

# CAPE NEWS NEWS LETTER OF THE INDIAN SOCIETY OF PEDIATRIC AND ADOLESCENT ENDOCRINOLOGY

www.ispae.org.in

Advisors: MP Desai, P Raghupathy, A Virmani, N Shah

President: Vaman Khadilkar, Pune vamankhadilkar@gmail.com

Joint Secretary: Ganesh Jevalikar, Gurgaon. gjevalikar@gmail.com

Executive Members: AbhishekKulkarni, Leena Priyambada, Meena Mohan, Riaz I, Saroj Patnaik, Shaila Bhattacharya, VijayaSarathi.

Ex-officio: PSN Menon (Immediate Past President); Preeti Dabadgao PET Coordinator

Web Master: Dr Shaila Bhattacharya

Editor CAPENEWS: Dr Archana Dayal Arya

Members of Editorial Board: Dr Sudha C Rao Dr Hemchand K Prasad Dr Shalmi Mehta Dr Sachin Mittal Dr Bhanu K Bhakri

# **MESSAGE FROM THE EDITOR**

### Dear Friends,

Wish you all a very Happy New Year and a warm welcome to all our new members and Dr. Sachin Mittal from Mumbai who has joined our editorial team.

I would like to thank my editorial team, for all the hard work that they have put in to bring out this issue.

At the outset in 2014, we propose to change the format of this newsletter to highlight one topic in every issue, for the benefit of all our members. This issue is dedicated to "Growth Charts and Approach to Short Stature" and the forthcoming issue would cover the "Management of Short Stature", followed by other aspects of Pediatric Endocrinology. We hope that you will appreciate the change and your valued comments are very welcome in this regard.

> Dr. Archana Dayal Arya Editor of CAPE NEWS (ISPAE Newsletter) 2013-2014

### **INSIDE THIS ISSUE:**

ISPAE 2013 Meeting – a report (Dr Shaila Bhattacharya)	page 2
Pearls from PET 2013	page 3
Update from PEDICON 2014	page 4
News from APPES fellow's School	page 5
Growth charts (Dr Vaman Khadilkar)	page 6
Approach to a child with short stature (Dr Sudha C Rao)	page 7
Patient information page (Dr Hemchand K P)	page 10
Pictorial quiz	page 11
Pedendoscan (Dr Sachin Mittal)	page 12
Useful information	page 14
Publications from our members	page 14
News from all over India	page 15
Miscellaneous	page 16

# ISPAE 2013 Bengaluru: 29<sup>th</sup> November to 1<sup>st</sup> December 2013 - A Report Dr. Shaila Bhattacharya, Organizing Secretary shailashamanur@gmail.com

Greetings from the Garden City, Bengaluru, the Venue of ISPAE 2013!

The main meeting was held at the Grand Ball room of Hotel JW Marriot, Bengaluru. It was held in association with Indian Academy of Pediatrics – Bangalore Paediatric Society (IAP -BPS), Department of Pediatrics, Manipal Hospital and Indira Gandhi Institute of Child Health, Bengaluru, EuropeanSociety for Pediatric Endocrinology(ESPE), Asia Pacific Paediatric Endocrine Society (APPES) and International Society of Pediatric and adolescent Diabetes (ISPAD).

Dr. Paul Hofman, President - APPES, was the Chief Guest and inaugurated the program by lighting the lamp. Dr P Raghupathy, Chairperson Organizing Committee, welcomed the gathering. DrVaman Khadilkar, President, ISPAE, gave the Presidential address and highlighted the achievements of ISPAE. Dr Sangeeta Yadav, Secretary, ISPAE, read the annual Report of the activities of the Society. Dr Shaila Bhattacharyya, Organizing Secretary, gave the vote of thanks. The inaugural ceremony was followed by a spectacular cultural program.

The scientific program was the highlight and really an academic feast for the 300 delegates who came from all over India and abroad. The invited faculty from abroad were Dr. Paul Hofman (President – APPES, Auckland, New Zealand), Dr Olaf Hiort (Lubeck, Germany), Dr Nick Bishop(Scheffield, UK), Dr Reiko Horikawa (Tokyo, Japan), Dr. Senthil Senniappan (UK),

Dr. Caroline Fall (Southampton, UK), Dr. Stephen Greene (President ISPAD, Dundee, UK), Dr Zulf Mughal (Manchester, UK) &Dr Margaret Zacharin (Melbourne, Australia).

The Indian faculty comprised Dr. VamanKhadilkar, Dr. PSN Menon, Dr. Raghupathy P, Dr. Vijayalakshmi Bhatia, Dr. Nalini Shah, Dr. SudhaRao, Dr. Sarah Mathai, Dr. Shaila Bhattacharyya, Dr. AnuragBajpai, Dr. Preeti Dabadgao, Dr. SangeetaYadav, Dr. Usha Shriram, Dr. Anuradha Khadilkar, Dr. Archana Dayal, Dr. Ahila, Dr. Anju Seth, Dr. Kavitha Bhat, Dr. Prasanna Kumar, Dr. Arpan Dev Bhattacharyya, Dr. Anna Simon, Dr. Rajesh Khadgawat and Dr. Subratadey.

The Scientific Program covered recent developments in Pediatric Endocrinology (Genetics, Molecular pathogenesis of Endocrine disorders), case discussions and practical tips for optimal management of endocrine disorders and diabetes.

The response to the call for abstracts was amazing with almost 40 posters being presented in the Conference. 8 abstracts were selected for Oral Paper Presentation.

The Organizing Committee gratefully acknowledges the financial support provided by the pharmaceutical industry (Novo Nordisk, Lilly, LG, Ranbaxy, Pfizer, Medtronics) for this meeting.





