosphamide can have a direct destructive effect on the gonads. Cyclophosphamide is commonly used in pediatric protocols. In females, this can result in delayed or arrested puberty, premature menopause and infertility. In males, delayed or arrested puberty, infertility, and testosterone deficiency or insufficiency can occur. Periodic evaluation of Tanner stage to monitor the start and progress of puberty is advisable starting at age 10y, with assessment of serum levels of luteinizing hormone and follicle stimulating hormone if puberty is delayed.

Bone metabolism: Anti-metabolites such as methotrexate and GCs can reduce bone mineral density and cause osteoporosis. The risk increases with concomitant use of steroids, cyclosporine, tacrolimus, and radiation.

Short stature: Although the cause is not clearly understood, childhood leukemia survivors treated with chemotherapy alone are at risk for short stature. The severity is more when both chemotherapy and radiation are used.

Late effects of radiation therapy: The incidence of endocrine complications secondary to radiation therapy varies, depending on the age at start of treatment, gender, radiation dose and the area of exposure. A prevalence of 56% was found with cranial radiation therapy of doses of 18Gy and above. Neuroendocrine abnormalities secondary to radiation to the hypothalamic-pituitary axis include deficiencies of multiple pituitary hormones, except central diabetes insipidus, which has not been reported as secondary to this therapy.

Table 1: Potential endocrine abnormalities that can occur with cranial radiation therapy:

Endocrine problem	**Radiotherapy doses at which effect can occur**
Growth hormone (GH) deficiency	Effect of dose >30Gy usually seen within 5y following treatment Effect of dose 18 – 24Gy: may not be seen until 10y after exposure
Precocious puberty	Dose >18Gy, increased risk for girls aged <5y
Hypogonadotropic hypogonadism	Dose >30Gy and increasing risk with increase in dose
ACTH deficiency	Dose > 30Gy
TSH deficiency	Dose > 30Gy
Obesity	Effect can occur even with minimum doses
Hyperprolactinemia	Dose > 40Gy

Recommendations for follow-up and periodic screening:

- All childhood leukemia survivors should have a yearly comprehensive health check.
- At the health screening, height, weight, BMI, and pubertal status should be documented, along with the child's overall wellbeing.
- Children who have received cranial radiation should be screened at 6 month intervals as their risk for developing pituitary hormone dysfunction is higher.
- If endocrine dysfunction is suspected, timely referral to a pediatric endocrinologist is necessary. Further evaluation would then be based on the suspected hormone dysfunction, and will include estimation of hormone levels along with radiological investigations as needed.

Summary:

Childhood leukemia is the most common childhood cancer with present survival rates nearing 80% with current advanced and intense treatment protocols. These regimens include combinations of multiple chemotherapy agents and cranial radiation, as a result of which endocrine dysfunction can occur during or even years after completion of therapy. Endocrine abnormalities that develop during leukemia therapy are usually identified and managed. However, late-onset endocrine dysfunction may go undiagnosed and untreated unless regular evaluation and screening is done in long-term follow-up clinics. Early detection and identification will allow timely intervention and thus reduce morbidity and mortality, so regular screening at least annually is recommended, starting 2y after completion of cancer therapy.

References

1. Arora R S, Eden T, Kapoor G. Epidemiology of childhood cancer in India. Indian J Cancer 2009;46:264-273.
2. Howard SC, Pui CH. Endocrine complications in pediatric patients with acute lymphoblastic leukemia. Blood Reviews 2002;16:225-243.
3. Hudson MM, Ness KK, Gurney JG, et al. Clinical ascertainment of health outcomes among adults treated for childhood cancer. JAMA 2013;309:2371-81.
4. Late Effects of Treatment for Childhood Cancer. National Cancer Institute.2015
5. Oeffinger KC, Mertens AC, sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006;355:1572-82.
6. Nandagopal R, Laverdière C, Mulrooney D, Hudson MM, Meacham L. Endocrine Late Effects of Childhood Cancer Therapy: A Report from the Children's Oncology Group. Horm Res 2008; 69:65-74.
7. Robinson LL, Bhatia S. Late effects among survivors of leukemia and lymphoma during childhood and adolescence. Br J Haematol 2003;122:345-359.
8. Wassim C, Charles A Sklar. Endocrine complications in long term survivors of childhood cancers. Endocrine – Related Cancer 2010;17:R141-R159.
9. Pan J, Chen C, Jin Y, Fuentes-Mattei E, Velazquez-Tores G, Benito JM, et al. Differential impact of structurally different anti-diabetic drugs on proliferation and chemosensitivity of acute lymphoblastic leukemia cells. Cell Cycle. 2012;11:2314–26.

Endocrinopathies in Children with Juvenile Idiopathic Arthritis

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Vydehi Institute of Medical Sciences and Research Center, Bengaluru

Introduction

Juvenile idiopathic arthritis (JIA) is the most common joint disorder in children, with an incidence of 20–30/100,000 children younger than 16 y, a prevalence of about 1 in 1000 and slight female preponderance [1]. JIA is associated with various endocrine abnormalities such as growth impairment, delayed puberty, hypothyroidism, type 1 diabetes mellitus (T1DM), and low bone mass.

Impairment of Growth and Puberty

Growth impairment is a common long-term complication of JIA, seen in 10-40% of affected children. Growth retardation is significantly more severe in children with the systemic and polyarticular subtypes of the disease (about 10–20% have compromised final height) [1], with longer duration of uncontrolled disease activity, and with use of glucocorticoids (GCs). In the systemic subtype, height loss is usually seen within 2y of diagnosis. Growth impairment results from loss of height in pre-pubertal years, delayed onset of puberty, and reduced duration and magnitude of the pubertal growth spurt. Compared to children with the oligoarticular type, peak height velocity and peak weight velocity occur a year later in those with polyarticular and systemic types [2].

Inflammatory cytokines, GCs and undernutrition contribute to the diminished growth by interfering with the growth hormone-insulin like growth factor-1 (GH-IGF-1) axis. JIA is characterised by resistance to GH, as a consequence of inflammation- and malnutrition-mediated decrease in the number of GH receptors on hepatocytes, or interference at the level of intracellular signalling pathways following GH binding to its receptor. Increase in plasma IGF-1 clearance due to raised proteolysis of IGFBP-3 during inflammation also contributes to GH inefficiency. Besides the systemic effects of cytokines on GH–IGF-1 axis, they also have a negative effect on chondrogenesis in the growth plate. GC therapy per se can influence GH secretion and IGF-I bioactivity through decreased expression of IGF-I receptor or binding proteins in target tissues including the growth plate [1].

While evaluating children with JIA and growth impairment, care should be taken to exclude the involved joints in bone age estimation, since the bone age may falsely advance in affected joints. A few patients with JIA may also have biochemical evidence of GH insufficiency. In a small study, nine of 46 short (height SDS < -2) JIA children had peak GH < 10 ng/dl in two stimulation tests [3].

The most important factors in the prevention and management of growth impairment are appropriate control of disease activity, and minimal use of GCs. Disease modifying anti-rheumatic drugs (DMARDs) usually do not negatively affect growth. Rather, good disease control (usually by use of biological agents) increases serum IGF-1 levels, height velocity (often in the range of catch-up growth) and height SDS. In JIA children treated with biological agents, improvement in disease activity score, lower baseline height SDS, and absence of GCs are the common positive predictors of improvement in height SDS [4].

Despite the best efforts to control disease activity, a few JIA children still continue to have growth impairment and may require additional therapy for optimisation of growth. In a randomised clinical trial (RCT), GH therapy (0.33 mg/kg/week, initiated at age 10.38±2.80y) in JIA children improved total pubertal growth (21.1±1.3 cm vs. 13.8±1.5 cm) and final height SDS (−1.67±1.20 vs. −3.20±1.84) [3]. In another RCT, GH therapy (0.46 mg/kg/wk, initiated at age 5.6±2.5y for 3y in JIA children on moderate doses (0.5±0.3 mg/kg/day) of GCs normalised height velocity and increased height SDS (0.37±1.5 vs. 0.96±1.2) [5]. GH therapy is effective in increasing pubertal height gain and final height in short JIA children, with or without GC therapy.

Thyroid autoimmunity and hypothyroidism

There are variable reports on autoimmune thyroid disease in JIA children. In a study by Stagi et al, among 120 patients with JIA (92 oligoarticular, 49 polyarticular and 10 systemic), 19 patients (18 of them girls) had evidence of autoimmune thyroiditis. A TSH of > 4.0 µIU/ml was found in 14 patients; however only two of them (age 13.2y and 14.9y) had associated elevation of thyroid autoantibodies. All patients had TSH < 7.0 µIU/ml [6]. Similar results were seen in another study from Israel (n=66), in which 11.3% and 7.9% of patients had increased anti-TG and anti-TPO antibodies respectively, compared to 2.2% and 1.1% respectively in healthy children [7]. In contrast, a Turkish study found autoimmune thyroid disease in only 5% of JIA patients, which was not different from healthy children [8].

Type 1 diabetes mellitus

In the USA, the prevalence of T1DM was reported to be 6-fold in 443 children with JIA. However, in Finland where the baseline prevalence of T1DM is very high, only a 2-fold increase was found in JIA patients. When JIA and T1DM coexist, it is best to avoid GC therapy, which can worsen glycaemic control. If GCs are initiated, glycemic control should be ensured, with close glucose monitoring and titration of insulin doses.

Low bone mass

Bone mineral density (BMD) in children with JIA is significantly lower than in controls. In a study of 103 JIA patients, 41% had low total-body bone mineral content (BMC) and 34% had low total-body BMD [9]. Another prospective study including 100 JIA patients and 100 healthy controls reported low or very low total-body BMC in 24% patients compared to 12% healthy children. The study also reported lesser gain in total-body BMC, distal radius BMC, and total-body lean mass in JIA patients than healthy controls. This was associated with reduction in both bone formation and bone resorption [10]. BMD is significantly more affected in systemic and polyarticular types than the oligoarticular type, in severe disease, with use of GCs and if there is delayed puberty. However, there is limited data on the occurrence fragility fractures in children with JIA.

Treatment with calcium and/or vitamin D modestly increases BMD Z-scores in JIA children. Though the benefits of bisphosphonates are not proven in RCTs, bisphosphonate treatment has been shown to increase BMD (4.5-19.1%) in JIA children with low bone mass [11].

Summary and Recommendations

1. Short stature is common in children with JIA, especially in those with polyarticular and systemic subtypes. Uncontrolled disease activity and use of GCs are the strongest predictors of growth impairment. Height, weight and height velocity should be closely monitored in all JIA patients to identify growth impairment at the earliest. The use of DMARDs should be optimised to have the best control of disease activity and the use of GCs should be minimal. Early initiation of GH therapy may be beneficial in JIA children who are persistently short despite the best use of anti-rheumatic agents.

2. Thyroid autoimmunity is more common in JIA children. TSH should be tested at diagnosis, and every 1-3y, or when growth impairment is out of proportion to disease activity/ GC use.

3. Low bone mass is a common complication. All JIA children should be encouraged to increase their dietary calcium intake. Those with low bone mass or on treatment with GCs should be supplemented with oral calcium and vitamin D. In those with very low bone mass, treatment with bisphosphonates may be considered.

