HUMAN GROWTH AND DEVELOPMENT

- the study of all aspects of human growth and development
- a highly multi-disciplinary science involving

1) **medicine** (paediatrics, endocrinology, physiology)
- growth hormone treatment of children after intrauterine growth retardation
- GH treatment of children after IU growth retardation - protocol:
- Participants - inclusion criteria:
1. birth weight less than P3 for gestational age
2. neonatal period without signs of severe asphyxia (defined by Apgar score less than 3 after 5 minutes), without signs of chronic lung disease
3. no catch-up growth defined as obtaining a height of P3 within the first 2 years of life or at a later stage
4. height velocity (cm/year) for chronological age P50
5. chronological age at the start of treatment: 3.0 - 7.99 years (boys and girls)
6. prepubertal signs defined as Tanner stage 1
7. well documented growth data from birth up to 2 years and at least 1 year before the start of the study
- Participants - exclusion criteria: any endocrine or metabolic disorder such as diabetes mellitus, diabetes insipidus, hypothyroidism or inborn errors of metabolism, ….

2) **nutrition - dietary recommendations for children:**
- **energy** should be adequate to support growth and development and to reach or maintain desirable body weight
- keep total fat intake between 30 to 35 percent of calories for children 2 to 3 years of age and between 25 to 35 percent of calories for children and adolescents 4 to 18 years of age
- choose a **variety** of foods to get enough carbohydrates, protein and other nutrients
- eat **only enough** calories to maintain a healthy weight for your height and build
- **don't overfeed**: estimated calories needed by children range from 900/day for a 1-year-old to 1,800 for a 14–18-year-old girl and 2,200 for a 14–18-year-old boy

3) **genetics**
- auxology is a valuable instrument for the **clinical diagnosis of SHOX** (short stature homeobox-containing gene) insuffiency in school-age children with unexplained short stature
- ~80% of SHOX mutations are complete gene deletions, diverse point mutations account for the rest
- SHOX mutation screening to children with an extremities-trunk ratio less than 1.95 + 1/2 height (m) and to add a critical judgment of the hand radiography

4) **socioeconomics, sociology**
- epidmiological auxology
- **children** living under **varying socioeconomic** conditions show **remarkable differences** in their **physical development**, further that later adult functional fitness as well as expected life span would suffer when growth and maturation had occurred under adverse circumstances
- **aim:** to utilize the research data on the relationship between socioeconomic environment and child growth or maturation is that the differences in the growth patterns of the children of subpopulations living under different socioeconomic conditions are primarily due to socio-demographic factors

5) **public health**
- by using growth charts to monitor children's growth
- growth charts are international (WHO) or national standards that show how healthy children should grow in environments believed to support optimal growth

6) **anthropology, anthropometry**
- **anthropology:** the study of humans, past and present: the study of human beings and their ancestors through time and space and in relation to physical characters, environmental and social relations, and culture, dealing with the origin, nature and destiny of human beings
- serves the other disciplines by serving anthropometric data (systematic data collections) for every age-group

Auxology studies:

- the **biological aspects** of physical growth and development both in the pre- and postnatal period
- the **morphological and physiological changes** that occur since the intrauterine stage through early life and that have an effect on the rest of the human life cycle
- within **socioeconomic** and cultural context
- both in **normal** and **pathological** conditions
- by taking into account their environmental, socioeconomic and emotional situations

- **the main aims of human ontogenic studies:**
  - to reveal the structural and functional changes during human development from the undifferentiated or immature state to a highly organized, specialized or mature state
  - to determine the normal range of these developmental processes

- **ontogeny:**
  - the origin and the development of an organism
  - starts with fertilization and ends with the attainment of an adult state, usually expressed in terms of both maximal body size and sexual maturity

- As individuals pass through the life stages, four main types of development occur:
  1) **Physical development**: progressive changes in size, shape and function of the body till complete maturity; the genetic potentials are translated into functioning adult systems
  2) **Mental development:** refers to development of psychical, cognitive and psychosocial characteristics
  3) **Emotional development:** refers to children's increasing awareness and control of their feelings and how they react to these feelings in a given situation
  4) **Social development:** refers to children's ability to interact with their peers and adults in a socially acceptable way

Development:

- **progression** of changes from undifferentiated or immature state to a highly organized, specialized or mature state
- a **sequence** of orderly, often irreversible changes; can occur with or without an increase in size
- results from **genetic plans** contained within the chromosomes
- the developmental process depends upon a precisely coordinated interaction of **genetic and environmental factors**
- **growth:** achieved via increased cell number or size or production of extracellular matrices
- **hyperplasia**: an increase in the number of the cells of an organ or tissue causing it to increase in size (due to any number of causes including increased demand, chronic inflammatory response, hormonal dysfunctions)
- **hypertrophy:** the increase of the size of an organ due to an increase in cell size rather than division (e.g. in muscle that has been actively stimulated)
- **differentiation:** one cell → many cell types and functions, the first cells are totipotent, later differentiation steps generate groups of pluripotent cells, terminal differentiation and dedifferentiation
- **totipotency**: the ability of a single cell to divide and produce all of the differentiated cells in an organism (e.g. zygotes)
- **pluripotency**: a stem cell that has the potential to differentiate into any of the three germ layers: endoderm (e.g. interior stomach lining, gastrointestinal tract, the lungs), mesoderm (e.g. muscle, bone, blood, urogenital), or ectoderm (e.g. epidermal tissues and nervous system)
- **multipotency:** progenitor cells which have the gene activation potential to differentiate into multiple, but limited cell types (e.g. blood stem cell can differentiate itself into several types of blood cell types like lymphocytes, monocytes, neutrophils, etc., but cannot differentiate into brain cells, bone cells or other non-blood cell types)
- **morphogenesis:** formation of anatomical structures (physical and chemical), process by which the adult assumes final shape along with the control of cell growth and cellular differentiation

- **Growth:** quantitative increase in size or mass, a component of development
- **Maturation:** the process and the state of reaching functional capacity in terms of biological, behavioural and cognitive capacities, a component of development – increasing complexity, a progression of changes
- all humans follow the same pattern of growth and maturation
- the sequence of each stage is predictable, although the time of onset, the length of stage and the effect of each stage vary with person
- the factors that influencing the growth and maturation are both genetic and environmental
- **genetic factors:** determine such characteristics such as sex, race, …
- **environmental factors:** affect an individual growth and maturation (family, religion, climate, culture, school, community and nutrition)

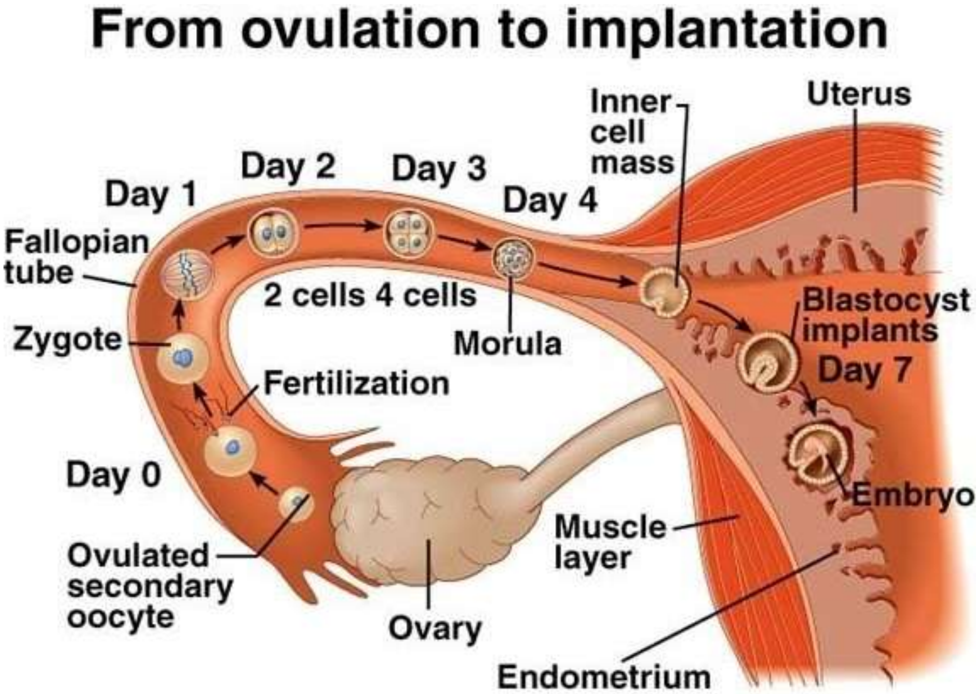
- **Life cycle:** stages of development (growth and maturation) **from conception to death** of any organism