### Pearls from PET-2013 (Pediatric Endocrine Training -2013, Bengaluru)

Contributors: Dr. Hari Mangtani, Dr Meghna Chawla, Dr. Ruchi Nadar, Dr Supriya Phanse, Dr Dhivyalakshmi J

### OBESITY & METABOLIC SYNDROME

In clinical settings, BMI is the standard measure of obesity, though there has been and ongoing criticism like the inability to differentiate between lean mass and fat mass and to capture the anatomical distribution of adipose tissue. DEXA is a better modality only in the research settings currently.

Visceral fat accumulation as represented by the waist circumference is strongly associated with metabolic syndrome in childhood and coronary artery disease in later life.

The homeostasis model assessment of insulin resistance (HOMA-IR) is a useful parameter to diagnose IR. HOMA IR = (Fasting glucose (mg%) x Insulin)/405. After the age of 10 years, a value >4.5 is considered abnormal.

Metformin is useful in children older than 10 years with insulin resistance (proven biochemically). Its use in younger children remains a grey zone.

Bariatric surgery is reserved for a child with a BMI greater than  $50 \text{kg/m}^2$  or BMI more than  $40 \text{kg/m}^2$  and significant, severe co-morbidities.

### <u>DSD</u>

Karyotyping is an absolute must in ALL cases of DSD. Sex assignment and psychological issues are still difficult to tackle and a team based management including a pediatric endocrinologist, pediatric endocrine surgeon and a psychologist is most helpful.

Inhibin levels can be used to determine presence of functioning testicular tissue.

### GROWTH

Go for GH therapy in all Turner girls. Consider ethical issues before prescribing GH for ISS.

### PUBERTY

Of all the features (clinical, biochemical and radiological) differentiating between true and pseudo precocious puberty, GnRH stimulation test remains the most reliable and reassuring.

Non ethnic pigmentation of nipple along with presence of pubertal signs, suggests external estrogen as a cause and should be probed. Exposure to estrogen may not be always due to estrogen tablets or creams, however some medications might be adulterated with estrogen.

### GLUCOSE

The finer aspects of DKA protocol don't matter so much and any protocol is fine, as long as the basic principles are followed.

In a case of Glucokinase mutation: management was accepting low blood sugarlevels as the baby has a physiologically low set point for hypoglycemia.

#### BONE

Interpretation of bone mineral density in children using the DEXA should not be only based on Z scores for BMD as it is a bone mineral areal density (difference between a narrow and a broad bone). It needs to be adjusted not only for age, but also the height and the pubertal status. Thus a short, prepubertal child will have less bone mineral content but may have normal bone mineral density.

The main indications for calcitriol are 1 alpha hydroxylase deficiency and renal disease. For others, cholecalciferol works as good as calcitriol.

1 alpha hydroxylase deficiency may be of varied severity depending upon the mutations. VDDR 1 may be present despite detectable low normal 1,25dihydroxyvit D,in the presence of changes of rickets, high alkaline phosphatase and low normal calcium and phosphorus levels.

### CAH

Recent studies shown that high doses of glucocorticoids are usually not required as:

a)No evidence of effect of androgens on bone age over the first 12 months of age

b)No evidence that gradually reducing post natal androgens appreciably adds to the virilisation occurring before birth in girls.

c)High doses of glucocorticoid causes major loss of height in the first year of life

This is because DHT is produced from 17 OH P through backdoor pathway (by 5 alpha reductase type 1 and various enzymes) without formation of testosterone.

# **CAPE NEWS**

This pathway is found active in CAH (usually 21 hydroxylase deficiency patients). Hence virilisation will progress even with suppressive doses of glucocorticoids (no need of increasing the dose). Bone age is not going to advance (no excess testosterone as only DHT is produced in excess) No need of chasing labs for good control, clinical monitoring is enough (height velocity, blood pressure).



## PEDICON 2014 (Indore) PEDIATRIC ENDOCRINOLOGY

PEDICON 2014 was held in Indore from January 9<sup>th</sup> to January 12<sup>th</sup>. There were a number of talks and panel discussions in Pediatric endocrinology. The topics discussed and the speakers were as follows:

1. Workshop on growth monitoring - Dr Vaman Khadilkar

2.Endocrinology chapter symposium – Theme adolescent endocrinology Chairpersons: Dr Sangeeta Yadav, Dr Rakesh Shukla
a)Adolescent obesity and metabolic syndrome – Dr Vaman Khadilkar
b)Type-1 Diabetes: Management in adolescents – Ganesh Jevalikar
c)Delayed puberty – Dr Sangeeta Yadav
d)Polycystic ovary disease – Dr Ahila Ayyavo
e)Panel discussion on Adolescent endocrine issues; Moderator - Dr I Riaz

3.Neonatal hypoglycaemia - Dr C Sudha Rao

4. Thyroid disorders - easy solutions; moderator - Dr Anju Virmani; Experts - Dr Sudha rao and Dr Anna Simon

5.Approach to short stature – a panel discussion; Moderator – Dr Abhishek Kulkarni; Paneslists – Dr Archana Dayal, Dr Hemchand Prasad and Dr Rajesh Khadgawat

6.Bedside endocrinology – Know your hormones well; Moderator – Dr Anurag Bajpai; Expert Dr Vaman Khadilkar, Dr Anju Virmani, Dr Shaila Bhattacharya, Dr Amit Lahoti

7. Precocious puberty - remedy earlier the better - Dr Anurag Bajpai

### NEWS from APPES Fellow School DrVeena V Nair, Thiruvananthapuram

The 15<sup>th</sup>APPES fellow School was conducted at Wuhan, China from 6-8<sup>th</sup>November 2013. It was a great academic experience to all the 38 fellows from the Asia Pacific regions. Five fellows from India attended the school Dr Veena V Nair (Thiruvananthapuram), Dr Aashima Dabas (New Delhi), Dr Vineet Surana (New Delhi), Dr Shyam Kishore (New Delhi) and Dr Deep Dutta (Kolkata). The case presentations and active participation from Indian fellows was well appreciated.

