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CAPENEWS

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

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Theme: Obesity

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From the Editor's Desk

Greetings from the Editorial Team of ISPAE CAPE News. It gives us a lot of delight to share this newsletter themed on obesity, with interesting review articles, excerpts from guidelines, journal scan, biochemistry corner, patient corner and history corner. You will also find learning pearls from ISPAE ACES meets and the solutions to the cross word on Growth: Congratulations to the winners! An interesting word hunt on obesity is there for trainees to crack: please do share your responses. There are many interesting activities from ISPAE members and office bearers.

The theme for the next issue is "Thyroid disorders". We look forward to contributions from members, feedback and suggestions at editor.capenews@gmail.com

With warm regards
ISPAE CAPE News Editorial Team 2021-22

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Message from ISPAE Office Bearers

As we have been through the lethal second wave of coronavirus, which ravaged our country and took many precious lives, we hope and pray that you and your family members are safe. The medical community has stood up to the challenge despite the helpless situation that we were in. This deserves special thanks to each and every member of the medical fraternity.

The EC has taken up several ambitious projects in these tough times. The monthly academic meeting 'ISPAE ACES' has been an immense success. We request all of you to encourage your students and young colleagues to participate with more enthusiasm in this monthly academic feast. We have completed the public awareness videos for popularizing newborn screening (NBS) for congenital hypothyroidism (CH) planned in collaboration with GPED, thanks to the immense efforts by Drs Sirisha, Sathyakala and Dhivyalakshmi. We are thankful to Prof Margaret Zacharin for her immense support in getting funding and giving ideas for dissemination of these videos. Now it is up to all of us to make these videos popular and bring out more material which will increase awareness of NBS for CH among the public. We are also working on writing to several state governments for initiating NBS in their states.

We all are aware of the gaps in the field of patient education for type 1 diabetes. In this regard, ISPAE has initiated an ambitious project – the 'ISPAE Diabetes Education and Learning' (IDEAL) program, which will create a workforce of diabetes educators trained in handling childhood diabetes. The core committee of Drs Aspi Irani, Anju Virmani, Sathosh Olety, Shaila Bhattacharyya, Rakesh Kumar, Sirisha Kusuma, Preeti Singh, Ganesh Jevalikar and Ms Sheryl Salis is working hard and on strict timelines to ensure a timely start of this program. Many of you have volunteered for this activity and we thank you for that.

We are also trying to bring uniformity amongst the various fellowship programs that have been running in this country. For this purpose, a committee led by Dr P Raghupathy and consisting of Drs PSN Menon, Sudha Rao, Rajesh Khadgawat, Anurag Bajpai, Ganesh Jevalikar and Shaila Bhattacharyya has been formed and will soon begin its work.

Another important milestone for our society is the launch of our journal named the "Journal of Pediatric Endocrinology and Diabetes". Many of you have sent articles for the inaugural issue; we request you to encourage all ISPAE members and pediatric colleagues to submit high quality scientific information to be shared amongst peers.

The registrations for the 7th biennial meeting of ISPAE have started. The organizing team led by Drs Vaman Khadilkar and Supriya Gupte, along with the ISPAE PET team of Drs Sarah Mathai and Ahila Ayyavoo are burning the midnight oil to organize this meeting at such a short notice. Please motivate them further by registering as early as possible, submitting abstracts and praying that we all can meet in person.

We congratulate Drs Hemchand Prasad, Sanjay Bhadada and Ravindra Kumar, who are the recipients of the Charity Awards for financial year 2020-21, as well as Drs Seema Rai and Nithya T, the recipients of the ISPAE Observership Award.

We heartily welcome all the new members to the ISPAE family.
Best Wishes,
Drs Shaila Bhattacharyya
Ganesh Jevalikar
Rakesh Kumar and Team ISPAE 2021-22

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Adolescent Obesity: Role of Health Care Providers.

Dr Ruchika Kumar, Asst. Professor & Dr Sangeeta Yadav, Professor of Excellence In-charge
Pediatric and Adolescent Endocrinology, Maulana Azad Medical College & Associated LN Hospital, University of Delhi, New Delhi. E-mail: yadav.sangita@hotmail.com

Obesity in children and adolescents is an international problem that is an increasing public health concern with several short and long-term health consequences. Globally, the prevalence of obesity has doubled between 1990 and 2015, and the rate of increase is higher in children than in adults. [1] ***In the last three decades, the burden of adolescents with obesity has increased 10-fold, from 11 million to 124 million.*** The prevalence varies from 30% in America to less than 2% in sub-Saharan Africa.[2]

The prevalence is plateauing in some developed countries, but continuing to rise steeply in the developing countries of Asia and Africa. The prevalence of overweight/obesity among Indian adolescents rose from 9.8% in 2006 to 11.7% in 2009.[3] In a school based study, we observed the prevalence of obesity which was 5.6% in 1998-1999 among 600 children, ages 9-10 years, had increased to 10.6% in 2006-2007 among 400 children ages 6-10 years. A systematic review conducted a decade ago by Gupta et al., reported a prevalence of 6.1 to 25.5% overweight, and 3.6 to 11.7% obesity among 5–19 year olds [4].

To address the issue of adolescent obesity, **the Society for Adolescent Health and Medicine (SAHM)** issued a position paper [5] to empower health care personnel (HCP).

Summary of "Position Paper of the Society for Adolescent Health and Medicine: Preventing and Treating Adolescent Obesity".

The position paper provides expert consensus and evidence to increase professionals' ability to prevent, screen, treat, and advocate for obesity prevention and healthy weight promotion. The salient points are as highlighted below:

Adolescent obesity is influenced by the physical, psychological, and social changes during adolescence. With the onset of puberty, in females, adiposity increases, while in males it decreases. Adolescents acquire increased autonomy, increased access to food and ability to purchase food, increased eating outside the home, and with the peers, contributing to increased caloric intake. Cognitively, they are also vulnerable to making food choices that may not support health.

All the physical, psychological, and social changes occurring during the adolescent's growth period greatly influence obesity development. Health care personnel should have the knowledge, skills, and resources to prevent and treat obesity ***while incorporating the biopsychosocial stages of adolescent development for their clients' positive self-esteem and empowerment.***

For all adolescent patients, the Committee recommended:

A. ***Primary prevention*** of obesity, supported by ***tracking patients' growth and by providing information to patients and families about maintaining a healthy weight from early on.*** To monitor weight, height and BMI serially at every visit, identifying BMI percentile for age and sex, the paper mentions use of CDC, WHO and IOTF BMI charts. For India, the IAP Growth charts and BMI charts are readily available.

B. *To screen for medical complications* with a thorough history, physical examination and investigations for co-morbidities: diabetes, dyslipidemia, hypertension, cardio-vascular disease, fatty liver disease, reproductive complications, alterations in puberty, obstructive sleep apnea, musculoskeletal complications and psychological problems.

C. *To screen for behaviors*, including nutrition and physical activity, and family history, that increase the risk of, or worsen, obesity. Detailed dietary history: eating habits including frequency, content, and location of meals, snacks and calorie dense foods. Physical activity assessment including details of time spent in physical activity as well as screen time. The adolescent population is especially vulnerable to development of eating disorders. Early identification and intervention for disordered eating behaviors can help to prevent them in the future.

D. ***The primary prevention tool is counseling*** as 5-2-1-0, i.e. daily consumption of 5 fruits and vegetables, less than 2 hours of screen time, at least 1 hour of physical activity, and 0/or limited consumption of sugar-sweetened beverages [5].

E. ***Secondary prevention individualizes the approach to risk reduction*** in adolescents and identifies other risk factors for obesity and related conditions.

F. ***Tertiary prevention*** is by the providers with expertise to screen for and manage physical and mental co-morbid conditions, including depression, anxiety, and disordered eating.

Treatment

The response and success of the treatment entirely depends on the BMI. Lower severity (BMI 85^{th}–97^{th}percentile), absence of any significant psychosocial or mental health barriers, availability of resources for physical activity as well as the inclusion of the entire family and family support, give the best results. The role of the HCP is to serve as a guide.

The guidelines recommend reinforcing healthy behaviors, counselling the adolescent and family together, keeping in mind emerging adolescent independence. Depending on the patient's pubertal status and BMI percentile, presence of physical and mental health co-morbidities, the treatment goal may be weight stabilization or loss. Motivational interviewing and promotion of incremental change have both shown good efficacy [6]. ***For adolescents the most effective methods are behavior change theory, specifically the use of skill-building techniques, and delivery of lifestyle counselling messages*** [7]. Counselling for decreasing sugar-sweetened beverages, sedentary behaviors, and screen time, while increasing dietary intake of fiber, fruits and vegetables, eating meals regularly, and having family meals is needed.

Recommendations

The paper mentions the WHO report of the Commission to End Childhood Obesity (2016) recommending a family-based, multicomponent approach that includes diet, physical activity, and psychosocial support from a multidisciplinary team consisting of the primary care provider, dietitian, exercise specialist, and behavioral counselor [8].

Based on the severity of obesity and response to treatment, the team would
(i) Guide the patient through initial assessment, including evaluation for co-morbidities;
(ii) Deliver evidence-based lifestyle counseling;
(iii) Refer to more intensive treatment options such as weight loss surgery (WLS) and monitored diets when appropriate.
(iv) Monitored diets are the key component of **intensive** behavioral therapy. Monitored diets are calorie restricted: they could be formula-based regimens, preprepared foods, or detailed meal plans. These approaches are available through commercially based programs or close monitoring with a clinic-based dietitian [9].

Patients with BMI > 97th percentile are unlikely to experience weight loss with clinic-based lifestyle counseling alone [9]. Therefore, weight stabilization may be the most reasonable goal. Intensive behavioral therapy, monitored diets, medication, and weight loss surgery (WLS) are becoming more common for the treatment of adolescents with extreme obesity [9,10].
Further, residential treatment, both inpatient and non-hospital-based programs, shows significant weight loss, but regain is common, most likely due to the families' inability to maintain the changes in the home environment. Through partnerships with mental health colleagues, some programs employ cognitive behavioral therapy or dialectical behavioral therapy, especially for patients with disordered eating and/or other mental health comorbidities [9].

Pharmacological therapy options are currently limited. The only FDA-approved medications for weight loss in those <18 years of age are orlistat and phentermine. Orlistat is approved for adolescents 12 years and older, but causes gastrointestinal side effects; rebound weight gain after discontinuation is common. Phentermine is approved for adolescents over 16 years. For those over 18 years of age, other drugs like combination phentermine/topiramate, and naltrexone/bupropion are also available. [9,11].

There is evidence to support WLS as a new treatment modality with positive initial outcomes, but long-term studies are lacking [10]. WLS options include the adjustable gastric band, sleeve gastrectomy, and the Roux-en-Y gastric bypass, although most promising results have been observed with sleeve gastrectomy [10].

Advocacy

HCPs should advocate for changes to promote healthy weight within and outside of clinic settings and efforts be made to reverse the obesity epidemic and promote healthy weight. They need to advocate on a variety of levels from the clinical settings, home and institutional environments, community responsibilities and initiatives, to the state, national or international level, and on topics ranging from food policy, the built environment, games, physical activity opportunities in various settings.

Summary

Adolescent obesity is a significant chronic health problem associated with developmental challenges. Effective and safe prevention and treatment of adolescent obesity, has many barriers like the complex societal and economic influences on adolescents' diets, space and time for physical activity, and body image ideals, added with the slow pace of pharmacologic and surgical interventions approved for use in adolescents.

- Based on the recommendations by SAHM, all HCPs caring for adolescents should be trained and supported in the assessment of obesity and its co-morbidities.
- Unhealthy eating behaviors must be looked at, and efforts should be made to prevent eating disorders.
- Primary prevention of obesity should be at the level of family and later at the community and national level.
- Management should be by a multidisciplinary team in case of poor response.
- Pharmacotherapy and/or weight loss surgery are options in adolescents with poor response to multidisciplinary approach.

Finally, HCPs caring for adolescents must understand that healthy weight loss is extremely difficult and is an enormous challenge for their patients.

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Excerpts from recent Guidelines on Obesity

Dr Ravindra Kumar, In-charge Pediatric & Adolescent Endocrinology
North DMC Medical College & Hindu Rao Hospital, Delhi

Recommendations

a) **Diagnosing overweight and obesity**

1. Children and adolescents > 2 years of age are diagnosed as overweight if the BMI is between 85th and 95th percentile; and obese if the BMI is > 95th percentile for age and gender on the growth chart**.**
2. A child < 2 years of age is obese if the weight for recumbent length is > 97.7th percentile of WHO growth standards**.**
3. Extreme obesity is defined as a BMI > 120% of the 95th percentile or > 35 kg/m2.
4. Routine laboratory evaluation for endocrine etiology of pediatric obesity is not needed, unless the patient's stature and/or height velocity are attenuated (assessed in relationship to genetic/ familial potential and pubertal stage). However, Albright hereditary osteodystrophy/ pseudohypoparathyroidism, although associated with short stature in adolescence, may be associated with increased growth velocity in the first 2-3 years of life.
5. Do not measure insulin levels when evaluating children or adolescents for obesity as it does not contribute to the diagnosis of insulin resistance.
6. Children or adolescents with a BMI > 85th percentile should be evaluated for potential co-morbidities.
7. The Indian Academy of Pediatrics recommends that children less than 5 years be considered as overweight if weight for height or BMI is above +2 SD and obese if weight for height or BMI is above +3 SD on the WHO charts. Children above 5 years are considered as overweight if their BMI is >23rd adult equivalent and obese if their BMI is > 27th adult equivalent

Clinicians should evaluate the following:

i. Weight, height, and BMI.
ii. Blood pressure, using height/ age/ sex percentile normalized BP tables to interpret the findings.
iii. Acanthosis nigricans and skin tags.
iv. Acne and hirsutism in pubertal girls.
v. Fundoscopic examination for pseudotumor cerebri.
vi. Tenderness and range of motion of the knee, leg and foot.
vii. Peripheral edema, thyroid examination for goiter.

Physical findings associated with syndromic obesity, particularly if there is a neurodevelopmental abnormality or short stature.