- developmentally functional stages
- life cycle begins with *fertilization*
- then proceeds through *prenatal growth and development*
- *birth*
- *postnatal growth and development (neonatal stage, infancy, childhood, puberty)*
- maturity
- senescence
- ends with death

Prenatal life

- **Prenatal age**
  - time elapsed since fertilization
  - mean duration is 38 weeks/264 days
    - germinal period: first 2 weeks
    - embryonic period: 2 to 8 weeks
    - foetal period: 2 to 9 months

- **intensity of prenatal development:**
  - oocyte: 0.2 mm, 4 μg
  - embryo (8th week): 30 mm, 2.0-2.7 g
  - newborn: 48-52 cm, 3000-3500 g



Female Reproductive System

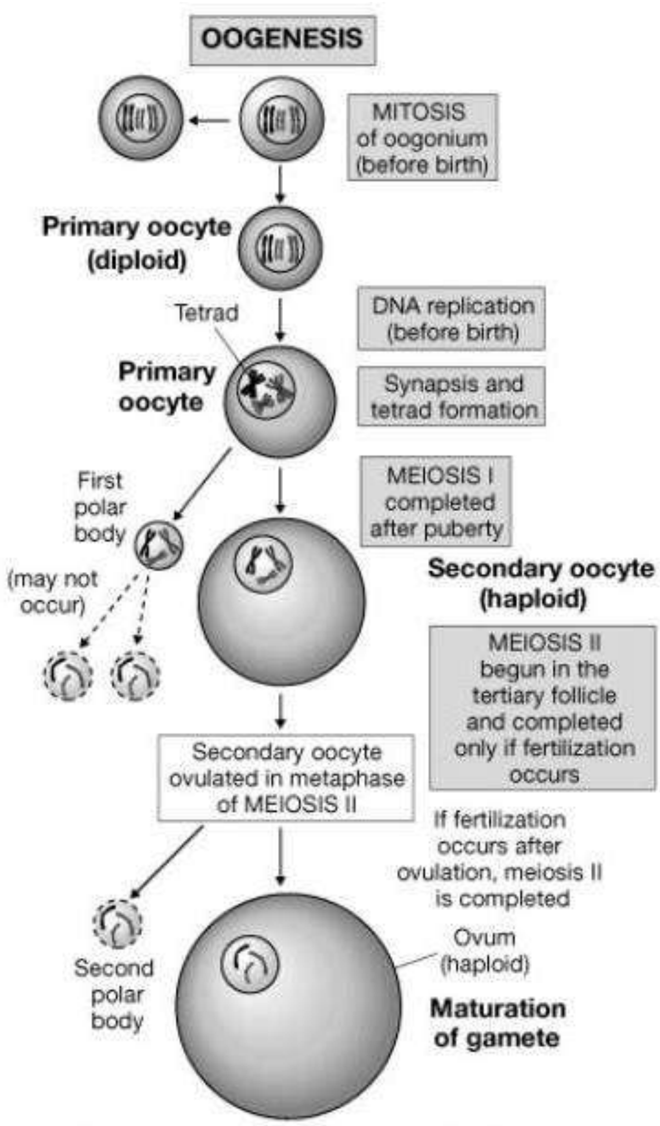
- produces sex hormones
- produces functioning gametes
- supports and protects developing embryo

- Inner and external organs:
  - ovaries (gonads)
  - uterine tubes (fallopian tubes)
  - uterus
  - vagina
  - accessory glands
  - external genitalia

- Ovaries
  ~ the size and shape of an almond
  - 2.5-5 cm long, 2 cm wide
  - they produce eggs (every female is born with a lifetime supply of eggs: 400,000 eggs at birth, ~400 ovulations till menopause)
  - they produce hormones: estrogen and progesterone

Oogensis

- when the girl becomes sexually mature, the primary oocytes recommence their development, usually one at a time and once a month
- the primary oocyte grows much larger and completes the meiosis I, forming a large secondary oocyte and a small polar body that receives little more than one set of chromosomes
- in humans, the first polar body does not go on to meiosis II, but the secondary oocyte does proceed as far as **metaphase of <u>meiosis II and then stops</u>**
- only if **fertilization occurs will meiosis II ever be completed**
- entry of the sperm restarts the cell cycle



Germinal period – first 2 weeks after fertilization

- oocyte: 0.10-0.15 mm

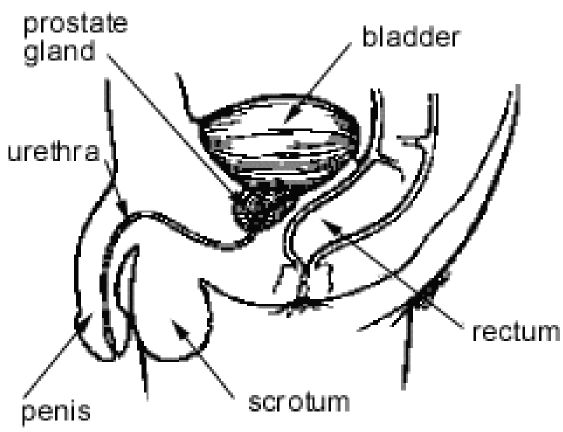
- female gamete (oocyte) is produced during the menstrual cycle and expelled during the ovulation
- during each ovarian cycle, only one follicle with an oocyte reaches full maturity
- at the 14th day in an average 28-day cycle this follicle bulges on the surface of the ovary
- inside the fallopian tube, a mature human egg waits in a state of arrested development
- it is the largest cell in the human body the egg is packed with nutrients, growth factors, enzymes and proteins
- if a sperm doesn't penetrate the egg's tough outer membrane to activate it within the next 24 hours, the egg will die
- it is surrounded by
  (1) several layers of the follicular cells arranged as the **corona radiata**
  (2) **zona pellucida**: a glycoprotein membrane surrounding the plasma membrane of the oocyte

Male reproductive system

-external genitalia:
- gonads (testes) undescended by birth
- scrotum
- penis

- internal genitalia:
- epididymis
- seminal vesicles
- prostate gland
- bulbourethral glands

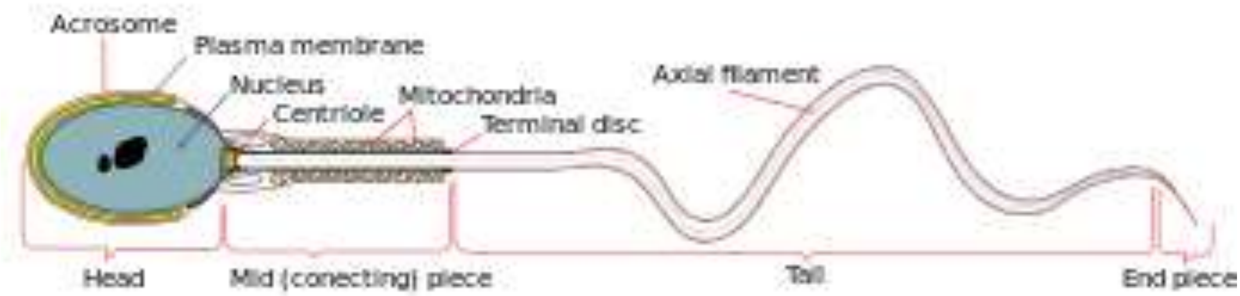
- testes:
~5 cm long and 3 cm in diameter
- covered by tunica albuginea
- located in the scrotum
- there are about 250 lobules in each testis
- each contains 1 to 4 seminiferous tubules that converge to form a single straight tubule, which leads into the rete testis
- short efferent ducts exit the testes
- interstitial cells (cells of Leydig), which produce male sex hormones, are located between the seminiferous tubules within a lobule



Male reproductive system

- sperm:

- consists of a head, a midpiece and a tail
- **head:** contains the nucleus with densely coiled chromatin fibres, surrounded anteriorly by an acrosome, which contains enzyme used for penetrating the female egg
- **midpiece:** has a central filamentous core with many mitochondria spiralled around it, used for ATP production for the journey through the female cervix, uterus and uterine tubes
- **tail (flagellum):** executes the lashing movements that propel the spermatocyte
- male gametes are produced during the spermatogenesis and stored in the epididymis
- upon ejaculation into the female genital tract, the spermatozoa are not capable of fertilizing the oocyte
- they must undergo a **capacitation** period that lasts approximately 7 hours, during which the glycoprotein coat and seminal proteins are removed from the surface of the sperm acrosome by the action of the substances secreted by uterus or uterine tubes
- **acrosomal reaction**: the capacitated spermatozoa come into contact with the corona radiata surrounding the secondary oocyte, the release of the acrosomal vesicles content that helps the sperm digest its way to the oocyte plasma membrane in order to fuse with it