The 2 day residential training was based on case based discussions and lectures by eminent faculty. In addition group discussions enabled sharing of ideas. The sessions started with thyroid disorders where cases like VanWyk Grumback syndrome, Grave's disease and thyroid hormone resistance were discussed. Dr Maria Craig (Australia) gave a vivid lecture on presentation and management of various thyroid disorders. In the session of endocrine emergencies Dr Peter Simm (Australia) did a case based discussion on SIADH, cerebral salt wasting, acute adrenal insufficiency, hyperinsulinemic hypoglycaemia neonatal thyrotoxicosis and diabetic ketoacidosis. Dr Pikto Cheung (Hongkong) delivered a detailed lecture on various lipid disorders in children. Insulin resistance and type 2 diabetes in children were also discussed. The session on monogenic diabetes was made very interesting by Dr Jan Lebl (Czech Republic) with his case histories. In the growth session, 2 cases on skeletal dysplasia and SGA with growth hormone deficiency were presented. Dr Gabriele Hauser (Austria) passionately discussed the biology and physiology of growth plates, endocrine regulators of growth and elaborated the diagnostic work up for short stature. Dr Reiko Horikawa (Japan) dealt with topics on pubertal disorders and covered various genetic factors involved in pubertal maturation. Dr Nalini Shah (India) did a beautiful discussion on various adrenal disorders in children. Dr Elaine Tham (Australia) discussed various causes of hypopituitarism and their management.



### WELCOME TO OUR NEW MEMBERS

- 1. Siddhnath Sudhanshu, Lucknow
- 2. Saroj Kumar Sahoo, Lucknow
- 3. VP Vipin ,Lucknow
- 4. Naina Bhat, Bengaluru

- 5. Mary Binsu Abraham, Perth, Australia
- 6. Bharat kumar Sharma, Surat
- 7. Shafi Kuchay, Srinagar
- 8. Pradip Dalwadi, Vadodara

### **Growth Charts**

Khadilkar V. V. Pediatric Endocrinologist, Jehangir Hospital and Bharati Vidyapeeth Medical College, Pune, India

#### Introduction:

Since production of WHO Multicenter Growth Reference Study(MGRS) growth standards in 2006, many countries have adopted the WHO charts for under five children. In UK, WHO growth charts are used until 4 years and in US only up to 2 years of age. Over-diagnosis of stunting and underweight in Asian children is likely with the use of these standards as Asian children are still thinner and lighter often with a near normal BMI. For children between the age of 5 to 18 years, no standard is available and every country has its own published and updated growth charts. It is not possible to produce a growth reference for children above the age of 5 years as environmental factors cannot be controlled as in case of underfive children. Therefore only reference curves (descriptive) are available. Every country must update these charts to document and incorporate the secular trends in children's growth

Growth Standard vs. Reference:

A growth reference simply describes the growth of a sample of individuals, whereas a standard describes the growth of a 'healthy' population and suggests an aspirational model. WHO MGRS under five growth charts are growth standards. A reference is representative of the existing growth pattern of children and allows us to study the secular trends in height, weight and obesity.

Advantages of WHO under five growth charts (standards):

WHO growth standards have given a platform to compare growth of under five children across all races and ethnicity against a single standard, thus assessment becomes objective and easy. They show more physiological growth pattern as the children in MGRS study were breast fed and hence leaner, promoting prevention of obesity from a younger age. The MGRS provides an unsurpassed foundation for a growth standard based on healthy children living under conditions that favored the achievement of full genetic potential.

Disadvantages of WHO under five growth standards: In developing nations the WHO 2006 standards tend to over-diagnose stunting and wasting. In a nationwide study done by the author on apparently healthy affluent Indian children the percentage of stunting was 13.6% for boys and 11.2% for girls and that for wasting was 8.5% for boys vs. 10.4% for girls. Similar concerns are expressed by authors from other developing countries such as Indonesia, and Malawi. In a study done by Kerac M et al on data from 21 countries it was concluded that use of WHO standards to define wasting results in a greater disease burden, in children under the age of 6 months.

#### Growth References:

Most other growth charts available today are growth references which merely describe the growth of a population at a given time. Examples of such charts are WHO 2007 references from year 5-19. In Indian context two national data sets which truly represent affluent Indian population in all five zones of India are available. First one is by K N Agarwal which is based on data collected from 1989 to 1992 (data collected nearly two and half decade ago) and second is from the authors group collected in 2007-8. Marwah et al have recently published data both on affluent and rural children from India in a multicentric study that predominantly involves the north Indian population (nearly 50%). These references highlight the fact that there is a mild secular trend in height in both sexes but it is more pronounced in boys as compared to girls. There is however an alarming rise in the overweight and obese children in the recent times and hence weight scales are tilted to the right. We therefore need prescriptive weight and BMI charts. It is not easy to construct prescriptive weight charts and hence WHO has also not produced weight charts for children between the age of 5-19. Authors group have made an attempt to produce prescriptive BMI charts for Indian children with the WHO recommended adult equivalent cut off of 23 and 28.

It is important that descriptive growth references are update once every decade so that under or over diagnosis or stunting, wasting and obesity is avoided. Conclusion:

WHO 2006 growth standards are useful for comparison of growth of children under the age of 5 years around the world but caution regarding referral for investigations of failure to thrive, changing infant feeding policies and intervention programs based on WHO 2006 standards for the developing part of the world is needed at least for the present time.

For children over the age of 5 years there is no standard (prescriptive) chart available in the world. Each country has its own references and in 2007 WHO has produced its own references based only on the same old American data used for CDC 2000 charts. Each country should update its own reference standards once in a decade and at the present time most updated growth reference curves for affluent Indian children are available from authors 2007-8 data published in Indian pediatrics.

