Original Article

PHYSIOLOGY OF GROWTH

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Growth is characterized by addition of newly formed protoplasmic mass to the existing cells or laying down of new cells.[1] Growth is a complex phenomenon which is affected not only by growth hormone and somatomedins but also by insulin, thyroid hormones, androgens estrogens and glucocorticoids. It is also affected by genetic and racial factors, and adequate nutrition. It is normally accompanied by a sequence of maturation changes and it involves protein synthesis and increase in length and size but not just an increase in weight. Which could reflect formation of fat or retention of salt and water rather than growth.[2] (Figure I).

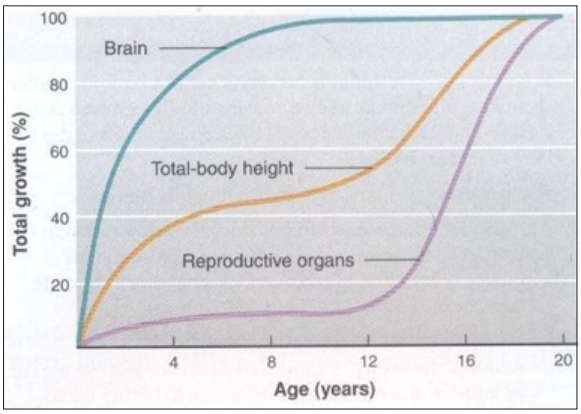

Fig-1: Relative growth in brain, total-body height (a measure of long-bone and vertebral growth), and reproductive organs. Note that brain growth is nearly complete by age 5, whereas maximal height (maximal bone lengthening) and reproductive organ size are not reached until late teens.[3]

The growth process involves cell division and net protein synthesis throughout the body, but a person, height is determined specifically by bone growth, particularly of the vertebral column and legs.[3] Ordered, controlled growth is essential for development and maintenance of normal human.[4]

Growth periods:

Patterns of growth vary from species to species. In humans, two periods of rapid growth occurs, the first in infancy and second in late puberty. The first period of accelerated growth is partly a continuation of the fetal growth period the second growth spurt, at the time of puberty is due to growth hormone, androgens and estrogens. The subsequent cessation of growth is mainly due to closure of epiphyses in the 18 years, after ward further increase in height is not possible. This growth spurt occurs earlier in girls.[2] (Figure - II).

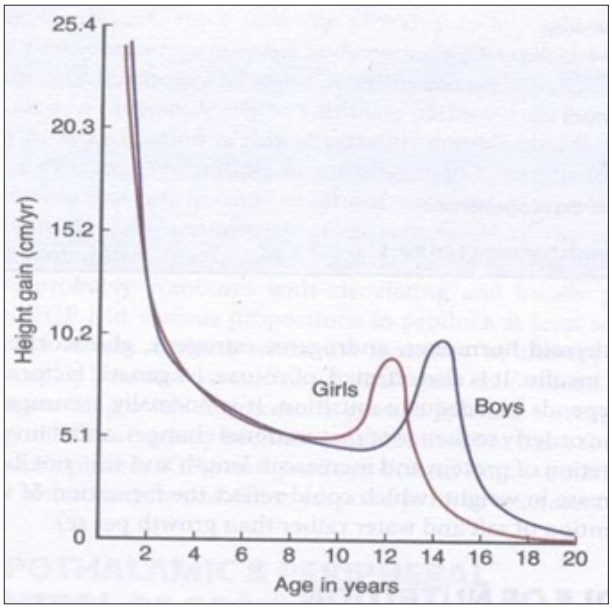

Fig-2: Rate of growth in boys and girls from birth to age 20.[3]

During childhood, height increases 5 7.5 cm/years and weight increases 2 -2.5 kg/year. In females, puberty begins at the age of approximately 11 years with breast budding followed by menarche at 13 years. Regular ovulatory menstrual cycles are established 2 - 3 years after menarche and linear growth ceases at age 16 -17 years. In males, testicular size begins to increase at age of 12 years followed 1 year later by penis enlargement and increased rates of linear growth. Secondary sexual characteristics appears approximately at age 14 15 years and growth ceases at approximately age 18 years. Impaired nutrition including diseases such as chronic diarrheal states, psychological disturbances and hormonal derangement are important causes of growth failure. The most common endocrine deficiencies are of growth hormone, thyroid hormone and insulin.[4]

Growth factors may facilitate cellular uptake of nutrients required for hypertrophy and division of one cell into two.[5] These growth factors include: epidermal growth factor (EGF), platelet derived

(PDGF). Fibroblast growth factor (FGF), insulin like growth factors (1GF) and nerve growth factor (NGF).[4]

Insulin like growth factor 1 (IGF1) is required for normal fetal total body growth and specifically for normal maturation of the fetal nervous system during prenatal life. It appears to be placental lactogen, a hormone released from the placenta, which is similar to growth hormone in structure.[3] Synthesis of insulin like growth factor (IGFI) mainly occurs in the liver stimulated by growth hormone[6] and all cells of the body express its receptors.[7] IGF1 helps to incorporate sulphate into chondroitin sulphate of epiphyseal cartilage.[8]

Factors controlling growth:

1- Genetic and racial factors. Offsprings of tall parents are usually tall. An Afghan is taller than a Japanese.[1]

