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GROWTH DISORDERS – A REVIEW ARTICLE

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ABSTRACT

Until quite recently, the management of children with growth hormone deficiency (GHD) had focussed on the use of recombinant human GH (rhGH) therapy to normalise final adult height. However, research over the past two decades that has demonstrated deficits in bone health and cardiac function, as well as impaired quality of life in adults with childhood-onset GHD (CO-GHD), has questioned this practice. Some of these studies suggested that there may be short-term benefits of rhGH in certain group of adolescents with GHD during transition, although the impact of GHD and replacement during the transition period has not been adequately investigated and its long-term benefits remain unclear. GH therapy remains expensive and well-designed long-term studies are needed to determine the cost effectiveness and clinical benefit of ongoing rhGH during transition and further into adulthood. In the absence of compelling data to justify widespread continuation of rhGH into adult life, there are several questions related to its use that remain unanswered. This paper reviews the effects of growth hormone deficiency on bone health, cardiovascular function, metabolic profile and quality of life during transition and young adulthood.

KEYWORDS: Growth Hormone Deficiency, Disorder of Growth Hormone.

I. INTRODUCTION OF GROWTH AND GROWTH DISORDER

Physical growth refers to bodily changes that happen as a child matures including weight, length or height and head circumference increases. Growth failure is by far one of the most common reasons for referrals to the pediatric endocrine office. Linear growth is most rapid in prenatal life when it is mainly regulated by maternal and placental factors. Postnatal growth is progressively slower and predominantly reflective of childs own genetic potential (see growth velocity figure). Another growth acceleration occurs at puberty.

Normal linear growth	
0-1 years	25 cm
1-2 years	10 cm/yr
3-5 years	7 cm/yr
4-7 years	6 cm/yr
7 years - puberty	5 cm/yr

A. Height and Length

- Patients < 2 years of age are measured lying flat on a board with one fixed and one moving end. The measurement is then plotted on the "birth to 36 month" growth chart. The most accurate growth chart for children under 2 years of age is the World Health Organization growth chart.
- Patients > 2 years are measured standing up against a calibrated wall stadiometer and plotted on the "2 to 20 year" growth chart.
- Ideally, height or length is measured thrice and the average is calculated.

Growth Velocity: Growth velocity (cm/yr) = (Height2-Height1) / (#months between times) x 12. It determines normal or abnormal growth by comparing height change over a period of time to gender-appropriate norms.

B. Body Proportions

- Arm Span (AS) is the distance from one end of child's arm (measured at the fingertips) to the other. AS is measured fingertip to fingertip while standing flat against a wall with arms outstretched. At

birth, AS is less than length by about 2.5 cm. By 10 years of age, AS is equal to height; and after 10 years in boys and 12 years in girls, AS exceeds height by up to 5 cm. If AS is greater than 5 cm, pathologic causes of tall stature such as Marfan's Syndrome or hypogonadism should be considered.

- Upper to lower segment ratio (U/L) reflects trunk vs legs ratio, where lower segment is the distance from the middle of pubic symphysis to the floor level and upper segment is height minus lower segment. At birth, U/L is about 1.7:1 or trunk longer than legs. U/L then decreases by 0.1 for every year of age until 10 years of age when it becomes 1:1 (trunk=legs). After 10 years, the ratio is <1.3. U/L segment is high in rickets, Turner, and achondroplasia and low in Marfan Syndrome and eunochoid habitus.
- Weight to length ratio (w/l) or BMI (Body Mass Index) is useful to assess pediatric overweight and obesity. BMI is calculated by dividing the patient's weight in kilograms by their height in meters squared. A BMI between the 85th to 95th percentiles is defined as overweight, and a BMI greater than the 95th percentile defines obesity. It is also informative for the differential diagnosis of short stature (e.g., w/l >1 and with short stature may suggest endocrinopathy, w/l <1 and with short stature may suggest nutritional deficiencies).