- **Germinal period** – first 2 weeks after fertilization

- conception: the union of the male sperm and female ovum
- life starts with a single cell, the fertilized ovum
- fertilization begins when a sperm penetrates an oocyte and it ends with the creation of the zygote: it takes about 24 hours
- a sperm can survive for up to 48 hours
- it takes about ten hours to navigate the female productive track, moving up the vaginal canal, through the cervix, and into the fallopian tube where fertilization begins
- though 300 million sperm may enter the upper part of the vagina, only 1%, 3 million, enter the uterus
- the next step is the **penetration** of the zona pellucida
- only one sperm needs to bind with the protein receptors in the zona pellucida to trigger an enzyme reaction allowing the zona to be pierced
- penetration of the zona pellucida takes about 20 min.
- within 11 hours following fertilization, the oocyte has extruded a polar body with its excess chromosomes
- the fusion of the oocyte and sperm nuclei marks the creation of the zygote and the end of fertilization

Prenatal life

spermatogenesis	oogenesis:
Principle: continuous production. Although from puberty to old age sperm cells are constantly being engendered, the production is subject to extreme fluctuations regarding both quantity and quality.	Principle: Using up the oocytes generated before birth. Continual decrease of the oocytes, beginning with the fetal period. Exhaustion of the supply at menopause.
Meiotic output	
Four functioning, small (head 4 mm), motile spermatozoids at the end of the meiosis	One large, immotile oocyte (diameter 120 mm) and three shriveled polar bodies are left at the end of the meiosis
Fetal period	
No meiotic divisions	Entering into meiosis (arrested in the dictyotene stage)

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Prenatal age

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- mean duration is 38 weeks/264 days
    - germinal period: first 2 weeks
    - embryonic period: 2 to 8 weeks
    - fetal period: 2 to 9 months

- divided into three-months periods, *trimesters*

First trimester:

- from fertilization to 3rd month
- *embryogenesis* (to 8th week): multiplication of a single cell, the fertilized ovum (zygote)
- *cellular differentiation*: separate groups of cells form germ layers: endo-, meso- and ectoderma
- by the 8th week the embryo has many phenothypic characteristics that may be recognized as human
- cellular growth: *hyperplasia* (cell division by mitosis) and
  hypertrophy (enlargement of already existing cells)
- the most active metabolic dynamics of human organism
- **Germinal period** – first 2 weeks after fertilization

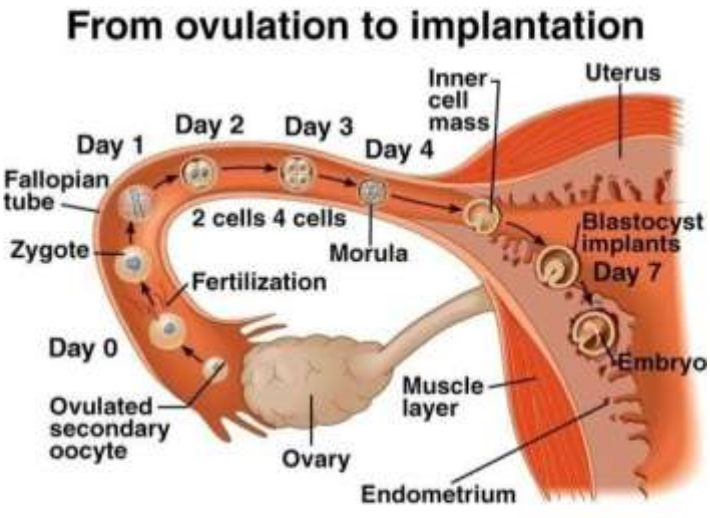
- inside the mother’s body, a fertilized egg moves through the fallopian tube, pushed toward the uterus by filaments lining the inside of the tube

- still dependent on nutrients and genetic instructions contributed by the egg, the embryo divides to form two cells, then four cells, then eight

- segmentation: growth by cell division in the early stages of gestation (with little or no increase in size) – the fertilized egg divides repeatedly into a mass of cells

- each division occurring into two cells called **blastomeres**

- each blastomere within the zona pellucida becomes smaller and smaller with each subsequent division



- the cell division generates about 16 cells, the zygote becomes a **morula** (mulberry shaped)
- it leaves the fallopian tube and enters the uterine cavity three to four days after fertilization

- the cells differentiate into 2 layers: inner and outer layers – the **blastocyst** is forming: a thin-walled hollow structure in early embryonic development that contains a cluster of cells called the inner cell mass from which the embryo arises
- inner cell mass: **embryoblast** (3, gives rise to the embryo and a part of the amnion)
- outer cell mass: **trophoblast** (1, forms most of the extraembryonic membranes, i.e., the bulk of the placenta)
- blastocyst loses the zona pellucida through the process called blastocyst hatching
- 6th day: the blastocyst attaches to the endometrial epithelium with it's embryonic pole
- **implantation:** fertilized egg (zygote) attaches to the inner wall of the uterus
- when the human embryo is around six days old, it starts making a nest in the wall of the mother's uterus
- begins at the end of the first week and is completed by the end of the second week

Germinal period, implantation:

- blastocyst **normally implants** in the endometrium along the posterior wall of the body of the uterust
- not infrequently, the blastocyst implants in **abnormal locations** outside the uterine body
- this usually leads to the **death of the embryo** and **severe hemorrhage** of the mother during the second month of pregnancy (extrauterine or ectopic pregnancy): this may occur in the abdominal cavity, the ovary, the uterine tube or pelvis
- **human chorionic gonadotropin** (HCG) is secreted by the trophoblast: ***stimulating*** the ***corpus luteum*** to continue progesterone production (progesterone maintains the blood rich lining of the uterus)
- the uterus is swollen with new blood capillaries and the circulation between mother and blastocyst begins (this process needed for the continuation of pregnancy)
- cells in the outer layer of the blastocyst stick to the uterine wall and grow long **projections** into it → the first step in developing a placenta with blood vessels linking mother and embryo
- the embryo will depend on oxygen and nutrients from the mother's bloodstream to survive
- as the placenta grows and embeds itself within the uterine wall, the inner cell mass divides to form the amniotic cavity and a flat disc with two layers of cells that is the embryo

Placental development

- **placenta:** the highly specialised organ of pregnancy that ***supports*** the normal growth and development of the fetus
- growth and maturation of the placenta as well as its function are precisely regulated and coordinated to ensure the ***exchange of nutrients*** and ***waste products*** between the maternal and fetal circulatory systems operates at maximal efficiency
- placenta is derived from both **fetal** and **maternal** cells
- it first takes shape when cells from the fetus, called **trophoblasts**, attach to the uterus wall and then proceed to invade the tissues of the uterus
- it connects with the mother's blood vessels
- a network is formed of finger-like projections, called **villi**, which project into spaces, or lacunae, that fill up with the mother's blood
- the baby's circulatory system is developing, and fetal blood vessels form in the placental villi
- these vessels connect back to the baby via blood vessels traveling through the **umbilical cord**, which attaches the baby to the placenta
- **gas and nutrient exchange** and **waste removal** take place across the villis' walls, which also serve to keep the baby's blood from mixing with the mother's blood
- placenta also functions as an **endocrine organ**, meaning it releases hormones, which enable both the mother and baby to have a successful pregnancy

- some of these, such as **progesterone**, help to maintain the pregnancy, while others increase the maternal blood supply to the fetus
- after the safe delivery of the baby, the placenta is delivered
- the umbilical cord is clamped and cut, and the site of attachment on the baby is commonly known as the umbilicus, navel or belly-button

Abnormal development in the first 2 weeks

- about 15% of oocytes fail to become fertilized
- about 10-15% of oocytes begin cleavage, but fail to implant
- of the 70-75% of oocytes that do implant, only about 58% survive until week 2
- of the above, about 16% are abnormal
- when the first expected menstruation is missed, only about 42% of the eggs exposed to sperm usually survive and, of these, a number will abort in subsequent weeks (poorly developed endometrium, chromosomal abnormalities in the embryo), and some will be abnormal at birth

