Gametogenesis

Oogenesis

Spermatogenesis

Primordial germ cells (PGCs)

- Fertilization
- Sperm & Oocyte unite to form zygote
- PGCs in second week from epiblast
- Move to wall of yolk sac
- In 4th week migrate to developing gonads
- By the end of 5th week they arrived there
- Mitosis
- Gametogenesis (Meiosis & differentiation)

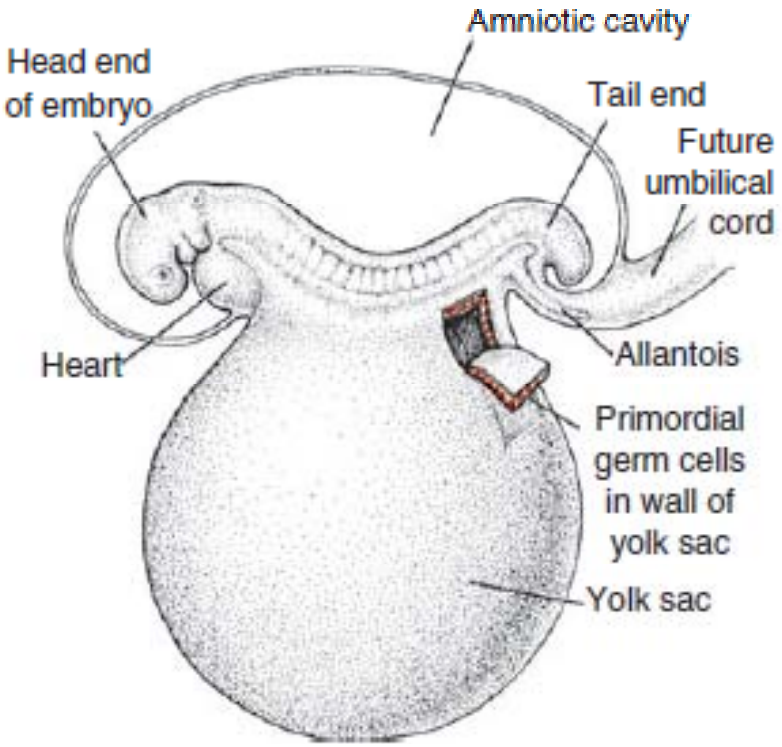


Figure 2.1 An embryo at the end of the third week, showing the position of PGCs in the wall of the yolk sac, close to the attachment of the future umbilical cord. From this location, these cells migrate to the developing gonad.

Clinical Correlates

Primordial Germ Cells and Teratomas

Teratomas are tumors of disputed origin that often contain a variety of tissues, such as bone, hair, muscle, gut epithelia, and others. It is thought that these tumors arise from pluripotent stem cells that can differentiate into any of the three germ layers or their derivatives. Some evidence suggests that PGCs that have strayed from their normal migratory paths could be responsible for some of these tumors (Fig. 2.2). Another source may be epiblast cells that give rise to all three germ layers during gastrulation

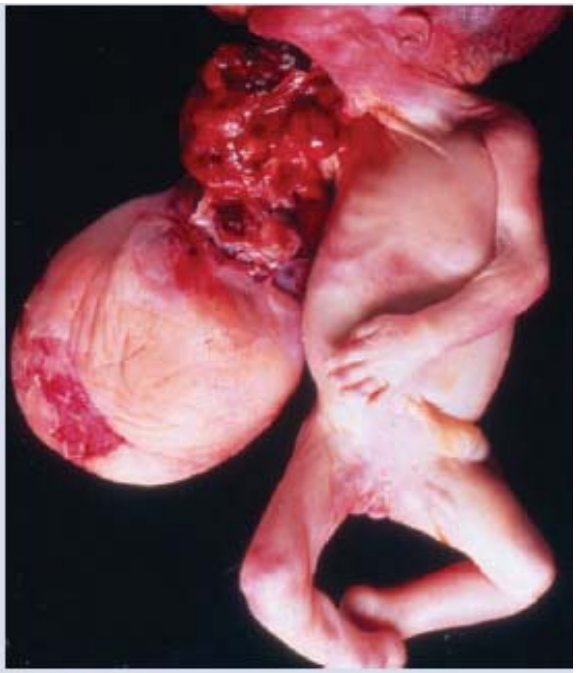
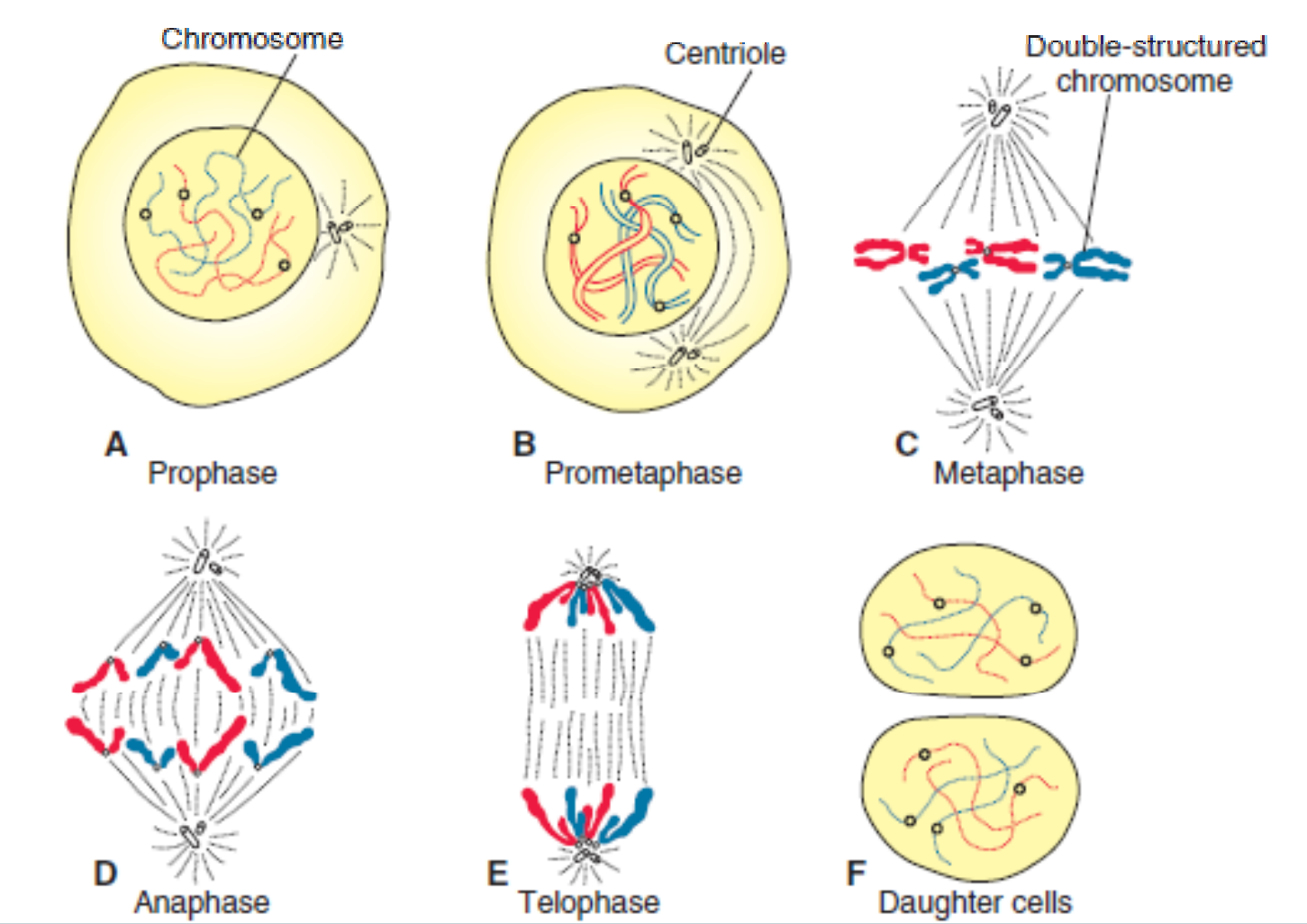


Figure 2.2 Oropharnyngeal teratoma. These tumors may arise from PGCs or from epiblast cells (see Chapter 5), both of which are pluripotent. Tissues within the tumors include derivatives of all three germ layers and may include gut, bone, skin, teeth, and so forth.