References

1. Bechtold S, Simon D. Growth abnormalities in children and adolescents with juvenile idiopathic arthritis. Rheumatol Int. 2014;34:1483-8.

2. Aggarwal B, Bhalla AK, Singh S. Longitudinal growth attainments of Indian boys with juvenile rheumatoid arthritis. Rheumatol Int. 2011;31:635-40.
3. Bechtold S, Beyerlein A, Ripperger P, et al. Total pubertal growth in patients with juvenile idiopathic arthritis treated with growth hormone: analysis of a single center. Growth Horm IGF Res. 2012;22:180-5.
4. De Benedetti F, Brunner H, Ruperto N, et al. Catch-up growth during tocilizumab therapy for systemic juvenile idiopathic arthritis: results from a phase III trial. Arthritis Rheum 2015; 67:840-8.
5. Simon D, Prieur AM, Quartier P, et al. Early recombinant human growth hormone treatment in glucocorticoid-treated children with juvenile idiopathic arthritis: a 3 year randomized study. J Clin Endocrinol Metab. 2007;92:2567-73
6. Stagi S, Giani T, Simonini G, et al. Thyroid function, autoimmune thyroiditis and coeliac disease in juvenile idiopathic arthritis. Rheumatology (Oxford). 2005; 44: 517-20.
7. Harel L, Prais D, Uziel Y et al. Increased prevalence of antithyroid antibodies and subclinical hypothyroidism in children with juvenile idiopathic arthritis. J Rheumatol. 2006;33:164-6.
8. Unsal E, Oren O, Salar K, et al. The frequency of autoimmune thyroid disorders in juvenile idiopathic arthritis. Turk J Pediatr. 2008;50:462-5.
9. Lien G, Flatø B, Haugen M, et al. Frequency of osteopenia in adolescents with early-onset juvenile idiopathic arthritis: a long-term outcome study of one hundred five patients. Arthritis Rheum. 2003;48:2214-23.
10. Lien G, Selvaag AM, Flatø B, et al. A two-year prospective controlled study of bone mass and bone turnover in children with early juvenile idiopathic arthritis. Arthritis Rheum 2005;52: 833-40.
11. Thornton J, Ashcroft D, O'Neill T, et al. A systematic review of the effectiveness of strategies for reducing fracture risk in children with juvenile idiopathic arthritis with additional data on long-term risk of fracture and cost of disease management. Health Technol Assess. 2008; 12(3):iii-ix, xi-xiv, 1-208.

Endocrinopathies in young people with thalassemia

Dr Veena V Nair, Consultant Paediatric and Adolescent Endocrinologist,
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Introduction:

Thalassemia is a group of inherited hematological disorders where defective synthesis of one or more of the globin chains results in production of abnormal haemoglobin molecules. Beta thalassemia is the most commonly seen genetic type. Bone marrow erythropoiesis becomes ineffective, leading to varying degrees of anemia and related manifestations, so frequent blood transfusions are required to maintain a reasonable haemoglobin level. Frequent transfusions lead to iron overload which in turn requires use of iron chelators. Unfortunately the endocrine glands are susceptible to damage due to the oxidative stress from excessive iron load, as well as chronic anemia and toxicity of chelating agents, resulting in a multitude of endocrine problems in children with thalassemia (Table 1). Newer transfusion protocols and introduction of new oral chelators have improved survival in thalassemia patients, at the expense of long term endocrine consequences. Studies from developing countries have shown early onset endocrinopathy in a significant proportion of young thalassemics [1].

Table 1: Endocrine problems in thalassemia patients	
Growth retardation	Hypogonadism
Diabetes mellitus	Primary Hypothyroidism
Hypoparathyroidism	Adrenocortical failure
Osteoporosis	

Mechanisms of endocrinopathy in thalassemia

One unit of blood contains 250 mg iron, 100 times the amount of iron that enters the circulation through gut. Moreover, anemia due to ineffective marrow erythropoiesis results in increased iron absorption from gut. Both these factors contribute to iron overload in various tissues, especially those that harbour high levels of transferrin-receptors such as liver, heart and endocrine glands. The non-transferrin bound iron-NTBI (free circulating form) is capable of generating hydroxyl radicals (reactive oxygen species) leading to lipid peroxidation in the cells. It also inhibits antioxidant defences such as superoxide dismutase. This causes oxidative damage to various cellular components. Chronic anemia and resulting tissue hypoxia due to the disease per se augment the cytotoxic effects of iron [2,3]. Regular chelation therapy is unavoidable in children who are adequately transfused. Parenteral (subcutaneous/intravenous) desferrioxamine (DFO) and oral deferiprone and deferasirox, alone or in combination are used. These agents, especially DFO, are cytotoxic even at therapeutic doses.

The International Network on Endocrine Complications in Thalassemia (I-CET) has proposed guidelines to monitor transfusion dependent patients with thalassemia major [4].

Clinical evaluation: Record height (standing and sitting), weight, head circumference (age <2y) and mid parental height; plot in appropriate growth charts; calculate growth velocity, height SD scores, BMI, and US: LS ratio. Check pubertal development (age >10y) every 6mo.

Table 2: Laboratory work up starting at age 10y

Complete blood count, Urinalysis, Liver function tests, Renal function tests, Serum Ferritin	Baseline screening
Serum total calcium, ionized calcium, inorganic phosphate, magnesium, alkaline phosphatase	Repeat annually
T4, TSH, 8:00 am Serum Cortisol	Repeat annually
Fasting and post prandial plasma glucose Fasting serum insulin: calculate HOMA IR (insulin IU/ml * glucose mg/dl/22.5)	Repeat annually
Bone age: X-ray hand AP view X ray spine and tibia	Repeat annually In case of disproportionate short stature
Provocative GH testing IGF-1 and IGFBP-3	In selected cases for evaluation of significant short stature
LH, FSH (basal and stimulated)	In pubertal age group, if there is delay/arrest of pubertal development

Management of specific endocrinopathies in thalassemia

Growth Failure

Short stature is the most common endocrine problem encountered in thalassemic children. Poor growth in thalassemia is multifactorial. In children who are under-transfused, chronic anemia and resulting hypoxia retards bone growth. In addition there is poor weight gain and reduced muscle mass. In well transfused children, iron overload leads to selective central hypogonadism, inhibiting the pubertal growth spurt. Hepatic iron deposition interferes with synthesis of insulin like growth factor-1 (IGF-1). Other possible mechanisms include abnormal growth hormone (GH) secretion, impaired GH response to GH releasing hormone (GHRH), abnormal GH receptors and reduced IGFBP-3 [5]. DFO, one of the widely used chelating agents, in therapeutic doses inhibits fibroblast proliferation and collagen formation, leading to metaphyseal dysplasia. DFO also chelates other metals like zinc, again adversely affecting cartilage growth. The growth failure usually manifests after 9y of age and predominantly affects the sitting height because of poor vertebral body development (platyspondyly) [6]. Children with height 2 SD below the mean height for age, sex and mid-parental height, or growth velocity consistently below 25th centile, should undergo provocative GH testing. The levels of IGF-1 and IGFBP-3 should be viewed cautiously in the background of liver dysfunction and malnutrition.

Correction of anemia, judicious chelation therapy, nutritional supplementation (including vitamin D and zinc), and pubertal induction at the appropriate age are important for ensuring maximum growth potential. Children who are proven to be GH deficient benefit from GH therapy, but in GH sufficient short children the benefit is not clear cut [7]. Moreover GH may increase the risk for insulin insensitivity and development of diabetes. For details on GH therapy, refer to CAPE NEWS, June 2014 issue.

Delayed puberty

The anterior pituitary, in particular the gonadotrophs, is highly sensitive and vulnerable to irreversible iron induced oxidative damage. Gonadal damage from iron deposition is rare. Most patients with thalassemia manifest delayed or arrested pubertal development. Even in women who do have menarche, poor chelation therapy can cause secondary amenorrhoea. Fertility prognosis is poor in both men and women in spite of early and aggressive chelation therapy. Fortunately ovaries respond to hormonal stimulation. The risk of ovarian damage from iron deposition is maximal in the peak reproductive age (25-30y) due to high vascular activity. Sex hormone replacement therapy, starting with low doses and building up slowly, should be started at the appropriate age, so that adolescent gain in height, muscle mass, bone density and body image are not adversely affected. Refer to CAPE NEWS February 2015 issue for approach to and management of delayed puberty.

Hypoparathyroidism

Parathyroid dysfunction due to chronic iron overload leads to symptomatic hypocalcemia, manifesting as neuromuscular irritability (tetany), paresthesias and abdominal cramps.

Hyperphosphatemia with low PTH levels clinches the diagnosis. Treatment includes vitamin D analogs (calcitriol 0.25-2µg/day), oral calcium (1g/d), and restriction of phosphorus in diet.

Diabetes mellitus

Chronic pancreatic iron overload in inadequately chelated patients leads to progressive beta cell damage and reduced insulin secretion, resulting in insulin dependent diabetes mellitus (DM). However, insulin resistance also has been demonstrated in thalassemic patients, though the mechanism is not clear [8]. DM usually manifests beyond 10y; the reported prevalence is 6-14%. In thalassemics, diabetes rarely present with ketoacidosis. Diagnosis is based on the standard biochemical criteria. Islet cell autoantibody screening is negative. These children require variable doses of insulin (0.15-1.72 U/kg) for glycemic control. Oral antidiabetic drugs including metformin are not well studied in these patients.

Being a hemoglobinopathy, HbA1C is not reliable for monitoring glycemic control; fructose-amine may be used instead. Though the long term complication rates are comparatively low, regular screening for end organ damage should be done as in any other diabetic child.

Hypothyroidism

Primary hypothyroidism, though not common, can occur in well transfused patients. It may be subclinical to overt in presentation. The onset is insidious and hence needs regular screening for early detection. Annual TSH and T4 are recommended from 9y of age, or earlier if symptomatic. Pituitary TSH deficiency leading to secondary hypothyroidism is very rare. Subclinical hypothyroidism (TSH <7µIU/ml) needs only regular follow up. L-thyroxine should be initiated in those with mild and overt hypothyroidism.

Adrenal insufficiency

Adrenal failure can be of primary (adrenal), secondary (pituitary) or hypothalamic in origin, but is rarely encountered, though the prevalence of biochemical hypocortisolemia has recently been reported to be quite high [9]. Early symptoms like tiredness, weight loss, muscle weakness, arthralgia, etc. may be missed. Adrenarche may be delayed or attenuated due to low levels of adrenal androgens. Diagnosis is established by low basal (8 AM) cortisol and low ACTH stimulated cortisol (< 18µg/dl, 60 minutes after 0.25µg ACTH IM/IV). In the absence of clinical adrenal insufficiency, only stress cover of steroids is required in subclinical adrenal impairment.