C. **Mid parental height calculation**

- Males = [mother's height (in) + father's height (in) + 5 inches]/2
- Females = [mother's height (in) + father's height (in) - 5 inches]/2
- Normal genetic height range is MPH +/- 3.5

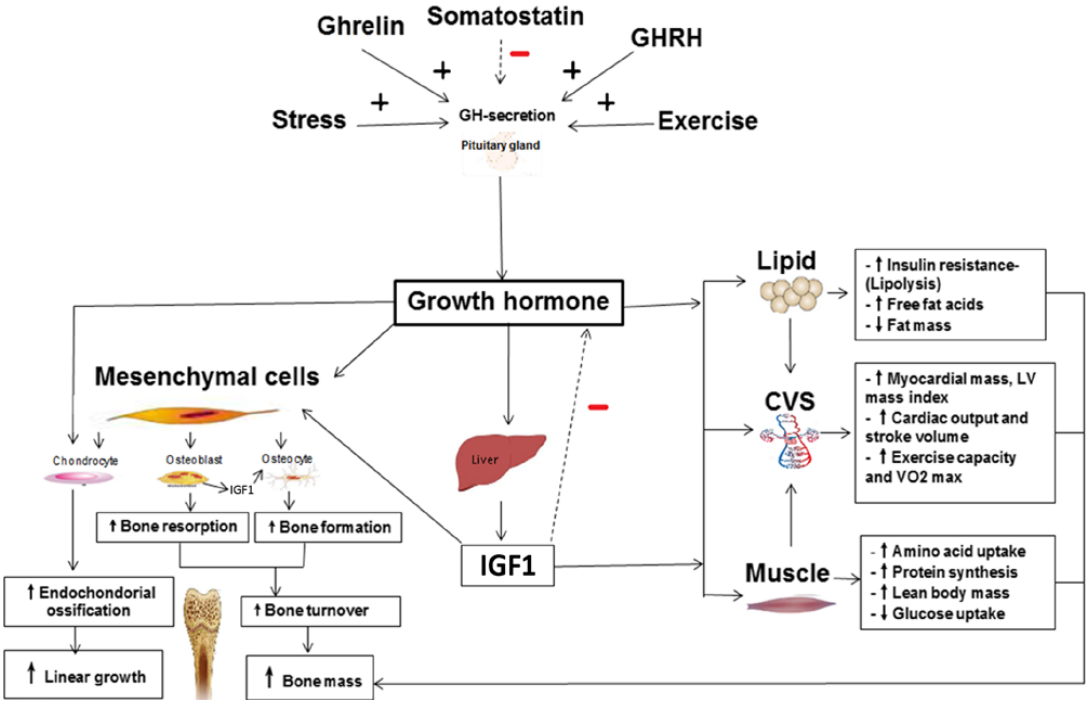

Fig. 1: Flow chart of Growth Hormone.

Bone Age x-ray: tool for assessment of skeletal maturation as it compares to the chronological age and for the prediction of child's final adult height (for films older than age 6 years). Bone age x-ray is typically delayed in thyroid hormone and growth hormone deficiency or constitutional delay of growth, normal in familial short stature and advanced in precocious puberty. Children < the 3rd %ile on the growth chart or > 2 standard deviations below MPH deserve a short stature evaluation.

II. Definition of Normal Growth

Kids and teens grow and go through **puberty** at different times. For girls, puberty usually begins between ages 7 and 13. For guys it often begins a bit later — between 9 and 15. Girls become more rounded in the hips and their breasts begin to develop. Usually, about 2 years after their breasts begin to develop, girls begin to **menstruate**, or get their periods. Guys' penises and testicles grow larger, and guys and girls both grow hair in their pubic areas and under their arms. Guys get more muscular, begin to grow hair on their faces, and their voices get deeper. During puberty, both guys and girls go through growth spurts.

Growth rates vary considerably from child to child. But measured in height, average "normal" growth is often described as.

- 0-12 months: about 10 inches a year
- 1-2 years: about 5 inches a year
- 2-3 years: about 3½ inches a year
- 3 years to puberty: about 2 to 2½ inches a year

If your child is less than the third percentile in height for a child of his age, that can be a red flag for growth hormone deficiency.

Some teens develop a lot earlier than their friends (called precocious puberty). Others can develop much later than other people of the same age. This is called delayed puberty. Kids and teens may not grow as fast as their peers for many reasons. If you're short, you may just have familial (genetic) short stature. In other words, short parents tend to have short children. If a doctor finds you're growing steadily and sexually maturing at the right age, then you can probably expect to grow to a normal size, although you may be somewhat shorter than average.