Embryonic period: 2 to 8 weeks

- the beginnings of all major internal and external structural (organ and organ systems) develop during which time the 3 germ layers give rise to specific tissues and organs – the period of **organogenesis**
- the shape of the embryo changes, major features of the external body form (morphogenesis) become recognizable by the end of month 2
- **embryo:** an early stage of growth and differentiation that is characterized by cleavage, the laying down of fundamental tissues, and the formation of primitive organs and organ systems
- the developing human individual from the time of implantation to the end of the eighth week after conception
- once the embryo is embedded in the wall of the uterus, it starts preparing for a transformation called **gastrulation** that takes place during the 3rd week
- during gastrulation: **every cell** in the flat disc will **migrate** to a ***new location*** and morph into one of three new cell types to form the inner, middle and outer layers of the 21-day-old embryo
- as the gastrulation is **complete**, the embryo will have **three distinct layers**
- the blastocyst inner cell mass differentiates into two layers:
- **epiblast:** the top layer of cells (6, dark blue) which will become the embryo and amniotic cavity
- **hypoblast:** lower layer of cells (8, yellow) which become the yolk sac
- the two-layered plate that will differentiate into the embryo is called the **embryonic disc**
- **gastrulation:** the blastula is reorganized into a trilaminar ("three-layered") structure (gastrula) - the germ layers: **ectoderm, mesoderm, endoderm**
- **by cell divisions, migrations and rearrangements**
- **the layers are the forerunners of specialized tissues and organs**
- **ectoderm:** the outermost primary tissue layer that forms first in all animal embryos,
  - it gives rise to the **central nervous system** (the brain and spinal cord); the **peripheral nervous system**; the **sensory epithelia** of the eye, ear, and nose; the **epidermis** and its appendages (the nails and hair); the **mammary glands**; the hypophysis; the subcutaneous glands; and the **enamel** of the teeth
  - ectodermal development is called **neurulation** in regard to nervous tissue
- **mesoderm:** the intermediate layer (last to arise evolutionarily), it is important in the formation of almost all organ systems

- it gives rise to **connective tissue**, **cartilage**, and **bone**; striated and smooth **muscles**; the **heart walls**, **blood and lymph vessels** and cells; the **kidneys**; the **gonads** (ovaries and testes) and genital ducts; the serous membranes lining the body cavities; the **spleen**; and the **suprarenal** (adrenal) cortices

- endoderm: the innermost layer, it forms the gut and structures derived from the gut

- it gives rise to the **epithelial** lining of the **gastrointestinal and respiratory tracts**; the **parenchyma of the tonsils**, the **liver**, the **thymus**, the **thyroid, the parathyroids**, and the **pancreas**; the **epithelial** lining of the **urinary bladder and urethra**; and the epithelial lining of the tympanic cavity, tympanic antrum, and auditory tube

- after these layers form, subpopulations of cells give rise to the organs – every body part develops from these 3 layers

- gastrulation:

- begins with an indentation called the **primitive streak**, which forms on top of the flat disc
- at the top of the streak is a small structure called the node
- the establishment of trilaminar embryonic disc and formation of three primary germ layers: ectoderm, mesoderm and endoderm
- 3 important structures form during the 3rd developmental week: the primitive streak, the notochord and the neural tube
- **primitive streak** (3): appears caudally in the midline of the dorsal aspect of the embryonic disc (a narrow line of cells appear on the surface of the formerly 2 layered embryonic disc)
- **primitive node** (2): in the region of the primitive streak and its cephalic end
- **epiblast** cells (6) move inward (invaginate) to form a new cell layer (intraembryonic mesoderm) between the epiblast and hypoblast
- some of the epiblast cells displace hypoblast, there by creating the embryonic **endoderm** (epiblast moves towards the primitive streak, dives down into it, and forms a new layer, called the endoderm, pushing the hypoblast out of the way)
- cells remaining in the epiblast form the **ectoderm**
- epiblast cells migrating cranially through the primitive node form the notochordal process,which defines the primitive axis of the embryo (vertebral column forms around the notochord)
- the developing notochord induces the overlying ectoderm to form the neural plate, e.g. the primordium of the **central nervous system**
- the mesoderm layer and the notochord separate the ectoderm and endoderm layers entirely, with the exception of the prechordal plate cranially (future oropharyngeal membrane) and the cloacal membrane (future anus) caudally

- gastrulation: directed by the node, cells move down and through the streak to be reborn on the other side as either endoderm (the inner layer of the embryo) or mesoderm (the middle layer), instead of going through the streak, the remaining cells of epiblast will fan out to form the outer layer of the embryo called the ectoderm

- **neurulation**: the neural tube formation
- begins with appearance of the neural plate, which invaginates along its central axis to form the neural groove (3), with ***neural folds*** (2) on each side
- the neural folds approach each other in the midline and ***fuse***
- the neural groove into a **neural tube**
- formation of the neural tube begins in the region of the future neck and proceeds in the cranial and caudal directions

- **somites:** somites are bilaterally paired blocks of **mesoderm** that form along the anterior-posterior axis of the developing human embryo
- somites give rise to skeletal muscle, cartilage, tendons, endothelial cells and dermis
- by the end of **week 4** the embryo has about **28 somites**, the ventral body wall has closed, and the major external features are somites and pharyngeal arches
- by the beginning of week 5, the fore- and hind-limbs appear as paddle-shaped buds
- the external appearance during month 2 changes due to the great size of the head and formation of the limbs, ears, nose, and eyes
- rapid cellular growth and change elongates the embryo and expands the yolk sac
- on each side of the neural tube: 4-12 pairs of somites (42-44 somite pairs develop by the end of week 5)
- somites give origin to the sclerotome, whose cells condense around the notochord and give rise to the vertebral primordia and the myotome, which gives rise to the vertebral muscles (myotome with the somatopleure gives origin to the muscles of the limbs and the anterior lateral body wall)
- cells (which become the eyes) appear as thickened circles just off of the neural folds
- the newly differentiated cells of the ears are also present
- heart tube takes on an S-shape establishing the asymmetry of the heart
- as the S-shape forms, cardiac muscle contraction begins
- during the second month, the intraembryonic coelom is divided into the body cavities, namely, the pericardial cavity, the pleural cavities, and the peritoneal cavity

- **Cardiovascular system development**

- early cardiovascular system formation can be related to the absence of a significant amount of yolk material in the ovum and yolk sac with the need for vessels to carry both nutrient materials and oxygen
- the primitive endothelial cardiac tubes form from mesenchymal cells in the cardiogenic area
- longitudinally paired endothelial channels, the heart tubes, develop before the end of week 3 and begin to fuse into the primitive heart tube
- by day 21, the paired tubes link up with blood vessels in the embryo, connecting stalk, chorion, and yolk sac to form a primitive cardiovascular system
- the CVS is the first organ system to reach a functional state
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Fetal period – 2 to 9 months
- growth and development continue dramatically
- 3 months after conception the fetus has become very active, moving its arms and legs, opening and closing its mouth, moving its head
- face, forehead, eyelids, nose, chin, arms, hands, lower limbs are distinguishable, the genitals can be identified as male or female
  - **Zygote:** the initial cell formed when two gamete cells are joined by means of sexual reproduction; in multicellular organisms, it is the earliest developmental stage of the embryo
  - **Embryo:** stage of prenatal development lasting from second to eight week following fertilization, characterized by the rapid differentiation of tissues and the formation of organs
  - **Fetus:** stage of prenatal development lasting from eight week following fertilization to birth.

First trimester
- enbryogenesis: multiplication of a single cell
- cellular differentiation: separate groups of cells from germ layers: endo-, ecto- and mesoderm
- cellular growth: hyperplasia (cell division by mitosis)
  hypertrophy (enlargement of already existing cells)
- by the 8th week the embryo has many phenotypic characteristics that may be recognized as human, and fetal heartbeat is detectable with ultrasound
- by the 12th week sex is distinguishable visually

Second trimester:
- rapid growth in length and weight
- differentiation of cells into tissues and organs is complete by the start of this trimester: embryo is a foetus

Third trimester:
- growth in weight takes place at a relatively faster rate
- development and maturation of circulatory, respiratory, digestive systems occur: preparing the foetus for the transition to extra-uterine life
- growth decreases by the end of this trimester: intrauterine space limitation, exchange of substances (nutrition, respiration, metabolic wastes) is blocked (- - -: predicted curve if no restriction takes place)
- from the 28th week: adding body fat
- by the end of this trimester: less active foetus

Ultrasonography in pregnancy:
- accurate method of gestational age
- fetal number, viability, placental location
- diagnose major fetal anomalies, diagnosis of fetal growth abnormalities
- safe for the fetus when used appropriately
- specific indication are the best basis for the use of ultrasonography in pregnancy
- optimal timing for single ultrasound examination: 16-20 weeks
- recommendation: every 4weeks
- fetal presentation, amniotic fluid volume, cardiac activity