For the diagnosis of overweight and obesity which is a very major public health problem, prescriptive BMI charts may be used. Such charts are produced by WHO, IOTF and by the authors group for Indian children in 2012.

### APPROACH TO A CHILD WITH SHORT STATURE

Dr. Sudha Rao Chandrashekhar, Mumbai

Short Stature (SS) is one of the common presenting symptoms in any pediatric outpatient clinic. Majority of these children do not have an underlying hormonal or genetic disease.

A child may be regarded as having growth retardation if his/ her height is

Less than the 3<sup>rd</sup> percentile or 2SD below the mean for age and sex of the population reference standard.

Demonstrates a growth velocity of less than  $25^{\text{th}}$  percentile on a velocity curve when assessed over a minimum period of 6 to 12 months.

### Normal growth velocity:

Intrauterine period is the period of most rapid growth. In the first year of life a child grows by 25cm, 12.5 cm in 2<sup>nd</sup> year, 6-7cm in 3<sup>rd</sup> & 4<sup>th</sup> year, 5cm per year from 5-9 years with a nadir of 4 cm per year pre pubertal.

During pubertal growth spurt 10-20 cm height is gained, with peak gain of 10 - 12 cm in boys and 7-9 cm in girls.

Body proportions (upper segment: lower segment) change from 1.7 at birth to 0.98-1 by 13-14 years of age and to 1 in adult hood.

### CAUSES OF SHORT STATURE

I. PHYSIOLOGICAL OR NORMAL VARIANTS Familial short stature (FSS) Constitutional delay of growth and puberty (CDGP)

II .PATHOLOGICAL CAUSES

A. DISPROPORTIONATE SHORT STATURE Rickets, Skeletal Dysplasia, Congenital hypothyroidism.

B. PROPORTIONATE SHORT STATURE

### Prenatal Causes.

#### IUGR

Dysmorphic syndromes - e.g. Russel Silver syndrome Chromosomal disorders - Down's syndrome, Turner's syndrome

### Postnatal Causes

1. Systemic diseases - Chronic anemia, Chronic renal failure, Chronic liver disease, Asthma, Congenital heart disease

- 2. Chronic undernutrition
- 3. Endocrine causes
- i. Growth hormone deficiency (ghd)
- ii. Hypothyroidism .- congenital /acquired
- iii. Cushing's syndrome
- iv. Diabetes mellitus uncontrolled
- v. Pseudohypoparathyroidism
- 4. Psychosocial dwarfism
- 5. Idiopathic

# EVALUATION OF A CHILD WITH SHORT STATURE (SS)

The key to initial evaluation of SS is the history, determination of auxological parameters and detailed clinical examination. Most centers report more than half of the cases presenting for SS to have a physiological cause. Thus the approach to short stature must be a careful balance designed not to miss pathology disorder without over evaluation.

### Facts to be elicited in the history (Etiology)

Age of onset- since when is the child not growing. Previous growth records at school, home or physician. Records of previous heights and weights must be sought and charted on growth charts.

Ante-natal History- Substance abuse, Medication, Infections (IUGR)

Birth History -- Birth weight /Gestational age IUGR H/O birth asphyxia (Hypopituitarism), Breech delivery, Neonatal hypoglycemia (GHD) Prolonged neonatal hyperbilirubinemia (Hypothyroidism)

Symptoms pertaining to illness. Shortness of breath, cyanosis, cough, fever (Heart disease, asthma,TB) Diarrhoea, Steatorrhoea, Abdominal pain (Malabsorption) Headache, vomiting, visual problems (Pituitary or hypothalamic mass) Constipation, lethargy, feeding difficulty (Hypothyroidism) Polyuria (RTA, Chronic renal failure) H/O Hepatitis, distension abdomen, malena (Chronic liver disease) Recurrent blood transfusions (Thalassemia and other chronic anemias)

Dietary history; to elicit weaning practice, to calculate calorie and protein intake

Drug history; prolonged use of corticosteroids, amphetamine derivatives.

Family history of SS in first /second degree relatives (FSS), Delay in puberty in one or both parent (CDGP)

Social history; child abuse, family discord, emotional deprivation (Psychosocial dwarfism)

### ANTHROPOMETRY

Measurement is the basis of growth assessment. Measurements made accurately and precisely and interpreted correctly are more specific and more sensitive than analyses of single hormone concentrations in children. It is required that the anthropometric measurements are accurate and reproducible with <0.1% of coefficient of variation .The measurements must be made on appropriately designed equipment and it is ideal to have the same person taking the readings to eliminate interpersonal errors.

### 1. Height (cms)

- For children < 2yrs of age supine length (TL) should be measured on an infantometer and two personnel are required to make an accurate measure.
- For children >2yrs of age standing height is measured on stadiometer.
- Plot the value on a reference curve.
- Calculate the height age ( the chronological age at which this measurement of height is on the 50<sup>th</sup> percentile of reference curve)
- Correlate the height to MPH range in children more than 2 yrs of age.

Mid Parental Height (MPH) or Target Height (TH) range is calculated as in

Boys MPH range = {(Father's height + (Mother's height+13)) / 2}+/-8.5cm

Girls .MPH range= {((Father's height 13) + Mother's height ) / 2}+/-8.5cm

### 2. Body proportions

US : LS ratio - Vertex to pubis: Pubis to sole of foot.
 (Normal .At birth-1.7:1, 3yrs-1.4:1, 5yrs-1.3:1, 6yr 1.2:1, At 8yrs -1:1, 10yrs-0.98:1)
 Lower segment longer than the upper segment by

Lower segment longer than the upper segment by more than 5cms after completion of puberty is considered disproportionate.

- Arm span / Total height . Arm span is usually within 5 cm of the height.
- 3. Weight, Head circumference and Chest circumference are the other parameters which need to be measured.