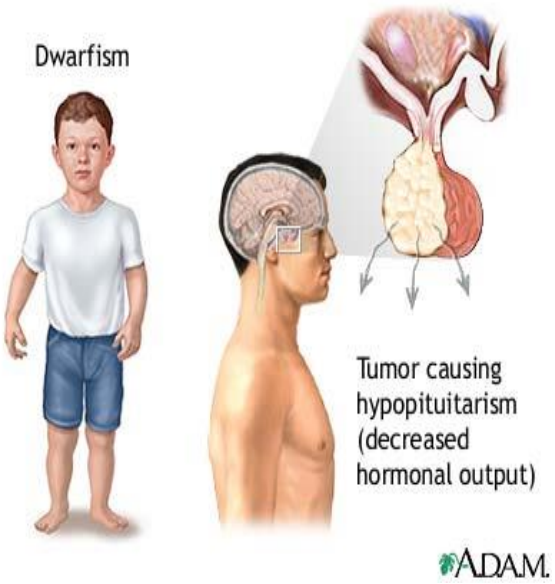

Fig. 2: Dwarfism-A Tumor Causes Hormonal Deficiency.

Teens who have constitutional growth delay grow at a normal rate when they're younger, but they lag behind and don't start their pubertal development and their growth spurt until after most of their peers. People who have constitutional growth delay are often referred to as "late bloomers." If a kid or teen might have constitutional growth delay, a doctor might take X-rays of the wrist and compare them with X-rays of what's considered average for that age. Teens with constitutional growth delay have bones that look younger than what's expected for their age. These teens will have a late growth spurt and continue growing and developing until an older age. They usually catch up with their peers by the time they're young adults.

Teens might have slower growth if they.

- Don’t get enough protein, calories, and other nutrients in their diet.
- Have a long-lasting (chronic) medical condition, such as problems with the kidneys, heart, lungs, and intestines.
- Have sickle cell anemia.

Following the treatment plan worked out with a doctor can help teens with health problems grow better.

III. Growth Disorders

Teens may have growth problems for other reasons. Growth is controlled by the hormones the body makes. Many diseases of the **endocrine system** can affect growth. Endocrine glands release hormones that travel throughout the body in the bloodstream.

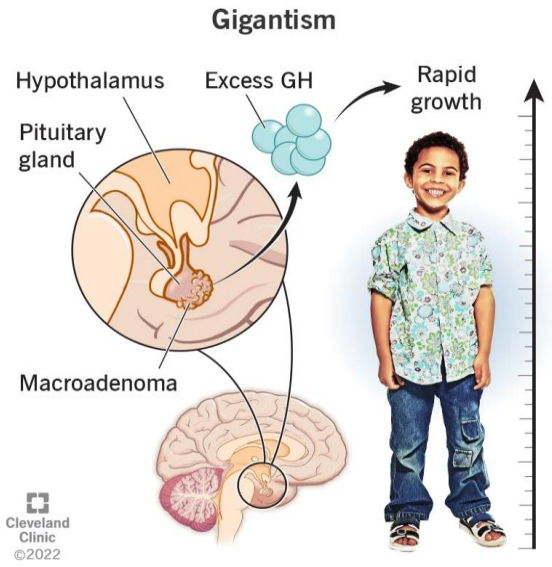

Fig. 3: Growth Hormone & its effect on Body.

The hypothalamus (part of the brain) controls the pituitary gland, which in turn releases some of the hormones that control growth and sexual development. Estrogen and testosterone are important hormones that drive sexual development and function and also play a role in growth. Hypothyroidism can cause slow growth because the thyroid gland isn't making enough thyroid hormone, which is needed to support normal growth. A blood test can show if someone has low thyroid hormone levels. Some causes of poor growth are genetic (a problem with a person’s genes). For example, **Turner syndrome** is a **genetic condition** that happens in girls. It is caused by a missing or abnormal X chromosome. Girls with Turner syndrome tend to be short and don't go through normal sexual development because their ovaries (which make eggs and female hormones) don't mature, so can’t work as they should. Another condition that can lead to significantly short stature is **dwarfism**. When a person has dwarfism, bones and cartilage don’t grow normally. In many types of dwarfism, the arms and legs are short and look out of proportion to the rest of the body.