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Screening for Co-morbidities of Pediatric Overweight or Obesity

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Co morbidity	Tests and Interpretation
Prediabetes (2) IFG (verify fasting status) IGT (if OGTT is used)	HbA1c 5.7% to < 6.5% (please remember the unpredictability of the test in the pediatric age group) Fasting Plasma glucose of ⩾100 but <126 mg/dL Two hour glucose of ⩾140 but <200 mg/dl
Diabetes mellitus (2)	HbA1C ⩾6.5% Fasting Plasma glucose of ⩾126 mg/dL Two hour plasma glucose of ⩾200 mg/dl during OGTT In a patient with classic symptoms of hyperglycemia, or a random plasma glucose of ⩾200 mg/dl
Dyslipidemia (4)	Fasting lipids (mg/dL) **Triglycerides** 0-9y: <75 (acceptable), 75-99 (borderline high), ⩾100 (high) 10-19y: <90 (acceptable), 90-129 (borderline high), ⩾130 (high) **LDL cholesterol** <110 (acceptable), 110-129 (borderline high), ⩾130 (high) **Total cholesterol** <170 (acceptable), 170-199 (borderline high), ⩾200 (high) **HDL Cholesterol** <40 (low), 40-45 (borderline low), >45 (acceptable) **Non-HDL Cholesterol** <120 (acceptable), 120-144 (borderline high), ⩾145 (high)
Prehypertension and hypertension (5)	(Standardized according to sex, age and height percentile) **3-11 y:** BP > 90th to < 95th percentile = prehypertension BP ⩾95th to < 99th percentile + 5 mm Hg = stage 1 HTN BP ⩾99th percentile + 5 mm Hg = stage 2 HTN **12-17 y:** BP > 90th to < 95th percentile or > 120/80 = prehypertension BP ⩾95th to < 99th percentile + 5 mm Hg = stage 1 HTN BP ⩾99th percentile + 5 mm Hg = stage 2 HTN **18-21 y:** BP ⩾120/80 to 139/89 mm Hg =prehypertension BP ⩾140/90 to 159/99 mm Hg = stage 1 HTN PP ⩾160/100 to 179/109 mm Hg = stage 2 HTN BP > 180/110 mm Hg = stage 3 HTN
NAFLD(6)	ALT> 25 U/L (boys) and > 22 U/L (girls)
PCOS(7)	Free and total testosterone and SHBG, as per Endocrine Society PCOS guidelines
Obstructive sleep apnea (8)	If suggestive history, refer to pulmonologist for nocturnal polysomnography; if not available, overnight oximetry
Psychiatric (9)	If suggestive history, refer to mental health specialist

Note: Individual clinician discretion should be used in Indian setting on using free testosterone in evaluation of PCOS. The ADA 2021 guidelines (3) complement the use of 2014 guidelines in assessment of type 2 diabetes in obese children and adolescents.

b) **Genetic obesity syndromes**

1. Genetic testing is suggested in patients with extreme early onset obesity (before 5 years of age), and/or clinical features of genetic obesity syndromes (in particular extreme hyperphagia), and/or a family history of extreme obesity.
2. Approximately 7% of patients with extreme pediatric obesity may have rare chromosomal abnormalities and/or highly penetrant genetic mutations that drive their obesity**.**
3. While assessing children and adolescents with extreme obesity, clinicians should consider potentially treatable causes and genetic conditions (figure 1).

c) **Prevention of obesity**

1. Clinicians should promote and participate in ongoing education of children and adolescents, parents, and communities about healthy dietary and activity habits.
2. Clinicians should encourage schools to provide adequate education about healthy eating, healthy options in school canteens, and adequate time and space for physical activity.
3. Clinicians should prescribe and support healthy eating habits such as:
   i. Avoiding consumption of calorie-dense, nutrient-poor foods (e.g., sugar-sweetened beverages, sports drinks, fruit drinks, most "fast foods" or those with added table sugar, high-fructose corn syrup (HFCS), high-fat or high-sodium processed foods, and calorie-dense snacks)
   ii. Encouraging consumption of whole fruits rather than fruit juices.
4. Children and adolescents should engage in at least 20 minutes, optimally 60 minutes, of vigorous physical activity at least 5 days per week, to improve metabolic health and reduce the likelihood of developing obesity.
5. Children and adolescents should have healthy sleep patterns to decrease the likelihood of developing obesity due to changes in caloric intake and metabolism related to disordered sleep.
6. The National Sleep Foundation recommends 8 to 11 hours of sleep for school age children and adolescents.
7. Balance unavoidable technology-related screen time with increased opportunities for physical activity.
8. Clinicians' obesity prevention efforts should start early and enlist the entire family rather than the individual child or adolescent.
9. Clinicians should assess family functioning, and make appropriate referrals to address family stressors to decrease the development of obesity.
10. School-based programs and community engagement have a high value in pediatric obesity prevention.
11. The following 6 techniques held promise for preventing obesity during a period of at least 6 months:
    I. Providing individualized information on the consequences of behaviour conducive to the development of obesity.
    II. Restructuring the environment to make individualized behaviour change more successful.
    III. Guiding practices expected to decrease the development of obesity.
    IV. Guiding the identification of role models or advocates to change behaviour.
    V. Implementing stress management/ emotional control training.
    VI. Providing general communication skills training.
12. Breast-feeding for the prevention of obesity is suggested, but evidence supporting the association between breast-feeding and subsequent obesity is inconsistent.

d) **Treating obesity**

1) **Lifestyle: general considerations**

I. Clinicians should prescribe and support intensive, age-appropriate, culturally sensitive, family-centered lifestyle modifications (dietary, physical activity, behavioral) to promote a healthy BMI.
II. Interventions which targeted family involvement with combined lifestyle interventions (diet and exercise) showed a modest but significant effect on obesity (equivalent to a decrease in BMI of 1.5 kg/m^2).

2) **Dietary**

Clinicians should prescribe and support healthy eating habits in accordance with the following guidelines:

i. US Department of Agriculture recommends intake of dietary fiber, fruits, and vegetables.
ii. Timely, regular meals and avoiding constant "grazing" during the day, especially after school and after supper.
iii. Recognizing eating cues in the child's or adolescent's environment, such as boredom, stress loneliness, or screen time.
iv. Portion control education.
v. Encouraging single portion packaging and improved food labeling for easier use by consumers.
vi. Consumption of whole fruit rather than fruit juices.
vii. Decreased consumption of fast foods.
viii. Decreased consumption of added table sugar; elimination of sugar-sweetened beverages.
ix. Decreased consumption of HFCS; improved labeling of foods containing HFCS, and increased awareness among family members.
x. Decreased consumption of high-fat, high-sodium, or processed foods.
xi. Reduced saturated dietary fat intake for children > 2y of age and adolescents.

3) **Physical activity**

i. Prescribe and support reduction of inactivity, and a minimum of 20 minutes daily of moderate to vigorous physical activity daily, with a goal of 60 minutes, all in the context of a calorie-controlled diet.
ii. Moderate to vigorous exercise is defined as causing some increase in breathing and heart rate; in a healthy person this is usually associated with brisk walking, dancing, swimming, or cycling.
iii. Encourage and support patients to limit non-academic screen time to 1 to 2 hours per day and decrease other sedentary behaviors, such as digital activities.

4) **Psychological complications of overweight and Obesity**

i. Identify maladaptive rearing patterns related to diet and activity and educate families about healthy food and exercise habits.
ii. Diagnose unhealthy intrafamily communication patterns; support rearing patterns that seek to enhance the child's or adolescent's self-esteem.
iii. Evaluate for psychosocial co-morbidities and prescribe assessment and counselling when psychosocial problems are suspected.

5) **Pharmacotherapy**

i. Pharmacotherapy should be used for children or adolescents with obesity only after a formal program of intensive lifestyle modification has failed to limit weight gain or to ameliorate co-morbidities.
ii. Do not use obesity medications in children and adolescents < 16 years of age, who are overweight but not obese, except in the context of clinical trials.
iii. FDA approved pharmacotherapy for obesity should be administered only with a concomitant lifestyle modification program of the highest intensity available.
iv. FDA approved medications are appropriate for those ≥ 16 years of age who have BMI ≥ 30 kg/m^2, or who have BMI ≥ 27 kg/m^2 and at least 1 weight-related co-morbid condition (e.g., hypertension or T2DM).
v. Discontinue medication and re-evaluate the patient if the patient does not have a > 4% BMI/BMI Z score reduction after taking anti-obesity medication for 12 weeks at the medication's full dosage.
vi. Among pharmacotherapeutic agents approved for adult obesity, only orlistat is FDA approved for obesity treatment of ages 12 to 16 years.
vii. Orlistat inhibits gastrointestinal lipases, reducing fat absorption by ≈ 30% and reducing BMI significantly by ≈ 0.7 to 1.7 kg/m^2; however, treatment is associated with significant gastrointestinal side effects.
viii. Orlistat must be taken with each meal and appears to affect the absorption of fat-soluble vitamins A and D.

Additional medications for treatment of pediatric obesity (not FDA approved)

a) Metformin

I It reduces hepatic glucose production, increases peripheral insulin sensitivity, may reduce appetite, and decreases BMI, but with a mean decrease of only 1.16 kg/m^2 over 6 to 12 months.
ii. It may possibly be useful in combating the weight gain observed in children and adolescents who are taking atypical psychotropic medications or who have PCOS.
iii. However, given its limited weight-loss efficacy, metformin is not considered a weight-loss treatment.

b) Phentermine and Diethylpropion

i. These are centrally active, amphetamine-like catecholaminergic and dopaminergic stimulants, FDA approved as short-term (a few weeks) monotherapy for obesity in adults.
ii. Lisdexamfetamine treatment was associated with short-term weight loss, but this medication is not FDA approved.
iii. Because of adverse effect profiles, abuse potential, and the absence of trials showing long-term weight loss efficacy, none of the amphetamine-like agents is recommended for obesity management in children and adolescents.

c) Growth Hormone

Although not FDA approved for the treatment of obesity, GH treatment of children and adolescents with Prader-Willi syndrome, particularly when started early, decreases body fat percentage and increases lean body mass, with effects that may be sustained for the long term.

d) Octreotide

I It limits the opening of voltage-gated calcium channels in beta cells, decreasing the magnitude of insulin response to glucose.

ii. In obese adults with insulin hypersecretion, treating with long-acting repeatable octreotide for 6 months resulted in ≈2% greater weight loss than in controls.

iii. Given its side effect profile, octreotide appears to be potentially beneficial only for those with hypothalamic obesity.

e) GLP-1 Analog

I Liraglutide is approved for long-term obesity treatment in adults.

ii. The effective 3 mg dose produced an additional weight loss of 4.5% vs. placebo at 1 year, with sustained effects for up to 2 years.

iii. Another analog, exenatide, may potentially have efficacy in adolescent obesity; used for > 3 months, exenatide reduced BMI by >1 kg/m^2 (compared with control), with continued BMI reduction during a 3 month open-label phase.

f) Leptin

I Leptin therapy in leptin-deficient patients produces significant loss of fat mass.

ii. Unfortunately, leptin therapy in adults who are not leptin deficient has little effect on body weight.

6) **Bariatric surgery**

Bariatric surgery is suggested only under the following conditions:

i. The patient has attained Tanner 4 or 5 pubertal development and final or near-final adult height andhas a BMI of > 40 kg/m^2 with mild co-morbidities (hypertension, dyslipidemia, moderate orthopedic problems, mild sleep apnea, nonalcoholic steatohepatitis, and extreme psychological distress secondary to the obesity)

or

has a BMI of > 35 kg/m^2 and significant co-morbidities (T2DM, moderate to extreme sleep apnea, pseudotumor cerebri, debilitating orthopedic problems, or nonalcoholic steatohepatitis with advanced fibrosis).

ii. Extreme obesity and co-morbidities persist despite compliance with a formal program of lifestyle modification, with or without pharmacotherapy.

iii. Psychological evaluation confirms the stability and competence of the family unit, psychological distress due to impaired QOL from obesity may be present, but the patient does not have an underlying untreated psychiatric illness.

iv. The patient demonstrates the ability to adhere to the principles of healthy dietary and activity habits.

v. The patient has access to an experienced surgeon in a pediatric bariatric surgery center of excellence providing the necessary infrastructure for patient care, including a team capable of long-term follow-up of the metabolic and psychosocial needs of the patient and family.

Bariatric surgery is not suggested in:

i. Preadolescent children;
ii. Pregnant or breast-feeding adolescents (or those planning to become pregnant within 2 years of surgery);
iii. Any patient who has not mastered the principles of healthy dietary and activity habits and/or has an unresolved substance abuse, eating disorder, or untreated psychiatric disorder.

Surgery can be malabsorptive, restrictive, or combination procedures, as follows:

i. Laparoscopic adjustable gastric banding (LAGB) is a purely restrictive procedure that isolates the upper stomach by placing an adjustable silicone ring around the entrance to the stomach.
ii. Roux-en-Y gastric bypass (RYGB) is a combination procedure in which the surgeon creates a small stomach pouch and the remainder of the stomach is bypassed.
iii. Vertical sleeve gastrectomy (VSG) is a restrictive procedure in which a surgeon resects ≈85% of the stomach, removing the fundus and greater curvature, leaving a narrow gastric remnant.

- Regardless of procedure, the percentage of weight loss is independent of initial BMI, so those who are extremely obese will still be obese following surgery.
- Even when obesity persists, most co-morbidities associated with obesity improve markedly following the surgery.
- As these procedures all have potential adverse events, it is important to have life-long monitoring for complications.
- Adherence to prescribed nutritional guidelines is essential for all weight-loss surgery patients.
- Iron, cholecalciferol, calcium, phosphorous, vitamins especially Vitamin B12, B1, folate, A, D and E deficiency may commonly occur.
- Annual screening is recommended for patients at risk for developing vitamin deficiencies.
- As RYGB can result in copper, selenium, and zinc deficiencies, it is recommended that all patients having bariatric surgery receive supplementation with a multivitamin with minerals.
- Despite the importance of nutritional supplementation following bariatric surgery, the Adolescent Morbid Obesity Surgery study found a 67% noncompliance rate with prescribed vitamin and mineral intake at 2 years following surgery.

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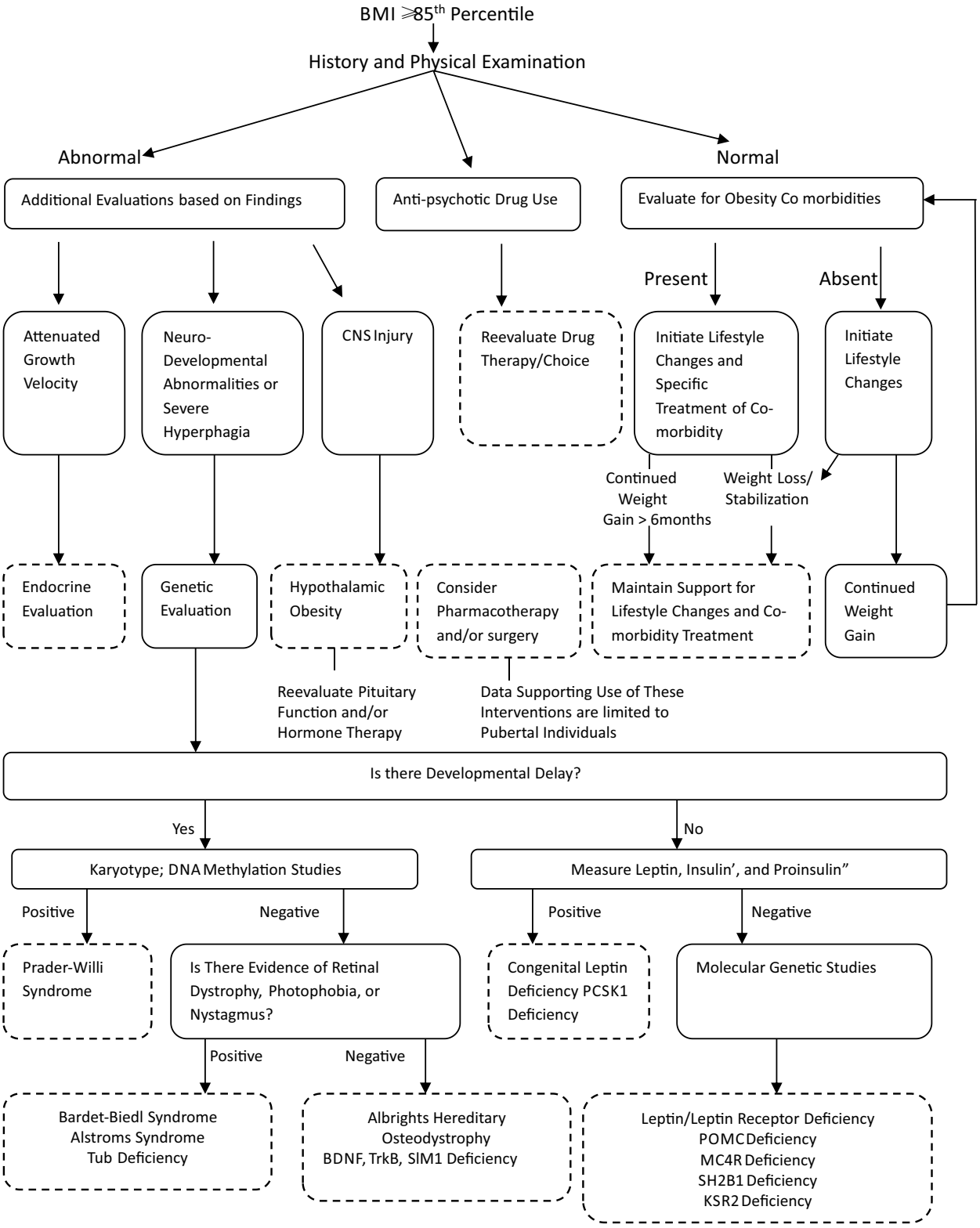
Figure-1 Diagnosis and management flowchart