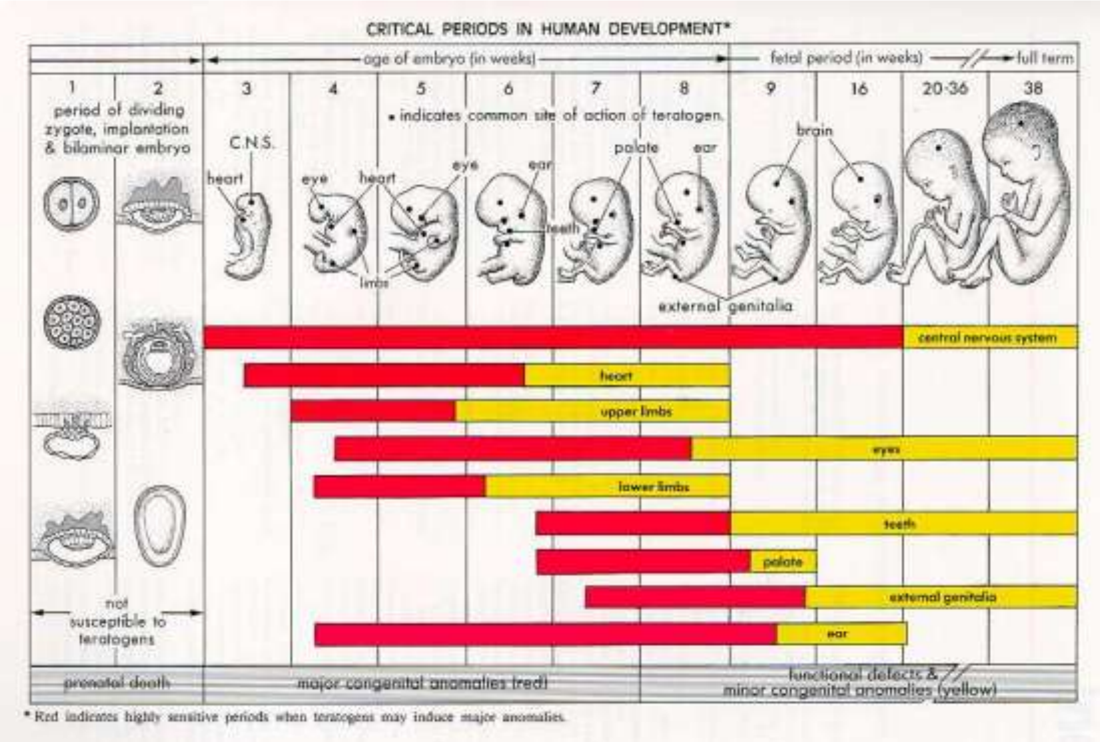
- placental position, fetal biometry
- anatomic survey: sex, evaluation of multiple gestation, umbilical cord vessel number, insertion site into fetal abdomen, spine, extremities, …
- after 16~20 weeks of gestation: can be difficult to visualize because of fetal size, position, movement, abdominal scar, increased maternal wall thickness

How safe is ultrasonography for the fetus?
- safe but, cannot be completely innocuous
- when there is a valid medical indication
- the lowest possible ultrasonic exposure setting
- physical effects: mechanical vibration, increased tissue temperature

Ultrasonography in pregnancy:
- **anomaly** is suspected on the basis of history, biochemical abnormalities or clinical evaluation, or suspiciousresults from standard exam
- indications: vaginal bleeding, pelvic pain, estimate gestational age, multiple gestations, uterine abnormality, …
- **gestational age**: it is defined in weeks beginning from the first day of the last menstrual period prior to conception
- accurate determination of gestational age is fundamental to obstetric care
- e.g.: the level of **α-fetoprotein** in both amniotic fluid and maternal serum is related to gestational age and when dates are inaccurate test results will be incorrect and misleading (**α-fetoprotein is** produced by the yolk sac and the liver during fetal development), diseases in which AFP will be elevated: hepatocellular carcinoma, neural tube defects, yolk sac tumor, etc.
- e.g.: **fetal growth** assessment relies on accurate assessment of gestational age, **fetal heart rate** activity and fetal breathing develop with advancing gestational age → the absence of these biophysical parameters may be interpreted as abnormal for fetuses in whom the gestational age has been overestimated, **obstetric management** is dependent on gestational age: preterm labor or postdate pregnancies are only possible when gestational age is accurately estimated

Methods of gestational age assessment:
- **in the past:** reliance was placed on the **menstrual history** and the **maternal sensation of fetal movement**, assessment of **uterine size** by bimanual examination in the first trimester, initial detection of **fetal heart tones** (Doppler 10–12 weeks, auscultation 19–21 weeks)
- 20% to 40% of women could not relate the gestational age with certainty (due to: oligomenorrhea, bleeding in the first trimester of pregnancy, pregnancy following use of oral contraceptives)
- in most pregnancies, the date of ovulation or conception could not be accurately predicted therefore gestational age must be established by other methods
- **nowadays:** the advent of **ultrasound** has allowed a more direct means of assessing fetal structures and development
- measurements of a wide variety of parameters have been devised to establish gestational age
- however: variations in the ultrasound measurements can be attributed to differences in fetal growth patterns, such differences are related to: maternal age and parity, prepregnancy maternal weight, geographic location, population characteristics

- a single parameter (CRL, BPD, HC, AC, or FL) may be used to assess gestational age
- the accuracy of a single parameter is dependent on the gestational age at the time of ultrasound examination
- **several** methods have been employed to improve the accuracy of gestational age assessment compared with the use of a single parameter
- when menstrual dates are unknown, assignment of dates should be based on ultrasound assessment of gestational age
- growth-adjusted sonographic age can be used: e.g. by obtaining paired BPD measurements (the first from 20 to 26 weeks' gestation and the second from 31 to 33 weeks' gestation) and assigning gestational age (since BPD growth from 20 to 33 weeks' gestation tends to progress within narrow percentile ranks)



Methods of gestational age assessment - ultrasonography:

- **First trimester: t**he gestational sac mean diameter and crown-rump length are used to establish fetal age
- **gestational sac mean diameter (GSMD):**
  - the gestational sac is the first identifiable structure routinely imaged in the first trimester
  - can be identified by trans-abdominal ultrasound as early as 5 weeks' gestation, or as early as 4 weeks' gestation by transvaginal ultrasound
- longitudinal, anteroposterior and transverse diameters are averaged to obtain the GSMD
- **gestational sac mean diameter (GSMD):**
  - gestational age can be estimated from GSMD from 5 to 12 weeks
- **crown-rump length:** the length from the tip of the cephalic pole to the tip of the caudal pole, gestational age can be estimated from CRL **from 7 to 13 weeks**
  - at 5 to 6 weeks' gestation, distinct landmarks cannot always be identified - after 12 weeks' gestation excessive curvature of the fetus may lead to shortening of CRL

- **Second and third trimesters:**
- **biparietal diameter:**
  - measured in the transaxial plane of the fetal head at a level depicting thalami in the midline, equidistant from the temporoparietal bones and usually the cavum septum pellucidum anteriorly, gestational age can be estimated from BPD from **12 weeks' gestation until the end of pregnancy**
  - the head circumference may be calculated using these diameters or measured directly
- **head circumference:**
  - the following formula using biparietal and fronto-occipital diameters may be used to calculate HC: $3.14 \times (D1 + D2)/2$
- **abdominal circumference:** gestational age can be estimated from AC from 15 weeks' gestation until the end of pregnancy
  - measured at the level of the fetal liver, using the umbilical portion of the left portal vein as a landmark
  - AC may be used to estimate gestational age but is less accurate than head measurements
- **femur length:** all the fetal long bones can be adequately examined and measured by ultrasound; however, the femur is the largest of the long bones, least moveable, and easiest to image, measured along the long axis of the bone; a straight measurement of the osseous portion is taken from one end to the other, disregarding bone curvatur
  - adequately visualized from 14 weeks' gestation until delivery
  - the accuracy of the FL and BPD measurements to be similar in the third trimester
- **fetal weight:** can be **estimated** by obtaining measurements such as the **biparietal diameter**, **head circumference**, **abdominal circumference** or **average abdominal diameter** and femoral **diaphysis length**
- results from various prediction models can be compared to fetal weight percentiles from published nomograms

- **Multiple gestations: t**he detection of multiple gestations is important: they are at **greater risk** for many complications, particularly fetal growth retardation
- fetal biometric data are available for twin gestations, however, triplet and quadruplet pregnancies have not been adequately studied owing to their infrequent occurrence
- ultrasound-derived fetal dating tables obtained for singleton pregnancies can be used accurately for twin pregnancies until approximately **30 weeks' gestation**
- during the last 10 weeks of pregnancy there is a **decrease** in **the growth rate** for twin fetuses compared with singleton fetuses
- the femur continues to grow normally throughout pregnancy in twin gestations, while the head (BPD and HC) and abdominal (AC) growth rates decrease in the last 10 weeks of pregnancy
- FL measurement may be a more reliable parameter to use for gestational age assessment in twin gestations during the third trimester
- gestational age estimations in twin pregnancies prior to 30 weeks' gestation should be performed in a similar manner to that for singleton pregnancies

How is ultrasonography used to detect disturbance in fetal growth - intrauterine growth restriction?

