CAPE NEWS

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INSIDE THIS ISSUE…

Delayed Puberty- Approach to management

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Delayed puberty is a common disorder presenting to the Pediatric Endocrinologist. Timely assessment and management is mandatory to achieve successful long-term outcome. Most children with delayed puberty represent physiological variations emphasizing the need for careful patient selection before extensive diagnostic workup.

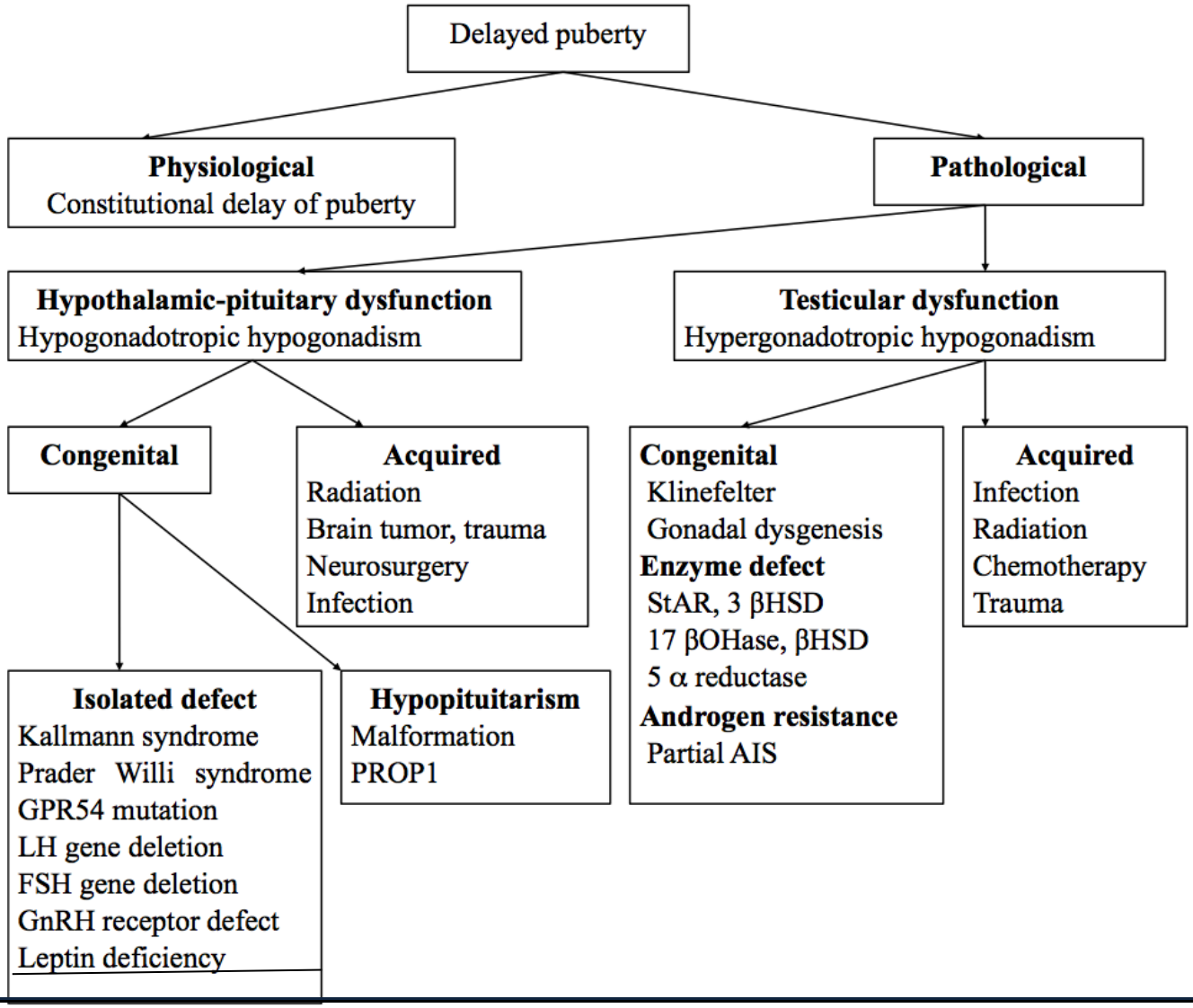
When to assess?

Boys- No pubertal development by 14 years of age.

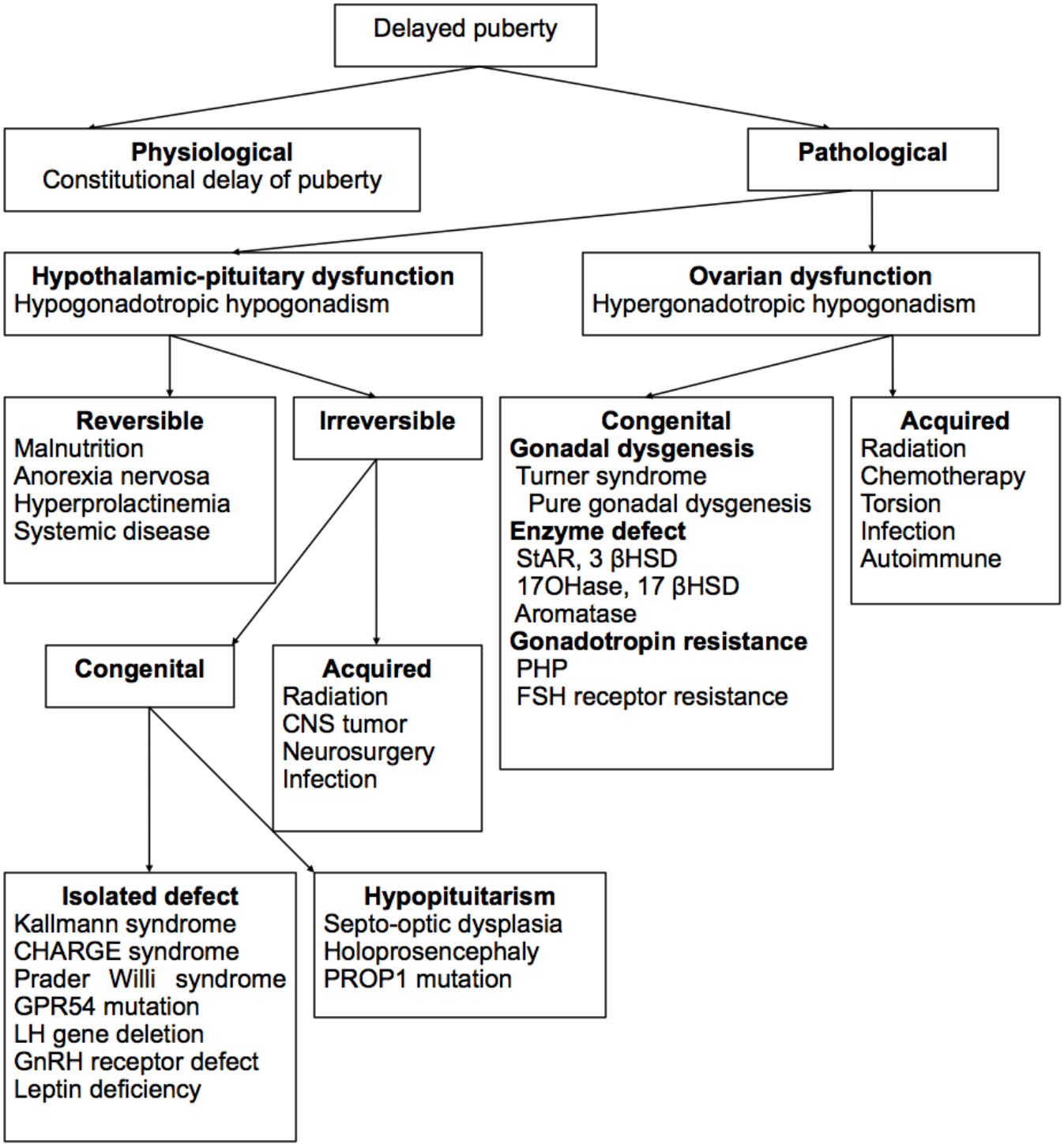
Girls- No thelarche by 13 years of age or no menarche 5 years after thelarche.