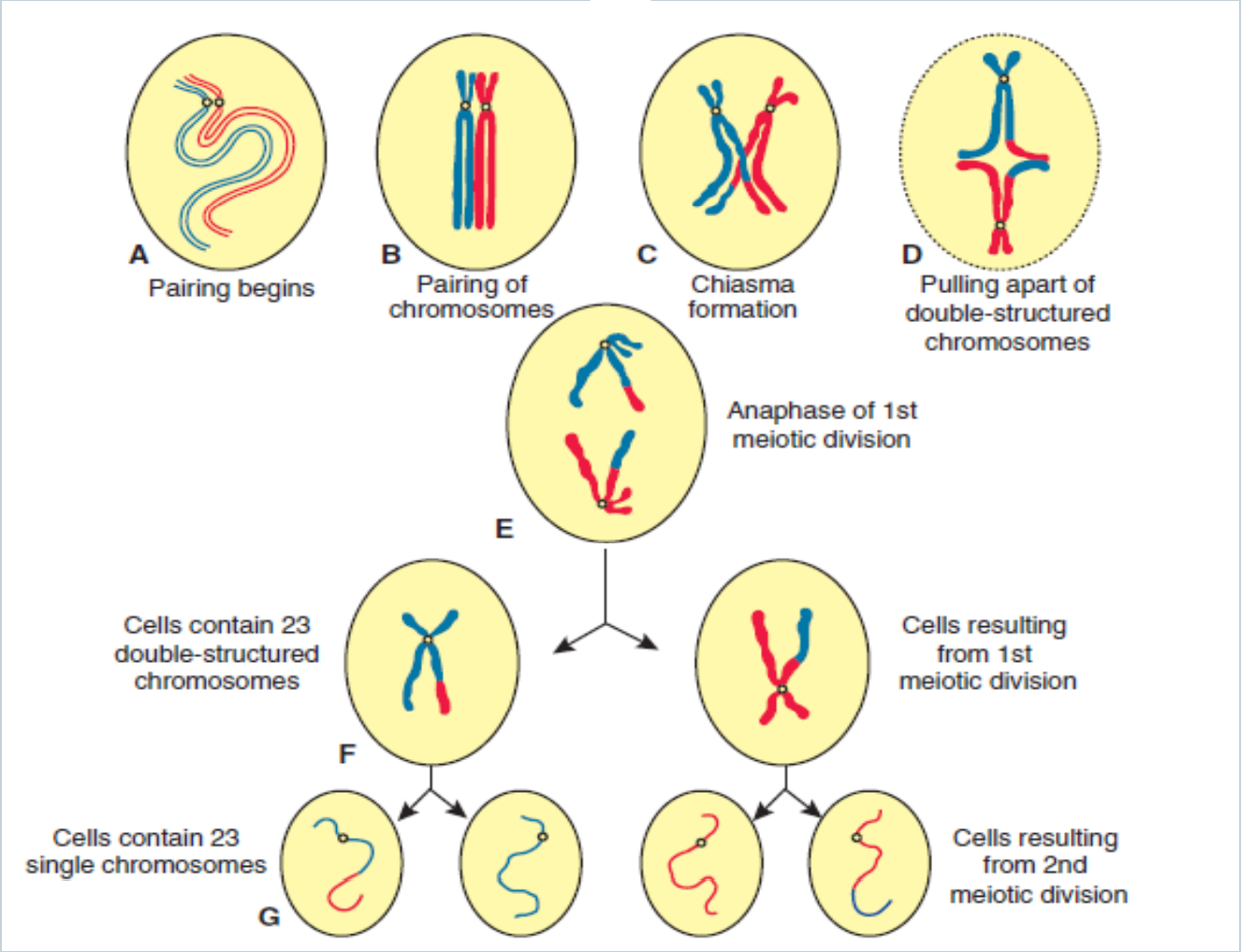
The chromosome theory of inheritance

- Traits of a new individual by inherited genes from the father and & mother.
- Humans genome 23,000 genes
- 46 chromosomes
- **linked genes**
- In somatic cells 23 **homologous pairs**
- 22 pairs are **autosomes**
- **one pair of sex chromosomes**
- **XX &** XY
- One chromosome of each pair is derived from the maternal gamete, the **oocyte, and one from the paternal gamete,** the **sperm**
- **each gamete contains a haploid** number of 23 chromosomes
- **fertilization restores the diploid** number of 46.