- **growth restriction:** <10th percentile (<5th or <3rd)
- 10% of infants in any population: not only pathologically but also familial & ethnic causes

- abdominal circumference, head circumference, biparietal diameter, femur length → calculates on the basis of formulas
- serial measurements of fetal biometric parameters → detailed ultrasound
- by recording growth velocity (2~4 weeks apart)
- amniotic fluid volume (oligohydramnios 77~83%)

Fetal period – 2 to 9 months
- weeks 9 to 12
- a broad face, eyes widely separated, ears low set
- the legs are short and thighs relatively small, the upper limbs reach relatively normal lengths
- external genitalia of male and female appear similar until end of week 9
- intestinal loops are clearly seen in the umbilical cord until the middle of week 10 when they return to the abdomen
- weeks 13 to 16
- period of rapid fetal growth, legs have become longer
- by end of week 16, the head is relatively small compared to a 12-week fetus
- skeletal ossification progresses rapidly and is seen on x-ray by week 16
- weeks 17 to 20
- growth slows, lower limbs reach their final relative proportions
- fetal movements are felt by mother
- skin is covered by the vernix caseosa (greasy, cheeselike material) by week 20 due to fetal sebaceous gland secretion and dead epithelial cells: protects fetal skin from abrasions, and hardening due to amniotic fluid around it
- by week 20, the fetus is covered by lanugo, a fine downy hair
- the eyebrows and head hair are visible, brown fat forms and is the site of heat production
- weeks 21 to 25
- intensive weight gain, the body is proportioned
- the skin is wrinkled but is very translucent and is pink to red in color, with blood in the capillaries visible
- if born at this time, the fetus usually dies due to an immature respiratory system
- weeks 26 to 29
- there is much subcutaneous fat formed, the wrinkles of skin smooth out
- white fat increases to 5%
- the fetus is viable and can survive if born prematurely, but the mortality is high as a result of respiratory problems, even though the lungs and pulmonary vasculature are developed for gas exchange
- weeks 30 to 34
- the skin is smooth and pink
- the body white fat is now about 7 to 8%
- weeks 35 to 38
- matured organs at birth

Birth

- transition between life in utero and independent life of uterine environment
- the most common indicator of inadequate prenatal growth is birth weight (BW)
- *low birth weight*: less than 2500 grams at birth)
- *prematurity*: birth before 37 weeks of gestation
- *SGA* (small for gestation age) *neonate*: BW lass than the P10 for gestation

- ☐ causes of low BW: congenital problems, placental insufficiency, maternal conditions: undernutrition, disease, smoking, alcohol consumption, maternal age, socioeconomic status (education, occupation, social prestige)
- ☐ other measures of growth at birth: recumbent length (person measured is lying down), circumference of the head, arm, chest, skinfolds
- ☐ small sexual dimorphism: boys are a bit longer, heavier and larger headed, have slightly less subcutaneous fat than girls
- ☐ physiological weight loss after birth (transient): volume of extracellular water decreases(insufficient renal activity and nutrition)
- ☐ body *proportions*: head circumference 70% of length (30% at maturity), growth of the brain proceeds faster rate than the growth of the body during fetal, infant and childhood growth, relative short limbs: length of limbs become longer relative to body length during growth
- ☐ *body composition*: 12% body fat, 20% muscle mass

Infancy (0 ys: birth – 3 ys: last deciduous tooth emergences)

- ☐ ***neonatal period*:** birth to 28 days
  - physiological weight loss after birth: the volume of extracellular water decreases (insufficient renal activity and nutrition)
  - leading causes of neonatal deaths:
    - birth defects
    - disorders related short gestation
    - maternal complications
- ☐ most rapid velocity of growth of any of the postnatal stages (rapid velocity during the first year, then very steep deceleration in velocity, continuation of the foetal pattern, peak of growth velocity in the 2. trimester lasts until childhood
- ☐ different patterns of growth:

lympoid type: thymus, lymph-nodes, …
neural type: brain, dura, spinal cord, …
general type: body as a whole, respiratory and digestive organs, kidneys, musculature as a whole, …
genital type: testis, ovarium, uterine tube, prostate, seminal vesicles, …

- ☐ mother provides all nourishment to her offspring via lactation until the end of infancy (until the 6th month, no teeth, fluid food)
- ☐ deciduous teeth emergency (milk teeth)
- ☐ rate and amount of growth in most infants is similar (no ethnic, socioeconomic difference, lactation)
- ☐ motor skills (physical ability, motor coordination) develop rapidly: by 7 month: infant can sit, by 8 month: crawl, by 12 month: walk with support, 2 years: walk, turn the pages of a book, 3 years: run, manipulate small objects
- ☐ similar progress of changes in problem solving, cognitive abilities of the infant
- ☐ brain grows more rapidly than any other tissue or organ

Childhood

(3 ys: last deciduous tooth emerged – 7 ys: permanent teeth emergence)

- ☐ *childhood diet*: easy to chew and swallow, low in total volume – immature dentition and small digestive system
- ☐ replacement of the deciduous teeth by the emergence of the first permanent teeth (4 first molars and 4 first incisors: sufficient to eat an adult-type diet)
- ☐ completion of growth of the brain in weight

- ☐ locomotive skills develop and mature
- ☐ these features indicate that the physically dependent children is moving on to independence
- ☐ moderate growth rate
- ☐ *mid-growth spurt*: at the end of childhood small increase in the velocity of growth

Juvenile (7 ys: permanent teeth emergence – ♀: 10 ys, ♂: 12 ys: growth rate increases again)
- ☐ prepubertal individuals those are no longer dependent on their mothers for survival
- ☐ juveniles have all the physical and cognitive abilities to provide much of their own food and provide themselves from accidents and disease (street children)
- ☐ rate of growth declines: juveniles growth at the slowest rate since birth

Adolescence (11-12 ys – 15-16 ys)
- a transitional stage of physical and psychological human development that generally occurs during the period from puberty to legal adulthood
- puberty: the stage of adolescence in which an individual becomes physiologically capable of sexual reproduction
- the reinitiation of activity of the hypothalamic-pituary-gonadal system of hormone reproduction
- adolescent growth spurt
- development of secondary sexual characteristics
- attainment of fertility
- establishment of individual sexual identity
- timing for puberty onset has wide variability - Girls: 8-12 years and Boys: 9-14 years of age
- changes of body composition
- changes of body proportions
- changes of body shape

adolescence growth spurt:
- period extends for 2.5 to 3 years
- height gain is 27-29 cm in boys and 24-26cm in girls
  (1 cm height will need 4500 Kcal)
- weight gain in both genders: 25-30 kg
    - PHV: peak height velocity
        - 7-12 cm/yr in boys, 6-11 cm/yr in girls
        - greater in adolescents who experience it earlier
    - PWV: peak weight velocity
        - adolescents experience it after PHV
        - greater in boys than in girls
- ☐ **factors account for sexual dimorphism in adult height:**
    - boys' greater amount of growth before adolescence (1.6 cm)
    - boys' delay in the onset of adolescence (6.4 cm, 2-year delay)
    - boys' greater intensity of growth spurt (6 cm)
    - girls' longer duration of growth following growth spurt (-1.4 cm)
    → males are taller than females with about 12 cm
- ☐ **compensating mechanisms:**
    - age of peak velocity inversely correlates with size of growth spurt
    - slow growth before puberty tends to have a longer-lasting adolescence spurt
    - chronic undernutrition, disease, child labor can prolong the total span of growth (by 25 ys)
    - most of the body measurements, inner organs increase in every dimension

- sexual dimorphism in body size, proportions, body composition and shape, deeping of voice in boys
- genitals are developing and secondary sexual characteristics are appearing
- very long transition from puberty to adulthood (full reproductive maturity: 5-8 years (monkey: 3 years): social and sexual maturation takes place
- differences among populations in timing of onset of adolescent maturation stages
- both boys and girls experience adolescent growth spurt (a rapid acceleration in the growth velocity), boys do it 2-3 years later than girls
- different parts of the body do not axperience AGS at the same time (foot, hand, leg, arm, stature, trunk)
- size of the spurt and age of peak velocity are not related to final adult height
- permanent tooth eruption completed (almost)
- the onset of puberty is followed within a few months by the appearance of the secondary sexual characteristics (pubic hair, axillary hair, …)
- usually every child experiences the same sequence in the order of appearance and timing of the secondary sexual characteristics
- the exact trigger is unknown, but distinct changes occur:
    1) onset of nocturnal sleep-related aug-mentation of pulsatile LHrelease (secondary to increased pulsatile GnRH release)
    2) decrease in sensitivity of the hypothalamus and pituitary to estrogen and testosterone (increased sensitivity to the gonadotropins LH and FSH secondary to maturation of the CNS)