Bone disease

Thalassemics are prone to develop osteopenia and osteoporosis, mainly due to delayed sexual maturation and attenuated peak bone mass acquisition. Other contributing factors include bone marrow expansion due to ineffective erythropoiesis, vitamin D deficiency, chronic liver disease, and untreated hypothyroidism. DXA studies show low BMD z-scores of the spine and femur (T scores are not reported in childhood and adolescence); since there may be short stature, the BMD z-scores should be corrected for height. Improved nutrition including increased dietary calcium and supplementation with vitamin D and zinc, sex hormone replacement at the appropriate age where necessary, and regular physical activity

are important in preventing poor bone density. In young adults, especially those with fractures, bisphosphonate therapy is beneficial to prevent bone loss and improve BMD, with continuous improvement in BMD demonstrated even after discontinuation of zoledronic acid [10]. Bisphosphonates have been shown to reduce the bone and back pain. Adverse events are reported rarely [11], but care must be taken as prolonged therapy can reduce bone turnover and thus bone formation.

Conclusion

Endocrine dysfunction is an unavoidable consequence of thalassemia treatment, but can be mitigated and quality of life improved with early identification and appropriate treatment. Hematologists must coordinate care with endocrinologists early on for optimal outcomes in these patients.

References

1. Gulati R, Bhatia V, Agarwal SS. Early onset endocrine abnormalities in beta thalassemia major in a developing country. J Pediatr Endocrinol Metab. 2000;13:651-6.

2. Galaris D, Pantopoulos K. Oxidative stress and iron homeostasis: mechanistic and health aspects. Crit Rev Clin Lab Sci. 2008;45:1-23..

3. Zhao M, Matter K, Laissue JA, Zimmermann A. Copper/zinc and manganese superoxide dismutase immunoreactivity in hepatic iron overload diseases. Histol Histopathol. 1995 Oct;10(4):925-35.

4. De Sanctis V, Soliman AT, Elsedfy H, SKordis N, Kattamis C, Angastiniotis M, et al. Growth and endocrine disorders in thalassemia: The international network on endocrine complications in thalassemia (I-CET) position statement and guidelines. Indian J Endocr Metab 2013;17:8-18.

5. Low LC. Growth of children with beta-thalassemia major. Indian J Pediatr. 2005;72:159-64.

6. Orzincolo C, Castaldi G, Scutellari PN. Platyspondyly in treated beta-thalassemia. Eur J Radiol. 1994;18:129-33.

7. Geffner ME, Karlsson H. Use of recombinant human growth hormone in children with thalassemia. Horm Res. 2009;71 Suppl 1:46-50.

8. Suvarna J, Ingle H, Deshmukh CT. Insulin resistance and beta cell function in chronically transfused patients of thalassemia major. Indian Pediatr. 2006;43:393-400.

9. Huang KE, Mittelman SD, Coates TD, Geffner ME, Wood JC.A significant proportion of thalassemia major patients have adrenal insufficiency detectable on provocative testing. J Pediatr Hematol Oncol. 2015;37:54-9.

10. Voskaridou E, Christoulas D, Konstantinidou M, Tsiftsakis E, Alexakos P, Terpos E. Continuous improvement of bone mineral density two years post zoledronic acid discontinuation in patients with thalassemia-induced osteoporosis: long-term follow-up of a randomized, placebo-controlled trial. Haematologica. 2008;93:1588-90.

11. Giusti A. Bisphosphonates in the management of thalassemia-associated osteoporosis: a systematic review of randomised controlled trials**.** J Bone Miner Metab. 2014;32:606-15.

Multiple endocrine dysfunctions in thalassemia major: case report

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A 14y 2mo old male, born of a non-consanguineous marriage, diagnosed as thalassemia major at age 6mo, on regular blood transfusions, was referred to our endocrine clinic at age 14y with polyuria, polydipsia, and polyphagia for 2 weeks. His weight was 23.2 kg (<3rd centile) and height was 124 cm (<3rd centile) with target height range of 170±6.5 cm (50th centile). On examination, he had haemolytic facies, generalised hyperpigmentation and hepatosplenomegaly. He was prepubertal with bilateral testicular volume of 2-3 ml. Bone age was 11y 6mo. Investigations revealed random blood glucose 556 mg/dl, simultaneous C peptide – 0.11 ng/ml (0.9-7.1), mild ketones in urine with blood bicarbonate of 14 mmol/L. Serum calcium was 7.6 mg/dl, ionic calcium 0.92 mmol/L (1.0-1.3), phosphorus 4.3 mg/dl, ALP 94 IU/ml, 25-OH vitaminD 10.5 ng/ml, serum ferritin 7408 ng/ml. Liver functions tests showed mildly raised transaminases, renal function tests were normal. HIV, HBSAg and HCV screen was negative by ELISA. FT3 1.4 pg/ml, FT4 0.6 ng/dl, TSH-28.9 µIU/ml were suggestive of primary hypothyroidism. There was mild LV dilatation on 2D ECHO.

Insulin infusion was started at 0.1 U/kg/hr and after stabilisation he was shifted to subcutaneous insulin (Split-mix regimen) with home monitoring of blood glucose. He was also started on 75 µg levothyroxine (LT4) daily, calcium and vitamin D replacement, and oral captopril for dilated cardiomyopathy. After initial intensive chelation therapy with deferoxamine injections, he was shifted to oral deferiprone. On follow up, thyroid function normalised on LT4 replacement of 125 µg/day, he needed insulin 1.5 U/ kg/day, growth velocity was 4.3 cm/y. At age 15y, he complained of tingling, lab tests showed low serum calcium (7.5 mg/dl), with inappropriately low iPTH levels (9.8 pg/ml}, so he was started on calcitriol 0.25 µg/day with 1.5 gm/day calcium, doses being titrated as per serum calcium and urine Ca/creatinine reports. Since in spite of adequate treatment, there was no progression in puberty, gonadal steroids were tested –serum testosterone <8 ng/dl, LH <0.4 mIU/ml, FSH- <0.5 mIU/ml, suggestive of hypogonadotrophic hypogonadism. He was started on testosterone depot injections 50 mg monthly, and the dose increased gradually to 200 mg monthly which he is on currently. GH testing was not done since the family could not afford GH therapy. DXA scan showed lumbar spine BMD z-score of -1.6. MRI revealed moderate myocardial and severe liver iron loading. He also acquired HCV infection at 18 years of age due to multiple transfusions.

Thus this boy with thalassemia major had several endocrine issues - **short stature, hypothyroidism, delayed puberty, insulin dependent diabetes, hypoparathyroidism** and **vitamin D deficiency,** apart from other problems. Hypocalcemia in this patient was multifactorial: impaired vitamin D metabolism due to chronic liver disease, malnutrition, and later hypoparathyroidism. Currently he is 21y old, 43.5 Kg, 143.2 cm (<3rd centile), Tanner stage P3 A2, on testosterone depot 200 mg IM monthly, subcutaneous insulin (1.3 U/kg/day), euthyroid on 125 µg/day thyroxine, normocalcemic on calcitriol 0.75 µg and calcium carbonate 1500/day, normal lipid profile, the latest serum ferritin being 3847 ng/ml on deferiprone (500 mg 4 tab/day).

The incidence of multiple endocrinopathies in thalassemic children increases with age and is directly related to serum ferritin levels (except for diabetes). Early detection and effective

iron chelation therapy can improve outcome and quality of life in these persons. To this end, Thalassemia International Federation has recommended endocrine evaluation of all thalassemic children beginning at 10y of age. Of course, the main aim is primary prevention, i.e. genetic counselling to prevent the occurrence of thalassemia major.

Congenital nephropathic cystinosis with multiple endocrinopathies

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Case summary

A 6y old girl was hospitalised with complaints of not gaining weight, polyuria, polydipsia, deformity of lower limbs and constipation. She was apparently normal until her first birthday (except for delay in motor milestones), after which the above complaints were noticed. On examination, height (74.5 cm) and weight (8.5 kg) were below the 3rd percentile (figure 1A); coarse facies, dry skin (fig 1A) and bony changes of rickets (figure 1C-1E), were noted. Investigations showed hypocalcemia, hypophosphaemia, increased alkaline phosphatase, increased intact parathyroid hormone (PTH), decreased 25(OH)Vitamin D, decreased 1,25$(OH)_2$ vitamin D, normal anion gap metabolic acidosis, hypokalemia and raised creatinine (table 1). She passed dilute urine, which showed proteinuria, glycosuria, generalised aminoaciduria, phosphaturia, bicarbonaturia, with a positive urine anion gap and normal calcium-to-creatinine ratio (table 2). Polyuria was confirmed by an output of 8ml/kg/hr. X-ray wrist showed bony changes of rickets with delayed bone age (figure 2A) and abdominal sonogram revealed grade III medical renal disease.

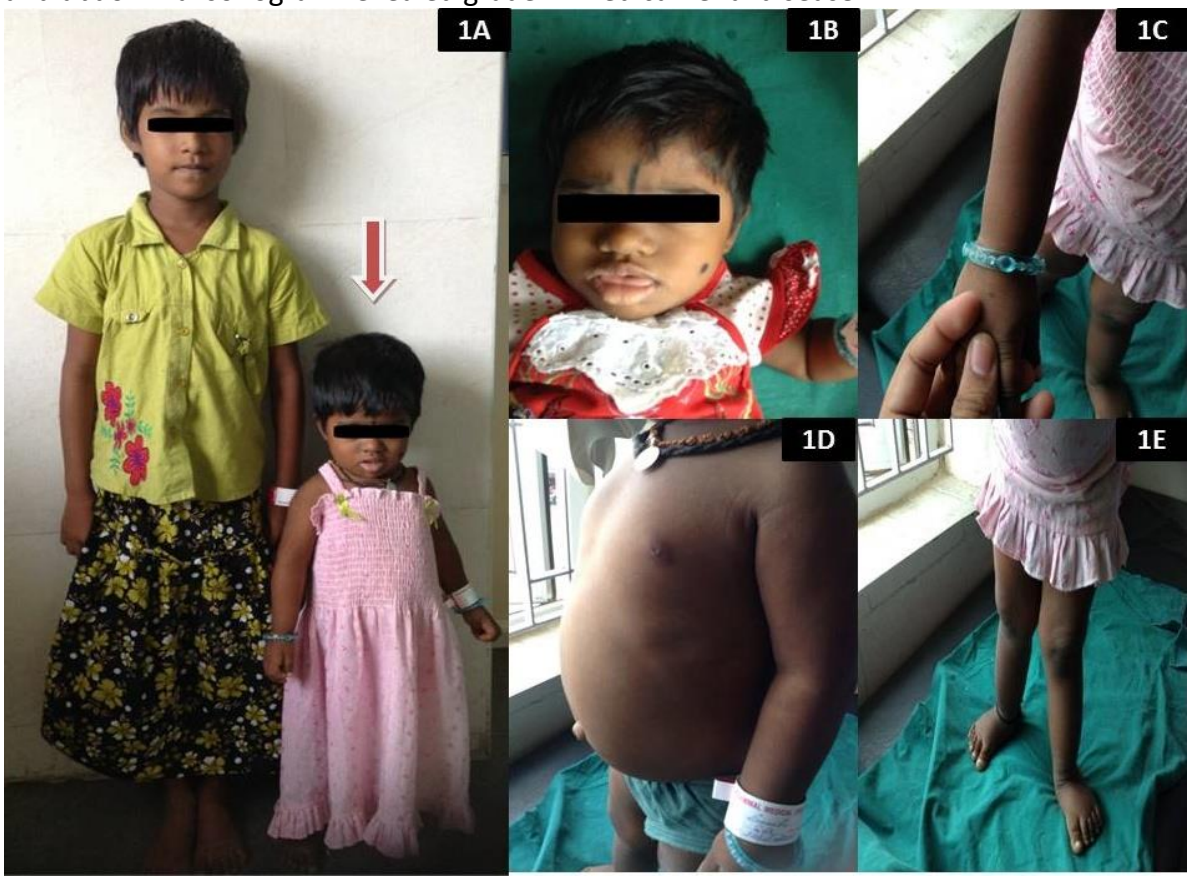

Figure 1, 1A: Patient with a normal 6y old girl; 1B: Hypothyroid facies; 1C: Widened wrist; 1D: Harrison sulcus and rachitic rosary; 1E: Genu valgum (left > right)