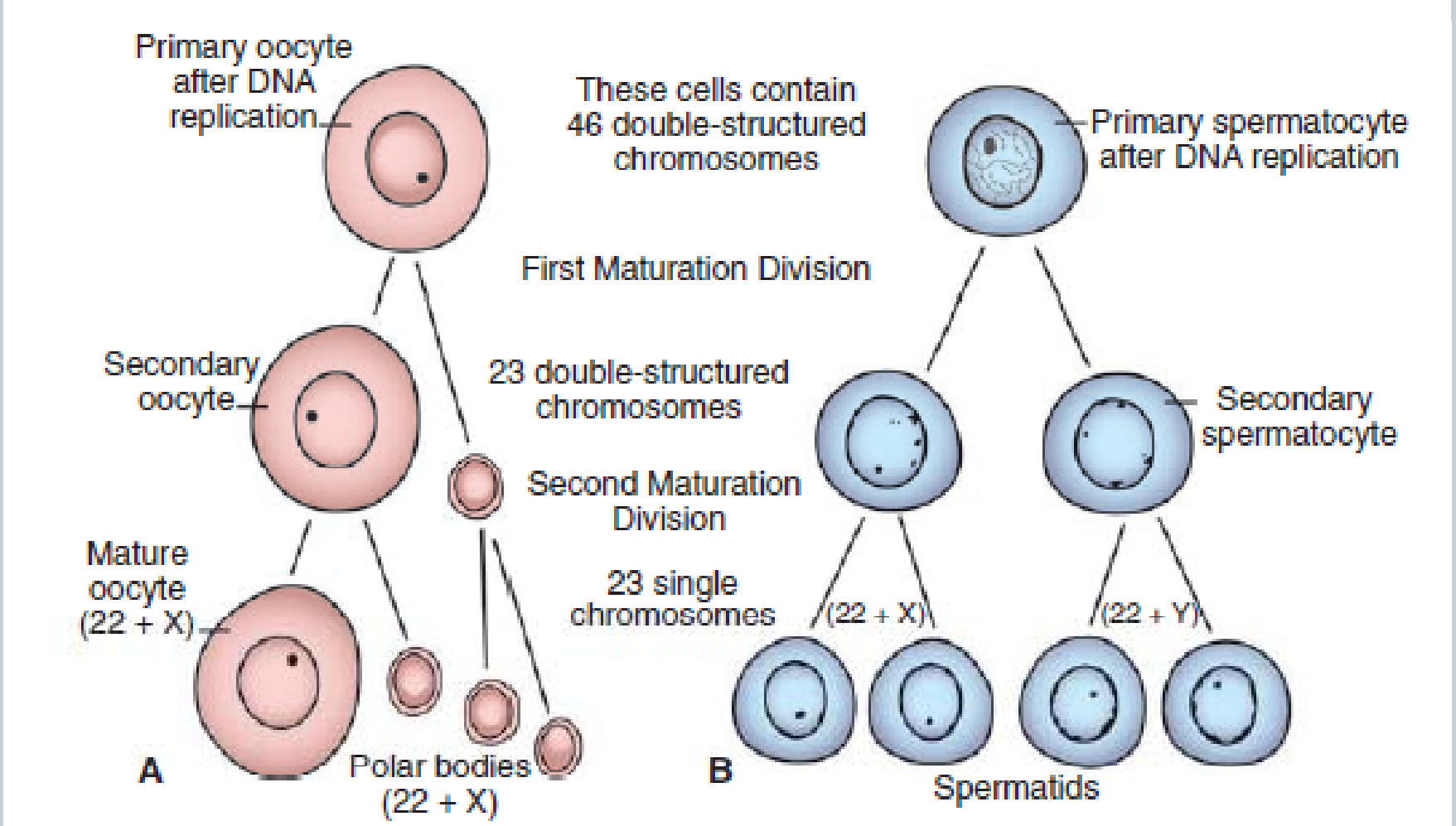
Mitosis


Chromosome
Centriole
Double-structured chromosome
A Prophase
B Prometaphase
C Metaphase
D Anaphase
E Telophase
F Daughter cells

Meiosis


A
Pairing begins
B
Pairing of chromosomes
C
Chiasma formation
D
Pulling apart of double-structured chromosomes
E
Anaphase of 1st meiotic division
Cells contain 23 double-structured chromosomes
F
Cells resulting from 1st meiotic division
Cells contain 23 single chromosomes
G
Cells resulting from 2nd meiotic division

Gametogenesis
& polar bodies



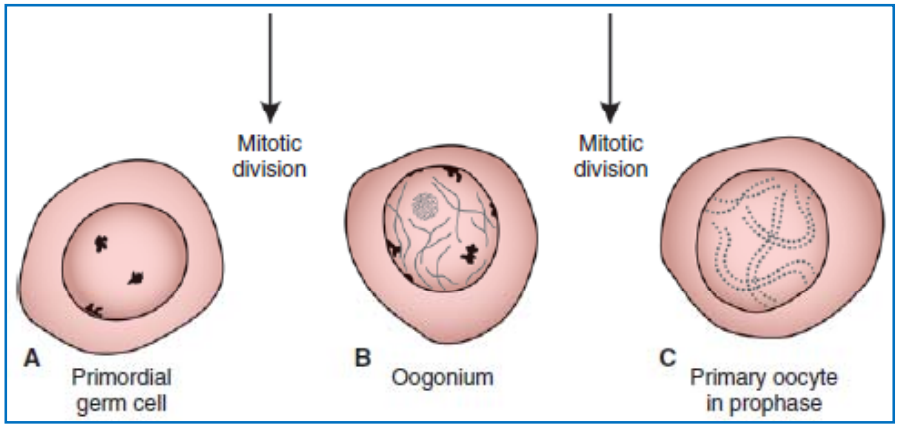
Oogenesis

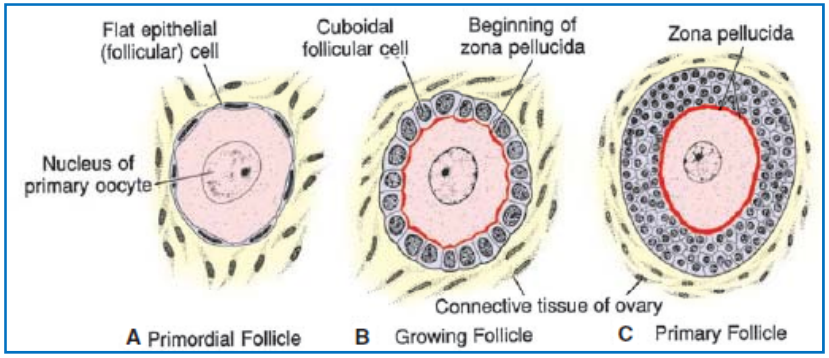
Maturation of Oocytes Begins Before Birth

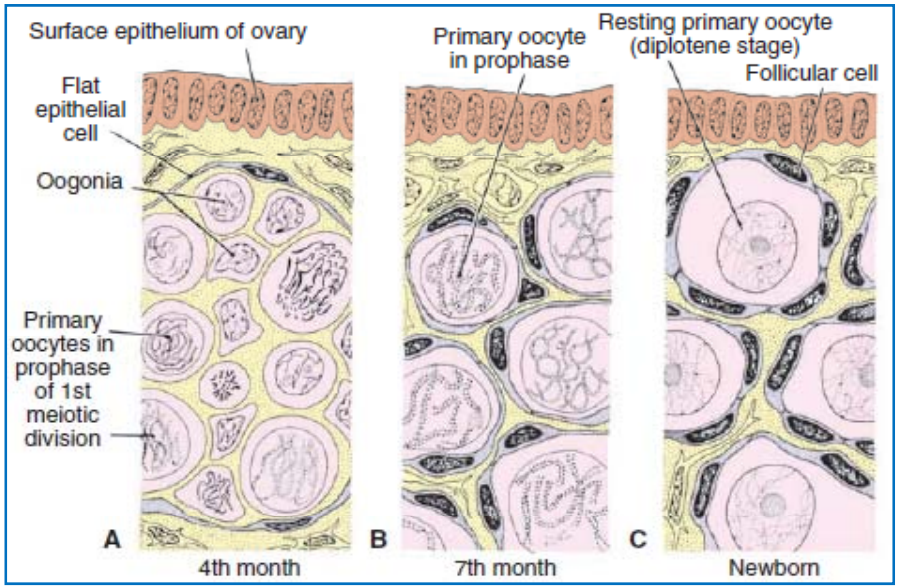
- PGCs have arrived to gonad (XX Genome)
- Differentiate to oogonia
- Mitosis
- By the end of third month
- Arrenged in clusters
- Cluster surround by layer of flat epithelial cells
- Follicular cell originated from

surface epithelium covering the ovary

- 5^{th} month 7 million germ cells
- 7^{th} month germ cells apoptosis & degeneration
- Prophase Meiosis I
- **Primordial follicle**