Why? - Most children with delayed puberty represent physiological variation in the form of constitutional delay of puberty and growth (CDPG, 80% in boys and 33% in girls). This condition is associated with low gonadotropin levels and needs to be differentiated from isolated hypogonadotropic hypogonadism. Turner syndrome and autoimmune polyendocrinopathy are common causes of delayed puberty in girls.

The causes of delayed puberty in boys include:



The causes of delayed puberty in girls include:

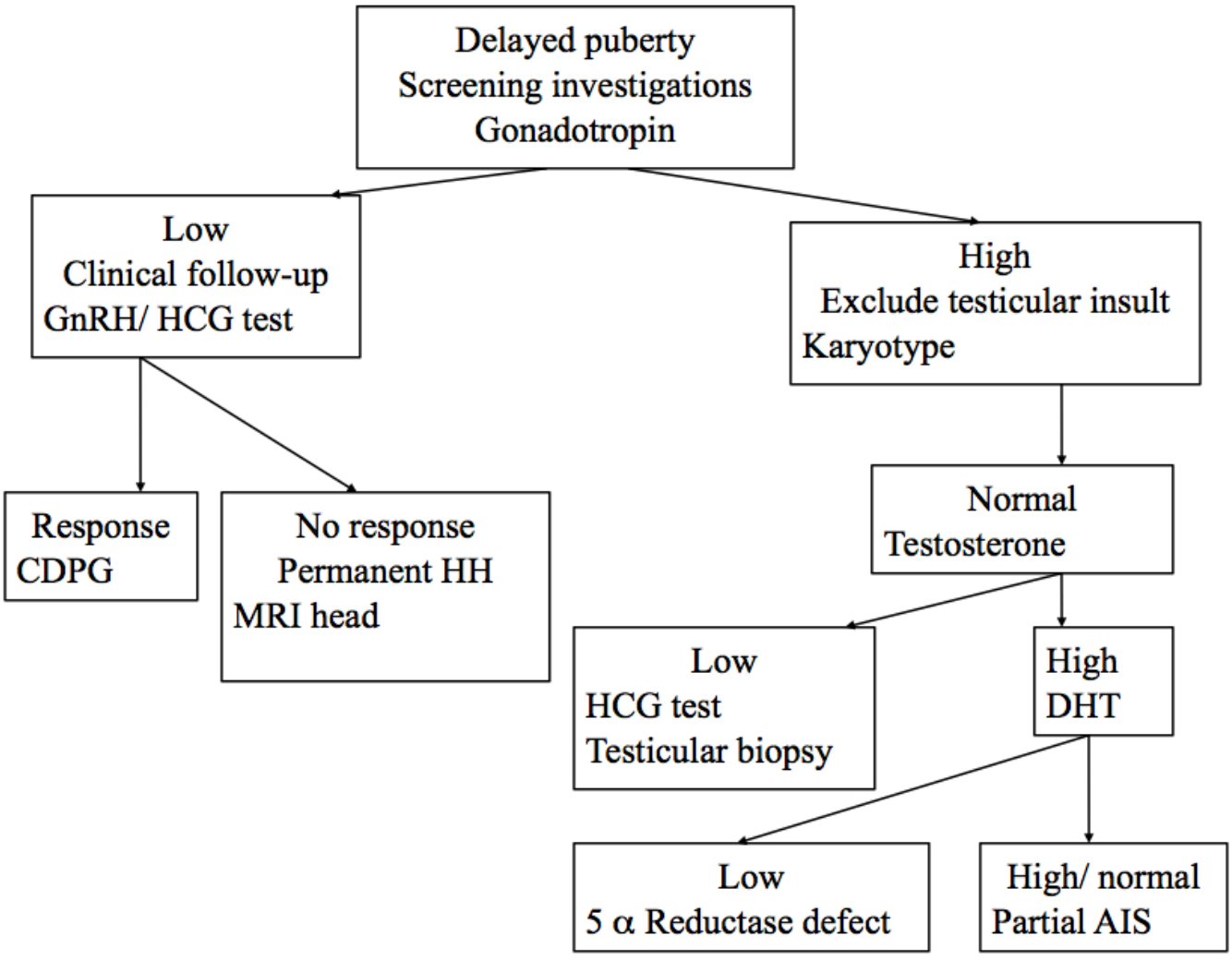


How to approach?

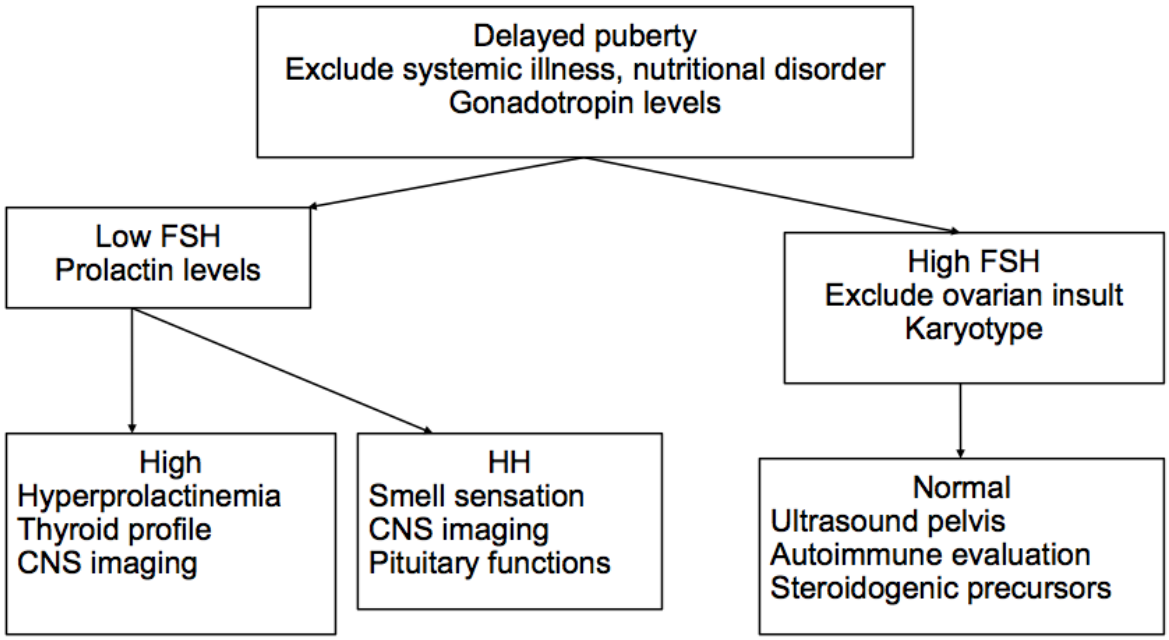
Initial evaluation includes work-up for systemic diseases, bone age and gonadotropin levels. Low gonadotropin levels indicate constitutional delay of puberty and growth (CDPG) or permanent hypogonadotropic hypogonadism (HH) while high gonadotropin levels suggest testicular failure. Follow-up for pubertal features is the gold standard for diagnosis of CDPG but requires prolonged observation. In boys short course of testosterone (100 mg testosterone ester per month for 3-6 months) helps in reducing the period

of follow-up. Morning testosterone levels greater than 20 ng/dL (0.7 nmol/L) are suggestive of CDPG while pubertal DHEAS indicate permanent HH. Positive response to HCG or GnRH stimulation test suggests CDPG. Boys with permanent HH should undergo neuroimaging). In girls with low gonadotropin levels reversible causes like hyperprolactinemia and hypothyroidism should be excluded. Neuroimaging and anterior pituitary evaluation is required in the setting of permanent HH. Hypergonadotropic hypogonadism should prompt karyotype and gonadal insult (trauma, torsion, radiation exposure, alkylating agent treatment) and Klinefelter syndrome (karyotype). Girls with no overt ovarian insult and normal karyotype should be evaluated for steroidogenic defects, autoimmune disorders and PHP (serum calcium and phosphate PHP).