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MINI-REVIEWS
ROLE OF APOB48-REMNANTS IN PEDIATRIC OBESITY

Dr Seema Rai, Assistant Professor
Dept of Pediatrics, Guru Gobind Singh Medical College, Faridkot, Punjab

Obesity is increasing alarmingly worldwide and so are the adverse effects of obesity on overall health. Adolescent obesity, especially, central adiposity, usually tracks onto adulthood and becomes a risk factor for premature cardiovascular disease (CVD). According to World Health Organization (WHO) reports, the number of children under 5y of age with obesity or overweight is 38.2 million; with a prevalence among 5-19 year olds of 18% in 2016. [1] ApoB48 has a stronger correlation with adiposity than the traditional lipid markers, with a significant association between obesity, dyslipidemia, and lipid subfraction like intestine-derived chylomicrons. Recent studies show that intestinal adaptation affects whole-body cholesterol production and the overall production of chylomicron remnants.[2] Intestinally derived apoB48-containing lipoproteins, chylomicrons (CM) and their remnants (CM-R) have been shown to have an integral role in atherogenesis and CVD risk. The impaired metabolism of remnant chylomicrons resulting from postprandial dyslipidemia has a direct relationship with plaque formation. Impaired metabolism of intestinally driven chylomicrons is not just the result of reduced clearance. [3] Overall, emerging data demonstrates that there is an accumulation of apoB48 remnants in youth with obesity at high cardiometabolic risk, which strongly suggests that these youth have postprandial dyslipidemia (fat intolerance) and potential increased susceptibility to subclinical CVD. The role of cytokines has been established in CVD; recently incretin (glucagon-like peptide GLP-2) has been implicated in the overproduction of chylomicrons, though the role has not been well established in pediatric obesity. [4] Fasting plasma apoB48 is associated with impaired insulin sensitivity and adipokine markers in adolescents. An increase in fasting plasma apoB48-remnants during insulin resistance has been attributed to the delayed clearance of apoB48-remnant particles from the circulation. The insulin resistance state is also known to modulate intestinal apoB48-remnant metabolism by increasing enterocyte *de novo* lipogenesis, including cholesterol ester and TG synthesis, as well as lipidation of primordial chylomicron particles.[5] Authors from western Australia studied 184 girls and observed that girls with cardiometabolic risk factors had higher ApoB48 cf. those without, and ApoB48 correlates with serum triglycerides. [6] It has been postulated that an increase in ApoB level by 1 mmol/L in the non-fasted state results in a 2.8 fold increase in ischemic heart disease. A follow up study on 570 children from Canada compared the utility of ApoB48 with traditional lipid markers in the assessment of central fat mass [7]. The authors observed that classical lipid markers improved with follow up, whereas ApoB48 worsened. For 1 kg/m^2 increase in central adiposity, increase in ApoB48 was higher (14 fold) in those with lower central fat mass cf. those with higher central fat mass. [7] Thus, ApoB48 may be an early marker of metabolic risk.

The present review suggests that elevated remnant lipoproteins may be associated with the early adaptation of the intestine during childhood obesity and represent a novel sex-independent biomarker for detection of CVD risk much earlier than traditional lipid markers, and may be useful in the evaluation of pediatric obesity. There is a need for more research for the formulation of normative data on ApoB48 in various age groups, to enable better understanding of its role as a biomarker in early identification of metabolic syndrome.

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BARDET BIEDL SYNDROME

Dr Priya Siva and Dr Hemchand K Prasad
Department of Pediatric Endocrinology, Mehta Multispeciality Hospitals India Pvt Ltd, Chennai, India

Bardet Biedl Syndrome (BBS) is an autosomal recessively inherited disorder of immotile cilia with a varied presentation. It was independently described by George Bardet in his work titled "Congenital obesity syndrome with polydactyly and retinitis pigmentosa" and Arthur Biedl in his description of "a pair of siblings with adiposogenital dystrophy". It is a multisystemic disorder that should be recognized early by the pediatrician and referred to a multidisciplinary team with expertise in the management.

Clinical features of BBS

Ocular features: Night blindness, photophobia and loss of central and color vision are the classical symptoms in BBS. The primary abnormality is rod cone dystrophy – where there is a primary loss of rod photoreceptors followed by destruction of cone photo receptors. An electroretinogram is the investigation of choice which shows abnormalities beyond 5 years of age. Cataract, myopia and strabismus has also been described. Most affected subjects are usually legally blind by the third decade of life.

Limb abnormalities: Post axial polydactyly is a classical manifestation of BBS. It involves the lower limbs more than the upper limbs. Other described features include: short metacarpals, short metatarsals, short phalanges, short ulna and clinodactyly of the fifth finger.

Obesity: Obesity in BBS is due to dysregulation of appetite, altered leptin resistance, altered neuroendocrine regulation and impaired leptin receptor signaling. Birth weight is usually normal, with obesity manifesting by 1 year of age. The pattern of obesity is diffuse in children and truncal in adulthood.

Developmental disabilities: Developmental delay, learning disability, cognitive defects, labile behavior with outbursts of frustration, lack of social dominance, and autistic spectrum disorder are the developmental disabilities encountered in BBS. Speech deficit, high pitched nasal speech, associated hearing loss and good response to speech therapy are observed in these children.

Renal disorder: An important cause for morbidity and mortality, cystic tubular disease, anatomical malformations and urine concentration defects are described in BBS.

Hypogonadism: Delayed onset of puberty, hypoplastic genitalia, genital abnormalities like vaginal atresia, hypoplastic uterus and ovaries and hypospadias, and low fertility rates can be seen in BBS.

Other abnormalities: Cardiac abnormalities like patent ductus arteriosus, left ventricular hypertrophy and cardiomyopathies are described. Gastrointestinal abnormalities include hepatic fibrosis and cystic dilatation of the bile duct. Neurological manifestations could be clumsiness, ataxia, poor coordination, dysdiadokokinesia, past pointing and difficulty in tandem walking.

Miscellaneous: Type 2 Diabetes mellitus, hyposmia, anosmia, nephrogenic diabetes insipidus are occasionally encountered.

Post axial polydacyly, with or without brachydactyly, should alert a neonatologist to look for development of features of BBS on post-natal follow up. Presence of echogenic kidneys and polydactyly on antenatal scans should alert clinician for the possibility of BBS.

Diagnosis: A diagnosis of BBS is made when 4 major criteria or 3 major and 2 minor criteria are satisfied. The major criteria include rod cone dystrophy, polydactyly, obesity, learning disability, hypogonadism in males and renal abnormalities. The minor criteria include: speech delay, brachydactyly/ syndactyly, developmental delay, ataxia and poor coordination, type 2 diabetes mellitus, anosmia/ hyposmia and left ventricular hypertrophy/ congenital heart disease.

Differential diagnosis: Lawrence Moon syndrome (no polydactyly, associated with spastic paraparesis, distal muscle weakness); Alstorm syndrome (hearing loss, no polydactyly or learning disability) and McKusick Kauffman syndrome (high prevalence of urological abnormalities, lack of obesity and rod cone dystrophy). However, one should remember that if all features are not expressed, the phenotype may be evolving - the child should be followed up prospectively for evolution of classical features of BBS.

Genetic evaluation: About 22 pathogenic genes are incriminated in the pathogenesis of BBS. Mutations in BBS10 and BBS1 genes are most commonly encountered. A triallelic pattern is often described wherein three mutations are needed for manifestation or the third locus acts as a disease modifier. The genotype phenotype correlation is often poor. Genetic testing helps in subsequent pregnancies: 25% are affected, 50% remain carriers and 25% are unaffected. Targeted gene sequencing should be carried out for families with BBS to complement clinical diagnosis.

Clinical assessment and management: Children with suspected BBS should be evaluated, managed and followed up by a team consisting of pediatric endocrinologist, ophthalmologist, pediatric nephrologist and child psychiatrist. The key aspects in evaluation and follow up of these children are described in Table-1.

Treatment: The key principles of treatment of a child with BBS are described in Table 1. In recent times, melanocortin receptor agonists are evolving as a promising modality of therapy. Defect in the hypothalamo-leptin-melanocortin axis resulting in leptin resistance has been described. Recent data has described the utility of setmelanotide in adolescents (age 12-17 years). It is initiated in a dose of 0.5 mg subcutaneously and increased up to a dose of 3 mg. A 9.3% decrement in fat mass and 5.5% decrement in body weight were observed at 3 months. No significant change was observed in blood pressure or lipid parameters, though injection site reactions and hyperpigmentation were seen. Thus, setmelanotide may emerge as a useful drug in control of obesity in subjects with BBS in the future.

Table: 1 Bardet Biedl Syndrome in a nut shell

Diagnosis	Differential diagnosis	Clinical assessment	Evaluation	Management
Presence of 4 major or 3 major and 2 minor criteria. Major criteria include: a. Rod cone dystrophy b. polydactyly c. obesity d. learning disability e. hypogonadism in males f. renal abnormalities. Minor criteria include: a. Speech delay b. brachydactyly/ syndactyly c. developmental delay e. ataxia & poor coordination f. type 2 diabetes mellitus g. anosmia/ hyposmia h. left ventricular hypertrophy/ congenital heart disease.	Lawrence Moon syndrome, Alstorm syndrome, McKusick Kauffman syndrome	Risk factors: screen time, physical activity and dietary intake pattern Clinical assessment of vision (for refractory error, cataract and visual acuity) and fundus assessment Clinical assessment: Body Mass index Waist circumference Blood pressure Sexual maturity rating Specialist assessment: Child guidance clinic assessment for developmental disabilities	One-time assessment: USG abdomen (for renal abnormalities and fatty liver) Electroretinogram (ERG beyond 5 years) Echocardiographic assessment for cardiac abnormalities Periodic assessment: Renal function testing (Serum creatinine and electrolytes) Urine routine assessment Blood glucose, glycosylated hemoglobin Lipid profile Periodic fundus assessment and visual acuity assessment	Lifestyle measures including diet and exercise Management of diabetes mellitus, dyslipidemia, hypogonadism as per standard guidelines Provision of visual aid and support

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Ketogenic Diet in Childhood Obesity

Mr. Swapan Banerjee
Dept. of Nutrition, Seacom Skills University, Kendradangal, Birbhum, West Bengal.

There is a growing interest in the ketogenic or keto diet (KD) by many people worldwide. Many obese individuals wish to achieve weight loss quickly without considering the side effects of a fad diet or inappropriate diet. However, as medical professionals, we are always concerned about health safety in prescribing, whether its medicines or diet[1]. One should also consider the long -term consequences of recommending such a diet to growing children.

The KD mainly focuses on fat consumption and its subsequent effects. In a KD, the total recommended kilocalories per day should come from 55-60% fat, 30-35% protein, and only 5-10% carbohydrates (CHO). The high fat low carbohydrate foods can be added (up to 50 g per day) as a low-carb diet, which, with a reasonable quantity of protein, leads to ketosis in a KD. Protein is usually recommended not less than 1-l.5g/kg body weight. Due to deprivation of CHO and resultant depletion of glycogen stores, the body generates energy through gluconeogenesis and ketogenesis[2].

Gluconeogenesis helps in energy generation in first 3-4 days in response to a low-calorie diet (LCD). Simultaneously, to meet the metabolic requirements of various organs in the body, additional energy can be sourced and managed by ketogenesis where fatty acids are broken down to ketone bodies (acetoacetate and β-hydroxybutyrate) which then work as substrates to supply primary energy[3]. Ketone bodies are utilized by the muscles, heart, kidneys and brain. Liver and RBCs are unable to utilize ketone bodies as an energy source. Ketone bodies in small quantities (without acidosis) are not harmful to the body. Ketones produce more ATP as compared to glucose, hence they are called *super fuel*. Ketones also reduce free radical damage and increase anti-oxidant capacity.

Some studies have described that the KD could be well-planned, with protein for growth and development. However, when dietary fats are in short supply, existing body fat is used for energy. Hence, a balance is required between the total fat intake and use of body fat as instant fuel. Overall, KD is a physiological model of starvation that allows body parts to use ketone bodies in place of glucose which is needed to fuel the brain [4].

The recommendation of KD should be particular, not generalized. Dietary intervention with the very-low-calorie ketogenic diet (VLCKD) has been observed to improve biochemical and anthropometric parameters in children. The results from KD have shown good results in achieving the desired level of total cholesterol, triglycerides, low-density lipoprotein-C, insulinemia, liver transaminases, and body mass index (BMI). The KD is an old dietary pattern, found to be very useful in inflammatory conditions for patients suffering from various cardiovascular diseases. Most importantly, this type of diet can be very effective in subjects with morbid obesity (BMI > 40 kg/m^2)[5,6].

Further, KD has good results in subjects with glucose transporter type 1 (GLUT1) deficiency and pyruvate dehydrogenase complex deficiency (PDCD). In addition, in myoclonic epilepsy, Dravet's syndrome, and Doose's syndrome, this diet has been shown to provide freedom fromseizure[7]. The benefits of KD in children with obesity include: reduction in weight, reduction in BMI, improved insulin sensitivity and reduced visceral fat.

Common short-term side effects include 'keto flu,' with flu like symptoms. This can be managed with supportive treatment and adequate hydration. In addition, there are many long-term side effects such as kidney stones, non-alcoholic steatohepatitis (NASH), hypoproteinemia, nephrolithiasis, urolithiasis, and hypovitaminosis D [8].

Contraindications for KD include inflammation of the pancreas, congenital disorders of lipid metabolism, carnitine translocase deficiency, and carnitine palmitoyl transferase deficiency. A team approach by a pediatric endocrinologist, dietician and social worker is pivotal before embarking upon such measures in growing children. The pros and cons of the therapeutic measure should be explained carefully to the families.

An online literature search and subsequent review show that most available studies had small sample sizes, and short duration of follow up[9]. A summary of some pediatric data from various centers is presented below:

Table-1 Pediatric data on KD

Study group	Diet pattern advised	Key observation
SM Willi et al (USA) KD in 6 adolescents (12-15 years)[10]	KD for 8 weeks (containing 80-100 gm proteins, 25 gm CHO and low fat) followed by 12 weeks of two extra CHO meals	Weight reduction 15.4±1.4 kg; BMI reduction of 2.3±2.9. Weight loss was predominantly fat: DXA scan showed reduced body fat by 6.9%.
Partsalaki I et al (Greece) 29 children[11]	No fat restriction with less than 20 grams of CHO for a period of 6 months	Significant reduction of weight, fat mass, waist circumference, fasting insulin and HOMA IR. Increased whole body insulin sensitivity index, & high molecular weight adiponectin.
Ghayour-Mobarhan et al (Iran) 38 children[12]	High protein and fat and low CHO diet in for a period of 3 months	Reduced body weight by 1.5 kg (2.2%), BMI by 1.01 (3.5%), body fat by 0.92%, and blood sugar by 6.6 mg/dL

Key Messages:

***** The ketogenic diet has been previously described to be useful in various neurological problems in children.

* The KD may be a promising measure in severe or morbidly obese children and adolescents in future only on a short-term basis, under strict medical supervision, considering all side effects and comorbidities. More pediatric studies are required to ascertain its safety, efficacy and long-term consequences.