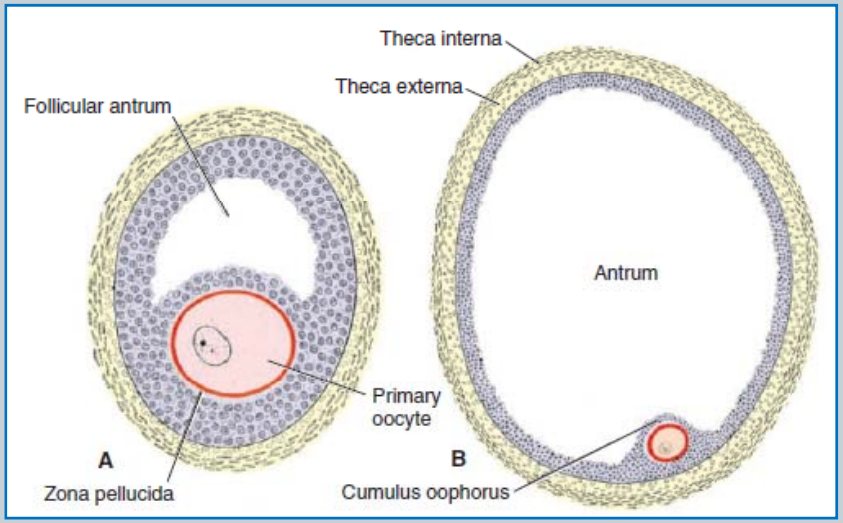
Maturation of Oocytes Continues at Puberty

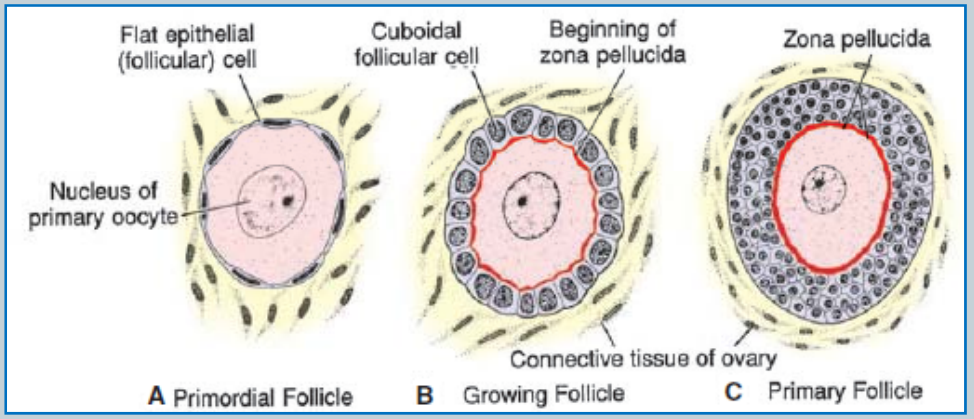
- Diplotene stage of prophase meiosis I
- Oocyte maturation inhibition (OMI)
- OMI from Follicular cells
- 600000-800000 follicles at birth
- 40000 at puberty
- 500 released

- Each month
- 15-20 follicle

- Antrum & antral or vesicular stage (longest stage)
- Graffian follicle or mature vesicular follicle
- 37 hours befor ovulation

- Follicular cells
- Flat cells
- Cuboid cells
- Multilayers of granulosa cells
- **Primary follicle**

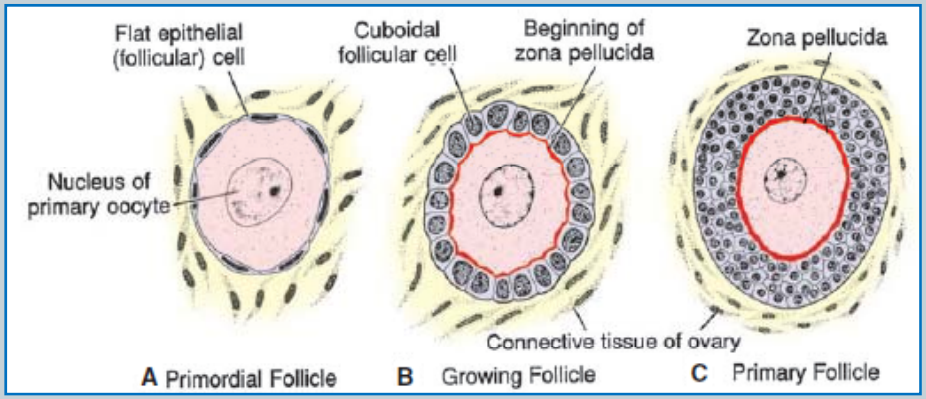




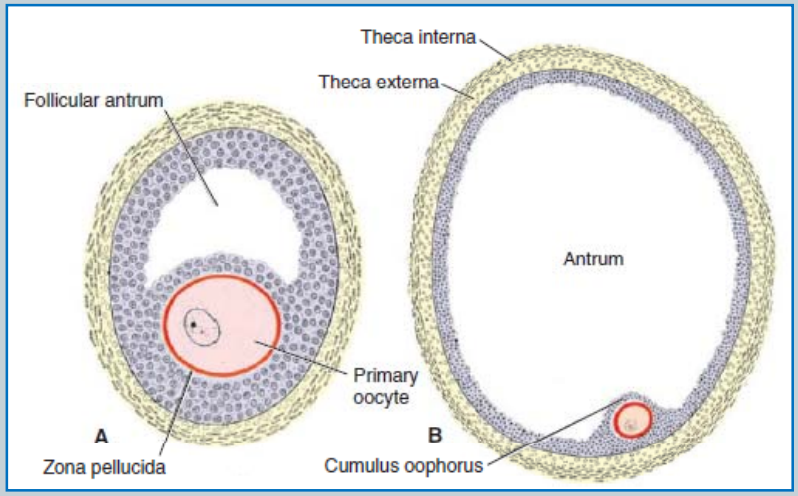
Follicle maturation

- Granulosa cell on basement membrane
- Theca folliculi
- Zona pllucida

- Theca interna
- Theca externa



- fluid-filled spaces
- Secondary follicle
- **Antrum formation**
- **the follicle is** termed
- a **vesicular or an antral follicle**
- **Cumulus oophorus**

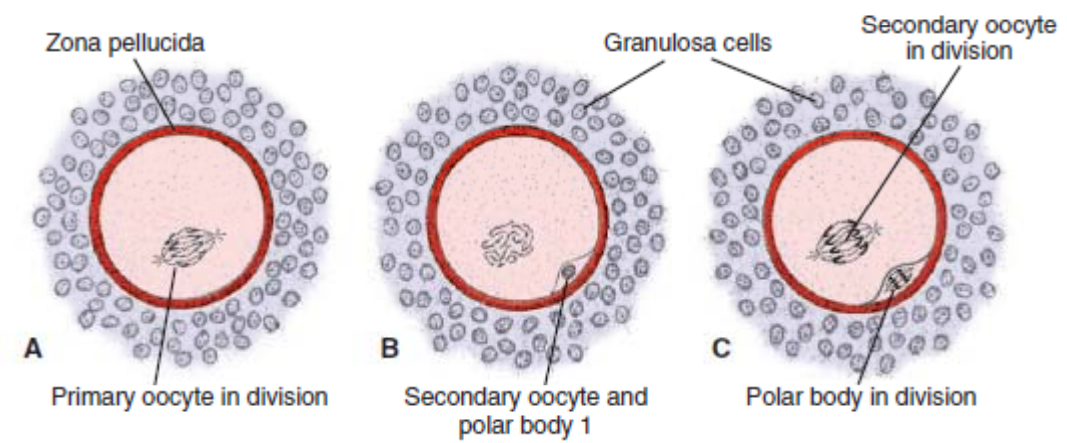


- **the mature vesicular (Graafian) follicle**
- 25 mm
- theca interna, steroid secretion & rich in blood vessels
- theca externa, merges with the ovarian connective tissue