The approach to Delayed puberty in boys is summarized as below:



The approach to Delayed puberty in girls is summarized as below:



How to manage?

The aim of management is to gradually induce puberty mimicking physiological development. Rapid pubertal induction is associated with inadvertent pubertal and skeletal maturation culminating in compromised final height, breast size and uterine size. Growth promoting therapy should be considered in children with Turner syndrome or concomitant growth hormone deficiency before pubertal induction.

Pubertal induction in Boys

Timing- After 14 years of age

Preparation- Injectable preferable over topical gel and oral preparation.

Dose

Preparation	Route	Frequency	Dose	
			Initial	Adult
Testosterone ester	Intramuscular	3-4 weekly	100 mg	300 mg
Testosterone pellets	SC Implant	3 monthly	300 mg	900 mg
Testo undeconate	Oral IM depot	Daily 3 monthly	5 mg 500 mg	10 mg 1000 mg

Protocol- Injection testosterone should be given at a dose of 100 mg monthly for 3-6 doses. Testosterone levels should be measured one month after last dose of testosterone. Normal levels confirm the diagnosis of constitutional delay of puberty and growth while low levels indicate need for long-term treatment. In boys requiring long term therapy the dose should be gradually

escalated to adult dose of 100 mg weekly (250 mg every 21 days or 1000 mg testosterone undeconate as a three monthly depot). The use of HCG in boys with permanent hypogonadotropic hypogonadism helps in increasing testicular volume and chances of subsequent fertility with combination gonadotropin therapy.

Girls

Timing- After the age of 13 years.

Preparation- Estradiol valerate and micronized progesterone are emerging as physiological alternatives to conjugated equine estradiol (CEE) and synthetic estrogen (ethinyl estradiol) and progesterone (medroxy progesterone acetate).

Route- Transdermal route is superior to oral estrogen replacement as oral estrogen suppresses hepatic IGF1 production. Transdermal estradiol also has the advantage of lower thrombotic risk.

Protocol- Estrogen should be started at 5-10% of adult dose (0.25 mg of estradiol valerate, 5 microgram of ethinyl estradiol or 0.12 of conjugated estrogen). The dose should be increased in quantums of 10-20% of adult dose every six months to adult dose (2 mg of estradiol valerate, 0.625 mg of conjugated estrogen and 30 microgram of ethinyl estradiol) over two years. Progesterone (200 microgram daily of micronized progesterone or 10 mg of medroxy progesterone acetate for 10 days) is added after two years of replacement or when withdrawal bleed occurs. This should be followed by cyclical estrogen-progesterone replacement (estradiol from day 1-21 and progestogen from day 11-21). Longer cycles with three monthly withdrawal bleeding may also be used is desired by the girls. Full adult dose of estrogen should be used till the age of 30 years to mimic physiological estradiol peak. Between 30 to 50 years the dose may be lowered to the minimum dose required to prevent osteoporosis. After the age of fifty years the need for estradiol replacement should be determined based on recommendations for postmenopausal women. Periodic monitoring of endometrial thickness and breast examination is required.

Guidelines for estrogen replacement in girls

Dose	Ethinyl estradiol	Equine estrogen	Estradiol valerate	Topical
Initial dose	2 μg/day	0.3 mg/day	0.25 mg	25 μg patch
Increment every 6 months	2-5 μg/day	0.3 mg/day	0.25 mg	25 μg patch
Adult dose	20 μg/day	1.25 mg/day	2 mg	100 μg patch
Preparation	Lynoral 20 and 50 μg	Premarin 0.625 mg	Progynova 1, 2 mg	Not available

Patient Information Page - DR. SHALMI MEHTA, AHMEDABAD

Delayed puberty is defined as the absence of sexual development in females by age 13 and in males by age 14. The condition also applies to adolescents that have begun sexual development but it is progressing slowly.

Several hormones regulate puberty or sexual development. Luteinizing hormone (LH) and Follicle stimulating hormone (FSH) are produced in the pituitary gland, which is located in the brain. These hormones stimulate the ovaries and testes. In combination with hormones from other glands in the body, sexual changes of puberty occur. In early to mid puberty, both males and females experience growth spurts and the growth of hair in the pubic and underarm areas.

The ovaries are stimulated to produce the hormone estrogen. This hormone is responsible for breast development and changes in body shape. In combination with other hormones, it also stimulates periods to begin. This usually occurs between the ages of 12 – 13 yrs. When the testes are stimulated to produce the hormone testosterone, the size of genitals increase and masculine body changes occur, usually by age 13-14 yrs.

WHAT CAUSES DELAYED PUBERTY?

Causes of delayed puberty include history of illnesses such as infection, cancer, kidney, heart or lung disease, eating disorders, taking certain medications, trauma or injury to pituitary gland, trauma or injury to the ovaries or testes, or congenital conditions. The most common cause of delayed puberty is "constitutional delay" in growth and puberty. This means that given time, without treatment, the child will grow and develop normal sexual characteristics. These children are usually referred to as "late bloomers, or late developers". This is seen more frequently in boys.

WHAT ARE THE POSSIBLE EFFECTS OF DELAYED PUBERTY?

If your child's body cannot make estrogen or testosterone, replacements with man-made forms of these hormones may be indicated. If the hormone is not replaced, normal adult sexual maturation may not occur. The child may be short for his/her age and/or look younger than their peers.

Late development can cause embarrassment for both boys and girls at a time when differences from peers are difficult. Children may experience teasing, which can be traumatic for some. It is important to talk to your child about how they are feeling and encourage them to discuss any concerns or worries they may be having.

HOW IS DELAYED PUBERTY DIAGNOSED?

Initially, your doctor will complete a thorough physical exam and will ask you many questions. At that time, some blood tests may be done to determine a possible cause of delayed puberty. This may include an estimation of several hormones. The doctor may also order an X-ray of the hand to determine your child's bone age or growth plate development. In some situations, the physician may order a chromosome study to check for an abnormality. He/she may also need a hormone stimulation test, which gives the physician a more thorough assessment of the body's ability to produce sex hormones. During this test, your child will be given medicine that should stimulate the production of certain hormones. Blood will be drawn at different times during this test to measure the hormone levels. Magnetic resonance imaging (MRI) of the brain or an ultrasound of the sex glands and organs may be ordered.

WHAT IS THE TREATMENT OF DELAYED PUBERTY?