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INTERESTING CASE REPORTS ON OBESITY FROM ISPAE MEMBERS

A Rare Case of Infantile Obesity – Leptin Receptor Gene mutation (LEPR)

Dr Meenakshi BR, Dr Namratha Upadhya, Dr Vani HN, Dr Raghupathy P.
Division of Pediatric and Adolescent Endocrinology, Indira Gandhi Institute of Child Health, Bangalore

Introduction

Obesity is a common problem that almost every healthcare professional encounters. Monogenic obesity, however, is rare. Leptin (LEP) and its receptor (LEPR) are key players in the regulation of body weight and energy homeostasis and genetic variations in the leptin receptor *(LEPR)* pathway are a significant cause of hyperphagia and severe early-onset obesity [1]. In these rare cases, genetic factors play a larger role than the behavioral and environmental factors; managing these children is challenging, given the fact that specific treatments are available only for specific types of monogenic obesity.

Here we describe a 5 months old infant with rapid, early onset obesity, highlighting the importance of early recognition and genetic diagnosis in these rare cases of early onset obesity.

Case report:

A 5 months old infant, first born to non-consanguineous parents, was brought with complaints of excessive weight gain since 3 months of age. She was born at term with a birth weight of 3.25 kg, and an uneventful perinatal history without feeding difficulties. She was exclusively breastfed for 2.5 months and was found to have rapidly increasing appetite, demanding more feeds with increased frequency of feeding at night (5 times from both breasts). To cater to the infant's increasing demands, the parents started her on top feeds with cow's milk (250ml/day). She was noticed to gain 8 kg over 5 months (average gain of 1.6 kg/month). Her milestones were normal and family history was not significant, with parents' BMI being in the normal range (Mother's BMI and father's BMI 23.2 and 24 kg/m2 respectively).

On examination she had prominent skin creases with no striae / hyperpigmentation, normal hair and no dysmorphic features, skeletal abnormalities or midline defects [Fig 1]. Her weight was 11.2 kg (99th centile; > +2 Z Score), length 68 cm (97thpercentile), OFC 42.8cm (50th-97th percentile), and weight for length > 99.7 percentile (+3.8 SDS). Systemic examination and external genitalia were normal. Her complete blood count (CBC), lipid profile and thyroid profile were normal, as were ultrasound abdomen and neuroimaging. Exclusive breast feeding was advised - at six weeks follow up, there was weight gain of 3 kg. With this presentation of early onset rapid weight gain with normal development and dysmorphism, a diagnosis of monogenic obesity was considered, and genetic analysis done. Clinical exome sequencing for monogenic obesity revealed a pathogenic homozygous single base pair deletion in exon 4 of Leptin receptor (*LEPR*) gene, that resulted in frameshift and premature truncation of the protein, suggestive of leptin receptor-related monogenic obesity. She is being managed with a structured diet plan and physical activity appropriate for age.

Discussion

Leptin is a hormone produced by the adipose tissue, with multiple actions in the endocrine and immune systems, including glucose homeostasis, reproduction, bone formation, tissue remodeling and inflammation. Leptin receptor deficiency is a very rare disorder with prevalence less than 3%. So far, 58 cases with more than 37 mutations have been reported in the world literature [1]. Congenital leptin deficiency is associated with early onset hyperphagia, rapid weight gain, hypogonadism, and reduced T-cell immunity and these symptoms are amenable to treatment with recombinant leptin therapy [2].

The phenotypic features of leptin receptor defect are similar or less severe than that of leptin deficiency; however, they do not respond to leptin therapy [3].

The genetic abnormalities described are mainly homozygous nonsense, missense and frameshift mutations of the *LEPR* gene [4]. Our patient was noted to have homozygous base pair deletion in exon 4 of the *LEPR* gene which resulted in a frameshift mutation causing premature truncation of the protein. Leptin therapy is not helpful in LEPR-deficient subjects. Setmelanotide, a potent Melanocortin-4 receptor *(*MC4R*)* agonist, is a peptide drug which binds to and restores the impaired MC4 receptor pathway activity arising due to genetic defects upstream of the MC4 receptor [5]. In Phase 3 clinical trials involving obese children above 6years of age with LEPR mutation, 46% patients achieved a ≥10% weight loss after 1year of Setmelanotide [6]. Currently, medical management is challenging and involves comprehensive multidisciplinary care with structured dietary framework and limited access to food, physical activities adapted to neurodevelopmental abilities, early recognition and management of co-morbidities and appropriate replacement therapy for endocrine deficits.

Learning Points

- Ø Obesity cannot always be attributed to environmental and behavioral factors. In patients with monogenic obesity, the hypothalamic neuroendocrine satiety system is affected, leading to hyperphagia and severe early onset obesity.
- Ø Infants with severe early onset obesity, should be offered genetic diagnosis as this would guide in further management, provide better insights into pathophysiology, and also help parents deal with stigmatization.
- Ø In non-syndromic monogenic obesity, the largest contribution to energy balance is excess calorie intake, hence intervention should focus on limiting access to food.
- Ø Setmelanotide has shown promising results in Phase III clinical trials, giving a ray of hope to children with LEPR deficiency.

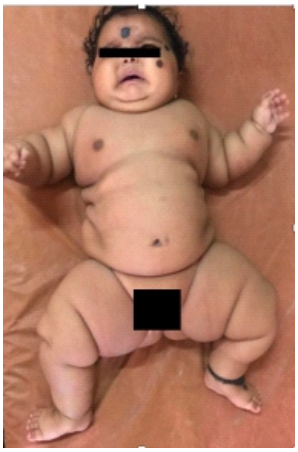

Fig 1 Image of the infant at 5 months showing severe obesity and accentuated skin creases.
(Authors have obtained permission to include this image)

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Bardet -Biedl Syndrome with Growth Hormone Deficiency

Dr Priti Phatale & Dr Hemant Phatale
Samrat Endocrine Institute of Diabetes Obesity and Thyroid, Aurangabad
Dr Kishor Kharche
Consultant Endocrinologist, United Ciigma Hospital, Aurangabad

Introduction - Biedl Syndrome (BBS), named after Georges Bardet and Arthur Biedl, is a rare autosomal recessive disorder characterized by obesity, polydactyly, rod cone dystrophy, cognitive impairment, hypogonadism, and renal abnormalities. The prevalence of BBS is estimated to be 1 in 125,000 to 160,000 in Europe, which is equivalent to around 400 cases in the United Kingdom (1,2). Only 11 cases have been reported from India, of which one case had documented end-stage renal disease (ESRD) requiring renal replacement therapy (3).

The diagnosis of BBS is clinical, requiring at least four of the primary features (obesity, polydactyly, learning disabilities, hypogonadism in male patients, renal anomalies) (4). Confirmation of the diagnosis can be done with direct genetic sequencing in 80% of patients.

Case Report - A 9.6 year old girl from a village near Aurangabad presented with complaints of gaining weight since 3- 4 years, night blindness, polydactyly, sluggish behavior, scholastic backwardness, and history of developmental delay. She was the product of a 3rd degree consanguineous marriage; one of twins delivered by LSCS, with birth weight 700 gm, needing NICU care for 15 days. She had undergone surgery twice for post-axial polydactyly in both hands, with no other major illness in past. The other twin girl had no obvious clinical abnormalities. Father was obese with family history of obesity, hypertension and thyroid disorders. On examination, she was obese - truncal obesity with waist circumference 70 cm (75-85th centile), with acanthosis nigricans, dysmorphism (small forehead) and retinitis pigmentosa; BP was normal; height was appropriate for target height (10th-25thpercentile). Intelligence Quotient was 61-67. On investigation, she had insulin resistance, dyslipidemia, Vitamin D deficiency, normal A1c, thyroid function and CBC. Next Generation Sequencing confirmed the diagnosis of BBS. Clinical Exome Sequencing was performed.

Compound heterozygous variant in BBS4 gene: Exon 6 – c.346 A >T and Exon 12 – c.953 dup A (pathogenic variant) was present. Another heterozygous variant was found in PRPF4 gene exon 11 C. 1138 G>A (variant of unknown significance). Genetic counseling was done, and the family advised about diet, exercise and behavioral therapy; D3 supplementation was started. After 14 mo, we found that lifestyle modification was being followed by the family, she was more active, weight stabilized from 31.7 kg to 32.5 kg, height increased 5 cm (117 to122 cm), BMI reduced by 1.4 from 23.2 to 21.8; waist circumference from 75 to 70 cm. Since height gain (5 cm in 14 months) was unsatisfactory, we investigated further: CBC and TFT were normal, but stimulated GH was low (1.6 ng/ml). Family was counseled and GH therapy started. Reviewed after 14 months, her height gain was 9.5 cm. Due to the home confinement during the current pandemic, she has gained 5.7 kg, but BMI remains the same due to height gain; waist circumference has reduced by 4 cm.

Discussion - A case report of 5 patients (3 girls, 2 boys) in a family of 12 sibs included one boy who had low growth hormone levels and grew 5.5 cm in 9 months of GH treatment (5). Our patient was also GH deficient and benefited with GH therapy, which may help not only in improving the metabolic parameters but also improving the level of confidence. Each patient with BBS should be assessed by an endocrinologist, ophthalmologist, nephrologist, clinical geneticist, and dietician.

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Secondary obesity: Exogenous Cushing Syndrome

Prof Vrind Kumar Bhardwaj
Former Head, Dept of Pediatrics, NSCB Medical College, Jabalpur

Cushing's syndrome due to exogenous glucocorticoid administration is far more common than endogenous hypercortisolemia. The life-saving potential of glucocorticoids is highlighted in the ongoing Covid 19 pandemic. Glucocorticoids play a crucial role in decreasing mortality due to the cytokine storm, but they are also responsible for at least some cases of newly detected hyperglycemia and high glycemic levels seen in Covid19 patients. More worrisome is the emergence of rhinocerebral mucormycosis (RCM) in patients who recovered from Covid 19. One reason for the RCM epidemic is the immunosuppression caused by prolonged use of glucocorticoids.

There is widespread misuse of glucocorticoids, many a times by patients/ parents. Misuse is undesirable at every age, but most distressing in infants and young children.

There are very few indications for glucocorticoid use in infants, viz. congenital adrenal hyperplasia (CAH), atopic dermatitis, congenital nephrotic syndrome, but none of them require long term use of oral betamethasone. CAH is an indication for long term glucocorticoid use in young children, but the drug of choice is oral hydrocortisone. Unfortunately, hydrocortisone is not available in drops or syrup formulation, while betamethasone and prednisolone are. It is particularly surprising that betamethasone, a very potent molecule (25 times more potent than hydrocortisone) with no indication for long term use in infants and young children, is available as drops containing 0.5 mg per ml. A child who is given 10 drops a day, receives 0.5 mg of betamethasone, equivalent to 12.5 mg of hydrocortisone. For a one year old 10 kg, 75 cm infant whose body surface area is approximately 0.5 m^2, 1 ml/ day of betamethasone drops translates into 25 mg/m^2/day of hydrocortisone, which is almost 3 times higher than the physiological dose. Betamethasone is sweet in taste, and being formulated in a flavored syrup base, it is very palatable. The quick resolution of cough, cold and fever, with improvement in appetite, impresses the parents; the ready availability at an affordable cost (15 ml bottle of betamethasone drops cost Rs 15/-) makes it suitable for misuse.

There is need for health authorities to regulate the necessity and availability of this unscientific preparation, so that its misuse is stopped.

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Figure: Image of child with exogenous Cushing syndrome
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Drug Corner - Liraglutide for management of pediatric obesity

Dr Pragya Mangla
Assistant Professor, Department of Endocrinology, GTB Hospital, Delhi

Introduction: Childhood obesity is one of the most burning public health issues at present. Even with intense lifestyle modifications, most obese children, especially adolescents, find it hard to lose weight substantially and sustainably; and ultimately land up as obese adults with significant co-morbidities. The use of approved drugs like orlistat and phentermine is limited due to their variable effect on weight loss, compounded with unacceptable side effects and poor tolerability. Another drug, metformin, is often used off-label for treatment of obesity in children with insulin resistance, with modest effects on weight, body composition and glucose homeostasis [1]. Recently, liraglutide has been approved as an adjunctive therapy to a reduced-calorie diet and greater physical activity in adolescents who are obese, as defined by specific body mass index (BMI) cut-offs for age and sex that correspond to a BMI of 30 kg/m^2 or higher for adults, and who weigh > 60 kg, or have a BMI of 27 kg/m^2 or higher, with at least one weight-related condition [2]. This drug was initially approved by US Food and Drug Administration (FDA) for treatment of type 2 diabetes in adults in 2005 and pediatric patients ≥10 years in 2019; and in 2014 as an adjunctive therapy for chronic weight management in adults.

Pharmacology: Liraglutide is a Glucagon-Like Peptide-1 receptor agonist (GLP-1RA), which has 97% amino acid sequence homology to native human GLP-1. Endogenous GLP-1 gets rapidly degraded by dipeptidyl peptidase-4 (DPP-4) and neutral endopeptidases (NEP). Liraglutide was created by recombinant DNA technology, by substituting arginine for lysine at position 34 in the GLP-1 peptide. Adding a palmitic acid (C-16 fatty acid) chain with a glutamic acid spacer on the remaining lysine residue at position 26 helped to improve the pharmacokinetic effects. After a single subcutaneous injection, liraglutide exhibits its maximum concentration after 8 to 12 hours. It has a half-life of 13 hours compared to 1-2 min of endogenous GLP-1. Liraglutide is highly protein bound (> 98%) with a large volume of distribution. The receptors for GLP-1 are found in pancreatic alpha and beta cells, the central and peripheral nervous systems, heart, lungs, and gastrointestinal (GI) tract. It causes cAMP mediated glucose dependent secretion of insulin, decreases excessive glucagon release, and increases sensitivity of insulin. It delays gastric emptying, promotes post-prandial satiety, suppresses appetite and thus helps in reduction of body weight. It also increases heart rate [3].

Pharmacokinetics and pharmacodynamics [4-8]**:** In obesity studies, individual and mean liraglutide concentration values appeared to be slightly higher in males and children (7-11 years); the concentrations were similar in adolescents and adults when adjusted to the 3.0 mg dose. However, when exposure was adjusted for differences in body weight, it came out similar across all age groups. Liraglutide concentrations were not different in adolescents in different stages of pubertal development (Tanner stage 2/3 vs. Tanner stage 4/5). An exposure-response relationship was seen in both adolescents and adults.

Dosage, administration and storage [4-9]**:** Liraglutide is available as 6 mg/ml prefilled 3 ml pen. It has to be given daily subcutaneously. Weekly stepwise escalation of doses from 0.6 mg to 3 mg, with close monitoring for side effects, helps in better GI tolerability. In studies on children (7-11 years), the dose was initiated at 0.3 mg daily and escalated till 1.2 mg in weekly increments of 0.3 mg, then followed with 0.6 mg weekly increments to a maximum dose of 3.0 mg or maximum tolerated dose. If the doses are missed for > 3 days, weekly stepwise escalation will be needed again. The injection can be given in thighs, arms or abdomen. It should be given ideally at the same time every day, irrespective of the meal time. New unused pens should be stored at 2-8 ; after first use, pens can be kept in the refrigerator (2-8) or at room temperature (15-30). In-use pens should not be used after 30 days. Safe injection practice should be followed. Needles should be discarded in a sharps' container.