Follicle maturation

- With each ovarian cycle,
- a number of follicles begin to develop,
- When the secondary follicle is mature,
- surge in **luteinizing hormone (LH) induces** the preovulatory growth phase
- Meiosis I is completed
- ***Secondary* oocyte, receives most of the cytoplasm;**
- **first polar body, receives practically** none

- Cell enters meiosis II but arrests in metaphase approximately 3 hours before ovulation
- Meiosis II is completed after fertilization

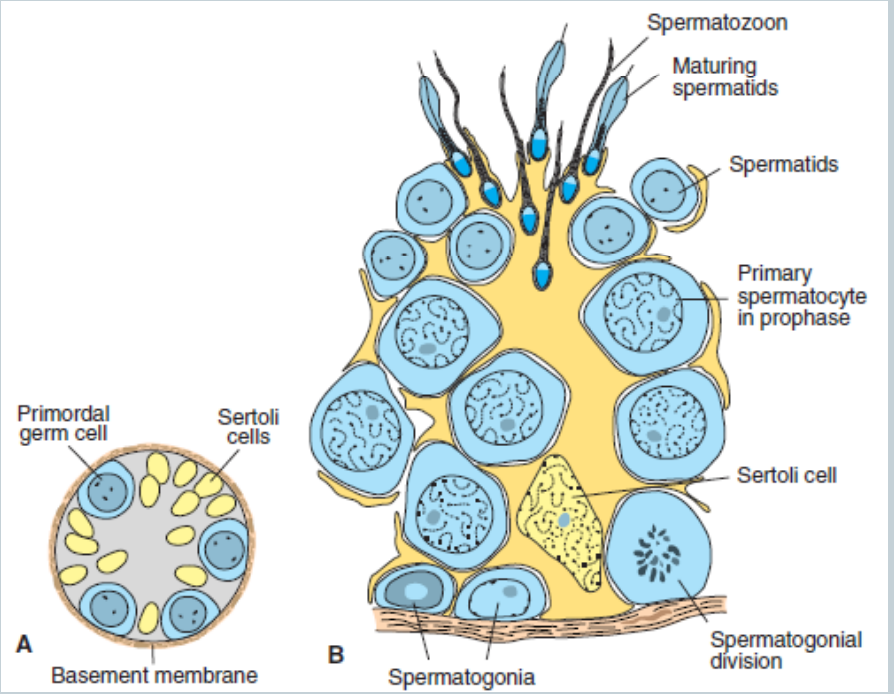


Spermatogenesis

- *Maturation of Sperm Begins at Puberty*
- **Spermatogonia** to **spermatozoa.**
- At male birth, germ cells in the sex cords of the testis
- Large, pale cells surrounded by supporting cells
- *Supporting cells*, are derived from the surface epithelium of the
- **sustentacular cells, or Sertoli cells**

Shortly before puberty

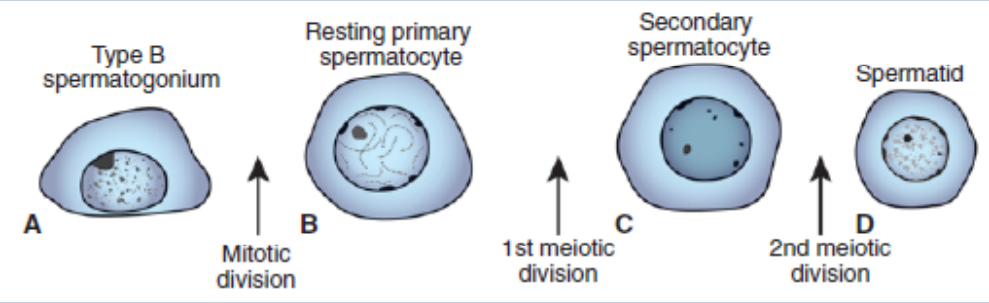
- the sex cords become the **seminiferous Tubules**
- PGCs give rise to spermatogonial stem cells.
- **type A spermatogonia**
- **type B spermatogonia,**
- **primary spermatocytes**

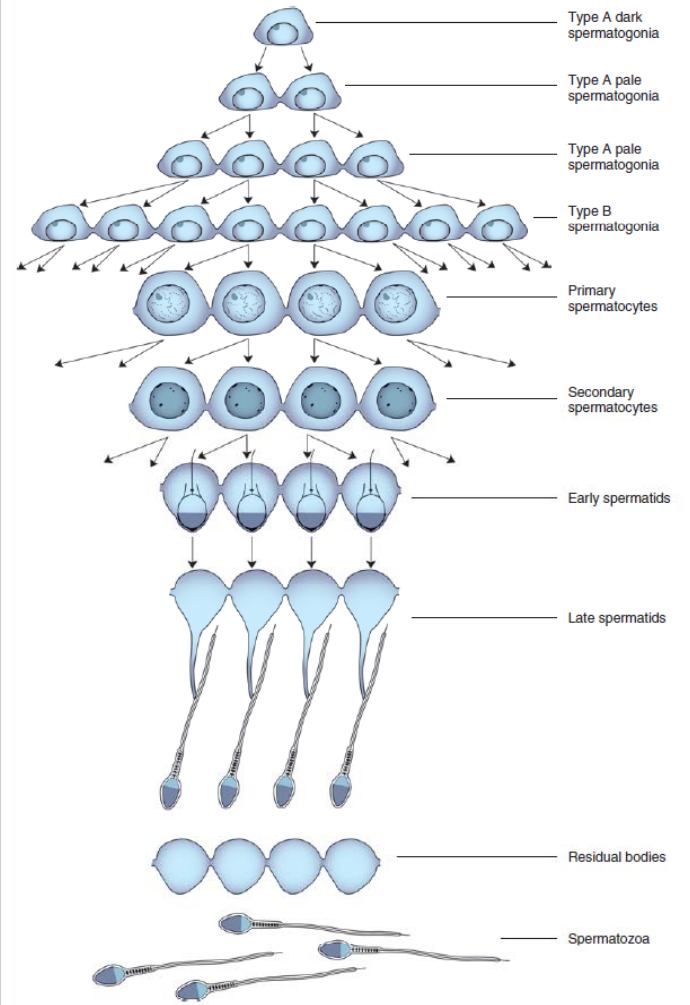


Spermatogenesis

- Primery spermatocytes enter a prolonged prophase (22 days)
- **Secondary spermatocytes**
- **spermatids**,
- incomplete cytokinesis
- remain embedded in deep recesses of Sertoli cells
- *Sertoli cells:*
- *support* and protect the germ cells
- participate in their nutrition
- assist in the release of mature spermatozoa