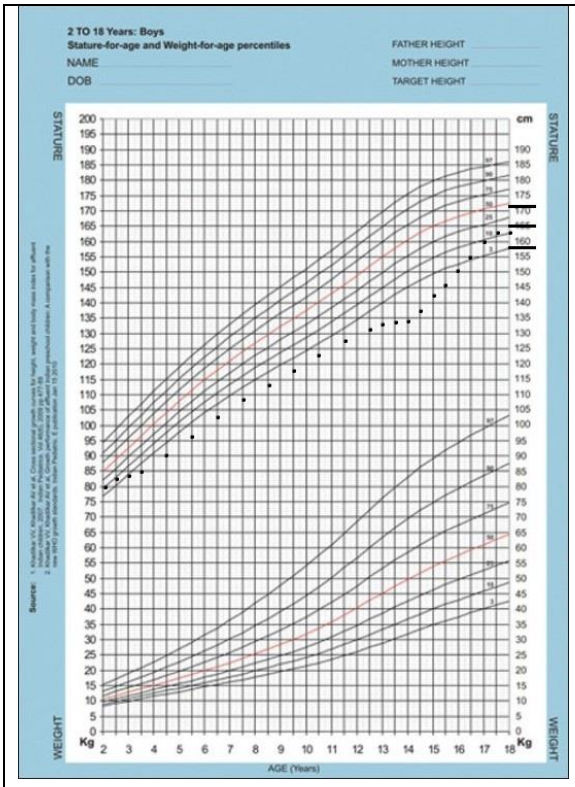
Illness or medication causing a delay in puberty should be corrected, if possible before any therapy is initiated and puberty may progress normally. There may not be any abnormalities identified and puberty will eventually occur. If your child is a "late developer" reassurance is needed that even without treatment, puberty will begin and sexual maturation will occur.

Hormone replacement is given if test results show that the body cannot produce adequate amounts of sex hormones. Sometimes the physician can prescribe low doses of testosterone for 3-6 months to start the puberty process in a boy. This may be referred to as a "jump start" into puberty.

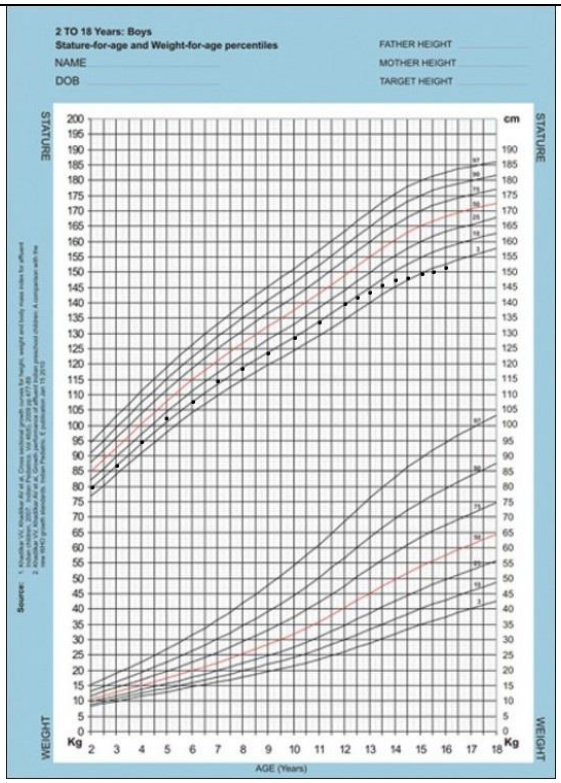
WHEN SHOULD THE DOCTOR SEE MY CHILD?

Most children with delayed puberty are seen by the Paediatric endocrinology clinic every 3-6 months to monitor the progression. Occasionally, your physician may order an ultrasound or additional X-rays. Remember to continue office visits to your child's primary care for routine medical care. If you have additional questions, contact your health care professional.

Growth chart quiz



GROWTH CHART 1



GROWTH CHART 2

Can you identify the two boys with delayed puberty from these growth charts? (solutions on last page)

FERTILITY TREATMENT IN AMENORRHEIC GIRLS –

Dr Ruma Satwik, Consultant, Centre of IVF and Human Reproduction
Sir Ganga Ram Hospital, New Delhi

Oligomenorrhea usually has a favorable fertility outcome since 95% of these cases are due to polycystic ovarian syndrome, hyperprolactinemia or thyroid dysfunction. In all these cases it is easy to induce ovulation with exogenously administered drugs and hence future fertility is not a challenge. Motherhood is achieved easily albeit with treatment.
It is the other group, namely amenorrheic girls that would run into fertility issues in future. It is important at this point to bring in the WHO classification of amenorrhoea to understand where the defect in the HPO axis lies and to device the most appropriate fertility treatment based on this knowledge.

WHO classification of amenorrhea

Group	Pathology	Other name	Hormonal profile
Group I	Hypothalamic non-function	Hypogonadotropic hypogonadism	Low FSH, Low LH, low estradiol
Group II	Hypothalamic pituitary dysfunction	normogonadotropic normogonadism	Normal FSH, high to normal LH, normal estradiol
Group III	Ovarian failure	hypergonadotropic hypogonadism	High FSH, High LH, low estradiol

Group I

Group 1 comprises about 30% of all cases of primary amenorrhea and about 5% of all cases of secondary amenorrhea. The defect here lies at the level of the hypothalamus or the pituitary causing absence of release of the stimulatory hormones, FSH and LH. Both these are necessary for ovarian follicular development. Follicular development sets into motion two processes that would give the female her feminine identity: first it brings about steroidogenesis leading to the cyclic production of estrogen and progesterone which develops secondary sexual characters and causes menses; and second it causes the gradual maturation and release of ovum, the female gamete, harbored within the follicle. These two ovarian functions are absent in hypogonadotropic hypogonadism, so girls afflicted with this condition do not menstruate, develop secondary sexual characters or naturally conceive. Luckily for these girls, different drugs in the form of synthetic hormones are now available that can do all of the above.

Treatment of girls with hypogonadotropic hypogonadism

Since the scope of this write-up is limited to fertility options in girls with amenorrhea, other treatments only just find a brief mention.

I*nvestigations* to look for etiology: Largely serum FSH, LH, E2, Prolactin TSH, Cranial imaging for prolactinomas, pituitary tumours, hemangiomas, empty sella etc.

Specific treatment: Bromocriptine treatment for hyperprolactinemia, surgery or radiotherapy for tumors.

Hormone replacement therapy: Oral contraceptives, or sequential estrogen progesterone to prevent bone mineral loss and for development of secondary sexual characteristics. Young women with primary amenorrhea in whom secondary sex characteristics have failed to develop should initially be exposed to very low doses of estrogen in an attempt to mimic the gradual pubertal maturation process. A typical regimen is as follows: 0.3 mg of conjugated equine estrogens or 25-µg estradiol patch unopposed (ie, no progestogen) daily for 6 months with incremental dose increases at 6-month intervals until the required maintenance dose is achieved. Gradual dose escalation often results in optimal breast development and allows time for the young woman to adjust psychologically to her physical maturation. Cyclical progestogen therapy, given 12-14 days per month, should be instituted toward the end of the second year of treatment.

Fertility treatment: Pregnancy is possible in girls with hypogonadotropic hypogonadism by use of two stimulation strategies. The first is with exogenous gonadotropins for ovulation induction. The second is with pulsatile GnRH analogue administered either subcutaneously or intravenously. The determination of which therapy to use, gonadotropins or gonadotropin releasing hormone pulses is related more to convenience and availability than to science. Therapies appear to be equally effective. GnRH agonist pump represents a more physiologic approach because the pulse of GnRH may be altered to mimic the natural process of ovulation. The disadvantage of treatment, other than the need to use a pump, is that it is available at specialized centers only due to pending approval by FDA for this indication.

Usually a prior priming of FSH receptors is needed before exogenous gonadotropins are introduced. A preparation with both FSH and LH is needed. Gonadotropins are continued in the same dose or stepped up or down according to ovarian response. An hCG trigger is essential for inducing final oocyte maturation. This is followed by either a timed intercourse, IUI or IVF as has been pre-determined based on prior infertility work-up. Luteal phase has to be supported by

human chorionic gonadotropin where OHSS risk is low. Where OHSS risk is high, progesterone and estradiol supplementation may suffice. Each cycle of ovulation induction in the first three months gives a fecundity rate of about 30% in such patients. Ovulation can also be induced by use of pulsatile GnRH therapy.