IV. Growth Hormone Deficiency

Growth hormone deficiency (GH deficiency) is a growth disorder related to the hormones that control growth. This condition involves the pituitary gland, the small gland at the base of the brain that makes growth hormone along with other hormones. If the pituitary gland doesn't

make enough hormones, normal growth slows down or stops. Kids and teens with GH deficiency grow less than 2 inches (5 centimeters) a year. GH deficiency happens if the pituitary gland or hypothalamus is damaged or doesn't work as it should. A person can be born with it, or it can happen later due to a head injury, brain infection, or brain surgery. Tumors near the pituitary gland, like **craniopharyngioma** (pronounced: kray-nee-o-far-un-jee-OH-muh), can also damage the hypothalamus and pituitary gland and slow growth.

As the name implies, growth hormone deficiency results when the pituitary gland doesn't produce enough growth hormone to stimulate the body to grow. This can result in noticeably short stature in children.

- Growth hormone deficiency may be partial (the pituitary gland produces insufficient amounts of growth hormone) or total (the pituitary gland produces no growth hormone).
- Growth hormone deficiency may occur during infancy or later in childhood.
- About one in 4,000 to 10,000 children have growth hormone deficiency.
- With early detection and treatment, many of these children can reach a normal height.

Damage to the pituitary gland or hypothalamus may be the result of an abnormal formation that occurred before your child was born (congenital) or something that occurred during or after birth (acquired).

Congenital growth hormone deficiency can occur if there are mutations in genes for factors that are important in pituitary gland development, or in receptors and factors (including growth hormone) along the growth hormone pathway; to date, however, the cause of most of these cases is unknown.

Acquired causes of growth hormone deficiency include.
- A brain tumor in the hypothalamus or pituitary.
- Head trauma.
- Radiation therapy for cancers, if the treatment field includes the hypothalamus and pituitary.
- Diseases that infiltrate the hypothalamus or its connection to the pituitary gland, such as histiocytosis.
- An autoimmune condition (lymphocytic hypophysitis).

It's also important to remember that growth hormone deficiency is only one of many conditions that may affect your child's growth. Your child's short stature may be caused by other syndromes, and growth failure may be due to decreased nutritional intake, gastrointestinal disorders, diseases that have increased metabolic demand, or hypothyroidism.

V. Symptoms of growth hormone deficiency

Since growth takes place over many years and since children grow at different rates, symptoms of growth hormone deficiency may be hard to identify. In addition to noticeably slow growth with normal body proportions, signs may include.
- Immature appearance, compared to peers
- A chubby body build
- A prominent forehead
- An underdeveloped bridge of the nose

Growth hormone deficiency has no effect on a child's intelligence.

These symptoms may resemble other conditions, so be sure to always consult your child's physician for a diagnosis.

VI. Complications of growth hormone deficiency

Some research suggests that there are additional complications from growth hormone deficiency, including:
- Decreased bone mineral density
- Increased cardiovascular risk factors
- Decreased energy level

You and your family are key players in your child's medical care. It's important that you share your observations and ideas with your child's health care provider and that you understand your provider's recommendations. If your child is experiencing symptoms of growth hormone deficiency and you've set up an appointment, you probably already have some ideas and questions on your mind. But at the appointment, it can be easy to forget the questions you wanted to ask. It's often helpful to jot them down ahead of time so that you can leave the appointment feeling like you have the information you need.

If your child is old enough, you may want to suggest that she write down what she wants to ask her health care provider, too.

Some of the questions you may want to ask include.
- What's causing my child's growth hormone deficiency?
- Will you be prescribing growth hormone replacement therapy?
- Are there any side effects or potentially dangerous risks to treatment?
- How long will my child have to remain on medication?
- How much can I expect my child to grow?

A. Short stature etiology

Common parental concerns about height tend to be gender biased (e.g. boys that are the shortest in their class or girls that are "too tall" or "taller than even her male classmates"). Referral for a short stature evaluation is also commonly prompted by concerns over bullying/ teasing at school for child's size/stature.