Adolescence - Girls
- puberty takes an average of 4 years to complete
- puberty begins with breast budding
- PHV occurs about 1 year after breast budding
- average age of menarche is 12 years occurring at Stage 3 or 4 Normal range of menarche 9-17 Occurs 3.3 years after the start of the growth spurt, 1.1 years after PHV and 2 years after breast budding growth slows after menarche

Adolescence - Boys
- puberty takes an average of 3 years to complete
- puberty begins with testicular enlargement, the bulk of testicular enlargement is attributed to the sperm producing tubules, androgen producing Leydig cell mass is small
- ejaculation usually occurs during Stage 3, Stage 4 is associated with nocturnal emissions, fertility
- spermarcheal age: 12-14
- peak height velocity occurs later for males than females corresponding to Stage 3-4

- **Boys and Girls:**
- girls tend to lose less of their body fat than boys
- an awkwardness as various body parts grow at different rates
- biologic changes in the brain causing dynamic emotional and cognitive changes
- the head, hands, and feet are the first parts of the body to reach their mature size, often the arms and legs lengthen before the trunk of the body, can cause awkwardness
- faster muscle growth in boys leads to greater strength
- girls begin puberty about 1-2 years earlier than boys

- **Sexual dimorphism:**
- shoulder growth in boys and hip growth in girls.
- they start puberty with similar fat and lean body mass content . Girls finally have 27% fat and boys 18%, from 16% . In boys gain in lean body mass is twice than the girls. But girls reduce LBM from 80% to 74%. These changes are due to sex hormones
- Maintenance cost of lean body mass needs more energy – boys have increased deposition of protein and minerals

- **Psychosocial changes**
- begin to separate from parents and identify with peers
- confrontational with parents, preoccupation with being like peers, conformity
- same gender in clique, interest in other gender for friendship
- greater need for privacy, mood swings/erratic behaviour, lack of impulse control

- **Cognitive development**
- beginning abstraction
- can consider facts and make better decisions based on knowledge of the consequences of their choices
- sensitive to criticism
- increased openness of feelings and sensitivity to the feelings of others
- ability for abstract thinking
- understanding consequences of behavioral choices
- increased thoughts about more global concepts such as justice, history, politics, patriotism and their emerging role in adult society

adulthood:
- the longest lasting stage in the human life cycle, stretching from age 20 to 50 ys
- the prime adulthood lasts until the end of child-bearing years and is a time of homeostasis in physiology, behaviour and cognition

senescence:
- characterized by a decline in the function of many body tissues or systems
- usually begins after the end of child-bearing years and lasts until death

Somatotyping

body shape estimation: Heath-Carter method

- the word used method to classify the morphological body shape by using anthropometric measurements

- **somatotype:** the quantification of the present shape and composition of the human body

- somatotype is expressed in a three-number rating: endomorphy, mesomorphy and ectomorphy components
  - endomorphy: relative fatness
  - mesomorphy: relative musculo-skeletal robustness
  - ectomorphy: the relative linearity or slenderness of a physique

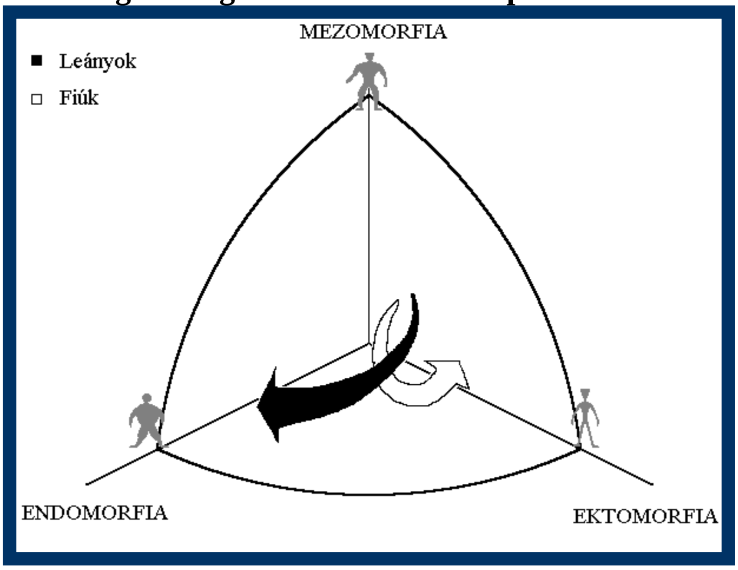
- **endomorphy** = - 0.7182 + 0.1451 (X) - 0.00068 (X2) + 0.0000014 (X3)

X = (sum of triceps, subscapular and supraspinale skinfolds) multiplied by (170.18/height in cm) – „height-corrected endomorphy"

- **mesomorphy** = 0.858 x humerus breadth + 0.601 x femur breadth + 0.188 x corrected arm girth + 0.161 x corrected calf girth – height 0.131 + 4.5
- **ectomorphy:** height-weight ratio (HWR): height is divided by the cube root of weight (stature/mass1/3)
  - if HWR is greater than or equal to 40.75 then ectomorphy = 0.732 HWR - 28.58
  - if HWR is less than 40.75 but greater than 38.25 then ectomorphy = 0.463 HWR - 17.63
  - if HWR is equal to or less than 38.25 then ectomorphy = 0.1

- **plotting the somatotype**
- X = ectomorphy - endomorphy
- Y = 2 x mesomorphy – (endomorphy + ectomorphy)
- these 2D points on the somatochart are called **somatoplots**

☐ **age changes and sexual dimorphism in somatotype**



Biological age

- estimates the functional status of an individual (organs or body parts) in reference to his or her chronological peers on the basis of how well he or she functions in comparison with others of the same chronological age
- it is based in large part to the “physiological development of the various organs and systems in the body (e.g. the adequate development of bones: skeletal age)

Biological ages

- Bone age
- Dental age
- Morphological age
- Physiological age

<u>Bone age (skeletal) estimation</u>

- methods for determining skeletal maturity and its relation to chronological age are based on the presence of ossification centers and on the forms these take from birth to the end of growth
- most subsequent studies were developed on the basis of analyses of the form taken by the ossification centers in the various segments of the skeleton (hand and wrist, elbow, shoulder, hip, foot, and knee)
- as research continued the hand and wrist emerged as the most studied skeletal segment.

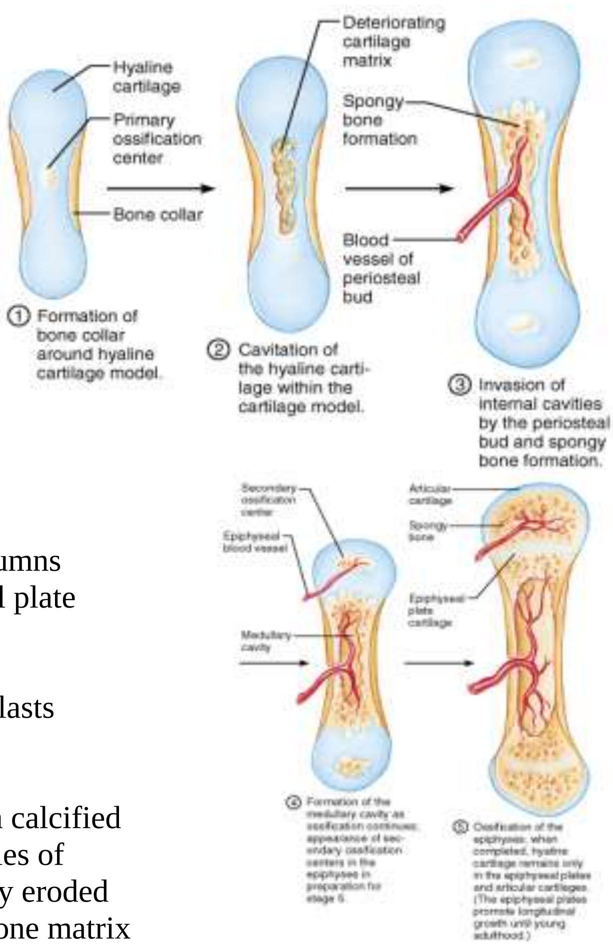
<u>Bone age (skeletal) estimation – purposes</u>

- at population level: to construct national references
  - Greulich-Pyle references
  - Tanner-Whitehouse references
  - criteria:
    - all healthy children’s bone development shows the same pattern
    - by considering the national references the bone age of children can be assessed
- at individual level:
  1) child endocrinology
     - suspicion of growth failure (growth hormone deficiency; congenital hypothyreosis)
     - diagnose of metabolic bone disease
  2) sport anthropometry
     - sport selection
     - final height estimation

Ossification (osteogenesis) begins around the 6th -7th week of embryonic life. At this time the embryonic skeleton is made of fibrous membranes and hyaline cartilage.