Group II:
Comprises about 30% of all cases of primary amenorrhoea and a whopping 85% of cases of secondary amenorrhoea. It is clinically useful to divide this group into two sub-groups based on anatomy. The first with either an absent uterus or a mullerian dysgenesis or agenesis. The second with normal uterus and mullerian tract. This anatomically normal subgroup is largely comprised of PCOS and other hormonal disturbances. PCOS leading to primary amenorrhoea is rare, but constitute a large group of individuals that present as secondary amenorrhoea.

Treatment of girls with Normogonadotropic normogonadism

Investigations : Pelvic imaging to establish the presence of uterus, functional endometrial cavity and to rule out any outflow tract obstruction. Hormonal analysis as above. In addition hormones like testosterone levels, DHEA, cortisol levels or 17 alpha hydroxy progesterone levels may be done where signs of severe hyperandrogenism are present.

Specific treatment: Surgical correction of mullerian anomaly where-ever possible. Hysteroscopic synechiaelysis in cases of asherman's syndrome. Hormonal treatment for correction of hormonal dysfunction like hyperandrogenemia, hyperinsulinemia, hyperprolactnemia hypercortisolemia, hypothyroidism, etc. Surgical resection of androgen producing tumours wherever needed.

Fertility treatment: The first subgroup of girls (with anatomic abnormality) is quite capable of conceiving normally if a normal, functional, unobstructed endometrial cavity and vaginal canal can be ensured after surgery. In those, where surgical reconstruction is not possible or has not given the desired results, conception through surrogacy is possible. All aspects of commercial and altruistic surrogacy should then be discussed with the parents in accordance with the guidelines laid down by ICMR. Also it should be made clear that the child so born will continue to be linked genetically to the affected girl and her future husband.
Very recently, cadaveric uterine transplants and uterine transplants from live donors in women with absent uteri have shown success in terms of graft acceptance, embryo implantation and quite remarkably the birth of a viable child at 32 weeks gestation. Although it is a long way off when this surgery becomes

commonplace, it nevertheless gives hope to such girls of becoming mothers without utilizing the agency of surrogate.

The second sub-group (namely amenorrhea due to hormonal disturbances) will conceive if the primary pathology (hypothyroidism, hyperprolactinemia, hypercortisolism etc.)is corrected. In the PCOS women comprising the larger chunk of this sub-group, lifestyle management for weight reduction coupled with ovulation induction strategies usually help the woman in realizing her goal of motherhood. Ovulation induction strategies include use of clomiphene citrate, tamoxifene, letrozole or gonadotropins. For descriptive details on their usage, refer to a book on infertility.

Group III

Comprises about 40% of cases of primary amenorrhea and about 12% of cases of secondary amenorrhea. Here there is a defect at the level of ovary and hence hormone production and ovulation are both absent.

Treatment of girls with Hypergonadotropic hypogonadism

Investigations: Apart from hormonal evaluation and pelvic imaging, a karyotype is essential. In doing so one determines the genetic make-up of this individual, 60% of times which is abnormal. When a Y chromosome is found, a gonadectomy is indicated after pubertal development is complete since the chance of gonadal cell tumours like dysgerminoma is alarmingly high in such gonads.
Hormone replacement therapy: Is needed as above since no endogenous source of sex-steroid hormones is available. This should continue under supervision in low doses in a cyclical way till 40 years of age in the absence of contra-indications to do so.
Fertility treatment: No exogenous stimulation can bring about ovulation. This is by far the most challenging group to treat. Such girls will eventually need an egg donor and IVF to conceive. There are case reports of occasional ovulation in women diagnosed with Turner's syndrome but these reports are by far too few to warrant waiting for spontaneous ovulation and pregnancy to occur. Pregnancy whenever it happens in such individuals (either with donor egg or very rarely with self eggs) is not different in terms of complications, ante partum period postpartum period or lactation. Women conceiving in IVF with donor eggs usually need exogenous progesterone and estradiol supplementation for a period of 7-12 weeks of gestation.

PEDENDOSCAN

Dr Sachin Mittal, Mumbai

Diabetes

Steck AK, Vehik K, Bonifacio E et al and the TEDDY Study Group. Predictors of Progression from the Appearance of Islet Autoantibodies to Early Childhood Diabetes: The Environmental Determinants of Diabetes in the Young (TEDDY). Diabetes Care. 2015 Feb 9.

The Environmental Determinants of Diabetes in the Young (TEDDY) study observed 8,503 children at increased genetic risk for autoimmune diabetes The authors concluded that children who progress to diabetes usually expressed two or more autoantibodies. Higher IAA and IA-2A levels, but not GADA levels, increased the risk of diabetes in those children who were persistently autoantibody positive.

Steck AK, Johnson K, Barriga KJ et al. Age of islet autoantibody appearance and mean levels of insulin, but not GAD or IA-2 autoantibodies, predict age of diagnosis of type 1 diabetes: diabetes autoimmunity study in the young. Diabetes Care. 2011 Jun;34(6):1397-9.

The Diabetes Autoimmunity Study in the Young (DAISY) followed 2,542 children with autoantibodies measured to GAD, IA-2, and insulin. Children expressing three autoantibodies showed a linear progression to diabetes with 74% cumulative incidence by the 10-year follow-up compared with 70% with two antibodies and 15% with one antibody (P <0.0001).

Growth and Puberty

Bhakhri BK, Prasad MS, Choudhary IP, Biswas K. Delayed puberty: experience of a tertiary care centre in India. Ann Trop Paediatr. 2010;30 (3):205-12.

A retrospective data of 42 patients (19 boys, 23 girls, age range 14-27 y) was analyzed to investigate the aetiology of delayed puberty in northern India. The authors concluded that chronic systemic illnesses are the major cause of pubertal delay in developing countries.

Watson SE, Greene A, Lewis K, Eugster EA. Bird's-Eye View of GnRH Analog Use in a Pediatric Endocrinology Referral Center. Endocr Pract. 2015 Feb 9:1-15.

While most patients were treated for CPP, ~27% were treated for other indications. Of girls with CPP, 39% were treated at an age (≥ 8 years) when benefit in terms of height is unlikely. This highlights the need for rigorous studies of GnRHa use for indications beyond CPP.

Pinto G, Cormier-Daire V, Le Merrer M, Samara-Boustani D, Baujat G, Fresneau L, Viaud M, Souberbielle JC, Pineau JC, Polak M. Efficacy and safety of growth hormone treatment in children with hypochondroplasia: comparison with an historical cohort. Horm Res Paediatr. 2014;82(6):355-63.

19 HCH patients with an initial height standard deviation score (SDS) ≤-2 and a mean age of 9.3 ± 3.1 years were treated with a mean r-hGH dose of 0.053 mg/kg/day over 3 years. Height gain in the treated population was +0.62 ± 0.81 SDS greater than in the general population, and +1.39 ± 0.9 SDS greater than in the historical untreated HCH cohort (mean gain of 7.4 ± 6.6 cm gain). A negative correlation between height gain and age at treatment initiation was reported (p = 0.04). No treatment-related serious adverse events were reported. The authors concluded that r-hGH treatment is well tolerated and effective in improving growth in HCH patients, particularly when started early.

Pituitary

Khan MJ, Humayun KN, Donaldson M, Ahmed SF, Shaikh MG. Longitudinal changes in body mass index in children with craniopharyngioma. Horm Res Paediatr. 2014;82(6):372-9.

Craniopharyngioma patients (n = 25) attending a tertiary pediatric endocrine center were divided into three groups based on their BMI at presentation [BMI ≥2 standard deviation scores (SDS), 0-1.99 SDS, and <0 SDS) and then analyzed for trends of BMI over a period of up to 5 years. At the 5-year follow-up, 100% of subjects with highest BMI and 25% of subjects with lowest BMI group were obese, indicating that obesity at presentation, rather than panhypopituitarism either at or after presentation, predicts obesity 5 years after diagnosis. The authors recommended that pediatric craniopharyngioma subjects who have BMI SDS ≥2 at presentation require early and aggressive intervention to help prevent the complications of obesity.