Effect on weight and glycemic parameters: In studies including mostly adolescents, after liraglutide treatment of 20-56 weeks duration, as compared to placebo, a modest reduction was observed for BMI [mean difference, −1.55 (95% CI -2.41, -0.70)], BMI z-score [−0.17 (-0.28, -0.06)] and body weight [−1.51 kg (-2.85, -0.17)]. After discontinuation, a greater increase in the BMI standard-deviation score was observed with liraglutide than with placebo [4]. The proportion of patients achieving at least 5% weight loss increased with increase in liraglutide exposure. No apparent differences were seen in growth or pubertal development [8]. Glycemic control improved in those with proven insulin resistance. No improvement in lipid profile was seen; only a few studies have shown a modest decrease in systolic blood pressure.

Specifically in children, after 7-8 weeks of liraglutide treatment, a statistically significant reduction in BMI Z score as compared to placebo (− 0.3 vs. −0.01; P = 0.0062) was observed, though the difference between body weight changes (-0.52 kg vs. +0.98 kg) was not significant. A minor reduction in FPG was observed in the liraglutide treated group, though there was no significant difference in the levels of serum insulin and HbA1c [5].

Adverse drug effects: On liraglutide therapy, gastrointestinal side effects like nausea, vomiting and abdominal pain, diarrhea and gastroenteritis are common. Other side effects are dizziness and hypoglycemia. Both gastrointestinal and endocrinological complications increase with dose escalation. In studies, side effects have led to treatment discontinuation in both the treatment and placebo groups, though the rate and severity of side effects were not significantly different. High transaminases and marginally elevated levels of lipase and sometimes amylase have been observed in children during treatment. Only one case of pancreatitis has been observed. In others, the levels resolved without any active intervention. It should be discontinued promptly in confirmed pancreatitis. Other side effects seen were local injection site pain, induration and pruritus. [4, 8]

Contraindications, warnings and precautions: This drug has been studied for very short term (8 weeks) in children 7-11 years of age; more studies are needed before it can be safely approved for use in this age group [5]. Very few studies have evaluated the effect of liraglutide (with and without lifestyle intervention) with any other anti-obesity medication; more studies are required in this area [10].
As liraglutide delays gastric emptying, it can affect the absorption of concomitantly administered oral drugs. Liraglutide should be used with caution in children and adolescents with psychiatric illnesses, as unusual changes in mood or behavior, and emergence or worsening of depression and suicidal thoughts have been seen. It should be avoided in patients with a history of suicidal attempts or active suicidal ideation.
Liraglutide is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in those with multiple endocrine neoplasia syndrome type-2 (MEN-2). Though in studies on mice and rats, increased incidence of MTC have been seen, this was not observed in human studies. In adolescent studies, calcitonin levels were found to be normal. [9] It is also contraindicated in pregnancy and in persons with known hypersensitivity to liraglutide and its excipients.

Conclusion: Liraglutide can be an effective drug along with reduced-calorie diet and greater physical activity in management of obesity in adolescents and children.

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Pedendoscan on Obesity

Dr Aashima Dabas
Associate Professor, Dept. of Pediatrics, Maulana Azad Medical College, New Delhi.

Hong J, Bo T, Xi L, *et al*. Reversal of functional brain activity related to gut microbiome and hormones after VSG surgery in patients with obesity. J Clin Endocrinol Metab. 2021 May 5:dgab297. doi: 10.1210/clinem/dgab297. Epub ahead of print.

Vertical sleeve gastrectomy (VSG) is an acceptable modality of bariatric surgery which reduces food intake and energy absorption. Similar to Roux-en-Y Gastric Bypass, another commonly performed bariatric surgery, VSG had also been shown on functional MRI (fMRI), to affect the neurohormonal control of satiety in the striatum, prefrontal cortex, cuneus and insula regions of the brain. The increased levels of glucagon-like-peptide 1 (GLP-1) and reduced ghrelin levels post-surgery in turn regulate the appetite center in the brain.

The present study enrolled 36 obese patients and compared them with 26 normal weight (NW) healthy controls. A total of 32 patients underwent VSG and 19 completed four months of follow-up. A food (eating) questionnaire was administered to all participants. The subjects underwent fMRI; blood testing for OGTT, GLP-1, ghrelin, leptin; and fecal sample collection and DNA extraction for functional profiling of microbiota. The results showed that the restraint score increased, with decrease in disinhibition and hunger score, post-VSG in obese subjects, suggesting an effect of VSG on cognitive control ability and disinhibition to feeding. FMRI showed comparable changes in post-VSG and NW subjects, who otherwise showed significant differences in the pre-VSG phase. The levels of GLP-1 were higher, and of ghrelin and leptin lower in the post-VSG than the pre-VSG state ($P < 0.001$). The AUCs of these hormones correlated with the fMRI parameters and eating questionnaire scores. The microbiota also changed post-VSG with an abundance of *B. thetaiotaomicron*, *Akkermansia muciniphila, Clostridum* and *Streptococcus.* These positively correlated with AUC of GLP-1, fMRI, and eating questionnaire, but not with other hormone levels. All these species were involved in production of short-chain fatty acids also suggesting their functional relevance in post-VSG patients. The authors concluded that VSG restored elevated functional connectivities with the right putamen and affected the neurohormonal regulation of appetite. This study provides objective evidence on the gut-brain circuit; however, the causality needs to be validated in further studies.

Ryan PM, Seltzer S, Hayward NE, Avelar Rodriguez D, Sless RT, Hawkes CP. Safety and Efficacy of GLP-1 Receptor Agonists in Children and Adolescents with Obesity: A Meta-Analysis. J Pediatr. 2021 May 10:S0022-3476(21)00432-7. doi: 10.1016/j.jpeds.2021.05.009. Epub ahead of print.

GLP-1 agonists (exenatide and liraglutide) are increasingly been researched for their use in pediatric obesity. This meta-analysis evaluated the effect of these agents on the weight, BMI, cardiometabolic and gastrointestinal (GI) effects in children with obesity. The Web of Science, PubMed/MEDLINE, and Scopus databases were searched for randomized placebo-controlled trials with either of these two drugs. Studies which enrolled subjects with type 1 diabetes, genetic obesity syndromes, hypothyroidism or eating disorders were excluded. The effect on weight/ BMI and cardiometabolic control was the primary outcome, while GI effects were the secondary outcomes. The meta-analysis compared nine studies (six with liraglutide) with 574 subjects with mean (SD) age of 14.15 (2.16) years. Only three studies provided details of lifestyle interventions which were administered to both placebo and case groups.

The dose of exenatide varied from 2 mcg to 10 mcg daily in three studies. For liraglutide, a 0.3 - 0.6 mg starting dose was escalated to 1.2 - 3 mg daily during the intervention period. The duration of intervention in seven studies varied from 5-26 weeks; two studies had a longer intervention period of 52-56 weeks. There was reduction in weight (mean difference [MD] -1.50 [-2.50, -0.50] kg), in BMI (MD -1.24 [-1.71, -0.77] kg/m^2, I^2 0%), and in BMI z-score (MD -0.14 [-0.23, -0.06], I^2 43%) reported with the use of these agents. With lifestyle intervention, weight reduction improved to -4.25 kg (-6.31, -2.20; I^2 0%), (subgroup heterogeneity I^2 90.1%) and BMI reduction improved to -1.60 kg/m2 (-2.32, -0.88; I^2 0%), (subgroup heterogeneity I2 41.1%). There was a decrease in systolic blood pressure (MD -2.30 [-4.11, -0.49] mmHg; I^2 0%), with a significant reduction in HbA1c (MD -1.05 [-1.93, -0.18, I^2 76%) in children with underlying insulin resistance, without any effect on fasting plasma glucose -16.26 [-41.23, 8.71] mg/dL, I^2 76%. There was no beneficial effect on lipid profile. An increased risk of nausea (risk ratio 2.11 [1.44,3.09]; I^2 0%) as a GI effect was reported.

The meta-analysis concluded that short-term (<3 months) use of GLP-1 agonists achieved a reduction in weight and BMI, with improvement in glycemic profile in obese subjects with insulin resistance. There was no difference in efficacy of exenatide and liraglutide in obese children, unlike data in adults. However, long term outcomes and rebound weight increase after stoppage of these drugs was not discussed. The variability in dosages of the drugs used also accounted for the heterogenicity of the results.

Davis JN, Pérez A, Asigbee FM, *et al*. School-based gardening, cooking and nutrition intervention increased vegetable intake but did not reduce BMI: Texas sprouts - a cluster randomized controlled trial. Int J Behav Nutr Phys Act. 2021;18(1):18. doi: 10.1186/s12966-021-01087-x.

The dismal fruit-vegetable intake in school children in the US is usually ascribed to lack of exposure to fruits and vegetables, with increasing cost and limited access to fresh vegetables. School gardens are being promoted as an educational strategy to promote healthier eating habits, food literacy and psychological well-being. This was a cluster-randomized controlled trial which recruited school children between 3rd-5th grade from 16 schools for a 12 month period. The students were involved in 18 60-min sessions on gardening, nutrition and cooking. Parental sessions (nine 60-min sessions) were focused additionally on importance of family eating, healthy shopping, and increasing access of healthy foods. The control group did not receive the intervention at the concurrent period but after 12 months in the delayed phase. A total of 3135 children with mean age of 9.2 years were enrolled, of which 2721 (intervention group n=1412) completed the study. The mean (SD) change in frequency of vegetable intake improved more in the intervention group 0.46 (0.25) than the control group 0.03 (0.23); P=0.02. There was no difference in the anthropometry, percentage body fat, blood pressure or intake of sugar-sweetened beverages; P > 0.05. The authors concluded that the role of this behavioral intervention, though not evident is the short observation period of the study, may have a long-term beneficial effect on adiposity.

Amat-Bou M, Garcia-Ribera S, Climent E, *et al*. Effects of *Bifidobacterium animalis* Subsp. *lactis* (BPL1) Supplementation in Children and Adolescents with Prader-Willi Syndrome: A Randomized Crossover Trial. Nutrients. 2020;12(10):3123. doi: 10.3390/nu12103123.

Prader Willi Syndrome (PWS) is one of the commonest genetic obesity syndromes, where obesity and mental health problems are the major challenges to treat. The role of gut microbiota has been earlier explored, with few beneficial outcomes in childhood and adult obesity and metabolic syndrome. This cross-over randomized controlled trial investigated children 2-19 years of age with genetically confirmed PWS for effect of this probiotic on adiposity and other metabolic parameters. Those with history of bariatric surgery or with other associated medical problems were excluded.

The intervention group received capsules containing 100 mg of *Bifidobacterium animalis* subsp. *lactis* (BPL1, CECT8145, 10^{10} colony forming units) with 200 mg of maltodextrin, while the placebo group received capsules with 200 mg maltodextrin, for the first 12 weeks period. This was followed by a 12 weeks washout period, then by crossover of treatment for 12 weeks duration. Adiposity measured by DXA was the main outcome measure; other outcomes were weight, height, BMI and metabolic profile. Stool samples were collected for DNA profiling of microbiota. All outcomes were collected at baseline and three other time points as 12 weeks interval each. A total of 35 subjects with mean age 10.4 years (17 in group A and 18 in group B) completed the study. The baseline characteristics were similar. An insignificant treatment effect (95% CI) of probiotic was noted in overall body fat % −0.18 (−1.08, 0.73) and abdominal fat % −0.23 (−0.53, 0.06). The treatment effect was significant in older children > 4.5 years for abdominal fat % −0.33 (−0.59, −0.06); P= 0.017. The treatment effect was significant for reduction of insulin −4.44 (−8.51, −0.38); P=0.033 and HOMA-IR levels −1.07 (−2.04, −0.10); P=0.031**,** but did not show any significant effect on energy consumption, or other metabolic parameters. There were no significant adverse events reported. The above trial suggested modest improvement in adiposity after short-term evaluation of BPL1 probiotic consumption in PWS, indicating the need for further long term studies.

Di Sessa A, Guarino S, Umano GR, *et al*. MAFLD in Obese Children: A Challenging Definition. Children (Basel). 2021 Mar 23;8(3):247. doi: 10.3390/children8030247.

Metabolic (dysfunction) associated fatty liver disease (MAFLD) has replaced the use of term NAFLD for signifying hepatic steatosis associated with a metabolic condition like obesity. Terms used earlier like metabolically healthy and unhealthy obesity have their own fallacies. MAFLD is diagnosed if there is radiological evidence of hepatic steatosis, with at least one of the following criteria: overweight/obesity, type 2 diabetes (T2D), or evidence of metabolic dysregulation defined as the presence of two or more of these conditions: (1) Waist circumference > 95^{th} percentile for age and sex, (2) blood pressure > 95^{th} percentile for age, sex, and height, (3) triglycerides >150 mg/dL, (4) HDL < 40 mg/dl, (5) prediabetes, (6) homeostasis model assessment -insulin resistance (HOMA-IR) score >2.5, (7) C-reactive protein (CRP) levels > 2 mg/L.

This study reviewed the retrospective records of 954 obese children and adolescents and analyzed them in three subgroups. Group 1 (n=142) where subjects were obese without NAFLD or metabolic dysfunction; Group II (n=139) where subjects were obese with NAFLD; and Group III (n=673) where obese subjects had NAFLD and metabolic dysfunction, fulfilling criteria of MAFLD. The BMI SDS and WHR were maximum in group III followed by Group II and I (P<0.001). Subjects in Group III showed higher proportion of prediabetes, elevated HOMA-IR, transaminases, triglycerides and lower HDL-C (P<0.001). The proportion of subjects with PNPLA3 gene polymorphism, the most important risk polymorphism for NAFLD, was maximum in group III (58.6%), followed by group I (51.9%) and II (40.3%) (P<0.001). The authors suggested the need for a more accurate definition in the context of pediatric obesity. These findings are similar to data on young obese adults, of severe hepatic steatosis even without MAFLD criteria. Moreover, all patients with NAFLD did not develop metabolic dysfunction.

Pfinder M, Heise TL, Hilton Boon M, *et al*. Taxation of unprocessed sugar or sugar-added foods for reducing their consumption and preventing obesity or other adverse health outcomes. Cochrane Database Syst Rev. 2020 Apr 9;4(4):CD012333. doi: 10.1002/14651858.CD012333.pub2.

Unprocessed sugar and sugar-added foods are unhealthy carbohydrates that may increase the risk of adverse metabolic outcomes. A few countries in Europe and the US have implemented food taxes on these products. This systematic review searched for the effect of taxation of food products with added sugars (bakery and confectionary) on the incidence of overweight/ obesity and diet-related health outcomes in children and adults. The primary outcome was to evaluate consumption pattern of sugar containing food products and overweight/ obesity, with secondary outcomes as substitution and diet, expenditure, demand and others. A total of 24,454 records were line-listed out of which 11 studies were found relevant. There was no study which reported tax on unprocessed sugar. A single study on 42,210 households which the Hungarian Household Budget and Living Conditions Survey, was included. The study reported a decrease in consumption of taxed sugar-containing products by 4% (standardized mean difference -0.04, 95% CI -0.07, -0.01). The authors concluded there was insufficient evidence of taxation in reducing consumption of sugary products or in decreasing obesity.