- Intramembranous (within the membrane) ossification: Bone develops from a fibrous membrane.
  - flat bones of skull, mandible and clavicles
  -mesenchymal cells become vascularized and become osteoprogenitor cells and then osteoblasts
  - organic matrix of bone is secreted, osteocytes are formed
  - calcium and mineral salts are deposited and bone tissue hardens
  - trabeculae develop and spongy bone is formed
  - red marrow fills spaces

- **Physiology of bone growth – long bones:**
  - epiphyseal plate (bone length)
  - 4 zones of bone growth under hGH.



1- Zone of resting cartilage:
- no bone growth
- located near the epiphyseal plate
- scattered chondrocytes
- anchors plate to bone

2- Zone of proliferating cartilage
- chondrocytes stacked like coins
- chondrocytes divide

3- Zone of hypertrophic (maturing) cartilage
- large chondrocytes arranged in columns
- lengthwise expansion of epiphyseal plate

4- Zone of calcified cartilage
- few cell layers thick
- occupied by osteoblasts and osteoclasts and capillaries from the diaphysis
- cells lay down bone
- dead chondrocytes surrounded by a calcified matrix. Matrix resembles long spicules of calcified cartilage. Spicules are partly eroded by osteoclasts and then covered in bone matrix from osteoblasts: spongy bone is formed

Age 18-21: Longitudinal bone growth ends when epiphysis fuses with the diaphysis.
- epiphyseal plate closure
- epiphyseal line is remnant of this
- last bone to stop growing: clavicle

<u>**Methodology**</u>

Tanner-Whitehouse method

- standard X-ray of the left wrist and hand
- in the TW2 method twenty regions of interest located in the main bones are considered for the bone age evaluation
- radius, ulna, ossa carpi, I-III-Vth finger metacarpi and phalanges
- TW2 20 bones: characterized by twenty bones including the bones of the first, third and fifth finger and the carpal bones
- RUS: considers the same bones of the TW2 method except the carpal bones;
- CARPAL: considers only the carpal bones
- maturity indicators:
- appearance and size of ossification centers
- changes in shape
- fusion of the epiphysis and the diaphysis
- development of each region is divided into discrete stages and each stage is given a letter (A,B,C,D, . . ., I)

Dental age estimation

- ☐ dental age can be estimated on the basis of the number of teeth at each chronological age or on the basis of stages of the formation of crowns and roots of the teeth
- ☐ eruption: the emergence of the tooth through the gingiva
- ☐ calcification or mineralization: the organic matrix of a tooth, root formation, and tooth eruption are important indicators of dental age
- ☐ caries, tooth loss and severe malnutrition may *influence* the emergence of teeth through the gingiva
- ☐ chronologies of the *eruption* of teeth are *less satisfactory* for dental age assessment than those based on tooth formation
- ☐ tooth formation may be divided appropriately into a *number of stages* that cover *continuously* the development of teeth, in contrast to the single episode of tooth eruption

Tooth formation standards

- ☐ How to create the standards? Events in the formation of human dentition are based primarily on data from studies of dissected *prenatal anatomic material* and from *radiographic imaging* of the teeth of the same subjects over time (longitudinal data) or of different subjects of different ages seen once (cross-sectional data)
- ☐ subjects surveyed in most studies of dental development are essentially of *European* derivation, and population differences can only be established by studies that share methodology and information on tooth formation in nonwhite/non-European-derived populations

Morphological age estimation

- ☐ by considering one or more body dimensions
- ☐ in the mirror of the adequate (in time and geographic region) references
  - Mészáros-Mohácsi method: body mass, stature, plastic index (shoulder width, lower arm circumference, hand circumference)

Adult height estimation

- ☐ reasons of adult height prediction:
  1) a common procedure in pediatric endocrinology, particularly when the stature of a child is unusual for its age (e.g. below 3rd percentile or above 97th percentile)
  2) it can be applicable in pediatric exercise science for talent identification, selection and development 3 or assignment to specific sport at early age
- o stature can play a significant role in *contributing to success in some sports* by offering certain natural advantages for short athletes in gymnastics, motorsport or weightlifting, while tall athletes have an advantage e.g. in basketball and volleyball
- o since children differ greatly in the timing and tempo of growth, an accurate method of estimating adult height needs to incorporate an indicator of biological maturity
- o methods that use skeletal age development to account for variation in biological maturity are the gold standard in the field
- o besides other methods, Tanner-Whitehouse technique seems to be valid procedure for prediction of adult height, with acceptable median errors and systematic objectivity
- o TW method accuracy: the studies verified the accuracy of TW method for predicting adult height (from 8 years of age) with significant correlation between predicted and final stature ($r = 0.96$; $P<0.0001$), mean adult height is usually underestimated by 3 cm on average

Physiological age estimation

- ☐ it is evidenced by auxological surveys that each healthy child follows the same growth pattern from birth till sexual maturity independently from gender or the genetic origin
- ☐ **Puberty:**
  - morphological changes in size
  - morphological changes in shape
  - changes of body proportions
  - changes in body composition
  - development of genitalia and secondary sex characteristics
  - the neuroendocrine events leading to onset of puberty remain largely unknown
  - the mechanisms underlying the reawakening of the hypothalamic-pituitary-gonadal (HPG) axis at puberty are unknown
  - the HPG axis is active during fetal development and continues to function in infancy until it enters a relative quiescent state, often referred to as the juvenile pause
- ☐ The timing and the length of pubertal events and stages can vary between individuals, populations and generations
- ☐ Pubertal timing is correlated highly within ethnic population groups, within families, and between monozygotic twins, with heritability estimates suggesting that 50% to 80% of the variation in pubertal timing is determined by genetic factors
- ☐ the understanding of normal variation in pubertal timing and likely provide further insight into pubertal disorders
- ☐ Disorders/abnormalities can be :
  - in the timing of sexual maturation (early or delayed)
  - in the onset of each stage of sexual maturation
- ☐ indicators of sexual maturation:
- ☐ breast, pubic hair, axillary hair development in girls
- ☐ external genitalia, pubic hair,axillary hair, face and body hair development in boys

- ☐ **stages of puberty in boys:**

stage 1: Normal Age Range: 9-12, Average: about 10

Male hormones are becoming active, but there are hardly, if any, outside signs of development. Testicles are maturing, and some boys start a period of rapid growth late in this stage.

stage 2: Normal Age Range: 9-15, Average: 12-13

Testicles and scrotum begin to enlarge, but penis size doesn't increase much. Very little, if any, pubic hair at the base of the penis. Increase in height and change in body shape.

stage 3: Normal Age Range: 11-16, Average: 13-14

Penis starts to grow in length, but not much in width. Testicles and scrotum still growing. Pubic hair starts to get darker and coarser and is spreading towards the legs. Voice begins to deepen. Some hair around the anus grows.

stage 4: Normal Age Range: 11-17, Average: 14-15

Penis width increases, as well as length. Testicles and scrotum still growing. Pubic hair begins to take adult texture, although covers a smaller area. Oigarche. Underarm hair develops. Facial hair increases on chin and upper lip. Voice gets deeper and skin gets more oily.

stage 5: Normal Age Range: 14-18, Average: around 16

Nearing full adult height and physique. Pubic hair and genitals have adult appearance. Facial hair grows more completely and shaving may begin now or soon.

- **stages of puberty in girls:**

stage 1: Normal Age Range: 8 to 11

There are no outside signs of development, but a girl's ovaries are enlarging and hormone production is beginning.

stage 2: Normal Age Range: 8-14. Average: 11-12

The first sign is typically the beginning of breast growth, including "breast buds." A girl may also grow considerable height and weight. The first signs of pubic hair start out fine and straight, rather than curly.

stage 3: Normal Age Range: 9-15. Average: 12-13

Breast growth continues, pubic hair coarsens and becomes darker.

stage 4: Normal Age Range: 10-16. Average: 13-14

Pubic hair growth takes on the triangular shape of adulthood, but doesn't quite cover the entire area. Underarm hair is likely to appear in this stage, as is menarche. Ovulation (release of egg cells) begins in some girls, but typically not in a regular monthly routine until Stage 5. Menarcheal age.

stage 5: Normal Age Range: 12-19. Average: 15

This is the final stage of development, when a girl is physically an adult. Breast and pubic hair growth are complete, and your full height is usually attained by this point. Menstrual periods are well established, and ovulation occurs monthly.