2- Role of adequate nutrition. The diet must be adequate not only in protein content but also in essential vitamins and minerals particularly in children and at the time of pubertal growth. During infancy and childhood, malnutrition can interfere with both intellectual development and total body growth.[2] A normal man requires only 20 essential organic compounds in addition to a source of calories and water. Eight amino acids, 11 vitamins and linoleic acid are essential. The most generalized deficiencies in humans are caloric malnutritcon (marasmus) and protein malnutrition (Kwashiorkor). These deficiencies are wide spread in underdeveloped countries and are more common in elderly, chronically ill and alcoholic persons in developed countries.[4]

Following a temporary period of stunted growth due to malnutrition or illness, if a child is given proper nutrition and recovery from the illness can manifest a remarkable growth spurt- "catchup growth", that brings a child to within the range of normal heights expected for his or her age.[3]

3. Hormonal effects. The contributions of hormones to growth after birth are shown in **Figure III.** Growth hormone Secreted from somatotropes of anterior pituitary gland. It promotes growth of many body tissues and stimulates cartilage and bone growth through somatomedins (insulin like growth factors), mainly somatomedinC (1GF1). It decreases glucose utilization for the energy but increases fat utilization for the energy. It promotes protein synthesis and its deposition in tissues and decreases catabolism of proteins and amino acids. There is necessity of insulin and carbohydrates for the growth promoting action of growth hormone. Growth hormone stimulates secretion of erythropoietin from kidney to increase erythropoiesis. The mean plasma growth hormone level in normal adults is 2 4 ng/ml and 5 8 ng/ml in children.[9] There is stunted growth in children with deficiency of growth hormone or somatomedinC (Levi Lorain dwarf) or due to defect in receptors (Laron dwarf).[2]

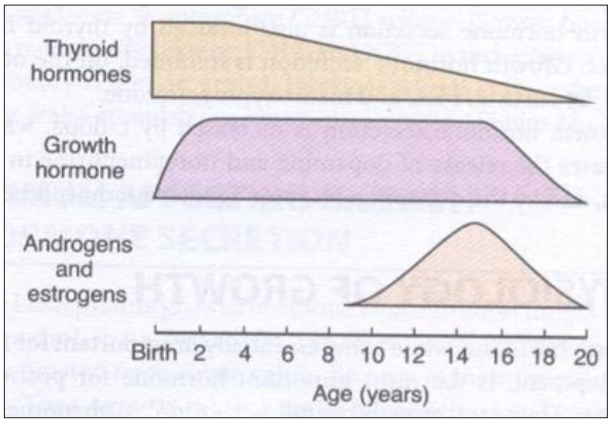

Fig-3: Relative importance of hormones in huma growth of various ages.[2]

Insulin Secreted from βcells of pancreatic islets. It is called "hormone of energy abundance", stores the excess of energy. Insulin promotes muscle glucose uptake and metabolism. It promotes liver uptake, storage and use of glucose. It increases fat synthesis and storage and also increases protein synthesis along with growth hormone to promote growth. It stimulates growth mainly during fetal life.

Thyroid hormones (Triiodothyronine and thyroxine) promote growth and development of brain during fetal life and for the first few years after birth. These stimulate almost all aspects of carbohydrate metabolism leading to hyperglycemia. Thyroid hormones decrease plasma cholesterol, phospholipids and triglycerides but increase plasma free fatty acids. These hormones increase basal metabolic rate. These promote protein synthesis in physiological concentration and protein catabolism in excessive secretion Thyroid hormones are required for growth hormone synthesis and growth promoting effect of this hormone. These are essential for normal growth during childhood.[10] Stunted growth and mental retardation occurs due to thyroid deficiency during fetal life and infancy is called cretinism. **(Figure-IV)**

Glucocorticoids are secreted by adrenal cortex. The main glucocorticoid is cortisol. It promotes gluconeogenesis and decreases glucose utilization by cells resulting into hyperglycemia. It increases liver and

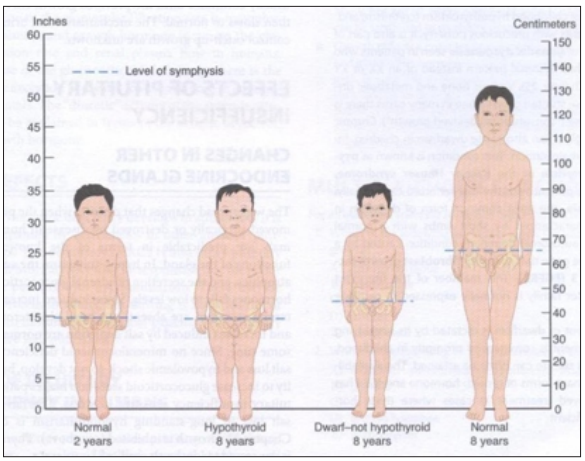

Fig-4: Normal and abnormal growth. Hypothyroid dwarfs (cretins) retain their infantile proportions. Whereas dwarfs of the constitutional type and to a lessor extent of the hypopituitary type have proportions characteristic of their chrorologic ages.[2]

Glucocorticoids are secreted by adrenal cortex. The main glucocorticoid is cortisol. It promotes gluconeogenesis and decreases glucose utilization by cells resulting into hyperglycemia. It increases liver and plasma protein synthesis but protein break down in extraheptic tissue leading to increase plasma amino acid. It causes mobilization of fatty acids to increase plasma fatty acids.[11]

Androgens. These include adrenal androgens (dehydroepiandrosterone and androstenedion) and testosterone from Leyding cells of testes. Androgen promotes protein synthesis and deposition to increases muscle mass and bone size.[12]

Estrogens. These are secreted form ovaries. These increase protein synthesis and deposition in breast, uterus, and bones.[13]

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