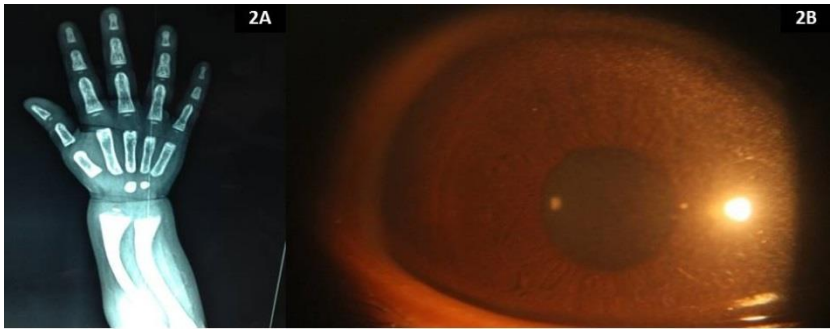

Figure 2,
2A: Rachitic changes with delayed bone age (BA=1 year); 2B: Cystine crystal deposits in cornea

With the above findings, the child was suspected to be a case of renal rickets; probably, Fanconi's proximal tubulopathy with renal failure. Since primary renal tubulopathies hardly ever present with renal failure during the first decade of life, further evaluation was done to look for a systemic cause for Fanconi syndrome. Ophthalmologic examination revealed the presence of cystine crystal keratopathy (figure 2B), suggesting the diagnosis of cystinosis. With the background diagnosis of cystinosis, extreme short stature, coarse facies (fig 1B), large tongue, history of constipation, and dry skin, prompted evaluation of thyroid status which revealed severe primary hypothyroidism. She was treated with oral L-thyroxine (6 µg/ kg/day, sodium bicarbonate (4mEq/kg/day), potassium chloride (2 mEq/kg/day), alfacalcidol (0.05 µg/kg/day) and calcium carbonate. She was registered with the Cystinosis Foundation of India for procurement of cysteamine for definitive therapy.

The patient has a 4y old younger sister who had history of polyuria and polydipsia, severe growth failure (height 71 cm; weight 5 kg). Her evaluation revealed similar renal findings with stage 3 chronic kidney disease; cystine crystal deposits in the cornea; and subclinical hypothyroidism (Table 1). She was started on L-thyroxine supplementation and treated with other supplements like her sister.

Discussion

Cystinosis is a form of lysosomal storage disorder, caused by defective lysosomal membrane transport protein, cystinosin. Its prevalence is approximately 1:100,000 to 1:200,000. There are three types of cystinosis. Nephropathic or classic infantile cystinosis (NC), the most severe form, inevitably leads to renal failure in the first decade of life. The intermediate form has all the manifestations of the nephropathic form, but its onset is generally during adolescence. Non-nephropathic or ocular cystinosis is characterized only by corneal crystals and photophobia. About 95% of patients have renal involvement [1]. All three forms are allelic recessive disorders caused by mutations in the *CTNS* gene.

The pathogenesis is due to intracellular accumulation of cystine in all the organs. Since cystine is poorly soluble, it forms crystals in various tissues, of which renal tissue is the most susceptible. Untreated nephropathic cystinosis is associated with poor growth and proximal tubular dysfunction (Fanconi syndrome) by 6–12 months of age, glomerular failure by age 10y, and various non-renal complications. Fanconi syndrome is characterized by the generalized failure of proximal tubules to reabsorb water, electrolytes, bicarbonate, calcium, glucose, phosphate, carnitine, amino acids, and tubular proteins [2]. Failure of the proximal tubules to reabsorb phosphate leads to vitamin D-resistant hypophosphatemic rickets, usually characterised by normocalcemia with normal or slightly elevated PTH levels. Hypocalcemia and high PTH in these patients are probably due to coexisting renal disease. Anorexia, vomiting, and feeding difficulties, combined with renal losses of nutrients, cause

poor nutritional status and failure to thrive. The renal phenotype consists of an overlap of Fanconi syndrome with progressive loss of glomerular function [3].

Table 1: Lab parameters in index child and younger sibling

Haemoglobin (g/dl)	9.1 **(Index child)**	7.5 **(Younger sibling)**
Serum creatinine (mg/dl)	2.3	0.8
Blood urea (mg/dl)	73	53
Serum sodium (mEq/L)	132	134
Serum potassium (mEq/L)	2.4	2.7
Serum chloride (mEq/L)	99	118
Serum calcium (mg/dl)	7.8	7.2
Serum phosphorus (mg/dl)	3.0	3.3
Serum alkaline phosphatase (IU/L)	632	625
Serum intact PTH (pg/ml)	1223.4	941
25(OH) vitamin D (ng/ml)	16.1	14.5
1,25 (OH)2 vitamin D (pmol/L)	27.6	30.2
Blood pH	7.33	7.3
Blood bicarbonate (mEq/L)	16	13
Urine bicarbonate (mEq/L)	12	6.2
FE bicarbonate (%)	16	14.8
Urine creatinine (mg/dl)	10.4	6.2
Urine phosphorus (mg/dl)	3.6	5.8
TMP/GFR	2.3	2.4
Uriine aminoacidogram	glutamic acid, valine, glycine	glutamic acid, valine, glycine
Urine specific gravity	1.005	1.010
Urine glucose	Trace	Nil
Urine protein	+++	+
Urine potassium (mEq/L)	13.6	9.6
Urine sodium (mEq/L)	62	75
Urine chloride (mEq/L)	63	66
Urine anion gap	11.6	18.6
Urine calcium/creatinine	0.18	0.2
T4	< 0.2 ng/dl (FT4)	6.96 µg/dl (Total T4)
TSH	>100	10.79

Fanconi syndrome is treated by replacement of renal losses, nutritional support, free access to water, and supplementation with citrate to alkalinize the blood. Oral potassium, phosphate and vitamin D supplements are also required. Renal transplantation may be needed if there is progressive renal failure with hypertension [6]. Cystine depleting therapy, in the form of oral cysteamine bitartrate (Cystagon) 1.3 gm/m^2/day given in divided doses, has revolutionized the management and prognosis of nephropathic cystinosis [7]. When started early, Cysteamine has successfully promoted growth and delayed complications, thereby improving life expectancy. Without therapy, patients may develop multiple endocrinopathies like primary hypothyroid-ism, delayed puberty and primary hypogonadism in males [4]. They also have photophobia [5], benign intracranial hypertension and neurobehavioral abnormalities.

Definitive diagnosis is based upon a high index of suspicion, supported by slit lamp exam of the corneas showing cysteine crystals, which are generally present around 16 months of age [5]. Measurement of cystine in a mixed white blood cell preparation enriched in polymorphonuclear leucocytes, performed using the cystine binding protein (CBP) assay or mass spectrometry, secures the diagnosis [9], but is presently not available in India.

Conclusion

Generalised proximal tubular dysfunction, including hypophosphatemic rickets and nephrogenic diabetes insipidus, and early renal failure, are characteristic of cystinosis. Primary hypothyroidism is the other endocrine manifestation of cystinosis. All these factors contribute for growth failure in cystinosis.

Bibliography

1. Gahl WA, Thoene J, Schneider JA. Cystinosis: a disorder of lysosomal membrane transport. In: Scriver CR, Beaudet AL, SlyWS, Valle D, Childs B, Kinzler KW, Vogelstein B. (eds) The metabolic and molecular basis of inherited disease, 8th edition 2001. McGraw-Hill Companies, Inc, pp. 5085-5108.

2. Roth KS, Foreman JW, Segal S. The Fanconi syndrome and mechanisms of tubular transport dysfunction. Kidney Int 1981;20:705–716.

3. Long WS, Seashore MR, Siegel NJ, Bia MJ. Idiopathic Fanconi syndrome with progressive renal failure: a case report and discussion. Yale J Biol Med 1990;63:15–28.

4. Chik CL, Friedman A, Merriam GR, Gahl WA. Pituitary testicular function in nephropathic cystinosis. Ann Intern Med 1993;119:568-75.

5. Gahl WA, Kuehl EM, Iwata F, Lindblad A, Kaiser-Kupfer MI. Corneal crystals in nephropathic cystinosis: natural history and treatment with cysteamine eye drops. Mol Genet Metab 2000; 71:100-20.

6. Nesterova G, Gahl W. Nephropathic cystinosis: late complications of a multisystemic disease. Pediatr Nephrol 2008;23:863-67.

7. Kleta R, Bernardini I, Ueda M, Varade WS, Phornphutkul C, Krasnewich D, Gahl WA. Long-term follow-up of well treated nephropathic cystinosis patients. J Pediatr 2004;145:555-60.

Pedendoscan

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Growth & Puberty

Human Chorionic Gonadotropin Stimulation Test in Prepubertal Children with Micropenis Can Accurately Predict Leydig Cell Function in Pubertal or Postpubertal Adolescents. Ishii T et al. Horm Res Paediatr. 2015;84 (5):305-10.

To evaluate the accuracy of the human chorionic gonadotropin (hCG) stimulation test in children with micropenis in predicting later Leydig cell function, a retrospective investigation of testosterone (T) response to a 3-day hCG test (3,000 IU/m2/day) was done in 50 Japanese boys with micropenis in prepuberty. Serum T levels after the hCG test in those who did not develop any pubertal signs without hormone replacement therapy (n=16) were significantly lower than in those who did spontaneously develop puberty (n= 34). The authors concluded that the hCG test in prepubertal children with micropenis can be useful for predicting peri-pubertal Leydig cell function; they recommend a post-hCG serum total T cut-off level of 1.1 ng/ml.

Hypogonadotropic Hypogonadism in Infants with Congenital Hypopituitarism: A Challenge to Diagnose at an Early Stage. Braslavsky D. Horm Res Paediatr. 2015;84(5):289-97.

To explore the functioning of the hypothalamic-pituitary-gonadal axis in the postnatal gonadotropic surge for an early diagnosis of CHH (Congenital Hypogonadotrophic Hypogonadism) in newborns or infants suspected of having CPHD (Combined Pituitary Hormone Deficiency), a cohort of 27 boys under 6 months and 19 girls under 24 months of age with suspected hypopituitarism was studied. Serum concentrations of LH, FSH, T, inhibin B, anti-Müllerian hormone (AMH) and estradiol were measured, and male external genitalia were characterized as normal or abnormal (micropenis, microorchidism and/or cryptorchidism). CPHD was confirmed in 36 of 46 patients. Low LH and T levels, in association with abnormal external genitalia, had a positive predictive value of 93% for CHH. No significant association was observed between serum FSH, AMH, and inhibin B and the patient's external genitalia.