Bessell E, Maunder A, Lauche R, *et al.* Efficacy of dietary supplements containing isolated organic compounds for weight loss: a systematic review and meta-analysis of randomised placebo-controlled trials. *Int J Obes* (2021). https://doi.org/10.1038/s41366-021-00839-w

Dietary supplements are frequent fads for achieving weight loss and a healthier body. They usually contain organic substances like chitosan, glucomannan, conjugated linoleic acid, green tea/ green coffee extracts or guargum. This article was a systematic review with meta-analysis to evaluate the efficacy of these dietary supplements in achieving weight loss. Sixty seven placebo-controlled RCTs from four electronic databases (Medline, Embase, Web of Science, Cinahl) to evaluate the effect of chitosan, glucomannan, conjugated linoleic acid, fructans, and multiple ingredient supplements on weight loss were included. The meta-analysis included adults with elevated BMI. The duration of the intervention was variable from 8-52 weeks. A modest (< 2.5 kg) but significant weight reduction (mean reduction, 95% CI) was observed with chitosan (−1.84 kg; 95% CI −2.79, −0.88; $p < 0.01$), glucomannan (−1.27 kg; 95%CI −2.45, −0.09; $p = 0.04$), and conjugated linoleic acid (−1.08 kg; 95%CI −1.61, −0.55; $p < 0.01$); there was no significant difference with fructans. The authors summarized that evidence of these isolated organic compounds in achieving significant weight loss was inconclusive.

PATIENT CORNER - ADOLESCENT WITH PRADER WILLI SYNDROME WINS BIG AT BEAUTY PAGEANT

Dr Priya Siva and Dr Hemchand K Prasad
Mehta Hospital, Chennai

Miss Anna Hankins is a 17 year old from Mississippi USA who has Prader Willi syndrome (PWS). She won the “Amazing Mississippi” beauty pageant state title three times. The problems faced by adolescents with PWS include constant hunger, slowed metabolism, and impaired cognition, but have not been an impediment to Anna Hankins’ success. Her co-morbidities include hypertension, heart failure and sleep apnea syndrome; she requires constant oxygen support. In spite of this, she shared her talent on stage and faced the interview by the judges boldly. Her achievement is an inspiration for children with PWS and doctors caring for them.

Reference

Mazziotta Julie. 15-Year-Old with Rare Disorder That Leaves Her 'Constantly Hungry' Wins Beauty Pageant. People.com; Health; March 28, 2018. Available at http://people.com/health/beauty-paegent-winner-prader-willi -syndrome/ Accessed on:28.5.2021

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HISTORY CORNER

Dr Nikhil Lohiya
Consultant Paediatric Endocrinologist, Silver Lining Pediatric Super Specialty Centre, Nagpur

Douglas Coleman (1931-2014)

Douglas Coleman was born in Stratford, Ontario, the only child of impoverished parents. He finished high school and attended college at McMaster University in Hamilton, Ontario where he also met the love of his life and future wife, Beverly Benallick, the only female chemistry major. Douglas attended graduate school at the University of Wisconsin in Madison where he pursued his interest in biochemistry in the laboratory of Professor Carl Baumann. He received his PhD in 1958 and accepted a position at The Jackson Laboratory in Bar Harbor, Maine (USA) where he spent his entire career.

In the 1960s he became interested in two strains of obese mice: ob/ob and db/db. While both of these mice strains are always hungry (hyperphagia) and consequently massively obese, the ob and db mutations are located on different chromosomes. The experiments during those days proved that diabetes is due to the result of insulin utilisation and genetics can have a profound effect on the disease. He wondered whether there was some circulating factor that controlled obesity. To find that factor he used a technique called parabiosis, where he linked the blood supplies of two mice by surgical skin-to-skin anastomosis.

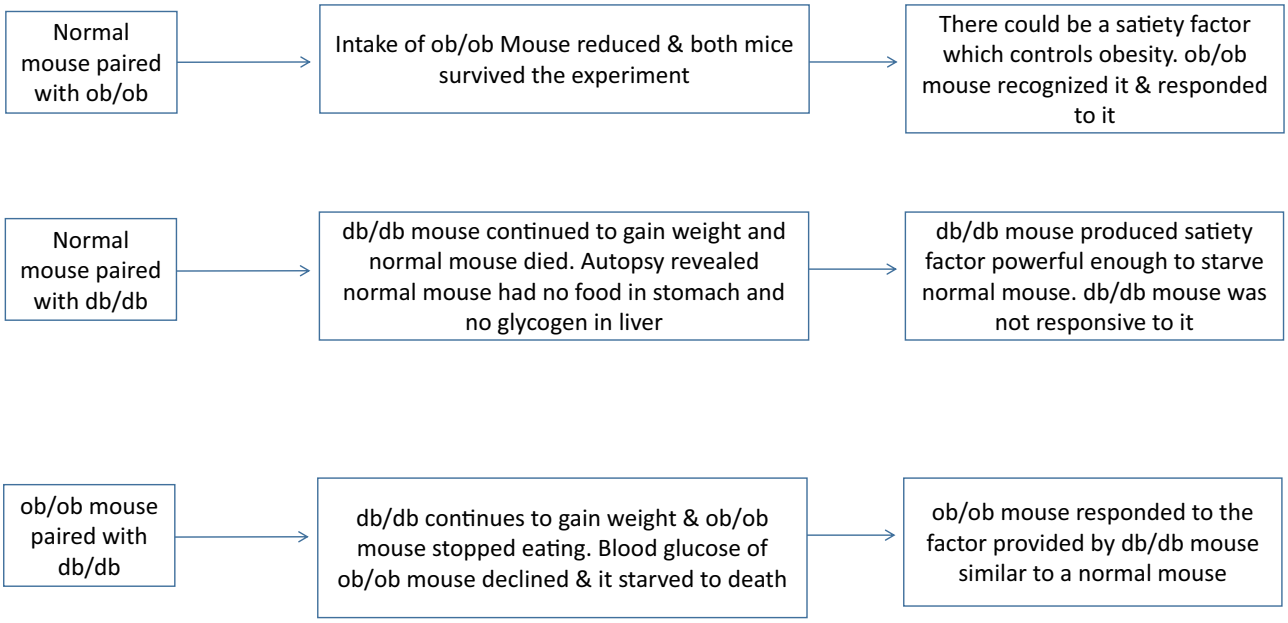

Image describing the experiment carried out by Coleman in normal, *ob/ob* & *db/db* mice by parabiosis.
The above experiment concluded that ob/ob mice respond to the satiety factor but could not produce it. On the other hand, the *db/db* mice produce the satiety factor in excess but do not respond to it, probably due to the lack of receptor.

He received the Claude Bernard Award from the European Diabetes Federation, but largely these discoveries were dismissed at the time. People working in the field of obesity felt that mice were overweight because of their behavior of overeating, not due to a genetic predisposition. Douglas correctly predicted that the factor is produced by adipose tissue, but was not able to isolate it. Decades later, in 1994, Dr Jeffrey Friedman and co-workers identified the satiety factor as a hormone, leptin; subsequently the leptin receptor was also identified, and the predictions made by the parabiosis experiments were proven.

Douglas was elected to the National Academy of Sciences in 1998 and received the Gairdner Foundation International Award (2005), the Shaw Prize (2009), the Albert Lasker Award for Basic Medical Research (2010), the King Faisal International Prize for Medicine (2013) and the BBVA Foundation Frontiers of Knowledge Award (2013).

He enjoyed working independently. His laboratory consisted primarily of himself and a single high school educated technician. Although he mentored one or two high school students each summer, he had only one graduate student and very few postdoctoral fellows during his career. He believed that because the public (through the NIH) paid for his research, the public owned his discoveries and, therefore, like many scientists of his generation, he had mixed feelings about patenting scientific discoveries for personal gain. Indeed, partly motivated by this line of thinking, he donated all of his scientific prize money to various charities.

He retired early in 1993 and made a clean break in his career, only returning to the laboratory to use the fitness centre. He entered retirement with great enthusiasm and spent his final years travelling and working on the town planning board as well as with forestry and conservation groups.
Douglas Coleman certainly left an impact on the way obesity is approached.

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BIOCHEMISTRY CORNER

Dr Nikhil Lohiya
Consultant Pediatric Endocrinologist, Silver Lining Pediatric Super Specialty Centre, Nagpur

A 17 year old girl presented with complaints of excessive weight gain and irregular menses. Her paternal grandfather and father had type 1 diabetes. She was 164 cm, 70 kg, BMI 26.8 (obese), waist circumference 91 cm. She had dorsal fat pad, hirsutism and round facies. Her initial work up revealed ACTH 76 pg/ml (6 – 48 pg/ml), serum cortisol 22 ug/dL (8.0 – 19 ug/dL) and normal fasting and PP blood glucose. She was referred for evaluation of Cushing syndrome. On further probing, she revealed that she was on combined estrogen and progesterone pills (OCP) for irregular menses and PCOS. Hence, before proceeding ahead, the hormonal therapy was stopped and the girl recalled after 6 weeks. Repeat investigations were normal: cortisol 15 ug/ml, ACTH 35 pg/ml; overnight dexamethasone suppression test showed cortisol 0.5 ng/ml. USG was suggestive of polycystic ovaries. On further follow-up, she lost weight, with BMI coming down to 22.4 kg/m^2, and resultant improvement in the frequency of her menstrual cycles.

Use of OCP leads to an increase in total cortisol levels by increasing levels of cortisol binding globulin, without altering the unbound fraction of cortisol (1). While measuring serum cortisol, it is the total cortisol which is assessed. The elevation of total cortisol depends on the dose of estrogen. Hence the Endocrine Society Guidelines recommend withdrawing OCP 6 weeks before testing or retesting (2). Similarly, many other drugs also interfere with serum cortisol levels by acting as inhibitors or inducers of *CYP3A4*. Itraconazole, Ritonavir, Aprepitant/ fosaprepitant, Fluoxetine, Diltiazem, Cimetidine are inhibitors of *CYP3A4.* Phenobarbitone, Carbamazepine, Ethosuximide, Phenytoin, Primidone, Pioglitazone, Rifampin, and Rifapentine are inducers of *CYP3A*. Medications increasing cortisol binding protein are estrogen and mitotane. Carbamazepine, synthetic glucocorticoids and fenofibrate increase urinary free cortisol levels. Hence, before evaluating for Cushing syndrome, one should take a detailed drug history.
Another point to notice is the initial high ACTH levels. In women with abdominal obesity there is an increased activity of the HPA axis (3)**.** There is increasing evidence which suggests that the cortisol clearance rates in patients with abdominal obesity are higher. This probably leads to a negative feedback on pituitary ACTH release (4).

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ISPAE-Academic and Clinical Education Series (ACES) - UPDATE

Dr Sirisha Kusuma B
Coordinator April, May, June 2021
Dr Dhivya Lakshmi
Coordinator Jan, Feb, March 2021

ISPAE's flagship academic program of 2021, the Academic and Clinical Education Series (ACES), is being conducted virtually on the last Saturday of every month since January 2021. With more than a 100 pediatric endocrinologists and trainees across India attending each session on the virtual platform, and another 50 watching it via ISPAE's YouTube channel, ACES has become an instant success, popular not only in India, but also with our neighboring colleagues from Pakistan and Sri Lanka as well.

In March, the theme of the program was "Thyroid". "An interesting case of Congenital Goitre" was presented by Dr Krishna Mori, moderated by Dr Raghupathy; and "An autonomous functional thyroid nodule" presented by Dr Dhanya Soodhana, moderated by Dr Rajni Sharma. Then followed engaging lectures on "An approach to subclinical hypothyroidism in children" by Dr Shriraam Mahadevan, and "An update on the management of thyroid nodules in children" by Dr Ari Wassner of Boston.

In April, the theme was "Pediatric Diabetes". We had two interesting cases: "A difficult to manage Type 2 diabetes" presented by Dr Navin Narayanan, moderated by Dr Nihal Thomas and "A rare cutaneous manifestation of T1D" by Dr Tejaswi, moderated by Dr Anju Virmani, following which Dr Sujoy Ghosh spoke on "T2D in children: What is new in management?". Then, Dr Linda DiMeglio, Indiana, US, gave insights into "Pediatric Diabetes: Insulin, Glucagon and future directions".

In May the theme was "Adrenal Gland". The cases were "A rare case of adrenal mass" presented by Dr Chirantap Oza, moderated by Dr Vijaya Sarathi, and "A short hyperpigmented girl with cyclical abdominal pain" presented by Dr Meenakshi BR, moderated by Dr Sudha Rao. This was followed by excellent lectures by Dr Anurag Lila on "Pediatric Cushing syndrome: Challenges in diagnosis and management", and Dr Tulay Guran, Turkey, on "Optimizing medical therapy in different forms of CAH".

The cases and lectures were received well by the attendees, who have been quite interactive in the Q&A sessions. We are looking forward to another exciting meeting on 26th June, with the theme "Pubertal disorders". We encourage you to visit our YouTube channel to access some of the cases and lectures from the last 5 meetings. The link to YouTube channel is available at the ISPAE official website: www.ispae.org.in

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PEARLS from ISPAE ACES meet on Childhood Diabetes

Dr Nikhil Lohiya
Consultant Pediatric Endocrinologist, Silver Lining Pediatric Super Specialty Centre, Kingsway Hospitals, Alexis Hospital, Nagpur

- Whenever there is disproportionate hepatomegaly with obesity, the differential diagnosis should be non-alcoholic fatty liver disease and genetic causes e.g. lipodystrophy. Body composition study can also help in such a scenario.
- Allostatic scoring system can suggest significant stress, which is suggestive of a diagnosis of type 2 diabetes.
- T2DM vs. MODY- heterozygous variants MODY 4 & 6 present with weight gain and diabetes.
- GAD-65 antibodies have a sensitivity of 80% to distinguish between T1DM and non-T1D.
- Beta cell dysfunction declines faster in adolescents or young children with T2DM. This can be preserved with weight loss.
- GLP-1 analogs should be started with the lowest possible dose, and gradually increased.
- The lipid profiles of T2DM and lipodystrophy can overlap. However, very high TGs i.e. > 500 mg/dL are more suggestive of lipodystrophy.
- Diabetes management in children is unique because there can be limitations in self-care, the insulin sensitivity changes with the physical age and sexual maturity, there is involvement of family dynamics, the developmental stages are different, they are neurologically vulnerable, and they can have adverse neurocognitive effects of diabetic ketoacidosis (DKA).
- In metabolically stable patients with T2DM, metformin can be used for treatment. However, if the HbA1c is high, and/or the patient is in DKA, insulin must be started.
- Insulin therapy may be needed early in children with T2DM to maintain tight glycemic control, otherwise the progression of complications is faster than in adults is faster.
- Degludec insulin can be very handy in children, and can be used in those over 1 year of age.
- Liraglutide is a promising GLP-1 analogue which can be used in children > 10 years of age for management of T2DM.

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Pearls from ISPAE ACES meet on Adrenal disorders

Dr Ravindra Kumar
In-charge Pediatric & Adolescent Endocrinology, North DMC Medical College & Hindu Rao Hospital, Delhi

Case presentations:

- Neurofibromatosis 1 may cause precocious puberty due to optic glioma in the suprasellar area.
- Hypertrichosis on the forehead and cheeks indicate steroid excess.
- In children with precocious puberty and hypertension, consider 11β hydroxylase deficiency, glucocorticoid resistance, adrenocortical tumor and neurofibromatosis type 1.
- Three possible reasons for hypertension in adrenocortical tumor are hypercortisolism, excess of aldosterone or deoxycorticosterone.
- Adrenocortical tumor is rare in children and follows a bimodal distribution, with peaks during the first and fourth decades; 65% present at age less than 5 years.
- Adrenal adenoma tends to secrete cortisol, while carcinoma secretes cortisol and androgen.
- 17-OHP could be high in adrenocortical tumor, and may cause confusion, hence values of testosterone and DHEAS must be checked in suspected cases.
- 46 XX females present with atypical genitalia ± salt losing crisis, while 46 XY males present with normal genitalia ± salt losing crisis.