Olsson DS, Andersson E, Bryngelsson IL, Nilsson AG, Johannsson G. Excess mortality and morbidity in patients with craniopharyngioma (CP), especially in patients with childhood onset: a population-based study in sweden. J Clin Endocrinol Metab. 2015 Feb;100(2):467-74

To investigate mortality and morbidity in patients with childhood-onset and adult-onset CP, a nationwide population-based study of 307 patients with a mean follow-up of 9 years was done. Patients with childhood-onset (n = 106) and adult-onset (n = 201) CP had SMRs of 17 (6.3-37) and 3.5 (2.6-4.6), respectively. This first nationwide population-based study of patients with CP demonstrated excess mortality that was especially marked in patients with childhood-onset disease and among women. Patients had increased disease burden related to type 2 diabetes mellitus, cerebral infarction, fracture, and severe infection.

Adrenal

Cartaya J, Misra M. The Low Dose ACTH Stimulation Test: Is 30 Minutes Long Enough? Endocr Pract. 2015 Feb 9:1-21.

Data in 82 patients was retrospectively reviewed to examine both 30 and 60 minute cortisol level to assess whether the interpretation of the test was affected when both cortisol levels were used. 54% of patients reached peak cortisol levels at 60 minutes and 11 patients who did not pass the test at 30 minutes, did so at 60 minutes. The only predictive characteristic was weight status such that overweight and obese individuals tended to peak at 30 minutes and normal and underweight individuals tended to peak at 60 minutes. The authors concluded that cortisol at both 30 and 60 minutes, following administration of synthetic ACTH may be necessary.

Claahsen-van der Grinten HL, Dehzad F, Kamphuis-van Ulzen K, de Korte CL. Increased prevalence of testicular adrenal rest tumours during adolescence in congenital adrenal hyperplasia. Horm Res Paediatr. 2014;82(4):238-44.

Retrospective analysis was done in 41 pediatric male CAH patients aged 0-19 years, regularly followed by high-frequency (12-MHz) ultrasound, to define the prevalence of TART. Above the age of 10 years, there was a clear increase in the prevalence of TART: 10-12 years, 28%, 13-14 years, 50%, and 15-16 years, 75% and above the age of 16 years, TART were detected in 100% of the patients. The tumours were not detectable by palpation. TART is already present in childhood with an increasing prevalence after onset of puberty. Authors recommend regular ultrasound from the onset of puberty in all boys with classic CAH.

DRUG INFORMATION PAGE – Cyclical Estrogen Progesterone therapy

Dr Bhanu K Bhakri
Consultant in Paediatric Endocrinology & Diabetes, AIIMS, Hrishikesh

Puberty can be induced using low dose estrogen therapy started once bone age approximates 12 years, allowing the induction of breast development without risking undue bone age advance. The starting dose of estrogen can be 0.3mg of conjugated estrogens every other day, 5 μg of ethinyl estradiol daily or transdermal estrogen preparations (0.025 mg) twice weekly. The dose of estrogen can be increased every 6 to 12 months in order to reach full replacement doses (daily doses of 0.625mg of conjugated estrogen or 20 μg ethinyl estradiol) after two to three years of therapy.

Replacement therapy, with the possible exception of those without internal reproductive structures, eventually involves cyclic estrogen-progesterone therapy, started once withdrawal bleeding occurs or the endometrial thickness exceeds 5 mm.

Cyclic estrogen-progesterone therapy can involve low-dosage estrogen birth control pills, a daily oral estrogen regimen or the transdermal form (on full replacement dose) for 21 days with the addition of progesterone (10 mg of medroxyprogesterone acetate or 200 to 400 mg of micronized progesterone daily) added for 12 days (day 10–21) followed by a week of no hormones.

Preparations with estrogen or progesterone alone were tabulated in previous issues; few commonly available combined preparations are listed below.

Brand name	Manufacturer	Preparation	Approx price (Rs)
Desogestrel + ethinylestradiol			
FEMILON	Organon	desogestrel 0.15 mg, ethinyl estradiol 0.02 mg X 21 TABS	200
OVULOC LD	Serum Institute	desogestrel 0.15 mg, ethinyl estradiol 0.02 mg X 21 TABS	120
LOCIPIL	Corona	desogestrel 0.15 mg, ethinyl estradiol 0.02 mg X 21 TABS	150
DESOLON	Dewcare	desogestrel 0.15 mg, ethinyl estradiol 0.02 mg X 21 TABS	150
DUOGEN DESO	Xeno	desogestrel 0.15 mg, ethinyl estradiol 0.02 mg X 21 TABS	150
Gestodene + ethinylestradiol			
MELIANE	Bayer	Gestodene 0.075 mg, ethinylestradiol 0.02 mg X 21 tabs	-
Drospirenone + ethinyl estradiol			
YASMIN	Zudus	drospirenone 3 mg, ethinyl estradiol 0.03 mg. X 21 tabs	400
GINETTE	Cipla	drospirenone 2 mg, ethinyl estradiol 0.03 mg. X 21 tabs	225

Revised IAP 2015 Growth Charts for 5-18 Year Old Indian Children

Dr. Vaman Khadilkar

Indian Academy of Pediatrics (IAP) in 2007 wrote growth monitoring guidelines for children from birth to 18 years. The growth charts produced at that time were based on 1989-91 data which is now nearly 25 years old. In a country like India which is in major economic and hence nutrition transition it is necessary to update growth references as suggested by many world experts and bodies. IAP therefore has recently released revised growth charts for 5-18 year old children. IAP growth chart committee was established in January 2014 with the following aims:

1. To produce updated contemporary nationally representative unified growth charts for 5-18 year old Indian children for Height, weight and BMI. by selecting a population of middle and upper middle class children that is representative of all five zones of India as designated by IAP.
2. To remove unhealthy weights from the population by using WHO recommended method so that obesity is not "normalized"
3. To produce BMI charts which are able to depict 23 and 27 adult equivalent cut offs for overweight and obesity respectively. (As these are more appropriate for Asian Indians due to their higher cardio-metabolic risk as lower BMI)

Process: Studies performed on Indian children's growth, nutritional assessment and anthropometry from upper and middle socioeconomic classes in last decade were identified using search engines viz. Pubmed, Embase and Google. Committee contacted 13 study groups; total number of children in the age group of 5 to 18 years were 87022 (54086 boys). Data from fourteen cities (Agartala, Ahmadabad, Chandigarh, Chennai, Delhi, Hyderabad, Kochi, Kolkata, Madurai, Mumbai, Mysore, Pune, Raipur and Surat) in India were collated. Data of children with weight for height Z scores >2 SD were removed from analyses. Data on 33148 children (18170 males, 14978 females) were used to construct growth charts using Cole's LMS method.

Growth Charts Salient features:

1. Height charts show secular trend in height both in boys and girls. At 18 years boys' height has increased by 2.8 cm and that of girls' by 1 cm on an average but at the 97th percentile the same difference is 5 cm in boys at about 3 cm in girls. Children at all ages are now taller as compared to 1989 data. The third percentile remains almost the same. As compared to the WHO or CDC charts, heights are comparable in both sexes until 13 years in boys and 11 years in girls but thereafter there is a significant difference in pubertal spurt in both sexes, Indian children falling short after puberty. Indian children's height charts are very similar to Chinese and Saudi children in terms of their final heights and growth curve characteristics.