Response to IGF-1 Generation Test in Short Prepubertal Children Born Very Preterm or at Term. Miles HL et al. Horm Res Paediatr. 2015;84(5):298-304.

26 prepubertal children (age 7.0 ± 2.0 y) with short stature, who were born appropriate for gestational age and either very preterm (n = 11) or at term (n = 15) were studied to investigate whether preterm (<32 weeks of gestation) exhibit features of growth hormone (GH) resistance by doing an insulin-like growth factor-1 (IGF-1) generation test. Preterm children who are short for genetic height potential showed no evidence of GH resistance that would explain their short stature. However, there was indirect evidence of insulin resistance in the preterm children, as insulin concentrations were significantly higher at baseline.

Adrenal disorders

Concurrent confirmation and differential diagnosis of congenital adrenal hyperplasia from dried blood spots: application of a second-tier LC-MS/MS assay in a cross-border cooperation for newborn screening. Monostori P et al. Horm Res Paediatr. 2015;84(5):311-8.

Newborn screening for congenital adrenal hyperplasia (CAH) by using 17- hydroxyprogesterone (17 OHP) is currently confirmed later with a fresh venous specimen due to the high initial false positive rate. The authors developed a single liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay for cortisol, 21-deoxycortisol, 11-deoxycortisol, 4-androstenedione and 17 OHP that allows both the confirmation and differential diagnosis of CAH using the same dried blood spot (DBS) as in primary screening. Of a total of 163 DBS samples tested positive in primary screening, the 21-hydroxylase-deficient form of CAH was confirmed in 1 sample. The assay allows concurrent confirmation and differential diagnosis of CAH and can be performed on the same DBS samples as in primary screening, enabling early diagnosis and treatment.

Diabetes

Effect of metformin added to insulin on glycemic control among overweight/obese adolescents with type 1 diabetes: a randomized clinical trial. Libman IM et al. JAMA 2015 Dec 1; 314(21): 2241-50.

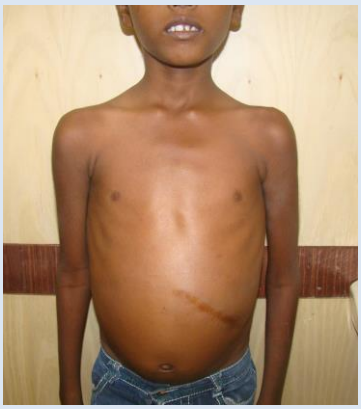
To assess the efficacy and safety of metformin as an adjunct to insulin in treating overweight adolescents with type 1 diabetes (T1D), a multicenter (26 pediatric endocrinology clinics), double-blind, placebo-controlled randomized clinical trial involving 140 adolescents, age 12.1-19.6y (mean 15.3y) with mean diabetes duration 7y, mean BMI 94th percentile, mean total daily insulin 1.1 U/kg, and mean HbA1c 8.8%, was conducted. The study showed that the addition of metformin to insulin did not improve glycemic control after 6 months. Of multiple secondary end points, findings favored metformin only for insulin dose and measures of adiposity. The use of metformin resulted in an increased risk for gastrointestinal adverse events. The authors concluded that results do not support prescribing metformin to overweight adolescents with T1D to improve glycemic control.

Higher glucose concentrations following protein- and fat-rich meals – the Tuebingen Grill Study: a pilot study in adolescents with type 1 diabetes. Neu A et al. Pediatr Diabetes. 2015 Dec;16(8):587-91.

Traditionally insulin dosage is focused on the carbohydrate (CHO) amount in meals. To investigate the influence of a fat- and protein-rich meal in the evening on glucose concentration overnight in adolescents with T1D, 15 patients, mean age 16.8y, participated in the study. Mean HbA1c was 6.9%. On two consecutive days, the patients received a standard meal (SM) and a fat-protein-rich evening meal (FPRM). The CHO amount remained identical; insulin was adjusted to this CHO amount with the individual CHO bolus. Glucose was measured continuously overnight during the 12h following the meal. Glucose area under the curve (AUC) for FPRM was significantly higher than for SM. Maximal AUC difference was at 6h after the meal. Glucose concentration in the morning was 91 mg/dL after SM and 153 mg/dL after FPRM. The authors concluded that after a FPRM, glucose concentration is significantly higher for 12h. Dietary counselling should include the effect of protein and fat on glucose levels in adolescents with T1D. The data indicates clearly a need for additional insulin for fat-protein-rich meals.

Photo Quiz

Dr Santhosh Olety, Paediatric and Adolescent Endocrinologist, Karnataka Institute of Diabetology, BengaluruBangalore



- A-9 years-old boy presented with symptoms of polyuria, polydipsia and tiredness.
- Investigations showed fasting plasma glucose of 350 mg/dl, HbA1c of 12% and fasting c-peptide of 0.71 ng/ml.
- What could be the possible cause of his diabetes?

ISAPE-PET 2015: A TRULY MEMORABLE EXPERIENCE

Aniish Kolly*, Dr Preeti Singh**,
*** Senior Resident, Department of Endocrinology, Vydehi Institute of Medical Sciences and Research Center, Bangalore; **Asst Prof, Pediatrics, LHMC-KSCH, New Delhi**

What do you get when you have some of the top stalwarts from the country and across, under one roof and who are eager to share their knowledge with you? A truly memorable and enriching experience! The ISPAE-PET 2015 program held in Gurgaon from 24th-27th November was the fourth of its kind. The first three programs were very successful, and all those who had attended those said this year's program was one of the best.

ISPAE PET is unique in many ways: intensive, residential, in a quiet environment (we could not get away!), for young entrants, with a high (under 3:1) participant faculty ratio, national and international faculty to give varying perspectives. It ensured maximum interaction, and provided a platform for long term relationships with faculty and amongst participants. ISPAE PET 2015 was held at Savoy Suites, Manesar, Haryana, in collaboration with European and Asia Pacific pediatric endocrine societies (ESPE, APPES), with Dr Preeti Dabadghao as PET Convener and Dr Ganesh Jevalikar the Organizing Secretary. The faculty comprised of 8 eminent Indian pediatric endocrinologists (Drs Vijayalakshmi Bhatia, Preeti Dabadghao, Vandana Jain, PSN Menon, P Raghupathy, Sudha Rao, Anna Simon, Nalini Shah, and Anju Virmani) as well as 6 international experts (Drs Jean-Claude Carel from Paris, Olaf Hiort from Lubeck, Paul Hofman from Auckland, Craig Munns from Sydney, Matthew Sabin and Margaret Zacharin from Melbourne). Thirty seven selected participants (35 from India, 1 each from Bangladesh and Nepal) attended.

For a training program to be successful, the most important thing to factor in is the training faculty. I would take this opportunity to say that it was an absolute privilege and a truly humbling experience to learn the subject under such an amazing group of people. Every one of them not only had a wealth of experience, but was also keen to share that expertise.

Even with outstanding teachers, a passive audience will not learn much. The PET program ensures active participation. After being selected, every trainee had to submit a couple of

paediatric endocrine cases seen by them, one of which was selected for presentation during the program. After that, the trainee was assigned mentors who guided the trainee in preparing the abstract and power point presentation, so we learnt not only the science of pediatric endocrinology, but also the art of presenting concisely yet precisely. When we reached the venue we were given a compilation of the abstracts, to go through all the cases.

We were divided into 6 groups of 6-8 trainees, one Indian and one foreign faculty member, for group discussions, which preceded each day's sessions. In these small group discussions, the mentors discussed the approach to some interesting and illustrative cases they had encountered. We got to discuss various perspectives and clinical practices followed across the world, and even various institutions in the country.

The main sessions covered different topics: in each session, three trainees briefly presented relevant cases, followed up a mentor building upon those cases to analyze and discuss the particular topic. Being case-based and largely interactive, they were very useful in clearing most of our doubts pertaining to practical aspects of the subject.

The first session was on disorders of growth, mentored by Dr J-C Carel. The second day we covered Thyroid disorders, Adrenal disorders, SGA and DSD, mentored by Dr Anna Simon, Dr Nalini shah, Dr Paul Hofman and Dr Olaf Hiort respectively. Day 3 consisted of sessions on bone disorders, diabetes, and obesity, mentored by Dr Craig Munns, Dr Vandana Jain and Dr Matt Sabin. In the evening we had a quiz conducted by Dr Rajni Sharma: 30 pediatric endocrine questions were asked: Dr Abraham Paulose from IGICH, Bangalore won. The last day we had sessions on puberty and fluid & electrolyte balance, covered by Dr Margaret Zacharin and Dr Preeti Dabadghao. Apart from the Quiz award, Dr Preeti Singh from LHMC, Delhi was awarded for the best case presentation.


It is hard to nitpick when something has been organised so well. The only grievance if any was that the program ended early with a few topics left out which could have been covered.


One of the best aspects of the training program was the interaction we could have with our fellow trainees. It is not often that you get to meet your colleagues from different places across the country, in such a close knit environment. We got to discuss interesting cases and clinical practices from our institutions, which we found was extremely helpful. A lot of new friendships were made which we hope would last the distance.

Lastly although the program was heavily academic, the organisers made sure that we were recharged daily with a host of fun activities. We had an introductory, ice-breaking dinner with *antarakshi*, karaoke and dumb charades, combined with a birthday celebration: Dr Anju Virmani, the backbone of CAPE NEWS.

A local sightseeing tour was arranged one evening. And if added incentive is needed, it's not every day that you get to play cricket with an Aussie and a Kiwi: we had two morning sessions of cricket by the MCC (Manesar Cricket Club) and Manesar Cricket Ground (MCG)!!

Pearls from ISPAE-PET 2015

Dr Preeti Singh, Asst Prof, Pediatrics, LHMC-KSCH, New Delhi

GROWTH – GH therapy in non GHD

1. Outside of severe permanent GHD, GH use increases adult height by ≈ 1 cm/yr of treatment for durations of up to ≈ 5 yrs.
2. The increases in height with GH therapy have no demonstrable effect on quality of life or psychosocial adjustment.
3. Routine use of the combination of GnRH agonist and GH in children born SGA as well as in children with GH deficiency cannot be suggested.

THYROID

Congenital hypothyroidism

1. Etiological diagnosis is useful in congenital hypothyroidism to confirm permanency and to plan long term treatment.
2. Age at initiation of treatment and starting dose of levothyroxine are critical factors that determine the long-term outcome.
3. The goals of therapy –frequently evaluate TT4 or FT4, maintain in the upper half of the reference range during the first 3y of life.
4. Doubtful cases should be reassessed at 2.5-3y, after discontinuing replacement thyroxine for 6-8 weeks.

Thyroid Cancers

1. Total thyroidectomy with central compartment LN dissection is the procedure of choice for Differentiated Thyroid Cancers.
2. RAI is required for residual disease treatment and remnant ablation (RAI doses have to be adjusted to age, nodal disease & distant metastasis).
3. TSH levels should be maintained: <0.1 mU/L for nodal/ distal metastases; 0.1-0.5 mU/L – when there is no active disease.
4. Long term follow up is to be done for decades.