Lecture:

- CAH because of 21 hydroxylase deficiency is deficient in glucocorticoid and mineralocorticoid hormone while sex hormone is in excess.Treatment is with oral hydrocortisone 10-15 mg/m^2/day in 3-4 divided doses.
- The aim of therapy for CAH is to normalize androstenedione and testosterone, not ACTH or 17OHP (aim for borderline high 17 OHP at 3-12 ng/ml). Hence, monitoring treatment should be with linear growth, weight, puberty and bone age, rather than ACTH or 17 OHP.
- The salt wasting form should be treated with fludrocortisone in the dose of 0.05-0.2 mg/day in two divided doses; monitored with electrolytes (at every visit) and renin (once a year).
- In children with advanced bone age, secondary central precocious puberty may occur, needing treatment with GnRH analog.
- In adolescents with hyperandrogenism, consider oral contraceptives and/or antiandrogens (spironolactone, flutamide, finasteride).
- Monitor for TART (Testicular Adrenal Rest Tumors) by periodic USG every 2-3 years in the adolescent age group.
- In 11β hydroxylase deficiency, in addition to glucocorticoid treatment and monitoring (same as in 21 hydroxylase deficiency), if hypertension is present, treat with mineralocorticoid receptor antagonist (spironolactone) or a calcium channel blocker.
- In 3β hydroxysteroid dehydrogenase deficiency, glucocorticoid, mineralocorticoid and sex hormone all are deficient, so sex hormone treatment may also be needed if they fail to progress through puberty.
- In 17α hydroxylase, 17,20 lyase, and P-450 oxidoreductase deficiency, sex steroid and glucocorticoid hormones are deficient, while mineralocorticoid is in excess. To manage these cases, glucocorticoid replacement is needed, and if hypertension is present, treatment with spironolactone or calcium channel blocker.

- In SCC/StAR deficiency CAH, glucocorticoid, mineralocorticoid and sex steroid all are deficient: hence physiological dose of glucocorticoid (6-8 mg/m^2/day); supplementation of salt in the newborn period, and mineralocorticoid replacement thereafter; and age and gender appropriate sex steroids at puberty are needed.
- The preferred steroid for treatment of CAH is hydrocortisone; prednisolone may be preferred for regulation of menstrual cycles or fertility induction; dexamethasone is indicated for fertility induction and TART treatment.
- Novel treatment strategies in the virilizing forms of CAH are modified released hydrocortisone (Plenadren, Chronocort) given orally, which provide good suppression of ACTH, and are in phase 3 trials.
- The hydrocortisone pump mimics the circadian rhythm but is expensive.
- Other trial drugs are CYP17A1 inhibitor (Abiraterone acetate) and CRH receptor type 1, used in adult women in addition to hydrocortisone.
- It is important to measure 17OHP in the early follicular phase in menstruating females.

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Pearls from ISPAE ACES meet on Thyroid disorders

Dr Aashima Dabas
Dept. of Pediatrics, Maulana Azad Medical College, New Delhi.

Sub clinical hypothyroidism

- Subclinical hypothyroidism (SCH) is a biochemical state of elevated TSH above the upper limit reference range, with normal levels of thyroid hormones, in the absence of any clinical features of hypothyroidism.
- The reversible causes of SCH are autoimmune thyroiditis, recovery from acute illness, obesity, laboratory error, or antithyroid drug administration.
- SCH could also be seen with underlying disease states like autoimmune thyroiditis, thyroid dysgenesis, hemithyroidectomy and Reidel's thyroiditis.
- An elevated TSH level should be documented in another sample before labelling as SCH. A morning sample in the fasting state is preferable for measurement of TSH.
- The natural history of SCH shows it to be a self-resolving state without risk of permanence of hypothyroidism, even with TSH levels up to 15 mIU/L.
- Children with underlying Down syndrome, Type 1 diabetes, Celiac disease and on antiepileptic drugs are at higher risk of SCH.
- Children with persistently elevated TSH >10 mIU/L and goiter, female gender or elevated serum anti thyroid peroxidise levels suggestive of autoimmunity will need a closer follow-up with repeat biochemical testing for thyroid function at 3-6 monthly intervals.
- Thyroxin replacement may be started in children with persistently elevated TSH, showing a progressive increase on follow-up.
- Thyroxin replacement is not recommended for improving neuropsychological outcomes in SCH.

Management of thyroid nodules in children

- Thyroid nodules are rare in children (0.76%) with relatively higher prevalence in females than males after puberty.
- The risk of cancer in a thyroid nodule is higher in a child than an adult.
- A detailed history for previous radiation exposure and family history of thyroid neoplasia should be taken in all children.
- Genetic syndromes like Familial adenosis Polyposis or MEN 2 and mutations in *PTEN, DICER1* genes are associated with an increased risk of thyroid cancer.
- A detailed head and neck examination should be performed for assessing lymphadenopathy.
- A TSH level should be measured in all thyroid nodules.
- An autonomous nodule which has low TSH, with uptake in the nodule, suppressing the rest of the thyroid which signifies low risk of malignancy.
- In case of a thyroid nodule if TSH is not low then ultrasound should be performed.
- Ultrasonographic features of a nodule like hypoechogenecity, being taller than wide, irregular margins, calcifications and abnormal lymph nodes signify higher risk for malignancy.
- The Thyroid Imaging Reporting and Data System (TI-RADS) used for scoring ultrasonographic features, is not sensitive in children, and may miss up to 22% of malignancies in them.
- Diffuse sclerosing variant of papillary thyroid carcinoma is commoner in children than adults, and has a good prognosis.

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MISCELLANEOUS INFORMATION USEFUL FOR ISPAE MEMBERS

Dr Aashima Dabas
Associate Professor, Dept of Pediatrics, Maulana Azad Medical College, New Delhi.

Announcement by the Indian Academy of Pediatrics (IAP)

1. Under the auspices of the IAP Action Plan 2021, IAP has come out with parental guidelines on identification, prevention and management of childhood overweight and OBESITY, prepared by Dr Rekha Harish, Dr Kavitha Sakumari, Dr Satish V Agarwal, and Dr Shilpa P Aroskar. Ten questions and answers are presented in a user friendly, practical, visually illustrative format to identify and tackle pediatric obesity and associated complications. The concepts covered include Body Mass Index calculation, lifestyle measures to be taken, healthy eating patterns to be adopted, physical activity guidelines, and preventive measures to be taken. **The link for the booklet is: https://iapindia.org/pdf/guideline-on-OBESITY-04032021.pdf**

2. Under the same IAP Action Plan 2021, guidelines for parents on normal growth "GROWTH: HOW SHOULD MY CHILD GROW" have been formulated, released and made freely available for use and dissemination. They were prepared by Dr Monika Sharma, Dr Anil Kumar, Dr Anju Seth and Dr Preeti Singh, specially written for parents seeking information on commonly encountered growth related issues in day-today life. The guidelines provide comprehensive answers to frequently asked questions on growth in children, sensitize parents on the importance of regular growth assessment and monitoring, help allay undue anxiety on misconceptions, and guide for early and timely referral. They serve as an important handy reckoner and a valuable pocket tool for parents for varied growth related issues. **The link for the booklet is: https://iapindia.org/pdf/Ch-22-IAP-Parental-Guide-for-How-My-Child-Grows.pdf.**

3. In the same IAP series of 101 guidelines for common pediatric problems, an early release was "CARE OF A CHILD WITH DIABETES MELLITUS", prepared by Dr Alok Gupta, Dr Anju Virmani, Dr Deepika Harit and Dr Neha Bhise Dighe. The format of 10 questions and answers covers basics of childhood diabetes care, including how diabetes occurs, how to suspect it, how to use insulin, home blood glucose monitoring and dose adjustment, simple diet concepts, encouraging regular play and exercise, handling going to school, acute and chronic complications, long term monitoring so these complications can be minimized, newer technologies available for diabetes care, and managing the stress of the condition. The booklet is brightly and profusely illustrated, making for easy understanding. A diabetes educator and a mother were consulted in the making of the Guidelines to ensure they are easily understood. **The link for the booklet is:https://iapindia.org/pdf/guidlines-for-Care-of-a-child-with-Diabetes-Mellitus.pdf**

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Activities by ISPAE members

Online event:
Childhood Obesity: Global Challenge on World Obesity Day:
Dr Priti H Phatale
The objective of this online event was to create public awareness about the exponential rise in childhood and adolescent obesity, and its future consequences. It was organized by Aurangabad Academy of Pediatrics, in association with All India Association of Advancing Research in Obesity (AIAARO) Maharashtra branch, Indian Medical Association Aurangabad, and Indian Medical Association Women's Wing Aurangabad. The scientific agenda was as per the World Obesity Day theme 2021 of "Every body needs Everybody". The event had 160 plus attendees, including overweight and obese children and their families, school teachers, nutritionists and authorities dealing with lifestyle diseases. The faculty for the workshop were childhood obesity specialist Dr Priti Hemant Phatale, pediatric endocrinologist Dr Sandhya Ulhas Kondpalle, nutritionist Ms Shilpa Joshi, activity specialist Dr Malhar Ganla, and child psychologist Dr Nidhi Navanadar.

Online CME:
Pediatric Diabetes:
Dr Hemchand K Prasad
An online CME was conducted by Mehta Multispeciality Hospitals India, the IAP Chennai city branch, and ISPAE on 16.5.2021 - 9 am to 1 pm - on various aspects of pediatric diabetes, including DKA, hypoglycemia, newer insulins, follow up care of type 1 diabetes (T1D), recent advances, CGMS, psychological aspects, nephropathy screening and social aspects of T1D. It was given positive feedback by the 250 members who registered for it, and 1 credit hour was awarded by the Tamil Nadu Medical Council.

Online CME:
Pediatric Endocrinology Emergencies:
Dr Deepa Anirudhan
IAP Kerala, ISPAE, and IAP Thrissur jointly organized a half day CME on Pediatric Endocrine Emergencies on 30th May 2021. The Presidential address was given by Dr TP Jayaraman, President of IAP Kerala. It was inaugurated by Dr Raghupathy, and addressed by Dr PSN Menon, Dr Shaila Bhattacharya, Dr Ganesh Jevalikar, Dr Veena V Nair, Dr Parvathy L, Dr Abraham Paulose and Dr Deepa Anirudhan. Interesting cases were presented by Dr Neethu, Dr Bivin, Dr Sithara (Residents) and Dr Vidhu Asok (Consultant Pediatrician, Calicut). The sessions were chaired by Dr Raghupathy, Dr PSN Menon, Dr Vijayakumar, Dr Riaz and Dr Sheeja Madhavan. More than 180 participants attended the well appreciated CME.

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Notes in Endocrinology by Dr Om J Lakhani

The current decade is the decade of "crowdsourcing", defined as "the practice of obtaining information or input into a task or project by enlisting the services of a large number of people".

Crowdsourcing has become a part of almost every field. The best example of crowdsourcing is "Wikipedia", a free digital encyclopedia written and edited by the common people; constantly updated by a vibrant community of people who support this movement.

Knowledge in the 21st century cannot be confined to physical books sitting on library shelves. Knowledge is more fluid in the digital space. It is often free, it is often crowdsourced, and it is constantly updated. At the same time, it is usually authentic because of the constant supervision by people who act as volunteer editors and peer reviewers.

Digital tools like "Roamresearch" and "Obsidian" have made it possible for all of us to develop our personal Wikipedia. You can call it a personal "digital garden" of knowledge curated by you, but available for all to see.

"Notes in Endocrinology" (available on the website www.endocrinology.co.in) is one such initiative of sharing our digital garden for all to read, share, criticize and update.

The idea is to become a one-stop shop for all the knowledge and updates in the field of Endocrinology. We have just started the first phase of this endeavour. The first step is to create a base on which we can build the library. This knowledge base is in a question and answer format, which makes it easy for people to read and learn, but also it is accessible for search engines, allowing more people to "stumble" upon our library.

Once we build a solid foundation, we will open the library for others to edit and contribute, making this a "Wikipedia of Endocrinology". This promises to become a living updated knowledge bank that will cater to all the future generations of doctors and researchers.

Please visit us at Endocrinology.co.in for "Notes in Endocrinology". It has just been a few months since we started, and we have already had more than 3000 unique visitors from 35 different countries around the world. Your suggestions, criticism, and comments are always welcome.

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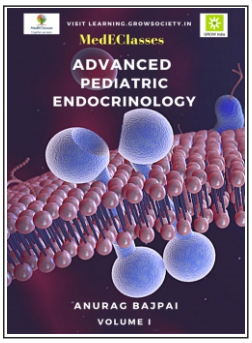
New Book release



Anurag Bajpai (Editor). MedEClasses Advanced Pediatric Endocrinology.
Publisher: MedEClasses Publications, April 2021
Volumes: Two, 63 chapters, 660 pages

MedEClasses Advanced Pediatric Endocrinology covers the entirety of Pediatric Endocrinology, with animated figures, approach, etiology, and management algorithms with illustrative cases. The two-volume book has 63 chapters across eight sections (Fundamentals, Pituitary, Adrenal, Cancer, Bone, Ovary, Testis, and Metabolic disorders). The Fundamentals sections include chapters on Endocrine Physiology, Pathology, Diagnostics, Therapeutics, Research, and Genetics, forming the basis of rational clinical assessment and management. Each section starts with chapters on physiology and assessment, before progressing to syndromic disorders. The chapters are organized into pathophysiology, pointers and criteria, algorithmic etiology, step-wise assessment, algorithmic approach, guideline-based management, illustrative case scenarios, and learning points. Extensive use of animated figures (over 500), algorithms (over 100), and cases (over 600) make the understanding of complicated endocrine disorders easy. The book is recommended for pediatric and adult endocrinology trainees and practitioners, and pediatricians with an interest in pediatric endocrinology.

Available at https://learning.growsociety.in/books.
E version at Amazon and Google Play store.
Price- INR 6000

Publication / Paper presentations by ISPAE members

1. Dr Bhanu K Bhakhri, Additional Professor of Pediatrics, SSPHPGTI Noida, UP, India

- Rai R, Singh DK, Bhakhri BK. Transient hypothyroxinemia of prematurity and its risk factors in an extramural neonatal intensive care unit. Arch Endocrinol Metab. 2021 Apr 27:2359-3997000000360. doi: 10.20945/2359-3997000000360. Online ahead of print.

- Goyal R, Bhakhri BK, Goyal JP, Lohiya N, Khadilkar V. Appropriateness of Lower Waist Circumference Cut offs for Predicting Derangement in Metabolic Parameters Among Asian Children and Adolescents: A Pilot Study. Indian Pediatr. 2021 Apr 15;58(4):392-394. doi: 10.1007/s13312-021-2203-9.

2. Dr Priti H Phatale, Childhood & Adolescent Obesity Specialist, Samrat Endocrine Institute of Diabetes, Obesity & Thyroid, Aurangabad

Certificate of achievement for winning best poster in Childhood & Adolescent Obesity track in Asia Oceania Conference on Obesity and Malaysian Association for the Study of Obesity Scientific Conference from 6-8 April 2021 in Kuala Lumpur. The title of the study was "Correlation for total body fat with Body Mass Index and triponderal Mass Index in overweight and obese children and adolescents".