2. Weight charts show that both boys and girls are heavier at all ages as compared to 1989 data with the median going up by 2.4 kgs in boys and 4 kgs in girls at 18 years while the difference in 97th percentile as compared to 1989 data is 5 kgs in boys and 0 in girls. The 3rd percentile remains almost the same. As compared to recent datasets by Khadilkar et al and Marwah et al these weight charts are much lower with nearly 15 kgs less weight in 97th percentile for boys and 10 kgs for girls. Thus these charts have managed to remove the unhealthy weights.

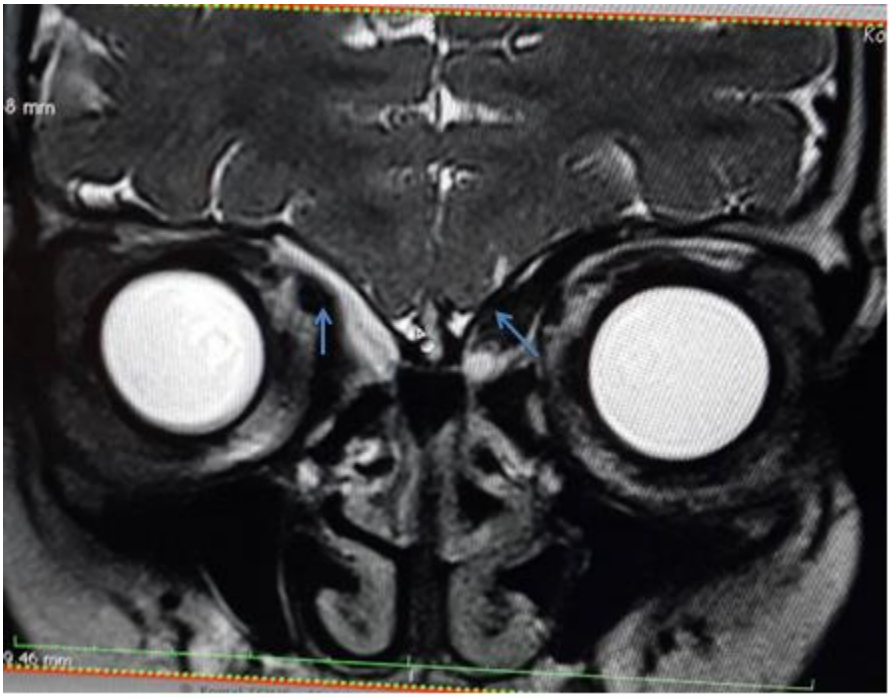
3. BMI charts are designed to depict 23 and 27 adult equivalent cut offs for diagnosis or overweight and obesity respectively as these are better suited for Asian Indian children due to their higher risk of cardiovascular morbidity and mortality at lower BMI. The 23 and 27 adult equivalent cut offs in this paper are very similar to International Obesity Task Force (IOTF) extended BMI cut offs and lower than WHO +1 and +2 Z scores which are better suited for populations of European descent.

Useful Links: These charts are free to download and use for all health care professional and can be downloaded for use from the following link:

http://www.iapindia.org/Revised-IAP-Growth-Charts-2015.php

The IAP growth committee recommends use of these revised growth charts for height, weight and body mass index (BMI) for assessment of growth of 5-18 year old Indian children to replace the previous IAP charts. IAP recommends use of WHO MGRS 2006 charts for growth monitoring in children under the age of 5 years.

PICTORIAL QUIZ FOR READERS (solution on last page) (images contributed by Dr Archana Dayal)



Identify the MRI findings in a child with Delayed puberty.

WELCOME TO OUR NEW MEMBERS

Welcome to our new members – Dr Preeti, Dr Neha and Dr Mudita to the ISPAE team. Looking forward to your participation in the academic activities of the body.

PUBLICATIONS FROM OUR MEMBERS

1. Agarwal M, Joshi K, Bhatia V, et al. Feasibility study of an outreach program of newborn screening in Uttar Pradesh. Indian J Pediatr 2014; Nov 1; Epub ahead of print.

2. Gopalakrishnan V, Joshi K, Phadke S, et al. Newborn screen for congenital hypothyroidism, galactosemia and biotinidase deficiency in Uttar Pradesh. Ind Pediatr 2014; 9: 701-705.

ACADEMIC ACTIVITIES BY ISPAE MEMBERS

National IAP meeting 2015 was held in New Delhi from 22/1/2015 to 25/1/2015. Topics covered in Pediatric Endocrinology include: Pediatric Medicine Surgery Jugalbandi (Dr Shaila Bhattacharya), Growth failure in systemic diseases (Dr P S N Menon), Case scenarios in Pediatric Endocrinology (Abhishek Kulkarni, M Vijaykumar, Anurag Bajpai, Archana Arya), Day to Day management of Diabetes (Riaz I), Turner Syndrome (Subrata Dey) and Vaman Khadilkar (Decoding the new IAP growth charts). Endocrinology chapter symposium chaired by Dr Anju Virmani and done by Dr Vaman Khadilkar and Dr Anju Seth. Panel Discussion of Neonatal endocrine disorders was held (Moderated by Dr Ganesh Jevalikar and panelists include Dr Vijayalakshmi Bhatia, Dr Vandana Jain, Dr M Vijaykumar and Dr Leena Priyambada).

Meeting of the **Delhi Pediatric Endocrine members** was held on 28th November at AIIMS.Two very interesting cases were discussed – an infant with hypernatremia and a child with severe short stature and knock knees.

Dr. Hemchand K P (Mehta Hospital Chennai): Guest lecture on "Approach to short stature" – by Dr Shuba Srinivasan from West mead, Australia; Guest lecture on "Diabetes in young – lessons from the TODAY study" – by Prof Stephen Greene, previous ISPAD president Guest lecture by Mrs Rathi from Western Australia on "type-1 diabetes mellitus – a Nurse educators perspective"

Dr. J Dhivyalakshmi (SRMC, Chennai) - Guest lecture on "Short term and long term complications of Childhood Diabetes" was given by Dr. K. G. Ravikumar (Consultant Intensivist & Paediatric Endocrinologist, KKCTH, Chennai).

Dr. Ramkumar S (Apollo Hospital Chennai) - Conducted Pediatric Endocrine CME in Apollo Children's Hospital consisting of: two lectures on 'approach to short stature' by Dr.Shivaprakash, Endocrinologist, Madras Medical College and 'approach to diabetes in children' by Dr.S.Ramkumar, Endocrinologist, Apollo Children's Hospital followed by discussion.

PATIENT RELATED ACTIVITIES BY ISPAE MEMBERS

Delhi: Dr. Meena Chhabra, Dr. Ganesh Jevalikar, and Dr. Anju Virmani: have been holding quarterly picnics (February, May, August, November) for children with type 1 diabetes and their families. Usually 40-50 kids, come. Everyone has a good time with yoga, races and games, while the parents discuss a different aspect each time.

Dr. Hemchand K P and Dr. Thangavelu S had organised a diabetic get to gether of all children with type-1 diabetes under the care of Mehta Children's hospital. About 50 families attended the program. Agenda included education and fun activities.

Dr. Shalmi Mehta and Dr. Ruchi Shah, Pediatric Endocrinologists from Ahmedabad celebrated the World Diabetes Day on 16th Nov. About 40 patients with their families attended the event. Diabetes education was imparted through fun filled activities. A thyroid checkup was done free of cost for all the patients and their family members. The story of Coco the monkey (Disney character who has type 1 DM-Courtesy Lilly) was narrated to the patients through a powerpoint presentation!

Diabetic Camp (Dr. Meena Mohan) - conducted in Masonic Medical Centre for Children. 33 children and their families attended make it a total of 120 people altogether. The day started off with a walk of 2.5 kms, followed by magic show for children and yoga, to stress the importance of daily exercises. Group discussion was held on preparing food for children with diabetes at home on a day to day basis for parents. Children were engaged in a separate discussion on managing hypoglycaemia in a school setting.