LONG TERM ENDOCRINE AND METABOLIC EFFECTS OF SGA

1. Fetal malnutrition is proposed as the cause of small birth size and programmed later adult disease (Barker's Hypothesis).
2. The endocrine consequences of being SGA are Insulin resistance, Leptin Resistance, Premature pubarche/ adrenarche, Polycystic ovarian syndrome, Early and rapid puberty, Elevated FSH, Short stature with partial growth hormone and IGF-I resistance and Altered body composition.
3. Insulin resistance and secondary hyperinsulinism appear to be the primary underlying metabolic abnormality. Most sequelae require an associated increase in fat mass/ adiposity to become apparent – probably causing a greater reduction in insulin sensitivity.
4. SGA children who rapidly gain weight from mid-childhood through early adult life are predisposed to diabetes in later life. Regular exercise is associated with a lower risk of type 2 diabetes in them.
5. Widespread epigenetic changes (DNA methylation/ histone modification and micro RNAs) resulting from SGA have been recognized, the precise epigenome of SGA remains obscure.
6. Lifestyle changes in childhood, and weight restriction, can prevent development of metabolic sequelae.

DIFFERENCES/DISORDERS OF SEX DEVELOPMENT (DSD)

1. Differences or Disorders of Sex Development (DSD) constitute a complex group of rare diseases caused by chromosomal, genetic and endocrine metabolic disturbances that affect the endocrine-reproductive system, thereby modulating the sexual phenotype of a given person.
2. Multi-Disciplinary Teams represent a new standard of care in the management of DSD, having been shown to provide improved support and care for children and their families
3. COST (European Cooperation in Science and Technology) Action DSD Net will link leading international scientists, clinicians and patients in this field, to characterize DSD with the aim of diagnosing all people with DSD to provide a structured, potentially personalized management.
4. Management of children with DSD requires correlation with diagnosis, using a thoughtful approach especially in minors, and no irreversible treatments should be offered in children and adolescents without informed consent.

ADRENALS

1. Neonatal cholestasis can be a presenting feature of Primary Adrenal Insufficiency which can be either glucocorticoid deficiency alone or both glucocorticoid and mineralocorticoid deficiency.
2. Diagnosis of adrenal insufficiency requires high index of suspicion and early diagnosis and treatment is the key to success.
3. In ACTH dependent Cushing, inferior petrosal sinus sampling may be required in difficult cases to localize the site of ACTH secretion.

PHEOCHROMOCYTOMA and PARAGANGLIOMAS

1. Endocrine Society Practice Guidelines recommend that initial biochemical testing for PPGLs should include supine measurements of plasma free metanephrines or urinary fractionated metanephrines by LCMS or electrochemical detection methods.
2. These Guidelines suggest computed tomography (CT) rather than magnetic resonance imaging (MRI) as the first-choice imaging modality because of its excellent spatial resolution for thorax, abdomen, and pelvis.
3. Search for syndromic associations and perform genetic testing in all.
4. Surgery is curative and follow up with clinical and biochemical parameters is important.

BONE

1. Treatment of Vitamin D Dependent Rickets type 2 (VDDR- 2) requires large doses of calcitriol or vitamin D_3; non responsive cases require intravenous Calcium to heal rickets.
2. In resistant rickets, alopecia is an important clue to the diagnosis of VDDR-2.
3. Vitamin D deficiency can present with severe proximal muscle weakness, a condition called as osteomalacic myopathy.
4. Recommended Vitamin D intake in 1^{st} year of life to prevent rickets is 400IU/day.
5. Beyond 12 months of age, all children and adults need to meet their nutritional requirement for vitamin D through diet and/ or supplementation, which is at least 600 IU/day (15µg), as recommended by the IOM.

6. Treatment of nutritional rickets requires daily therapeutic dose of vitamin D of 2000 IU, 3000-6000 IU, and 6000 IU for infants below 12 months, 12mo-12y, and more than 12y respectively, for total duration of 12 wk, along with calcium supplementation (500mg/day).
7. Since vitamin D deficiency is widespread, all lactating mothers can be given 1.2 lakhs of cholecalciferol

DIABETES AND OBESITY

1. Thyroid disorders are associated with type 1 DM with the prevalence ranging from 12 to 24% for hypothyroidism and 1-2% for hyperthyroidism.
2. Wolfram syndrome is a very rare type of diabetes in children, which should be suspected in a diabetic child with unusual complaints like early visual impairment and polyuria that persists despite glycemic control.
3. Recommendations for frequency of SMBG and targets need to be *individualized* based on factors such as SES, educational and motivational level of the family, age and insulin regime.
4. Multi-dose insulin regimens are now standard of care.
5. Use BMI charts to diagnose and track obesity, and look for underlying causes - other than just diet and exercise.
6. There are no clear criteria to define Insulin Resistance in children; surrogate markers such as fasting Insulin levels are poor indicators of Insulin sensitivity.
7. Life style interventions such as diet and exercise can improve Insulin sensitivity; drugs should be implemented only in selected cases.
8. Diagnosing Type 2 DM especially in the acute setting is extremely difficult; if in doubt then treat as Type 1 DM.
9. Small interventions done at a young age to keep a check on abnormal weight gain can have improved effects on BMI and therefore long-term health.

PUBERTY

1. Pubertal induction with hCG and rFSH for boys with hypothalamic hypogonadism would result in effective testicular growth and spermatogenesis over a time span similar to that of natural puberty.
2. The cause of precocious puberty in girls is 90% functional, in boys 70% organic pathology.
3. Currently MKRN3 defects represent the most frequent known genetic cause of familial CPP, inactivation of MKRN3 results in in premature reactivation of GnRH secretion.
4. Consequences of precocious and delayed puberty may be underestimated, both short and long term and follow up may be needed for several years after completion of initial management.

WATER AND ELECTROLYTE DISTURBANCES DUE TO PITUITARY DISORDERS

1. In craniopharyngioma, pre-operative central diabetes insipidus (CDI) has been reported in 8-35% of patients and after surgery in 70-90%.
2. After surgery for craniopharyngioma, a classical triphasic response is observed in the post-op period which requires appropriate management in order to avoid life-threatening electrolyte disturbances.
3. The most common etiology of CDI in childhood and adolescence is idiopathic.
4. Careful and intensive follow up is required in cases of idiopathic CDI to identify other anterior pituitary hormone defects (correlated with stalk thickening).

Additional Pearls from ISPAE PET 2015

Dr Anju Virmani, Senior Consultant Pediatric Endocrinologist, Max, Pentamed, SLJ & Apollo Hospitals, Delhi

1. Hypocalcemia can, rarely cause diarrhea (hypocalcemic sprue): once serum calcium improves, the diarrhea improves.
2. Vitamin D deficiency can cause developmental regression is small children.
3. QCT is not a good investigation for the spine; DXA is very good for this area.
4. Multiple fractures in a young child: never miss leukemia!
5. In a child presenting with DKA, get into the habit of calculating corrected serum sodium, since hyperglycemia is inevitable.
6. Waist circumference should be ½ the height, or less.
7. Spironolactone works well in boys with gonadotropin independent precocious puberty.
8. Children with precocious puberty do well in languages and Maths, since their brain also matures somewhat faster.
9. hCG is better for inducing puberty, since the primed testes respond better and sooner, when fertility is desired later.

PEARLS FROM ISPAE 2015

10. Goa was the first Indian state to start newborn thyroid screening in 2008.
11. In primary TSH screening, if the TSH is very low, suspect and rule out central hypothyroidism.
12. In Vellore, of newborns recalled for confirmation, 22% did not come back.
13. Incidence of congenital hypothyroidism (CH) reported from Lucknow is 1: 1220, from Chandigarh 1: 3400, from Vellore 1: 1290.
14. If sampling was done after 24 hours, missed newborns were 16% in Lucknow and 14% in Chandigarh. Also, care is needed that age be recorded accurately in hours, at time of sampling.
15. With filter paper tests for thyroid screening, double the value reported, since the test is done using whole blood, not serum.
16. In New Zealand, T4 and TSH are tested weekly for the first 6 weeks, and monthly for the first year in CH.
17. ESPE recommends starting with a loading dose of 10-15 µg/kg/day, and rapidly decreasing dose to 4-5 µg/kg/day in 1-2 weeks time, to avoid hyperthyroidism.
18. In all studies on GH, only 6% studies have looked at final height; the rest are short term studies.
19. In idiopathic short stature, gain in final height with GH therapy is about 1 cm per year of therapy.
20. Early clitoroplasty can be considered in CAH since sex of rearing is known unlike in other DSD where sex of rearing is more likely to be uncertain.
21. Fludrocortisone has significant glucocorticoid activity, and this must be factored in when calculating dose of glucocorticoid replacement.
22. In western populations, pregnant women need 600 IU/day of vitamin D, and RDA of calcium is similar to the non-pregnant state; lactating women also need 600 IU/day of vitamin D, and do not need to take supplemental calcium.
23. Bisphosphonates decrease osteclastic activity. In children this results in increased cortical thickness and bone density. Reduced bone pain → more activity → better muscle strength.
24. However, decreased turnover means slower bone healing, and eventually decreased bone formation. So doses have to be titrated very carefully. In fracturing bones, Dr Margaret Zacharin suggested treating hard for 3-5y, then decrease to maintenance dose for 3-5y.
25. Progynova (natural estradiol) is cheap and easily available across India and should be the preferred estrogen, as it has fewer side effects than Premarin (conjugated estrogen) and ethinyl estradiol.
26. In France, MRI pituitary and head is mandatory for all children suspected to have GHD.
27. In McCune Albright syndrome, radiotherapy should not be given to fibrous dysplasia lesions as they are prone to sarcomatous change.

ISPAE Biennial Meet 2015: A Report

Dr Ganesh Jevalikar, Organising Secretary

The 4th biennial meeting of the Indian Society for Pediatric and Adolescent Endocrinology, ISPAE 2015, was held on 27th-29th November 2015, at the Epicentre, Gurgaon. It was attended by a total of 184 delegates. Eminent national and International faculty deliberated on a wide range of topics in pediatric endocrinology. It was preceded by a highly successful ISPAE-PET program from 24-27th November. The main meeting was inaugurated by Dr

Naresh Trehan, Chairman, Medanta the Medicity Hospital, and Dr Narender Yadav, President, IAP Haryana. A video clip of Dr Desia's award presentation at ESPE was screened. ISPAE bestowed honorary membership to Dr Jean-Claude Carel and Dr Olaf Hiort for their continuous support and contribution to ISPAE PET and ISPAE meetings.

The event was also enlivened by the cultural program - a beautiful Odissi dance performance by Padmashri Ms Madhavi Mudgal and her team.

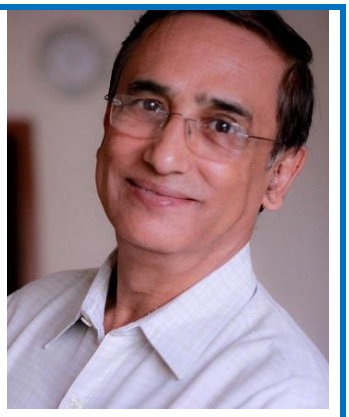
Clinical and research experience from across India was also shared in the form of scientific posters and oral presentations. Six abstracts were selected for oral presentations. The paper by David Chandy et al from SGPGIMS, Lucknow on "Effect Of Vitamin D supplementation vs. sunshine for term infants on bone mineral, infection and dentition outcomes: a randomized controlled trial" was adjudged the best oral presentation.