### CLINICAL EXAMINATION FEATURES AND ETIOLOGY

- Dysmorphism , congenital malformation-Genetic syndromes.
- Midline defects, Single upper central incisor
- o Micropenis GHD, Hypopituitarism
- Signs of vitamin deficiencies, Malabsorption -Rickets
- Jaundice , clubbing Chronic liver disease
- Pallor, Chronic anemia Renal failure, Liver disease
- Central obesity, striae, proximal weakness-Cushing's syndrome
- Hypertension Chronic renal failure
- Goitre, coarse & dry skin, delayed relaxation of tendon jerks - Hypothyroidism
- Round face, short 4 metacarpal -Pseudohypoparathyroidism
- Pubertal staging delayed puberty
- Webbed neck, wide spaced nipples, increased carrying angle in a short girl Turner's syndrome

### LABORATORY INVESTIGATIONS

• Bone age Xray left hand wrist to tips of fingers (to assess by Atlas or Scoring method) (Counting the number of carpal bones is an inaccurate method of calculation of bone age and should not be attempted).

### Screening tests

Hemogram - Hb, CBC, ESR, Peripheral smear examination

RFT/LFT -S. Creatinine, Blood gas analysis, S.Electrolyte, SGPT, S. Proteins , Albumin, RBS, S. Calcium, S. Phosphorous, Alk PO4. Tissue transglutaminase IgA as coeliac screening test. Urine examination routine & microscopic Stool examination for ova & cysts

- Karyotyping if suspected Turner's syndrome, Buccal smear is unreliable and should not be used to diagnose Turner's syndrome.
- Hormone studies ( if indicated) Thyroid profile, Provocative tests for growth hormone assay. IGF1, IGFBP3 as screening test for GHD (if available)

### **Indications for hormone studies**

Subnormal growth velocity Markedly stunted height Height below MPH range Retarded bone age Other causes of pathological SS ruled out. Single basal GH level has no diagnostic value and should not be done.

### APPROACH TO EVALUATION OF SHORT STATURE



Syndrome specific charts are availab	le for use for the following conditions:
Down's syndrome	Achondroplasia
Turner syndrome	Hypochondroplasia
Noonan Syndrome	Spondylo epiphyseal dysplasia
Prader Willi Syndrome	Marfans syndrome
Russell Silver syndrome	

9

### PATIENT INFORMATION PAGE

DrHemchand K Prasad, Consultant, Department of Paediatric Endocrinology Mehta Childrens Hospital, Chennai

### SHORT STATURE

# 1. HOW DO I KNOW IF MY CHILD IS SHORT OR NOT GROWING WELL?

- **ü** Common reasons why children come up with concerns of short stature include when your child is the shortest in the class and being bullied for the same;
- **ü** Has very tall parents and yet the child is short, this is being discussed when the child is taken to a social gathering;
- **ü** The younger sibling had raced past your child; or a cousin born later than your child is almost as tall as her
- **ü** Your child's shoe size or size of his clothes are the same for more than two consecutive years.
- **ü** Previously he was the tallest child, sitting in the last bench. Now he is counted as being amongst the short kids of the class
- **ü** People who look at your child and ask if he is studying more than two grades of what he currently is in.

# 2. WHAT ARE THE COMMON CAUSES FOR SHORT STATURE IN CHILDREN?

There are many reasons why your child may be short or is growing poorly. You must consult your pediatric endocrine specialist (specialist in growth and hormonal problems in children) for this. Common causes include:

- Familial You and your spouse or either of you may be very short. This may have a genetic effect on your child's height.
- Your child may have a systemic disease which needs to tested and treated. conditions include celiac disease; gut problems and childhood tuberculosis.
- Your child may be a late bloomer, i.e. he is a normal child who is slow and steady and ultimately going to win the race. He may be growing slowly and may shoot up late.
- Sometimes your child may have a skeletal problem like achondroplasia where he needs to be seeing a bone specialist (orthopedician) for surgical help.
- Your child may have a chromosomal problem and hence is growing slowly.
- Rarely your child may have a hormonal deficiency like a defect in thyroid gland or his growth hormone and hence may have a poor height.

# 3. WHAT SHOULD I ASK MY DOCTOR IF I HAVE CONCERNS ABOUT MY CHILD'S HEIGHT?

- ü Is my child really short?
- **ü** Does he need tests for the same?
- **ü** Does he have a potential to grow?

# 1. WHAT INFORMATION SHOULD I GIVE THE DOCTOR?

Please tell the following things to your doctor:

- a) What was your child's birth weight?
- b) Are there any members of your family who are very short ?
- c) When your child was a baby did he have problems like low sugars ?
- d) Does he drink a lot of water ?
- e) Does he pee a lot ?
- f) Does he have a disturbed sleep?
- g) Does he have lot of headaches?
- h) Does he have frequent tummy upsets ?
- i) Does your child have any neck swelling?
- j) Does your child have any cold intolerance or constipation ?
- k) If your daughter has periods, are they regular?

# 1. HOW WILL MY DOCTOR EVALUATE MY CHILD?

Your pediatric endocrinologist will measure your child's height, your and your spouses' height and plot it on a chart called a "GROWTH CHART". By this he will be able to compare your child's growth to his age and sex matched peers of the world and say whether his height is normal for

- a) The population
- b) The parents

Your doctor will measure the proportions of the different parts of the body to see if your child has a skeletal problem. Then he will meticulously examine your child for any systemic disease. If your child is >9years, he will check whether your child's reproductive organs are growing appropriately for their age.

# 6. WHAT TESTS DOES MY CHILD NEED TO UNDERGO?

Your child will need to undergo a few blood tests early in the morning. Your child may also need an X-ray to assess the maturity of the bones of your child.

### 7. ARE THERE MEDICINES AVAILABLE FOR CHILDREN WHO ARE SHORT?

Yes there are safe medicines that can be given to help your child if your child has a genuine hormonal defect. If your child gets the correct dose of the medicine for the correct period, he will grow normally.