- LH on Leydig cells
- FSH on sertoli cell





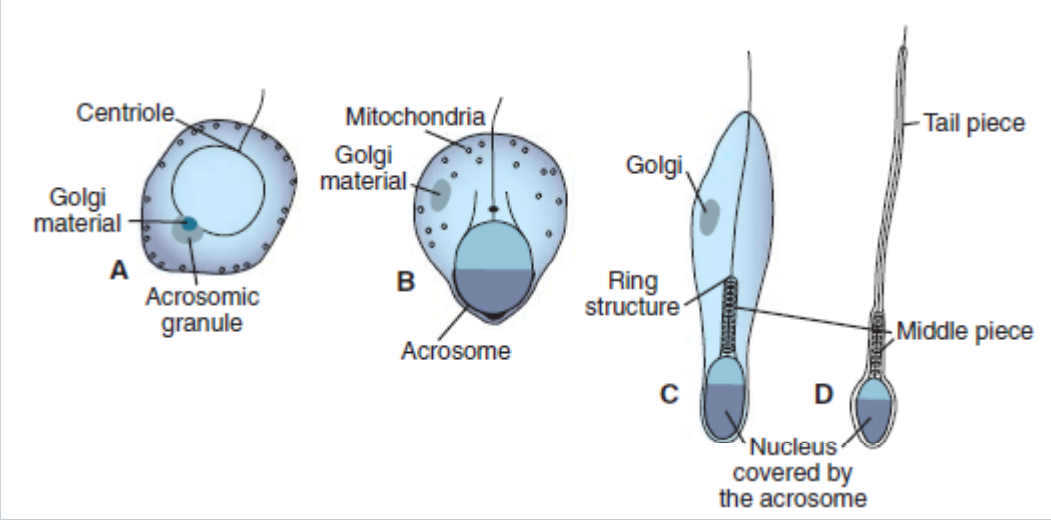
Spermiogenesis

- spermatids into spermatozoa

changes include:

- (1) formation of the **acrosome,**
- (2) condensation of the nucleus;
- (3) formation of neck, middle piece, and tail;
- (4) shedding of most of the cytoplasm

- In humans, 74 days, daily 300 million sperm
- obtain full motility in the epididymis



Clinical Correlates

Abnormal Gametes

In humans and in most mammals, one ovarian follicle occasionally contains two or three clearly distinguishable primary oocytes (Fig. 2.25*A*). Although these oocytes may give rise to twins or triplets, they usually degenerate before reaching maturity. In rare cases, one primary oocyte contains two or even three nuclei (Fig. 2.25*B*). Such binucleated or trinucleated oocytes die before reaching maturity.

In contrast to atypical oocytes, abnormal spermatozoa are seen frequently, and up to 10% of all spermatozoa have observable defects. The head or the tail may be abnormal, spermatozoa may be giants or dwarfs, and sometimes they are joined (Fig. 2.25*C*). Sperm with morphologic abnormalities lack normal motility and probably do not fertilize oocytes

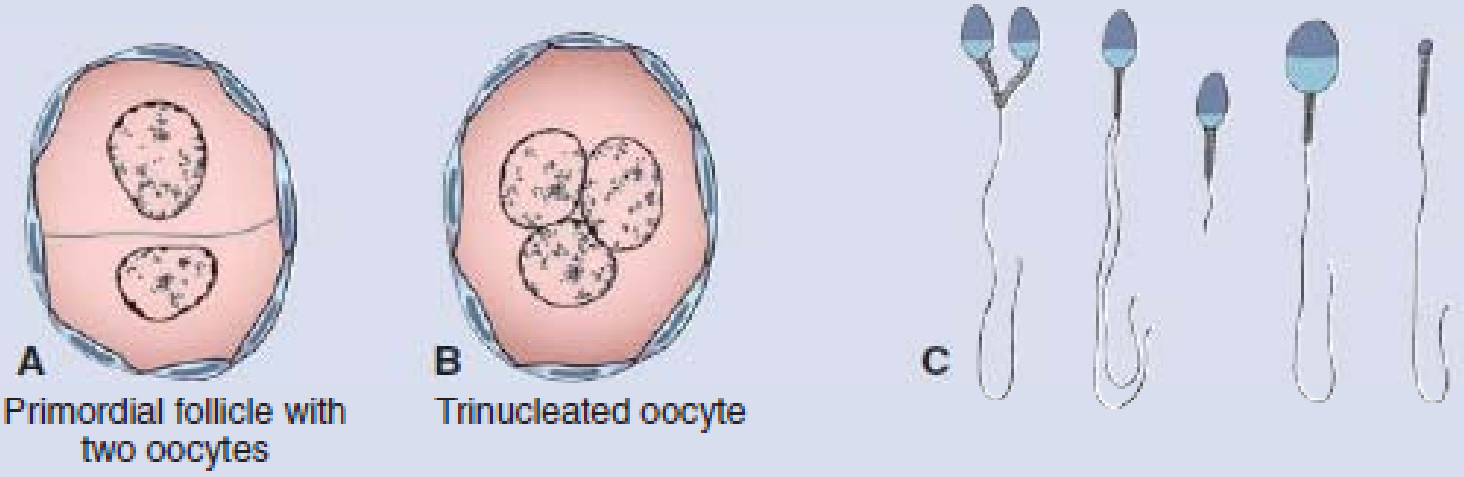


Figure 2.25 Abnormal germ cells. **A.** Primordial follicle with two oocytes. **B.** Trinucleated oocyte. **C.** Various types of abnormal spermatozoa.

Birth defects & spontaneous abortion

chromosomal & genetic factors

Chromosomal abnormalities:

- Numerical
- Structural

25% of all pregnancy & 50 of abortions by chromosomal abnormalities

- Turner s.
- Triploidy
- Trisomy 16

birth defects

- 10% (chromosomal abnormalities)
- 8% (gene mutation)

Numerical abnormality

Human somatic cell

- 46 chromosomes & diploid(2n)

Human gamete

- 23 chromosomes & haploid(n)

- Euploid
- Aneuploid
- Trisomy
- Monosomy
- Nondisjunction
- Translocation

Balanced & unbalanced

(13,14,15,21,22)

Down syndrome

- **Trisomy 21**

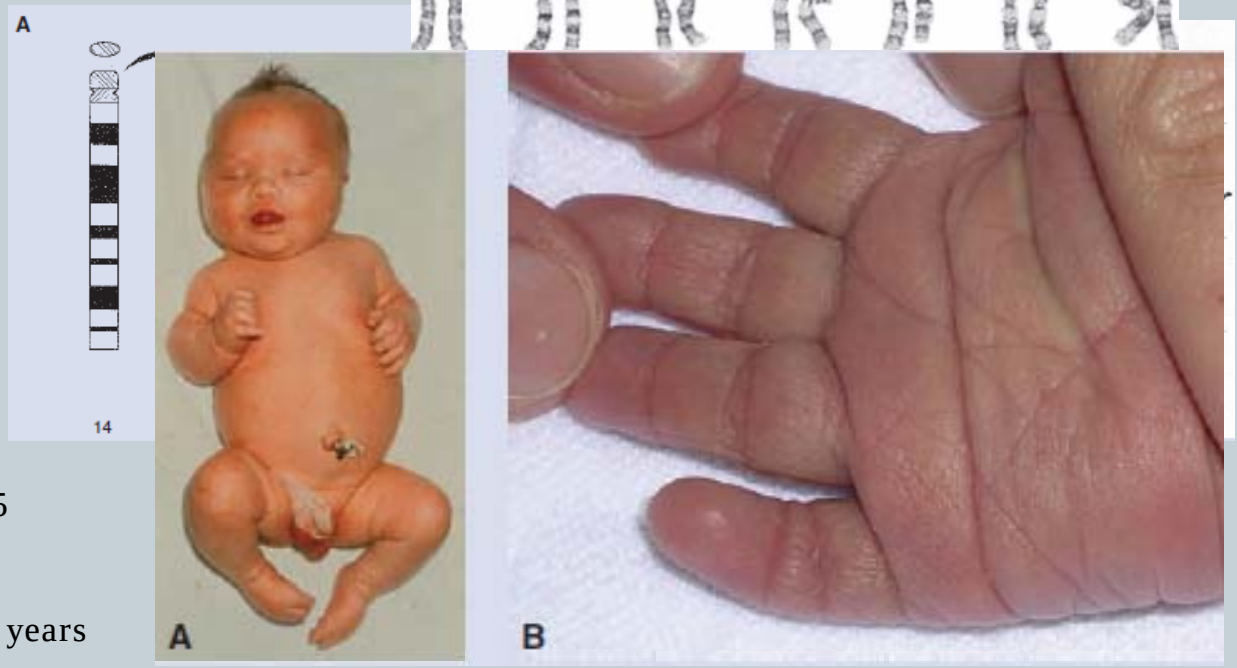
Children features

- Growth retardation
- Intellectual disability
- Craniofacial abnormalities
- Flat faces
- Small ears
- Cardiac defects
- Hypotonia