Diabetic Camp was held in Kurinji Hospital (**Dr. Meena Mohan)**. 29 children and families attended, make it to 100 numbers in total. The importance of exercise through Yoga was stressed. Lunch with millets was provided to provide information about low GI foods.

Paediatric Endocrinology Clinic, Sri Ramachandra Medical College & RI, Chennai organized a Childhood obesity awareness camp from 14th to 26th November 2014. Around 70 children benefited. Endocrinology consultation (**Dr. J. Dhivyalakshmi**), Dietary assessment, Diet counseling and investigations for metabolic complications were given free of cost.

Dr. Ravindra Kumar (Hindu Rao Hospital, Delhi) organised a camp for children with type-1 diabetes on 20/11/2014. A talk on diabetes was delivered by Dr Rajesh Khadgawat from AIIMS.

CONGRATULATIONS TO ISPAE MEMBERS

Dr. Ambrish Mithal - for being conferred with Padma Bhushan by the President of India for his distinguished services in the field of medicine.

Dr. Nikhil Tandon - for being conferred with Padma Bhushan by the President of India for his distinguished services in the field of medicine.

Dr. Rakesh Kumar, Associate Professor, Dept of Paediatrics, PGIMER, Chandigarh has been awarded Commonwealth Clinical Training Fellowship in Paediatric Endocrinology for the year 2014-15 to Dept. Of Paediatric Endocrinology, Royal Manchester Children's Hospital, Central Manchester University Hospitals, Manchester, UK.

Dr.S.Ramkumar was awarded 'ALLAN DRASH Clinical Fellowship' by International Society of Pediatric and Adolescent Diabetes (ISPAD) for the year 2014.

Dr. Ashu Rastogi got prestigious "Outstanding Abstract award" and a "travel grant" by much coveted "US Endocrine Society" to present his research paper at San Diego, USA.

Dr. Ashu Rastogi elected as "Governing council member" of "Diabetic Foot Society of India".

Dr. Anju Virmani – elected to the advisory board of ISPAD

Dr. Vaman Khadilkar – elected to the Executive council of the APPES

Dr. Anju Virmani - invited to speak in the ADA meeting in Boston in June 2015.

Dr. Nalini Shah – best faculty award by the APPES fellow's school. She was also the faculty for the fellow's school at the APPES. Invited speakers in APPES meeting 2014 at Darwin – **Dr. Nalini Shah** (Pheochromocytoma), **Dr. Preeti** (PCOS) and **Dr. Hemchand K P** (Type-1 diabetes mellitus)

ISPAE OBSERVERSHIP 2015 GUIDELINES

Indian Society for Pediatric and Adolescent Endocrinology (ISPAE) announces the invitation of applications for the **ISPAE Observership Award 2015**. The objective of the award is to inculcate interest and disseminate knowledge in pediatric endocrinology among pediatricians and physicians with interest in pediatric endocrinology. The process and procedures are as follows:

1. The award is meant as a reimbursement to partially defray the expenses of the selected candidate in spending one to three months (1-3 months) with a Pediatric Endocrinology centre *or* an Endocrinology centre with facilities for exposure and training in pediatric endocrinology.
2. The training centre should have at least (1) two pediatric endocrinologists or (2) one pediatric endocrinologist and one adult endocrinologist interested in pediatric endocrinology as faculty/trainers. The centers which have on-going training and/or fellowship programs would be preferred. For more information please visit www.ispae.org.in
3. The applicant must communicate with the training centre/ mentor in advance. Documentation of acceptance by the Centre/ Mentor/ Institute concerned should be submitted along with the application. The **observership should occur preferably in the Calendar Year 2015**, and should be completed **no later than March 31st 2016**.
4. It is planned to grant travel award to 2 persons this year if applicants are found suitable.
5. The award consists of an amount of Rs 25,000/-, and will be given after the candidate successfully completes his/her tenure and the course report duly signed by the mentor, which is submitted to the executive committee of ISPAE is approved.
6. The applicant must be a member of ISPAE. Those who are not would have to become members immediately upon selection, else the offer will automatically go to the next on the short list. Please check the details regarding ISPAE membership at our web-site www.ispae.org.in
7. Preference will be given to young faculty members, who are in a position to start pediatric endocrine clinics in their hospital, or are already running a clinic but have not had the benefit of a formal training program. However, the award is not limited to this group. Those who have done endocrinology or pediatric endocrinology training earlier and wish to do a refresher course in pediatric endocrinology may also apply.
8. Upper age limit is 45 years.

9. The application must be accompanied by a recommendation note from one active ISPAE member.
10. It is desirable that the applicant plans for & submits a brief synopsis of a research plan that he/she would like to commence during the period.
11. **Applicants should send in their applications for the award by 15th April 2015.** The awardees will be announced by 30st April 2015.
12. Interested candidates must submit their applications in the prescribed application form. This application must be forwarded by the Head of the Department, if the applicant is a student or trainee and those working in a government institutions.

Completed applications should be sent by email to Dr. M Vijayakumar (Secretary, ISPAE) **and** Dr. Bhanu Kiran Bhakhri (Joint Secretary, ISPAE) at drmvijaycalicut@gmail.com and drbhanu04@yahoo.co.in. Hard copies should be additionally sent to Dr. M Vijayakumar, Additional Professor, Department of Pediatrics, Institute of Maternal and Child Health, Government Medical College, Kozhikode, Kerala: Pin 673008

Report on ISPAE 2015 and ISPAE PET 2015
(4th Biennial Conference of Indian Society for Pediatric and Adolescent Endocrinology)
In association with European Society of Pediatric Endocrinology (ESPE) and Asia Pacific Pediatric Endocrine Society (APPES)
Hosted by Medanta The Medicity Hospital, Gurgaon

On behalf of the organizing committee of ISPAE 2015, I wish to thank ISPAE office bearers for giving us the opportunity of hosting the most prestigious event of ISPAE !

The preparations for ISPAE 2015 and ISPAE 2015 are in full swing. The conference, ISPAE 2015 will be held between 27-29 Nov 2015 at The Epicenter, Gurgaon (managed by the same company as the India Habitat Center, New Delhi). The venue is centrally located in Gurgaon near Huda City Center Metro station and is easily accessible from Delhi. ISPAE PET will be held between 24-27 Nov 2015 at Hotel Ibis, Delhi Aerocity, an easily accessible venue from New Delhi

International Airport and New Delhi railway station (by the airport Metro. The process of application for ISPAE PET will be soon advertised in Indian pediatrics and on the conference website.

The International faculty confirmed to participate in both the events include Dr Matthew Sabin, Dr Craig Munns, Dr Margaret Zacharin, Dr Paul Hofman, Dr Olaf Hiort and Dr Jean Claude Carel.

On behalf of the organizing committee, I would request all ISPAE members to use this opportunity to showcase the massive amount of clinical work that is going on in pediatric endocrinology in India. The unique strength of our conferences in the past has been our scientific program and we will make sure that it is of a very high quality this time too!

I wish to inform ISPAE members that the process of registration is now open and queries related to the same may be directed to me on gjevalikar@gmail.com and ispae2015 @gmail.com. I would be happy to take your calls/sms on +91-9711539359

Regards

Dr PSN Menon (Organizing Chairperson)
Dr Ambrish Mithal (Organizing Chairperson)
Dr Anju Seth (Scientific Committee Chairperson)
Dr Preeti Dabadghao (ISPAE PET Convener)
Dr Ganesh Jevalikar (Organizing Secretary)

UPCOMING ISSUE:

OBESITY AND METABOLIC SYNDROME

Solution to pictorial quiz

Absent Olfactory bulb in Kallman syndrome

Solution to Growth chart quiz

a) CDGP

b) IHH