The best posters were those of Aashima Dabas et al from AIIMS, New Delhi on "Subclinical atherosclerosis and glucose homeostasis in Indian obese children" and Sidhnath Sudhanshu et al from SGPGIMS, Lucknow on "Sun exposure, ultraviolet (UV) irradiance and serum 25OHD in pregnant women in rural north India".

The annual general body meeting was held on 28 November.

The meeting evoked appreciation and positive feedback from all delegates and faculty with respect to the venue, scientific program, the quality of the discussions, and the adherence to time.

Tribute to Legend: Dr Panna Choudhury



Dr Panna Choudhury was literally well named. A gem of a person, he was well known to and admired by all pediatricians across India as he served as Editor-in-Chief of Indian Pediatrics (2002-2007), and National President of IAP (2009), apart from advising on national and international public health programs and committees too numerous to list, and receiving awards too numerous to count! Even after retiring as Consultant Pediatrician at LNJP Hospital-MAMC, New Delhi, after 35 years of service, he had his hands full providing guidance to many agencies. Born in Nagaon, Assam, in January 1947, he lost his mother when he was just 5 years old. A brilliant student, he studied in Nagaon, Guwahati, Shillong, and Dibrugarh,before coming to Maulana Azad Medical College (MAMC) for MD Pediatrics, where he also met Dr Monisha, whom he married in 1978. After brief stints in Safderjung Hospital, Delhi, and JIPMER, Pondicherry, he joined LNJP-MAMC, his karma-bhumi till March 2009. With several papers and books to his credit, no one would doubt his academic worth. However, what was truly amazing about him was his other qualities: his softness and kindness, his ability to carry his honors lightly, his warmth and willingness to help whoever turned to him, and his genuine love for life. With a twinkle in his eyes, he would give truly sage advice, especially when it came to disputes and disagreements. His advice helped our Chapter tide over rough waters on more than one occasion. His untimely and shocking demise on 1st September 2015, at just 68 years, has left a huge void which will be hard to fill. He is survived by Dr Monisha Choudhury, currently Director Professor of Pathology in LHMC, New Delhi, two adoring daughters Pallavi and Surabhi, and sons-in-law, and three grandchildren, apart from a vast number of people whose lives he touched and who will greatly miss him.

Dr Anju Virmani

Award Winning Abstracts from ISPAE and ISPAE-PET, 2015

Best oral paper award

Sun exposure, ultraviolet (UV) irradiance and serum 25 hydroxycholecalciferol (25OHD) in pregnant women in rural north India

Siddhnath Sudhanshu, Pramod Upadhyay Monashish Sahu, Vinita Rawat, Vijayalakshmi Bhatia

Objective: We aimed to estimate the amount of cutaneous vitamin D synthesis in village women, in different seasons. We also documented variations in surface UV energy in areas of variable environmental pollution and crowding.
Methods: Measurements of UVB radiation energy were obtained at different times of the day, in different seasons and at different locations. Serum 25OHD measured in 139 pregnant women.
Results: The average peak UV irradiance calculated during April and May was significantly higher at our institute and in the villages, than at the crowded inner city location (p=0.03). The average daily cutaneous vitamin D synthesis was estimated to be 769 IU during winter and 1487 IU during summer. The mean serum 25OHD was 11.3 ± 5.0 ng/ml in women tested during winter (92 % < 20 ng/ml) and 16.6 ± 8.1 ng/ml in women tested during the rest of the year (70 % < 20 ng/ml). Mean dietary calcium intake was 270 mg.
Conclusion: Poor skin exposure, poor UVB energy in winter season and low dietary calcium intake are major limiting factors. The environmental pollution affects the UVB energy adversely.

Best Poster award

Subclinical atherosclerosis and glucose homeostasis in Indian obese children

Aashima Dabas, Tushanth Thomas, Rajesh Khadgawat, N Gupta, M Gahlot, Devasenathipathy K .

Objective: To evaluate the role of carotid intima-medial thickness (CIMT), as a marker of subclinical atherosclerosis in Indian obese children. .
Methods: Prospective case-control study. Cases: 80 children aged 6-17 years with constitutional obesity. Controls: 23 age and gender matched with normal body mass index (BMI). Detailed anthropometric and clinical evaluation was followed by biochemical analysis and body fat estimation by DXA scan in cases. Similar parameters were measured for controls except laboratory parameters. CIMT was measured with B-mode ultrasonography in both cases and controls. .
Results: The mean age of cases was 12.8 ±3 y, with mean BMI of 29.2±4.8 Kg/m^2. The mean CIMT was significantly higher in cases (0.54±0.13) than controls (0.42±0.08); P<0.001 across all ages. CIMT was significantly higher in hypertensive than non-hypertensive. CIMT showed a positive correlation with BMI (P=0.02), percentage body fat and fat mass index (P<0.01), but not with waist: hip ratio or waist circumference. CIMT correlated significantly with blood glucose and serum insulin at 1 hrr and Matsuda index but not with lipid profile or HOMA-IR.
Conclusion: CIMT correlated significantly to cardio-metabolic risk factors and can serve as a screening tool for cardio-vascular risk in obese Indian children.

Best case presentation at ISPAE-PET

Vitamin D Dependent Rickets Type II

Dr Preethi Singh, Asst Prof, Pediatrics, LHMC-KSCH, New Delhi (Mentor Dr Craig Munns)

Background: In developing countries nutritional rickets is the most common form of rickets and establishing an early diagnosis to the rare genetic forms in resource limited settings remains a challenge. .

Methods and Results: A 3 year old boy, born to non-consanguineous parents presented with inability to walk independently, progressive bowing of legs and loss of scalp hair. On examination he had short stature (Height 77 cm; < 3rd centile), frontal bossing, wrist and ankle widening and alopecia totalis with absent eyebrows and eyelashes. In setting of resistant rickets, alopecia and laboratory features of secondary hyperparathyroidism, normal 25(OH) D & high 1,25(OH) $_2$D, low 24 hour urinary phosphate and calcium excretion a diagnosis of Vitamin D Dependent Rickets –II (VDDR-II) was made. He was started on calcitriol @ 80-140 ng/kg/day along with oral calcium supplements (1 g/d) with periodic biochemical, radiological and growth monitoring. Within 1 year of treatment, he started walking independently and gained height. In view of financial constraints he has been started on Vitamin D3 (60000 IU fortnightly) instead of calcitriol with equally rewarding clinical and biochemical response. There has been reappearance of few scant eyelashes but alopecia at other sites persisted. .

Conclusion: VDDR II is an autosomal recessive disorder caused by mutations on the vitamin D receptor gene preventing normal physiological response to 1,25(OH)2 vitamin D. Alopecia is an important clue to diagnosis. Treatment requires large doses of calcitriol or vitamin D; non responsive cases require intravenous Calcium to heal rickets.

A short report of activities

Dr Santhosh Olety, Paediatric and Adolescent Endocrinologist,
Karnataka Institute of Diabetology, Bangalore, Email: docsanthosh@yahoo.com

Education booklets about understanding diabetes in children and gaining self-management skills are available, free of cost, in both Kannada and English versions for children and their family members. They are written in simple language with animated descriptions.

You-tube video upload ref

1. https://youtu.be/ki9QC2deZUc - Slides on celebrities with diabetes, for motivating children with diabetes. Audio in Kannada.
2. http://youtu.be/xTXUTbSWBHw - Understanding type 1 diabetes and its management. Animation video for educating children and families with audio in Kannada.

Publications by ISPAE Members

Dr Devi Dayal, Professor, Department of Pediatrics, PGIMER, Chandigarh

1. **Dayal D**, Kumar S, Sachdeva N, et al. Fall in vitamin D levels during hospitalization in children. **Int J Pediatr.** Volume 2014 (2014), Article ID 291856.
2. Sawatkar GU, Kanwar AJ, Dogra S, Bhadada SK, **Dayal D**. Spectrum of cutaneous manifestations of type 1 diabetes mellitus in 500 south Asian patients. Br J Dermatol. 2014;171(6):1402-6.
3. Ganvir RH, Bhalla AK, **Dayal D**. Growth attainments of Indian children with Type 1 diabetes: a mixed longitudinal study. **Indian J Pediatr** 2015;82(3):245-52.
4. **Dayal D**, Sharma S, Sachdeva N, et al. Efficacy of insulin detemir compared to insulin NPH on glycemic control in Indian children with Type 1 Diabetes. **J Diabetology** 2014; 2:2.
5. **Dayal D**, Jain H, Attri SV, et al. Relationship of high sensitivity C-reactive protein levels to anthropometric and other metabolic parameters in Indian children with simple overweight and obesity. **J Clin Diag Res** 2014;8(8): PC05.
6. **Dayal D,** Jain P, Panigrahi I, et al. Thyroid dysfunction in North Indian children with Down syndrome. **Indian Pediatr** 2014;15:751-2.
7. **Dayal D**, Sindhuja L, Bhattacharya A, et al. Agenesis and not ectopia is common in North Indian children with thyroid dysgenesis. **Indian J Endocr Metab** 2014; 18, Suppl S1:97-9.
8. **Dayal D,** Bakshi J, Jain P, Singhi S. Outcome of rhinosinus mucormycosis in North Indian children with Type 1 diabetes. **Indian J Pediatr** 2015; epub ahead of print.
9. **Dayal D**, Saini AG, Jayashree M, et al. Hospital based incidence, patterns of presentation and outcome of Type 1 diabetes: 12 years' data from a tertiary care center in North India. **Int J Diab Dev ctries** 2015; epub ahead of print.
10. **Dayal D**, Sindhuja L, Bhattacharya A, Bharti B. Advanced maternal age in Indian children with thyroid dysgenesis. **Clin Pediatr Endocrinol** 2015;24(2):59-62.
11. **Dayal D**, Samprati M, Kaur N, et al. Prevalence of beta-cell, thyroid and celiac autoimmunity in North Indian children with recent onset Type 1 Diabetes. **J Clin Diagn Res**. 2015; 9(3): SM01-SM02.
12. **Dayal D**, Naganur S, Singh B, Saikia B. Thyroid dysfunction and autoantibodies in first degree relatives of North Indian children with autoimmune thyroiditis. **Thyroid Res Pract** 2015; 12(3):96-99.

Dr S Ramkumar, Endocrinologist, Apollo Hospitals, Chennai

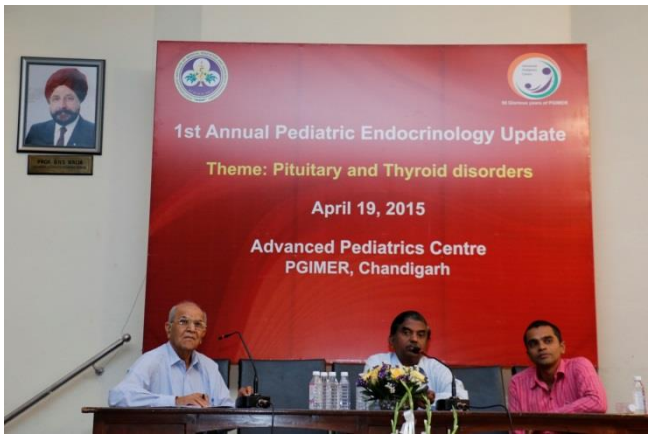
1. Praveen PA, **Kumar SR**, Tandon N. Type 2 diabetes in youth in South Asia. Curr Diab Rep. 2015;15(2):571.