B. Normal variants

- **Familial short stature.** Parents are short; therefore, their children are likely to be short. Growth velocity is typically normal along with body proportions, labs and bone age. However, since some pathological causes of short stature are familial, an evaluation may be warranted for children who are very short on the growth chart despite growing along their genetic target height trajectory.
- **Constitutional growth delay ("late blooming").** Children's growth velocity is usually normal in childhood but progressively declines and it can be associated with delayed puberty. However, catch-up growth occurs without assistance and children eventually achieve heights within their genetic target height range (although typically below their mid-parental height). Bone age x-ray is typically delayed for chronological age.

VII. Pathological causes of Growth Disorder

- **Nutritional deficiency:** Under nutrition (global nutritional deprivation or marasmus, inadequate protein intake or Kwashiorkor, anorexia nervosa, zinc deficiency)
- **Psychosocial dwarfism:** Extreme emotional deprivation can result in failure to thrive (both poor height and weight growth) or even short stature with normal BMI.
- **IUGR or small for gestational age:** Poor growth due to maternal, placental or chromosomal factors. About 10% of children born SGA fail to "catch-up" to normal growth percentiles by age 2 years.
- **Systemic disease:** malabsorption, heart disease, renal disease, heme/onc disease, pulmonary disease, diabetes mellitus, inborn errors of metabolism, chronic infection, inflammatory disease
- **Chromosomal abnormalities/genetic syndromes:** Turner Syndrome, Prader-Willi Syndrome, Russel Sliver Syndrome, Noonan Syndrome
- **Skeletal dysplasias:** achondroplasia or hypochonodroplasia etc.
- **Endocrinopathy:** thyroid hormone deficiency, growth hormone deficiency, Cushing Syndrome
- **Chronic drug intake:** supra physiologic glucocorticoid exposure, high-dose estrogens or androgens, stimulent medications (e.g., methylphenidate, dextroamphetamine)
- **Idiopathic short stature:** Height < 2 SD below the corresponding mean height for a given age, sex and population group without evidence of systemic, endocrine, nutritional or chromosomal abnormalities.

VIII. Diagnosis of Growth Disorder

Bone age x-ray (to assess skeletal maturation), CBC, CMP, ESR, UA to screen for systemic disease, free T4, TSH, IGF-1, and IGFBP-3 to screen for endocrinopathy. Celiac screen optional, Pituitary/brain MRI as needed. Karyotype/microarray or specialized genetic testing as clinically indicated.

IX. Treatment of Growth Disorder

Typically, growth hormone replacement is reserved for true growth hormone deficiency. Many causes of short stature are due to an underlying disease and by treating this disease, you are simultaneously able to treat the short stature. For example, levothyroxine treatment for hypothyroidism and growth hormone for growth hormone deficiency typically restores linear growth. However, growth hormone treatment is also FDA approved for Turner Syndrome, small-for-gestational age with failure to catch up, Prader-Willi Syndrome, idiopathic short stature, SHOX gene haplo insufficiency, Noonan Syndrome and chronic kidney disease. **Tall stature** is defined as predicted adult stature greater than two standard deviations above the mean height for age and gender. Tall stature can represent a normal variant of growth such as familial tall stature or it may be pathological.

X. Unani aspects of Growth Disorder

A. Asnan-e-arba and their temperament

There are four periods of life.

- *Sinn-i-Numū*(the period of growth and development): It is dominated as the early period and lasts about twenty five years. The peoples of this period are hot and wet in temperament.
- *Sinn-i-Shabāb or Sinn-i-wuqūf*(manhood/the period of stability): It is the period of youth/middle age and lasts upto thirty five or forty years depending upon the state of the health and temperament of individual. The people in this period are Motadil mail ba hararat in temperament.
- *Sinn-i-Kuhūlat* (Aetus verelis / the period of decline with continuing vigor): It is the period of the middle age and extends to about sixty years. The people in this period are cold and dry in temperament but then old age.
- *Sinn-i-Shaykhūkhah* (old age or Aetus cripita / the period of decline with the appearance of weakness in vigour): It is the age of the old to the end of life.[1,2,5,6]