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CAPENEWS | ISPAE

Welcome to New ISPAE members

Hema Ram Dogiyal, Fellow, Pediatric Endocrinology, AIIMS Jodhpur

Ramawtar Mitharwal, Senior Resident, Pediatrics, JLN Medical College, Ajmer

Kochurani Abraham, Fellow, Dept. of Pediatric Endocrinology, Bai Jerbai Wadia Hospital for Children, Mumbai

Ajinkya Patil, Dept. of Pediatrics, Bharati Hospital, Bharati Vidyapeeth Deemed University, Pune

Namratha Upadhya, Consultant Pediatric Endocrinologist, Bengaluru

Dhanya Soodhana Mohan, Fellow in Pediatric and Adolescent Endocrinology, Indira Gandhi Institute of Child Health, Bengaluru

Shruthi Bettegowda, Senior Resident, Sri Venkateshwara Institute of Medical Sciences, Tirupati

Likhitha Butukuri, Senior Resident, Sri Venkateshwara Institute of Medical Sciences, Tirupati

Sayan Banerjee, Fellow, Regency Hospital, Kanpur

Narayanan R, Fellow, Regency Hospital, Kanpur

Manoj Kumar, Fellow, Regency Hospital, Kanpur

Rajesh TV, Professor, Govt. Medical College, Kozhikode

Krishna Janakbhai Kaswala, Fellow, Bai Jerbai Wadia Hospital for Children, Mumbai

Arun George, Senior Resident, Christian Medical College, Vellore

Vikas Katewa, Asst. Professor, Dept of Pediatrics, Dr SN Medical College, Jodhpur

Smriti Rohatgi, Asst. Professor, Pediatrics, ESI PGIMSR, Basaidrapur, New Delhi

Pamali Nanda, DM Senior Resident (Pediatric Endocrinology), PGIMER, Chandigarh

Nitin Pandey, Dr RP Clinic, Pakri Pul, VIP Road, Alambagh, Lucknow

Divya Vilas Pujari, Bai Jerbai Wadia Hospital for Children, Mumbai

Reshma Manayankath, Asst. Professor, Pediatrics, Alappuzha, Kerala

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Obesogenic Word Hunt

Dr Diksha Shirodkar
Asst. Professor, Pediatrics and Pediatric Endocrinologist, Yenepoya Medical College and Hospital, Yenepoya University, Mangalore, Karnataka

Search for all the words using the clues given below related to the genetics, neuroendocrine mechanisms, treatment and syndromes of obesity. The words could be arranged in a horizontal, diagonal or a vertical fashion. Look for the colored alphabets to guide you in this maze.
Good luck and Happy Word-Hunting!
Clues:

1. An afferent nerve conveying hunger signals to the Nucleus-Tractus-Solitarius
2. An orexigenic hormone/ peptide.
3. Cocaine/_____Related transcript (CART).
4. The "Reward" neurotransmitter.
5. "Fetal origin of adult disease" is synonymous with the _____Hypothesis
6. IgG2 monoclonal antibody against proprotein convertase subtilisin–kexin type 9 for reduction of LDL.
7. Name the syndrome with retinitis pigmentosa, obesity, kidney dysfunction, polydactyly, behavioural dysfunction and hypogonadism.
8. Name the syndrome with acrocephaly, soft tissue syndactyly, brachy- or agenesis mesophalangy of the hands and feet, preaxial polydactyly, congenital heart disease, mental retardation, hypogonadism, obesity and umbilical hernia.
9. Name the syndrome with intellectual disability, facial dysmorphism, microcephaly, retinal dystrophy, truncal obesity, joint laxity and intermittent neutropenia.
10. Mutation of this gene causes obesity, hypocortisolism and red hair.
11. The _____(one of the vertices of the limbic triangle) transduces fear and stress, which results in increased cortisol release from the adrenal cortex.
12. The children who have a BMI between the 85th to 95th centile on the BMI chart are _____.
13. This part of the hypothalamus is called the central processing unit, integrating the afferent signals and central stimuli for food intake and hunger.
14. This study is performed to assess the severity of obstructive-sleep apnea
15. What does "A" stand for in the abbreviation ROHHAD (a rare serious respiratory and obesity disorder)?
16. An autosomal recessive disorder characterized by progressive cone-rod dystrophy leading to blindness, sensorineural hearing loss, childhood obesity associated with hyperinsulinemia, type 2 diabetes mellitus and dilated cardiomyopathy.
17. A type of gastric-bypass bariatric surgery.
18. US-FDA approved drug for children above 12 years with obesity.
19. An anti-epileptic drug which causes weight loss.
20. A hypothesis in which favorable genes during famine or calorie deficient environment become obesogenic/diabetogenic in the modern world.

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Obesogenic Word Hunt

Dr Diksha Shirodkar
Asst. Professor, Pediatrics and Pediatric Endocrinologist, Yenepoya Medical College and Hospital, Yenepoya University, Mangalore, Karnataka

	Q	M	P	**C**	N	P	B	W	R	E	K	R	A	**B**	V	Z	A	C	F	**P**	
	U	C	W	H	A	K	X	E	R	V	Y	L	L	W	Q	I	L	Y	O	Y	
	T	Q	N	K	L	R	R	U	F	H	**O**	A	I	F	J	C	H	M	E	N	
	H	H	D	E	A	U	P	H	P	R	T	I	E	N	O	P	C	B	Y	**A**	
	G	F	T	C	D	I	P	E	L	E	Z	D	G	W	A	S	**A**	D	L	G	
	I	J	F	S	G	Y	T	I	N	Q	U	E	V	R	S	M	O	S	A	B	
	E	F	Y	C	Y	V	S	R	Y	T	L	M	G	**C**	P	U	T	E	J	A	
	W	H	P	Y	M	T	N	F	I	J	E	O	Z	H	O	R	G	Z	B	J	
	R	Y	S	Y	**A**	I	G	K	D	N	N	R	E	U	O	H	C	A	L	F	
	E	I	I	T	O	K	W	F	K	M	J	T	S	M	N	**B**	E	J	**V**	X	
	V	E	Y	F	S	Q	D	P	O	Z	A	N	V	U	U	A	R	N	Q	**R**	
	O	N	Q	I	V	X	N	S	W	M	A	E	U	H	K	R	P	K	I	O	
	U	I	B	R	N	R	Y	Q	I	K	E	**V**	L	J	W	D	W	H	H	U	
	R	M	I	H	T	L	X	N	Y	D	L	T	N	I	L	E	R	H	**G**	X	
	S	A	S	**T**	O	N	E	X	I	D	Y	L	O	C	W	T	G	T	H	E	
	F	P	G	**P**	J	Z	E	P	L	Q	K	W	R	L	O	B	Q	I	J	N	
	W	O	F	I	E	U	E	H	**A**	U	T	O	N	O	M	I	C	A	R	Y	
	O	**D**	B	D	R	I	D	A	L	E	N	G	R	F	K	E	W	N	K	U	
	G	J	O	R	W	**E**	V	O	L	O	C	U	M	A	B	D	Q	A	V	O	
	T	I	R	T	E	T	A	M	A	R	I	P	O	**T**	S	L	B	Q	N	J	

Please mail your answers to editor.capenews@gmail.com
All successful entries will be acknowledged in the next issue of CAPE News.

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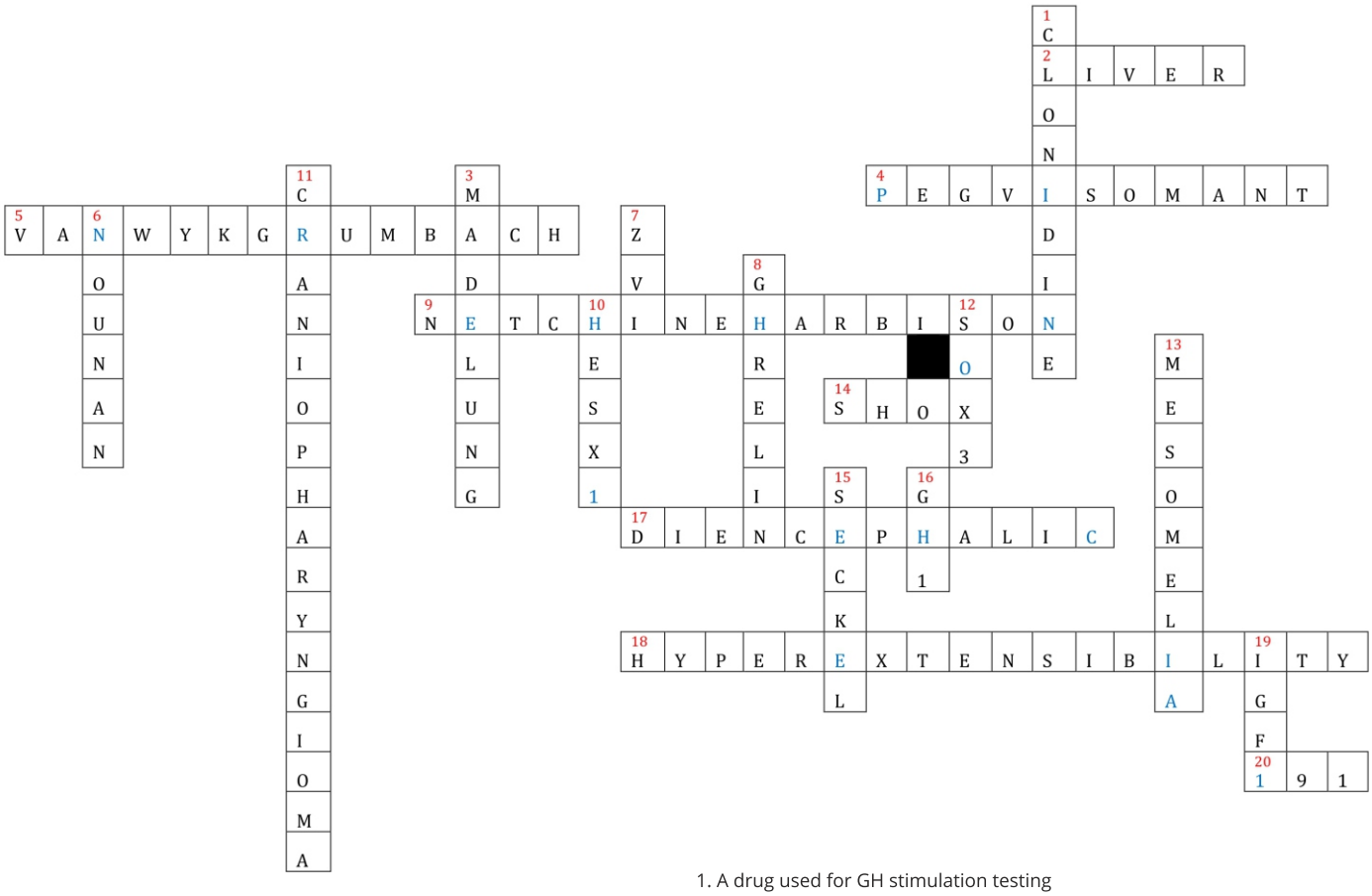
WINNERS OF PREVIOUS ISSUE OF CROSSWORD QUIZ ON GROWTH:

1. Dr. Aaradhana, *Associate Professor, Dept. of Pediatrics, UCMS and GTBH, Delhi.*

2. Dr Noor Fathima S Zohra, *MD Pediatrics, Yenepoya Medical College, Mangalore.*

Hearty congratulations to the winners!



Clues

Across

2. IGF1 is produced by this organ
4. GH antagonist
5. Acquired hypothyroidism, short stature, precocious puberty and delayed bone age.
9. The scoring criteria for Silver Russell syndrome
14. One of the pseudo autosomal regions - absence of which causes short stature
17. A rare syndrome of failure to thrive in infants with hypothalamic tumors
18. What 'H' denotes in SHORT Syndrome
20. The total number of amino acids in GH

1. A drug used for GH stimulation testing
3. Deformity seen in Leri Weill Dyschondrosteosis.
6. Syndrome caused mostly due to PTPN 11 mutation
7. First name of the famous Pediatric Endocrinologist after whom Laron syndrome is named
8. The most common hormone responsible for hyperphagia in Prader Willi syndrome
10. Mutation of this gene is associated with septo-optic dysplasia
11. What are adamantinomatous and papillary histological types of ?
12. The mutant gene responsible for X linked-classic pituitary stalk interruption, cysts and craniopharyngeal canal
13. Shortening of the middle segments of the limb eg. Radius, ulna
15. Bird headed dwarfism
16. The gene attributed to GH deficiency which results in anti-GH antibodies post administration of rhGH
19. Treatment of Growth hormone Insensitivity

Please find information about the Journal of Pediatric Endocrinology and Diabetes - the official journal of the ISPAE.
All members are encouraged to submit their research work to the journal.

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Please find information about the upcoming ISPAE meeting in Pune and ISPAE PET School. All members are encouraged to register for the conference. All fellows are encouraged to apply for the Fellows' School.

ISPAE 2021

PUNE

IAP Pune Branch

7TH BIENNIAL MEETING OF INDIAN SOCIETY FOR PEDIATRIC AND ADOLESCENT ENDOCRINOLOGY (ISPAE)

12TH - 14TH NOVEMBER 2021

Theme:

"From Bedside Basics to Molecular Pediatric Endocrinology"

ISPAE PET FELLOWS SCHOOL

9TH - 12TH NOVEMBER 2021

IN ASSOCIATION WITH APPES, ESPE & ISPAD

APPES ESPE European Society for Paediatric Endocrinology ISPAD International Society for Pediatric and Adolescent Diabetes

www.ispaepune2021.com

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Please find information about the upcoming ISPAE meeting in Pune and ISPAE PET School. All members are encouraged to register for the conference. All fellows are encouraged to apply for the Fellows' School.

A galaxy of international speakers from ESPE, APPES and ISPAD will be participating in the conference.

CONFERENCE HIGHLIGHTS

The theme of the conference this year is:
"From Bedside Basics to Molecular Pediatric Endocrinology".
Topics addressing various aspects of Pediatric Endocrinology, recent advances and new technology in Type 1 Diabetes will be covered.

Single day program for Pediatricians, Postgraduates and General Practitioners

REGISTRATION DETAILS

DATES	ISPAE MEMBERS	NON-ISPAE MEMBERS	STUDENTS & ACCOMPANYING PERSON
Early bird registration Upto 15th June 2021	Rs. 6,000/-	Rs. 7,000/-	Rs. 4,500/-
16th June - 15th October 2021	Rs. 7,500/-	Rs. 8,500/-	Rs. 5,000/-
16th October 2021 onwards	Rs. 9,000/-	Rs. 10,000/-	Rs. 5,500/-

International delegates $150. Spot registration: TBA. All fees inclusive of 18% GST

For 14th November 2021	Rs. 1,000

To register online please visit **www.ispaepune2021.com**

Cancellation Policy
Up to 15th June 2021 - 75% of the fee
up to 15th August 2021 - 50% of the fee
After 15th August 2021 - No Refund



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ISPAE PET Fellows School 2021

Tuesday, 9th November to Friday, 12th November 2021

The much-awaited ISPAE PET School is scheduled from 9th-12th November this year, immediately preceding the ISPAE Scientific meeting. It is a 3-day intensive residential training program for young entrants in pediatric endocrinology and a refresher course for those already working in the field of pediatric endocrinology. The PET school provides opportunity for Fellows to learn from excellent national and international faculty with immense experience, explore career options, and network with their peers from institutions all over India.

The venue this year is The Corinthians Resort & Club, Pune with its beautiful ambience conducive for learning and promoting interaction between Fellows and faculty.

Registrations are limited to 36 seats only.

Course registration is fees Rs. 8,750/- **(to be paid only after selection).**

Please complete the application form and return by email to **Dr. Sarah Mathai** (ISPAE - PET 2021 Convener) at **ispae.pets2021@gmail.com** and **Dr. Ahila Ayyavoo** (ISPAE - PET 2021 Co- convener) at **ahila.ayyavoo@gmail.com** along with your CV (not more than 2 pages) and a reference letter from the Head of the Department.

It is mandatory that all applicants become member of ISPAE.

Important Dates

Last date of application	15th July 2021
Notification of selected candidates	15th August 2021

Dr. Sarah Mathai
PET Convener

Dr. Ahila Ayyavoo
PET Co-Convener

Dr. Vaman Khadilkar
Organizing Chairperson
ISPAECON 2021

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