### 8. WHOM SHOULD I CONTACT IF I HAVE CONCERNS REGARDING MY CHILD'S GROWTH?

If you have concerns about the growth of your child, please contact your Pediatrician and ask him to refer you to a Pediatric Endocrinologist for growth assessment

Image 6

## PICTORIAL QUIZ ON GROWTH



Image 4





Contributors: Dr Archana Dayal, Dr Bhanu, Dr Vaman Khadilkar, Dr Sudha Rao) (Solution on last page)

11

# PEDENDOSCAN

Dr SachinMittal, Mumbai

### Diagnosis

The utility of the IGF-I generation test in childr en with chronic kidney disease. Al-Uzri A et alPediatrNephr ol. 2013 Dec;28(12):2323-33

To determine if the insulin-like-growth factor (IGF-I) generation test, can be used as a marker for growth hormone (GH) sensitivity in children with chronic kidney disease (CKD), a randomized cross-over study, with low-dose (0.025 mg/kg/day) and high-dose (0.05 mg/kg/day) GH therapy was conducted in the framework of a 7-day IGF-I generation test. Children with CKD were able to respond to GH therapy with both growth and an increase in serum IGF-I levels, but the IGF-I generation test was not a good predictor of growth response.

Development of additional pituitary hormone deficiencies in pediatric patients originally diagnosed with idiopathic isolated GH deficiency . Blum WF et alEur J Endocrinol. 2013 Nov 22;170(1):13-21.

5805 children initially diagnosed with idiopathic isolated GH deficiency (IGHD) were evaluated for the later development of additional (multiple) pituitary hormone deficiencies (MPHD). MPHD is more likely to develop in patients with more severe idiopathic IGHD. Older baseline age, lower baseline height SDS, and longer follow-up duration are associated with increased risk of development of MPHD. Delivery complications, congenital anomalies, and perinatal/neonatal adverse events occurred more frequently in patients who developed MPHD. The most frequent additional deficiency was TSH.

Prepubertal girls with Turner syndrome and children with isolated SHOX deficiency have similar bone geometry at the radius. Soucek O, et al. J ClinEndocrinolMetab. 2013 Jul;98(7):E1241-7.

The similar bone geometry changes of the radius in TS and SHOX-D patients support the hypothesis that loss of 1 copy of SHOX is responsible for the radial bone phenotype associated with TS.

### Follow up

A four-year, open-label, multi-center, randomized, two-arm study of Genotropin® in patients with idiopathic short stature: comparison of an individualized, target-driven treatment regimen to standard dosing of Genotropin® - analysis of two-year data. Counts DR, et al; ISS Study Group. Horm Res Paediatr. 2013;80(4):242-51.

An individualized, formula-based, target-driven GH regimen for children with ISS, did not meet the primary endpoint achieving targeted gain with lower variability compared to a standard weight-based dosing. No new safety concerns were found.

Carel JC et al. Long-term mortality after recombinant growth hormone treatment for isolatedgrowth hormone deficiency or childhood short stature: preliminary report of theFrench SAGhE study. J ClinEndocrinolMetab. 2012 Feb;97(2):416-25. doi: 10.1210/jc.2011-1995

a population-based cohort study based on a French population register of 6928 children, who started treatment between 1985 and 1996.Mortality rates were increased in this population of adults treated as children with recombinant GH, particularly in those who had received the highest doses. Specific effects were detected in terms of death due to bone tumors or cerebral hemorrhage but not for all cancers, highlighting the need for additional studies of long-term mortality and morbidity after GH treatment in childhood.

Growth hormone therapy and respiratory disorders: long-term follow-up in PWS children. Genetic Obesity Study Group of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED).J ClinEndocrinolMetab. 2013 Sep;98(9):E1516-23.

Long-term GH treatment in patients with PWS is safe; however, annual polysomnography and adenotonsillar evaluation is recommended

### Treatment

A long-acting human growth hormone with delayed clearance (VRS-317): results of a double-blind, placebo-controlled, single ascending dose study in growth hormone-deficient adults. Yuen KC, et al. J ClinEndocrinolMetab. 2013 Jun;98(6):2595-603.

The elimination half-life for VRS-317 is 30- to 60-fold longer and stimulates more durable IGF-I responses than previously studied rhGH products. Prolonged IGF-I responses do not come at the expense of overexposure to high IGF-I levels. The pharmacokinetics and pharmacodynamics combined with the observed safety profile indicate the potential for safe and effective monthly dosing. No unexpected or serious adverse events were observed.

# Eight years of growth hormone treatment in children with Prader-Willisyndrome:maintaining the positive effects. Bakker NE, Kuppens RJ, Siemensma EP et al. J ClinEndocrinolMetab. 2013 Oct;98(10):4013-22.

In this multicenter prospective cohort study, after 8 years of GH treatment, height SDS and head circumference SDS had completely normalized. IGF-1 SDS increased to +2.36 SDS during the first year of treatment (P < .0001) and remained stable since then. GH treatment did not adversely affect glucose homeostasis, serum lipids, blood pressure, and bone maturation.

Effects of recombinant human growth hormone (rhGH) for 1 year on body composition and muscle strength in children on long-term steroid therapy: randomized controlled, delayed-start study. Simon D, et al J ClinEndocrinolMetab. 2013 Jul;98(7):2746-54

rhGH increased height, lean mass (LM) and thigh muscle area (MA). However, muscle strength did not improve significantly.

# Expensive therapies in children: benefit versus cost of combined treatment of recombinant human growth hormone and gonadotropin-releasing hormone analogue in girls with poor height potential. Toumba M, Kokotsis V, Savva SC, Skordis N. J PediatrEndocrinolMetab.2013 Oct 25:1-6.