B. *Sinn-i-Numū* / Period of growth: It is further divided into five periods.

- *Sinn-i-Ṭufūlat* (Infancy): It is upto 4 years of age. It is the period before the limbs are fitted for walking.
- *Sinn-i-Ṣabā* (Babyhood): It is from 4 upto 7 years of age. It is the period of appearance of teeth. Walking has been learnt, but is not steady. The gums are not full of teeth.
- *Sinn-i-Tara'ru_* (Childhood): It is from 7yers upto 14 years. The body shows strength of movement. The teeth are fully out. Pollutions have not yet appeared.
- *Sinn-i-murahiqah or Sinn-i-Bulūgh* (Juvenility/puberty): it is from 14 years upto 21 years of age. The period up to the development of hairs on the face andpubes. Pollutions begin.

- *Sinn-i-Fatā* (Youth): It is upto 30 years. It is the period up to the limit of growth of the body.[2,7,1]

C. Relation between *Ruṭūbat Gharīziyya* and Growth

The period of growth is hot and moist and in this period both *Ruṭūbat Gharīziyya* as well as *Ḥararāt Gharīziyyah* are dominant.[1] Ibn Nafees in Kulliyat nafisi says that hotness of sibyan is because of their higher metabolic rate than adults and olds.[8] In this period *Ruṭūbat Gharīziyya* exceeds the quantity of sufficient for the preservation of *Ḥararāt Gharīziyyah* (normal body heat) or in the other words it is more than sufficient for various metabolic processes of the body. In this period the organs of the body continue to grow.[1,8]

In the period of *wuqūf*, the quantity of *Ruṭūbat Gharīziyya* is only equal to the quantity sufficient for the preservation of *Ḥararāt Gharīziyyah* i.e. neither it is excessive nor deficient than the quantity required for the preservation of normal heat, or for the continuance of normal metabolism. So that in this period, there is no growth or dissolution/degeneration takes place.[1,8]

In the period of *Kuhūlat*, the quantity of *Ruṭūbat Gharīziyya* is lesser than the quantity required for the preservation of *Ḥararāt Gharīziyyah* or bodily metabolism. But there is no domination of *Ruṭūbat Gharībah ballah* (abnormal metabolic compounds). In this period the powers and faculties begin to deteriorate but there is no marked dissolution.

In the period of *Shaykhūkhah*, the quantity of *Ruṭūbat Gharīziyya* is deficient and lesser than the quantity required for the preservation of *Ḥararāt Gharīziyyah* and tocontinue the bodily normal metabolism and super added with and dominated by *Ruṭūbat Gharībah ballah*(abnormal metabolic products). In this period deterioration in the powers and faculties of the body is marked. *Ruṭūbat Gharīziyya* and *Ḥararāt Gharīziyyah* are markedly reduced. Hence the *Mizāj* becomes *Bārid* (cold) and *Yābis* (dry).[1,8]

D. Rate of growth at different phases of *Sinn-i-Numū*

Growth of the body does not proceed at a uniform rate. At different age itshows different rate of growth. During infancy, especially in the first year growth is very rapid. Between three and twelve years, growth proceeds at a lower rate. At puberty growth again becomes very rapid. After puberty the rate slows down. Growth of skeleton continues upto 25 years of age, thereafter epiphyseal cartilages ossify andgrowth is arrested.[1]

Regarding this Ibn Sina says in his book –Alqanoon Fit-Tib that, the temperament during the whole of this period of life (period of growth) is almost equable as regards "heat", but "moisture" is in excess. There has been not a little controversy among older writers about the degree of heat during the period of juvenility as compared with that of youth. Some argue that the heat is greater in the former than the latter, and that this accounts for their growth, Others argue that the innate heat of youth is far greater than that of juvenility, and the process of growth, greater in juveniles, requires adequate moisture rather than heat. These then are the two theories and the facts on which they are based.