Fellowships and Awards

1. Dr S Ramkumar was selected for the **ISPAD Allan Drash Clinical Fellowship in Diabetes** in Auckland City Hospital, New Zealand under Dr Craig Jeffereies, in February-March 2015.
2. Dr S Ramkumar attended the 15th ISPAD Research School for Physicians in Milan, Italy 19-24th April 2015.

Activities by ISPAE Members

First Annual Pediatric Endocrinology Meet at Advanced Pediatrics Center, PGIMER, Chandigarh



The 1st Annual Pediatric Endocrinology Update was organized by the Dept of Pediatrics at the Advanced Pediatric Center, PGIMER, Chandigarh on April 19, 2015. This one day CME focussed on pituitary and thyroid disorders and was attended by 85 delegates. The faculty included Dr Murlidharan, Dr SK Mathur, Dr Leena Priyamada, Dr Amaresh Reddy, and faculty from Pediatrics and other departments of the Institute.

Dr Veena V Nair, Consultant Pediatric and Adolescent Endocrinologist, Ananthapuri Hospitals and Reserach Institute, Thiruvananthapuram

Osteogenesis Imperfect Parent Awareness and Patient Support Campaign

Ananthapuri Hospital & Research Institute, Thiruvananthapuram, together with IMA, Thiruvananthapuram branch, and Amritha-varshini Charitable Society for Osteo-genesis Imperfecta, organized a one day camp for parents and patients on 23rd November 2015 at IMA Headquarters Hall, Thiruvananthapuram. IMA National President Padmashree Dr Marthanda Pillai inaugurated the event. Prof. Margaret Zacharin, Pediatric Endocrinologist, Royal Children's Hospital, Melbourne, Australia was the chief guest. She addressed the parents on 'Caring for children with OI'. Medical consultation, including orthopaedic and physiotherapy services, were provided. Twenty young people with OI and their caretakers from different parts of Kerala benefitted from the camp.

Guest Lecture

Prof Margaret Zacharin, Pediatric Endocrinologist, Royal Children's Hospital, Melborne, Australia, gave a guest lecture on 'Endocrine problems in young people with disabilities' on 23rd November at IMA Headquarters Hall, Thiruvananthapuram. The session was chaired by

Dr S. Noel Narayanan, retired Professor and HOD, Pediatrics, Govt Medical College, Thiruvananthapuram. It was organised by Ananathapuri Hospital and Research Institute, and IMA Thiruvananthapuram branch. Doctors from various specialities attended the program.

Dr Sangeeta Yadav, Professor, Dept of Pediatrics, Maulana Azad Medical College, Delhi

A workshop on **Adolescent Endocrinology** was held on 21st November, 2015 at Department of Pediatrics, MAMC, New Delhi under the aegis of Adolescent Health Academy, Delhi.

The chairperson was Dr Sangeeta Yadav, Director Professor & Head & In-charge Pediatric and Adolescent Endocrinology, MAMC; the other faculty included Dr Bindu Kulshreshtha, Dr Anjali Saxena, Dr Aashima Dabas and Dr Sumaira Khalil. It aimed to provide knowledge and skills required to understand office practice of common adolescent endocrine issues which are intertwined with adolescence, since adolescence itself is a dynamic period of growth. There were sessions on interpretation of normal variations in growth, assessment of growth and puberty, investigations for growth and pubertal disorders, abnormal patterns of pubertal growth, managing diabetes during adolescence, polycystic ovarian syndrome and metabolic syndrome. It was structured on case-based learning, followed by skill stations and group discussions. The workshop was attended by over 35 delegates from Delhi, most of whom rated the workshop and lectures and the methodology, as excellent to very good, as per their feedback performas. It not only enhanced their skills and knowledge but instilled confidence and also how to approach and manage an adolescent presenting with various issues as enumerated above.

Dr S Ramkumar, Endocrinologist, Apollo Hospitals, Chennai

1. Organized a Diabetes Education program for parents of children with Type 1 Diabetes on Diabetes Day/ Children's Day (14 Nov 2015) in Apollo Children Hospital.
2. Organised a Childhood Obesity Awareness Program on World Obesity Day (25 Oct 2015) in Apollo Children Hospital. In addition to free consultations with the endocrinologist,

physiotherapist, dietician and psychologist, the program also included a health talk and dietary practical workshop on preparing healthy snacks.

3. Presented posters in ISPAD-APEG 2015:
    a. Partial remission by standard and IDAA1c definitions in children with new-onset type 1 diabetes mellitus in Auckland, New Zealand (2000-2013).
    b. Acute complications in children with type 1 diabetes from a regional cohort setting in Auckland, New Zealand (2000-2014).

Dr Anurag Bajpai, Pediatric & Adolescent Endocrinologist, Regency hospital, Kanpur, UP

Conducted Pediatric Endocrinology Workshops at

1. Pre Congress Workshop on Endocrinology, at Adolescon, Mangalore, 14 August 2015
2. Growth & Puberty Workshop, Rajpedicon, Jaipur, 11 September 2015
3. Glucose Disorders Workshop, IAP Faridabad, 26 September 2015
4. Diabetes Workshop, IAP Varanasi, 18 October 2015
5. Diabetes Workshop, IAP Kanpur, 1 November 2015.

Delivered invited talks at

1. Polycystic Ovarian Syndrome: Adolescon, Mangalore, 15 August 2015.
2. Mathametics of Short Stature, Rajpedicon, Jaipur, 12 Sep 2015
3. Approach to Growth Failure, North GRS Symposium, Delhi, 27 Sep 2015
4. Growth failure- When, why and how? MP PEDICON, Bhopal, 28 Nov 2015
5. HPG axis modification. ISPAE, Gurgaon, 29 Nov 2015
6. Short stature- Clinical approach. UP Pedicon, Jaunpur, 19 Dec 2015.

GROW India World Diabetes Day Empowerment Program, 15 Nov 2015, Kanpur

VI Annual GROW India Type 1 DM Empowerment program was organized at KDMA World, Keshavpuram, Kanpur. The program was attended by over 100 children with diabetes and their parents, Principals, Teachers and Students from 12 schools and social groups. The theme of the program was "Type 1 DM- From being ruled by it to ruling it.: The key highlights of the program included release of educational book "Type 1 DM- From problem to solution", release of Type 1 DM documentary, awareness skit "Type 1 DM- Karlo Apni Mutthi Mai", Launch of GROW India Type 1 DM School Initiative, Release of awareness posters and multimedia, Grow India T1DM identification pendant, Design solutions by school students and Launch of afforadable Insulin program. The proposals included training programs for teachers and primary healthcare workers, mentorship program and push for indegenous insulin pump in collaboration with IIT Kanpur.

Dr Shalmi Mehta, Pediatric Endocrinologist, Endokids Clinic, Ahmedabad, Gujarat

World Diabetes Day 2015 was celebrated on 1st November in Ahmedabad by Dr Shalmi Mehta and Dr Ruchi Shah (Endokids Clinic, Ahmedabad). About 60 patients of Type 1 diabetes and their families participated. A talent Evening was organized for the teens, to showcase the budding stars. A Fashion Parade for toddlers saw enthusiastic participation of the toddlers and their mothers. Two adults with Type 1 diabetes talked about their experiences, providing a great boost to the parents. A Dance Workshop managed by an adult with Type 1 Diabetes was held before dinner. Overall, the whole evening was filled with fun and entertainment and the kids and their parents enjoyed a lot.

Dr Ravindra Kumar, Senior Specialist, Dept of Pediatrics, Hindu Rao Hospital, Delhi

The Dept of Pediatrics, Hindu Rao Hospital, Delhi, along with Indian Academy of Pediatrics, Delhi Branch, celebrated **World Diabetes Day** with a CME on Wednesday 18th Nov 2015. Dr Ravindra Kumar presented a brief overview on Type 1 diabetes. The program also included training and counselling of patients and parents.

Dr Hemchand K Prasad, Dr Mehta's Hospital, Chennai

Delivered lectures at

1. National IJPP CME, Chennai, on "Management of Metabolic Syndrome" on 14.06.15
2. State PEDICON, Vellore, on "OPD management of Diabetes" on 15.08.15
3. Pedendo 2015, Chennai, on "New treatment modalities in Diabetes" on 30.08.15
4. Panel discussion in Pedendo 2015, Chennai, on "Thyroid dilemmas" on 30.08.15
5. Cochin IMA on "Growth charts" on 09.08.2015
6. Hyderabad meeting on "IAP 2015 growth charts" on 07.08.15
7. New Delhi "IAP 2015 Growth Charts and Growth Monitoring" on 13.09.15
8. IAP Pune meeting Pedimeet on "OPD management of Diabetes" 05.07.15
9. IAP Pedimeet on "Adrenal crisis" 05.07.15

World Diabetes Day celebrations in Mehta Children's Hospital was organised by Dr Thangavelu S and Dr Hemchand KP on 14.11.2015. A support group was formed, and patient education was done. The event was attended by over 40 families with type 1 diabetes.

Upcoming Events by ISPAE Members

V Practical Pediatric Endocrinology Course, JK Lon Hospital, Jaipur, Feb 21 2016

This course would focus on practical issues related to pediatric endocrinology encountered by pediatricians in their daily practice. Six case based modules on Growth, Puberty, Thyroid, Calcium and bone, Glucose metabolism, and Electrolyte imbalance would be executed by eminent pediatric endocrinologists. The program is particularly suited for pediatric PG trainees and practicing pediatricians. The participants would be provided a comprehensive resource book with algorithms and case based approach to all topics covered during the program. The number of delegates would be limited to ensure active interaction.

For registration please contact Dr Anurag Bajpai, Consultant Pediatric & Adolescent Endocrinologist, Dept of Pediatric Endocrinology, Regency Hospital Ltd, A2 Sarvodaya Nagar, Kanpur 208005. email dr_anuragbajpai@yahoo.com, Ph +919454081769, Fax 0512-2213407

'Manchester Insulin Pump Course' at Bengaluru

A workshop including practical hands-on session on Insulin Pump therapy and CGMS is organized at Hotel La Marvella, No.1, 14th Cross, South-End Circle, 2nd Block, Jayanagar, Bengaluru. Maximum of 20 participants could only be accommodated. Course fee is INR 5000 (Early Bird registration) till 31st December 2015 and INR 6500, 1st January 2016 onwards. Contact Dr Santhosh Olety for further details or enquiry: docsanthosh@yahoo.com, 9945459530

Answer to Photo Quiz

Diagnosis: Hemolytic anemia (Thalassemia major) with surgical scar of splenectomy. Patient received multiple blood transfusions and is on desferoxiamine (chelating agent). His ferritin levels were significantly high. He developed secondary diabetes due to secondary hemosiderosis.