The cost benefit of combination therapy of gonadotropin-releasing hormone analogues (GnRHa) and recombinant human growth hormone (rhGH) in girls with central precocious puberty (CPP) and poor height prognosis and in girls with idiopathic short stature (ISS) and early puberty was analyzed. The authors concluded that the treatment is very expensive with each centimetre costing about 2700 Euro per patient. It should be considered only in patients with extremely low height prediction and very early pubertal onset.

### Change in total body water as a predictive tool for growth hormone treatment response. Ernst MA et al. Horm Res Paediatr. 2012;78(1):18-23

To investigate whether changes in body composition as a result of growth hormone therapy could be used to predict its growth effect after 1 year, total body water (TBW) and height were measured in 88 GHD children and 99 SGA children. The authors concluded that changes in body composition, measured by TBW are a valuable tool to correctly predict 75% of the GHD children and are only useful in SGA children when the change in TBW is above the cut-off value of  $0.7 \text{ l/m}^2$ 

13

# USEFUL INFORMATION IGF-1 NORMAL LEVELS

Rajbinder Kaur Dehiya, Deepa Bhartiya, Chhaya Kapadia, Meena P. Desai. Insulin like Growth Factor-1, Insulin Like Growth Factor Binding Protein-3 and Acid Labile Subunit Levels in Health children and Adolescents residing in Mumbai Suburbs Indian Pediatrics 2000;37: 990-997

Juul A, Bang P, Hertel NT, Main K, Dalgaard P, Jørgensen K, Müller J, Hall K, SkakkebaekNE.

Serum Insulin-like Growth Factor-I in 1030 healthy children, adolescents, and adults: relation to age, sex, stage of puberty, testicular size, and body mass index.J ClinEndocrinolMetab. 1994 Mar;78(3):744-52.

### IMPORTANT CONSENSUS STATEMENTS IN AREA OF GH

AUTHOR	TOPIC	Reference
Clayton P et al	SGA	J ClinEndocrinolMetab. 2007 Mar;92(3):804-10.
Cohen P et al	ISS	J ClinEndocrinolMetab. 2008 Nov;93(11):4210-7
Clayton P E et al	GHD during transition	Eur J Endocrinol. 2005 Feb;152(2):165-70. Review.
Wilson T A et al	GHD (LWPES) GHD (GHRS)	<u>J Pediatr.</u> 2003 Oct;143(4):415-21 J ClinEndocrinolMetab. 2000 Nov;85(11):3990-3.
Ho KK et al	Adults	Eur J Endocrinol <u>.</u> 2007 Dec;157(6):695-700.
Mahan J D et al	CKD	PediatrNephrol. 2006 Jul;21(7):917-30. Epub 2006 May 30

### PUBLICATIONS FROM OUR MEMBERS

- 1. Devidayal, Bhalla AK, Sachdeva N. A boy with prepubertalgynecomastia, hyperprolactinemia, and hypothyroidism. J PediatrEndocr Met 2013; 26 (3-4): 357-60.
- 2. Sawatkar GU, Kanwar RAJ, Dogra S, Bhadada SK, Dayal D. Spectrum of skin changes secondary to insulin injections in Type 1 diabetes mellitus patients. J EurAcadDermatolVenereol 2013. DOI: 10.1111/jdv.12068
- 3. Jauhari P, Sahu JK, Singhi P, Dayal D, Khandelwal N. An Indian Boy With a Novel Leukodystrophy: 4H Syndrome. J Child Neurol. 2013 Jan 9.
- 4. Devidayal, Singh MK, Sachdeva N, Singhi S, Attri SV, Jayashree M, Bhalla AK. Vitamin D levels during and after resolution of ketoacidosis in children with new onset Type 1 diabetes. Diabetic Med 2013; 30(7): 829-34. DOI: 10.1111/dme.12200
- 5. Dayal D, Dekate P, Sharda S, Das A, Attri SV. An Indian girl with FanconiBickel syndrome without SLC2A2 gene mutation. J Pediatr Genetics 2013; 2: 109112.
- 6. Dayal D, Saini L, Attri SV, Singh B, Bhalla AK. Daily versus alternate day thyroxine therapy to maintain euthyroidism in children with congenital hypothyroidism. Int J EndocrinolMetab 2013; 11(4): e9499.
- 7. Abdusalam K, Bhalla AK, Dayal D. Early onset and slow progression of sexual maturation in North Indian boys with exogenous obesity. ActaEndocrinologica (Buc) 2013; 9(4): 589-96.
- Md. Saif, Akshay Kapoor, IPS Kochar, And Radhika Jindal Continuous Glucose Monitoring System for Congenital Hyperinsulinemia. Indian Pediatr 2013;50: 421-422
- 9. IPS Kochar, Radhika Jindal.Glibenclamide for Neonatal Diabetes Indian Pediatr 2013;50: 428-429
- 10. Inder Pal Singh Kochar. Infantile Onset Diabetes Mellitus. Indianpaediatrics/aug2013/737

# **NEWS FROM ALL OVER INDIA**

### WORLD DIABETES DAY CELEBRATIONS

### COIMBATORE (Dr. Meena Mohan)

On world diabetes day, about 15 children and their families were taken to a water theme park. Basic concepts of regular follow up, SMBG and complication screening were emphasized. An insulin pump training workshop was conducted with children who were using insulin pumps and families who were interested in using pumps. All the parents and children thoroughly enjoyed the day.

#### CHENNAI (DrHemchand K P)

World diabetes day was celebrated by 50 children on follow-up at Mehta children's Hospital Chennai. All children were taken on a one day trip to Birla Planetorium. There were fun activities and education sessions. The head of the department DrThangavelu arranged the program, and Prof P Ramachandran from SRMC was the chief guest. The camp was supported by a grant from Indian journal of Pediatrics.

#### KANPUR (DrAnuragBajpai)

World Diabetes Day Meeting was organized at Regency Hospital Limited. The meeting discussed recent advances on Diabetes management and future of Diabetes.