- **Galen s teaching:** Galen is opposed to both. In his opinion the heat is actually the same in each. The difference is that in puberty its quantity is great but its acuity is less. In youth the heat is less in quantity but greater in acuity. At the outset of life, the innate moisture suffices for the two requirements- maintenance of innate heat and growth. But there comes a time when one or other or both must fail. Innate heat must be adequate to enable growth to take place, yet the basis of growth (innate moisture) is failing, so that growth must be cease.[2]

- **As regards the second theory:** During juvenility growth is in virtue of moisture rather than in virtue of heat. This cannot be true because moisture is the material cause of growth and moisture does not unfold or construct itself. It is not a self created, it only changes in virtue of a formative power acting upon it. As amatter of fact this formative power is F- the "soul" or "nature "- that which is in the decree of Allah ('Umr-i-Allah). This "nature" requires an instrument where with to work, and this instrument is the innate heat.

This completes Galen's teaching about the temperaments of juvenility and youth. The temperament of youth is nearer to equipoise than that of juveniles but compared with them, its temperament is dry and compared with the third and fourth periods of life, the temperament of youth is moist.[2]

E. Factors affecting *Quwwat Nāmiya*

Following factors affect *Quwwat Nāmiya* (faculty of augmentation) and controls growth of the body.

- Warathah (heredity): As a result of transmission of hereditary character of parents to their off springs, children of tall person usually grow tall and so on. The internal and external environments also play their role in affecting *Quwwat Nāmiya*in stimulating or retarding growth.
- *Ghidhā* (food): Ibn Sina says that *Quwwat Nāmiya* (augmentative faculty) is served by *Quwwat Ghādhiya* (nutritive faculty) and growth is possible only when it supplies food exceeds the *Taḥallul.*
- *Ruṭūbat*: Factors producing *Ruṭūbat* (moisture) in the *Mizāj* of internal environment of the body enhance growth, and effect of *yubusāt* (dryness) is contrary to this. *Akhlāṭmuḥarrikah* (hormones): Hormones which exert strong effect on the *Mizāj* (temperament) of the internal environment of the body and thereby affect growth, are the following.

a) Growth hormone of the anterior pituitary, thyroid hormones and insulin help in the replacement of wear and tear and enhancement of growth. Thus, the

Quwwat Nāmiya takes its work from these hormones.

b) Growth of the gonads and secretion of sex hormones is controlled by *Quwwat Nāmiya* through the gonadotropic hormones of the anterior pituitary. Sex hormones are required for the development of secondary sex characters with the growth of the *A'ḍā' Ṭanāsulliyya* (accessory sex organs).

c) Growth of the thyroid and adrenal cortex and their functions are controlled by the thyrotrophic hormones and ACTH, respectively.

d) Growth of bones is controlled through the parathyroid hormones.[1]

F. Mechanism of *Quwwat Nāmiya*

This can be understood by the mechanism of bone growth as an example. During embryonic development most bones of the body are first seen in the form of cartilage. The replacement of these cartilages by bone is called ossification.[9] Most bones are formed by a process of Endochondral ossification, in which performed cartilage templates (models) define their initial shapes and positions, and their cartilage is replaced by bone in an ordered sequence. Bones such as those in the cranial vault are laid down within a fibro-cellular membrane, by a process known as intra-membranous ossification.[10]

- In most bones, ossification begins during intrauterine life at an area called the primary centre of ossification.
- The part of the bone formed by extension of bone formation from the primary centre is called the diaphysis.
- However, the ends of long bones are still cartilaginous at birth. These are ossified from secondary centers that (as rule) appear after birth.
- Each part ossified from a secondary centre is called an epiphysis.
- For many years after birth, the bone of epiphysis and diaphysis is separated by a plate of cartilage called epiphyseal plate.
- This plate is a site of active bone growth. Growth in length of a bone is possible only as long as the plate exists.
- When a bone has attained its full length the epiphyseal plate disappears and the diaphysis and epiphysis fuse with each other. This is referred to as fusion of the epiphysis.[9]

Fusion of epiphysis and diaphysis starts at puberty and is complete by the age of 25 years, after which no more bone growth take place. Bone grows in length by multiplication of cells in the epiphyseal plate of cartilage and in the thickness by multiplication of cells in the deeper layer of periosteum. Bone grows by deposition of new bone on the surface and at the ends. This process of bone deposition by osteoblast is called oppositional growth or surface accretion.[11]

G. GH-A basic tool of *Quwwat Nāmiya*

Quwwat Nāmiya performs their functions with the help ofGrowth hormone also called somato-tropic hormone or somatotropin. It is a peptide hormone synthesized by somato-tropic cells within the lateral wings of the anterior pituitary and stored in very large amount in pituitary gland. It is Single un-branched polypeptide chain containing 191 amino acid and of molecular weight-22,005Daltons.[12]

H. Metabolic effects of human growth hormone

Growth hormone (GH) exerts its multiple effects on every cell. The metabolic actions of human growth hormone may be considered in four broad categories.