- Leukemia
- Infections
- Thyroid dysfunctions
- Premature aging
- Alzheimer

- 95% meiotic nodisjunction
- 75% maternal
- 4% translocation 21 with 13,14,15
- 1% mosaism in mitosis

- 1 in 2000 mothers age under 25 years
- 1 in 300 mothers age 35 years
- 1 in 100 mothers age 40 years



Trisomy 18

- Intllectual disability
- Congenital heart defect
- Low-set ears
- Fingers & hands flection
- Micrognathia
- Renal anomaly
- Syndactyly
- Skeletal system malformations

- 1 in 5000
- 85% lost between 10 weeks of gestation & term
- Those born alive die by 2month age
- 5% live beyond 1 year

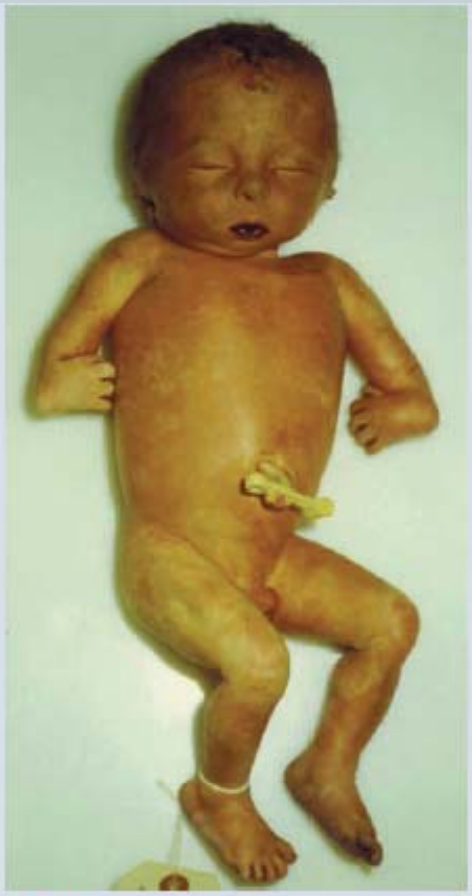


Figure 2.10 Child with trisomy 18. Note the low-set ears, small mouth, deficient mandible (micrognathia), flexion of the hands, and absent and/or hypoplasia of the radius and ulna.

Trisomy 13

- Intllectual disability
- Holoprosencephaly
- Congenital heart defect
- Deafness
- Cleft lip & palate
- Eye defects (microphthalmia, anophthalmia, cloboma)
- 1 in 20000 live birth
- 90% die in first month
- 5% live beyond 1 year

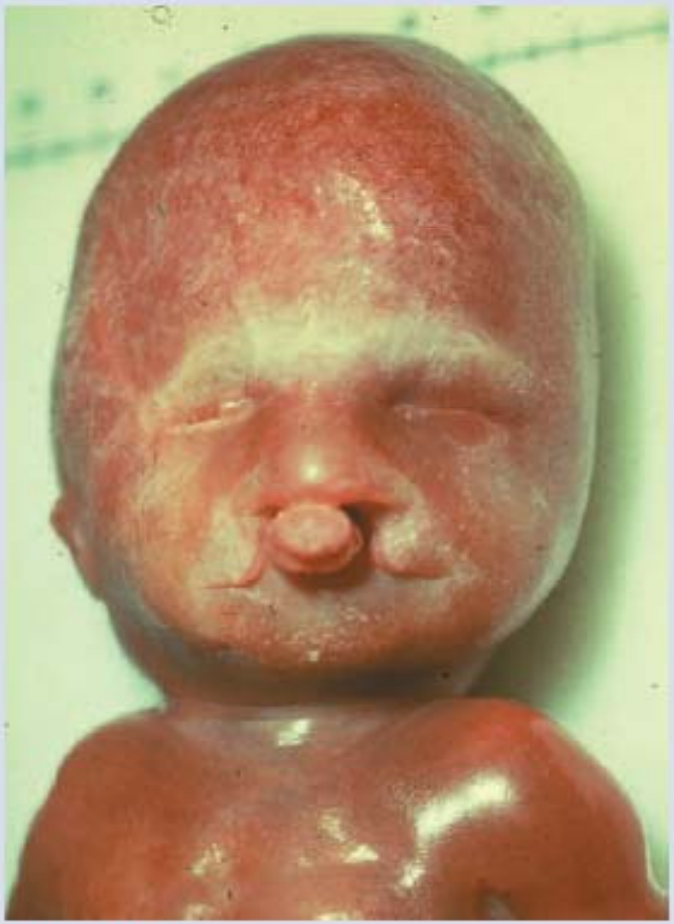


Figure 2.11 Child with trisomy 13. Note the bilateral cleft lip, the sloping forehead, and anophthalmia.

Klinefelter syndrome

- In male
- XXY
- XX nondisjunction

- Strility
- Testicular atrophy
- Somniferous tubule hyalinization
- Gynecomastia