#### NEW DELHI (Dr IPS Kochar)

A camp was organized in Noida on Diabetes day, where patients and parents interacted and shared their experiences and knowledge of insulin, Insulin pumps, glucosemonitoring. A painting competition was also held. A meeting was also organized at talkotara stadium for children with type 1 diabetes.

#### KANNUR (DrReetha)

World diabetic day was observed Pariyaram medical college ,Kannur, Kerala on november 14<sup>th</sup> attended by about 20 children and their families. there were talks on various aspects of diabetes, a patient support group for type I diabetic children was formed and there were fun activities

#### AHMEDABAD (Dr Shalmi)

30 children with type-1 diabetes with their families attended the meet. They were educated on various aspects of type-1 diabetes including diet (dietician), insulin dose adjustment and exercise (by physiotherapist). Fun activities were also conducted.

### **ENDOCRINE ACTIVITIES FOR PATIENTS**

### Growth Hormone Support Group Meeting Kanpur (Dr. Anurag Bajpai)

GROW India organized Growth Hormone Support Group meeting at Regency Hospital on October 25. The meeting was attended by 30 children and witnessed the release of educational DVD "Growth & Me". In the meeting,DrsYuthika, RN Chaurasia and Anurag Bajpai educated parents about the impact of growth hormone on children with GHD.

### **ACADEMIC MEETINGS**

Puberty Workshop, FOGSI Kanpur, Dec 25 2013 (Dr. Anurag Bajpai)

GROW India organized its 2<sup>nd</sup> puberty workshop under the banner of FOGSI Kanpur. The program used case based approaches to highlight key issues in assessment and treatment of early and delayed puberty in girls. The workshop was attended by 120 gynecologists.

A symposium was organized on growth disorders by GROW India in association with IMA Kanpur on Nov 17, 2013. The symposium covered key issues related to growth and pubertal disorders.

### Growth Workshop at Rajkot (DrVamanKhadilkar)

A Growth workshop cum symposia was organized at Rajkot on 22<sup>nd</sup> September, 2013 by the Academy of Pediatrics (Rajkot Branch, Gujarat) and was attended by more than 50 pediatricians from Rajkot and nearby towns. The growth monitoring workshop was conducted by Dr. Vaman Khadilkar, Dr. Shalmi Mehta and Dr. Supriya Phanse-Gupte

### **MISCELLANEOUS USEFUL INFORMATION**

### **ISPAE 2013**

### **CONGRATULATIONS**

The Winners of **Oral Presentation** (Judges- Dr. Meena Desai, Dr. P. Raghupathy):

1<sup>st</sup>Prize: Influence of pubertal development and body composition on bone mass accrual in apparently healthy school children aged 6-17 years - **Dabas A.** 

2<sup>nd</sup> Prize: Carotid intima media thickness and its association with metabolic variables in obese children and adolescents - **Rajendra Prasad.** 

The Winners of best **posters** (Judges Dr. Shaila Bhattacharyya, Dr. Sarah Mathai):

1<sup>st</sup>Prize: Body image perception in urban school going adolescents - Jain V

2<sup>nd</sup> Prize: Lipoid congenital adrenal hyperplasia due to StAR mutation A case series - **Ruchi Shah** 

### **UPCOMING MEETINGS**

**Pedendocon 2014** - Aloft Hotel, Coimbatore on 23.02.14 by DrMeena Mohan

**Pedendo 2014** - Prof P Venkatraman (SRMC, Chennai) and Prof P G Sundararaman at SRMC University Porur, Chennai on 15/2/14

# GENETIC TESTING AT PUNE FOR ENDOCRINE DISORDERS

GenePathDx offers a broad range of molecular diagnostic tests including Ambiguous Genitalia (SRY/DYS14), Congenital Adrenal Hyperplasia (CYP21A2, CYP21A1P, C4A, C4B, TNXB), Intersex disorders of sex development - (SRY, ZFY, NR0B1/DAX1, WNT4, SOX9, NR5A1), Growth Hormone Disorder - gene dosage (GH1, POU1F1/PIT1, PROP1, GHRHR, LHX3, LHX4, HESX1), Achondroplasia (G380R ie. G1138A/C) + Hypochondroplasia (N450K ie.C1620A/G) common mutations study and SHOX gene analysis for short stature. Contact info: +91 96234 95511 or contactus@genepathdx.com Pediatric Endocrine Disorders, 3rd edition Editors: Meena P Desai, PSN Menon&Vijayalakshmi Bhatia

The new lucid and concise third edition of the book, Pediatric Endocrine Disorders, was released on 30 November 2013 during 3rd Biennial Meeting of ISPAE, held at Bengaluru. With contribution from experts on the subject from all over the world, this comprehensively updated edition aims to present current knowledge about diagnostic techniques and treatment in a simple yet erudite manner. Incorporating suggestions received over the years, new color photos and new research data, this edition will be helpful to all medical professionals involved in caring for children.

Regards, P S N on behalf of all three editors

### **Solutions to pictorial Quiz**

- 1. Clinodactyly
- 2. Metaphyseal dysplasia
- 3. Micropenis
- 4. Shortening of <sup>4</sup> and 5<sup>th</sup>metacarpals in Pseudohypoparathyroidism
- 5. Larons dwarfism
- 6. Hypothyroidism

### Gilsanz&Ratib's bone age assessment method: Dr. VamanKhadilkar

In the recent years (2005) VincenteGilsaz and Osman Ratib from LA in USA have developed a digital atlas of skeletal maturity. This digital atlas is produced by the creation of artificial, idealized, sex- and agespecific images of skeletal development. The models were generated through rigorous analyses of the maturation of each ossification center in the hands and wrists of healthy children This computer generated set of images should serve as a practical alternative to the reference books currently available.Gilsanz and Ratib's atlas is available for clinical use as an application for iphone and ipad. Similarly the TW3 atlas is available as application for the Android os.