- Anabolic effects: i.e. effects which may be considered reflections of an increase in protoplasmic mass. It causes growthof all tissues of the body that are capableof growing. It enhances almost all facets of amino acid uptake and protein synthesis by cells, while at the same time reducing the breakdown of proteins.
- Skeletal effects-bone growth anddevelopment.
- Effects on carbohydrate and fat metabolism: It enhances body protein, uses up fat stores and conserves carbohydrates.
- Miscellaneous effects: It increase glomerular filtration rate and renal plasma flow and also increases tubular reabsorption of phosphate.[12,13]

I. Mode of Action of GH

GH acts on bones, growth and protein metabolism occurs through somatomedin secreted by liver. GH stimulates the liver to secrete somatomedin. Somatomedin is defined as a substance through which growth hormone acts. It is a polypeptide with the molecular weight of about 7,500.Somatomedins are of two types: first one is Insulin-like growth factor-I (somatomedin C), and other one is Insulin- like growth factor-II.[14] The insulin like growth factors (IGFs) are members of the family of insulin related peptides, which includes insulin, IGF-I and IGF-II. The IGFs are potent mitogens for many different cell types, including those of the immune system, and these factors play a central role in growth and development.[15]

J. Regulation of growth hormone secretion

GH secretion is under negative feedback control. Hypothalamus releases GHRH and GHRP, which in turn promote the release of GH from anterior pituitary. GH acts on various tissues. It also activates the liver cells to secrete somatomedin C (IGF- I). Now, the somatomedin C increases the release of GHIH from hypothalamus. GHIH, in turn inhibits the release of GH from pituitary. Somatomedin also inhibits release of GHRP from hypothalamus. It actson pituitary directly and inhibits the secretion of GH. GH inhibits its own secretion by stimulating the release of GHIH from hypothalamus. This type of feedback is called short-loop feedback control. Similarly, GHRH inhibits its own release by short-loop feedback Control.[14]

K . Factors affecting Growth

There are various efficient and coefficient factors that affects growth including especially environmental factors. The ways to increase human growth hormone naturally are- lose body fat, try an Arginine supplement, fast intermittently, reduce sugar intake, take a GABA supplement, exercise at a high intensity, don‘t eat a lot before bedtime, take a melatonin supplement, take beta- alanine and/or a sports drink around your workouts, try other natural supplements including- glutamine, creatinine, ornithine, L-dopa, glycine, Optimize your sleep.[21] Specific exercises which help in maintaining the normal functioning of the pituitary gland are- Triangle pose, Pushups, Seated wide leg forward bend, Childs pose.[22] Pituitary gland can also be activated through Yoga. In yoga, the third-eye chakra governs the pituitary gland. This is Locatedin the middle of the eye brows.[23]

CONCLUSION

GHD is an important condition that has detrimental effects on both physical and psychological health throughout life, whereas rhGH therapy shows benefits in both children and young adults with GHD throughout each stage of their life. It seems from the current data that rhGH has less direct impact on bone density, with a greater impact on body composition and cardiovascular risk factors, including improvement in serum lipid profiles, and to a lesser extent on insulin sensitivity and QoL. Even with scarce evidence, substantial short-term studies during transition revealed that untreated GHD has a risk of alteration in somatic and metabolic consequences, although it is difficult to establish whether these mild alterations represent the early long-term consequences and whether subsequent rhGH treatment improves long-term health. Larger studies of longer duration of rhGH therapy will be required to determine whether the metabolic alterations in adolescent GH-deficient patients persist in later adulthood and if recommencement of rhGH therapy has a positive impact on these aspects.

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