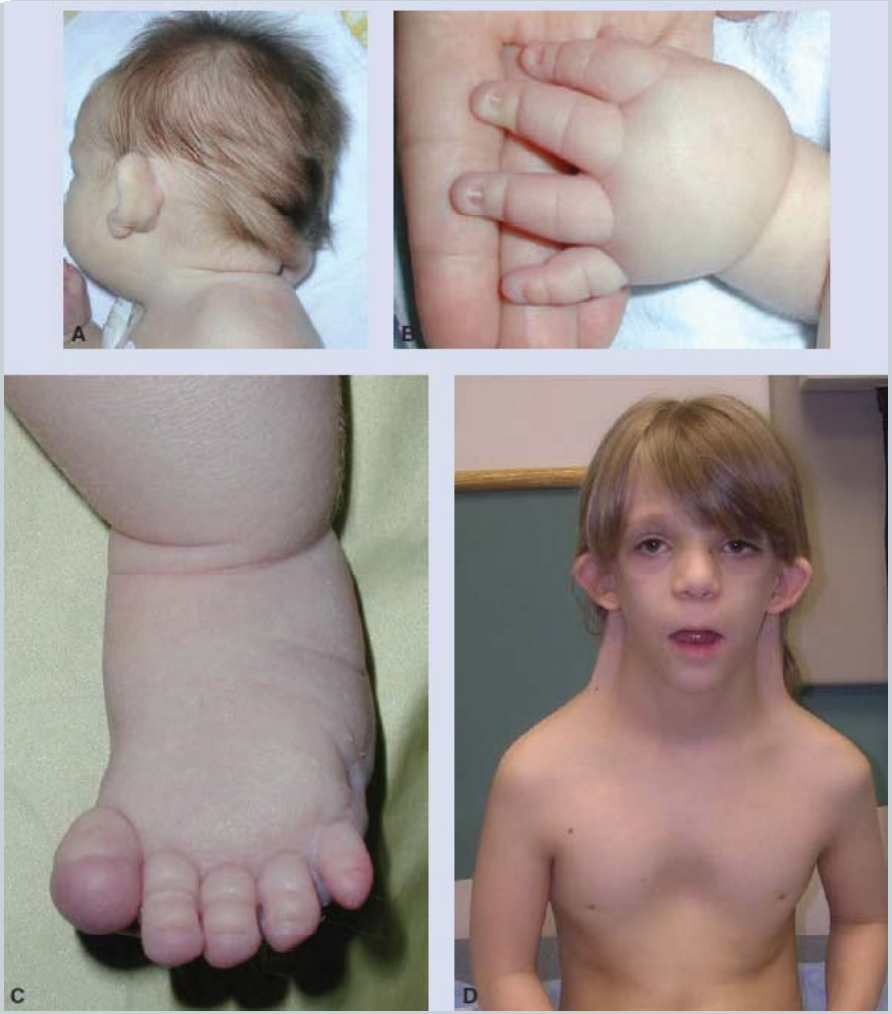
- Bar body (80%)
- 1 in 500 males

- Detect by amniosynthesis

Turner syndrome

- 45 X
- Monosomy
- 98% spontaneous aborted

- Female appearance
- Absence of ovaries (Gonadal dysgenesis)
- short stature
- Webbed neck
- Extremity lymphedema
- skeletal deformation
- Broad chest
- Widely spaced nipple
- 55% meiosis nondisjunction
- 80% in male gamete
- Mitosis nondisjunction & mosaism



Triple X syndrome

- Speech
- Self esteem
- 2 bar body

Structural chromosome abnormalities

- Chromosome breakage
- Environmental factors

Viruses

Radiation

Drugs

Deletion

Short arm of chromosome 5(cry-du-chat syndrome)

Children features

- Cat-like cry
- Microcephaly
- Intellectual disability
- Congenital heart disease

Microdeletion

- Contiguous genes
- Microdeletion or contiguous syndrome
- Detect by FISH
- 15q11-15q13
- Maternal (angelman syndrome)

Children features

- Intellectual disability
- Cannot speak
- poor motor development
- Unprovoked & prolonged period of laughter

- Paternal (prader willi syndrome)
- Children features
- Hypotonia
- Obesity
- Intellectual disability
- Hypogonadism
- Undecendant testis

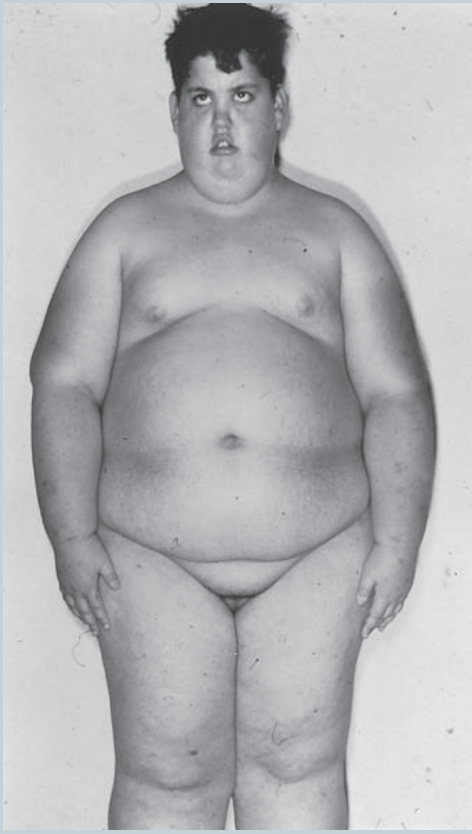
- Genomic imprinting

- Miller-dicker syndrom
- Lissencephaly

(lack of development of brain folds & grooves)

- Developmental delay
- Seizures
- Cardiac & facial abnormalities

- 17p13



Fragile sites

- CGG repeats

- Fragile X syndrome
- Xq27
- 200 repeat near promoter instead of 6-54 repeats

Children features

- Intellectual disability
- Large ear
- Prominent jaw
- Large testes
- Blue iris
- 1 in 5000 (mostly in male)

- The second cause of intellectual disability after down syndrome

Gene mutations

- Mendelian pattern
- Gene Structural & functional change
- Single gene mutation
- 8% of all human abnormalities
- Dominant mutation
- Recessive mutation

- Inborn errors of metabolism
- Phenylketonuria (impaired metabolism of phenylalanine)
- Hemocystinuria (disorder of the metabolism of the amino acid methionine)
- Galactosemia (disorder that affects sugar galactose metabolism)

Diagnostic techniques for identifying genetic abnormalities

- Cytogenetic analysis
- Giemsa stained
- High resolution metaphase banding technique

- FISH
- microarrays

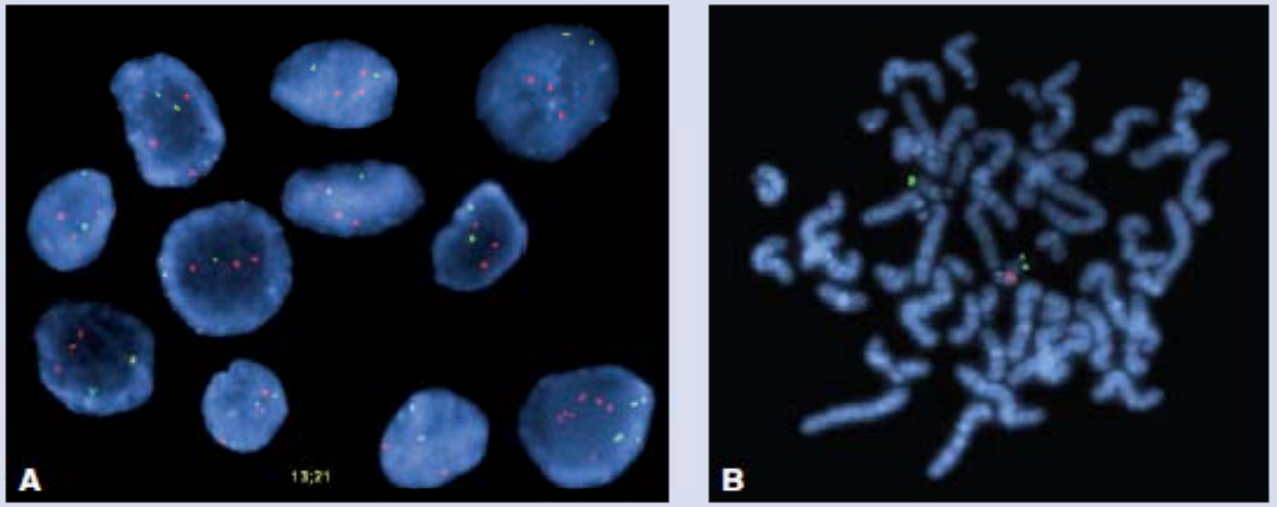


Figure 2.15 A. FISH, using a probe for chromosome 21 (*red dots*). Note that there are three red dots in each cell, indicating trisomy 21 (Down syndrome). The *green dots* represent a control probe for chromosome 13. Two cells are superimposed on the lower right, giving the impression of the presence of multiple probes. **B.** FISH analysis of 22q11 deletion syndrome. The green signals identify chromosome 22; the red signal represents FISH probe N25, which is in the q11 region. It is present on only one of the pairs of chromosome 22 indicating the other has the 22q11 deletion.