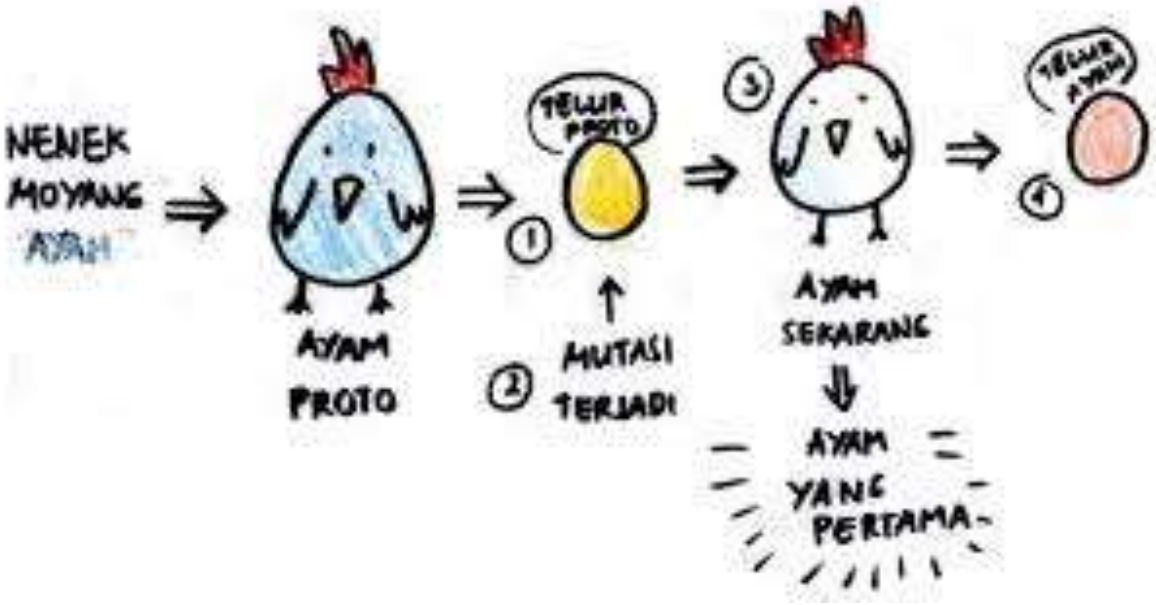
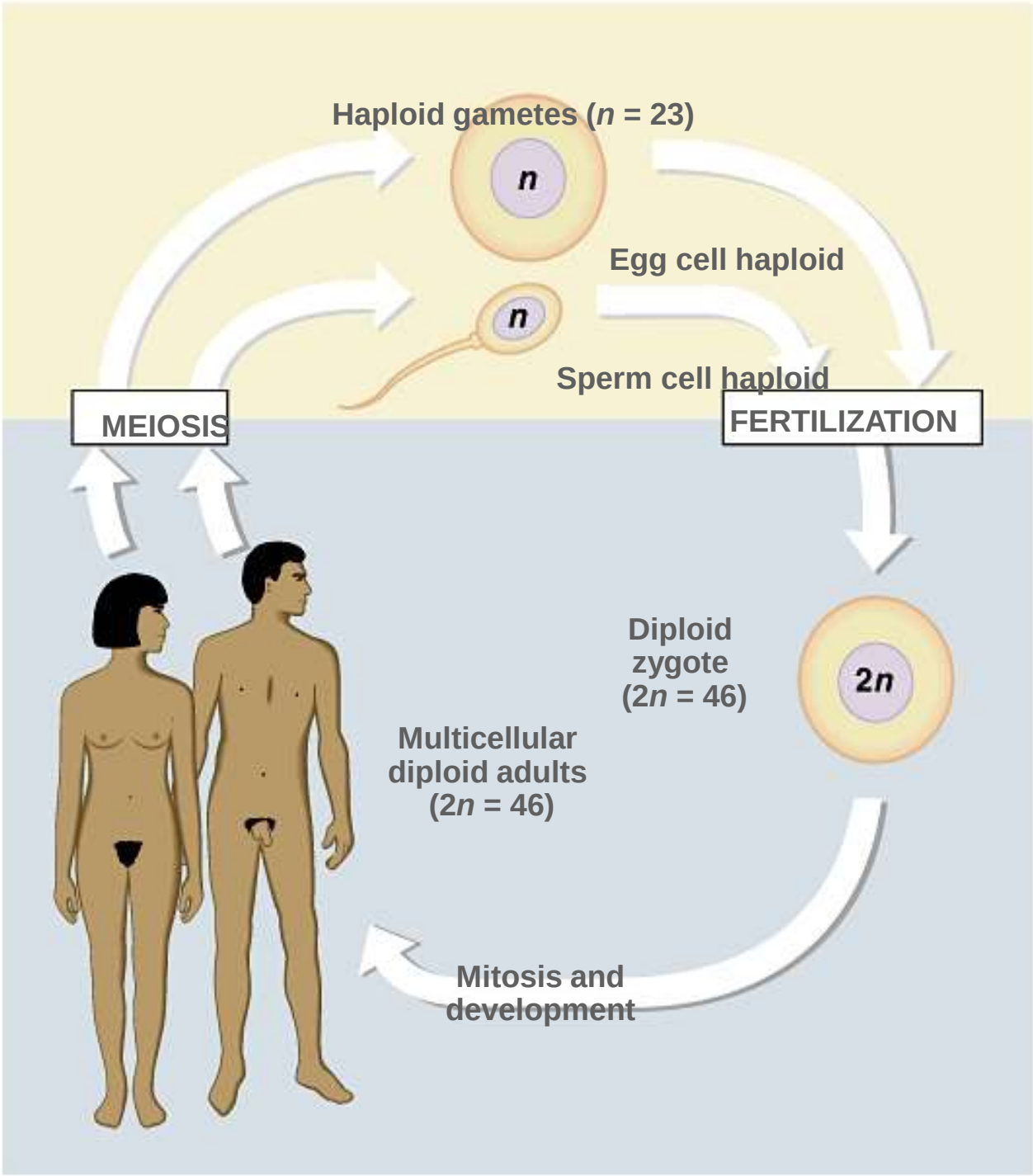
mutasi

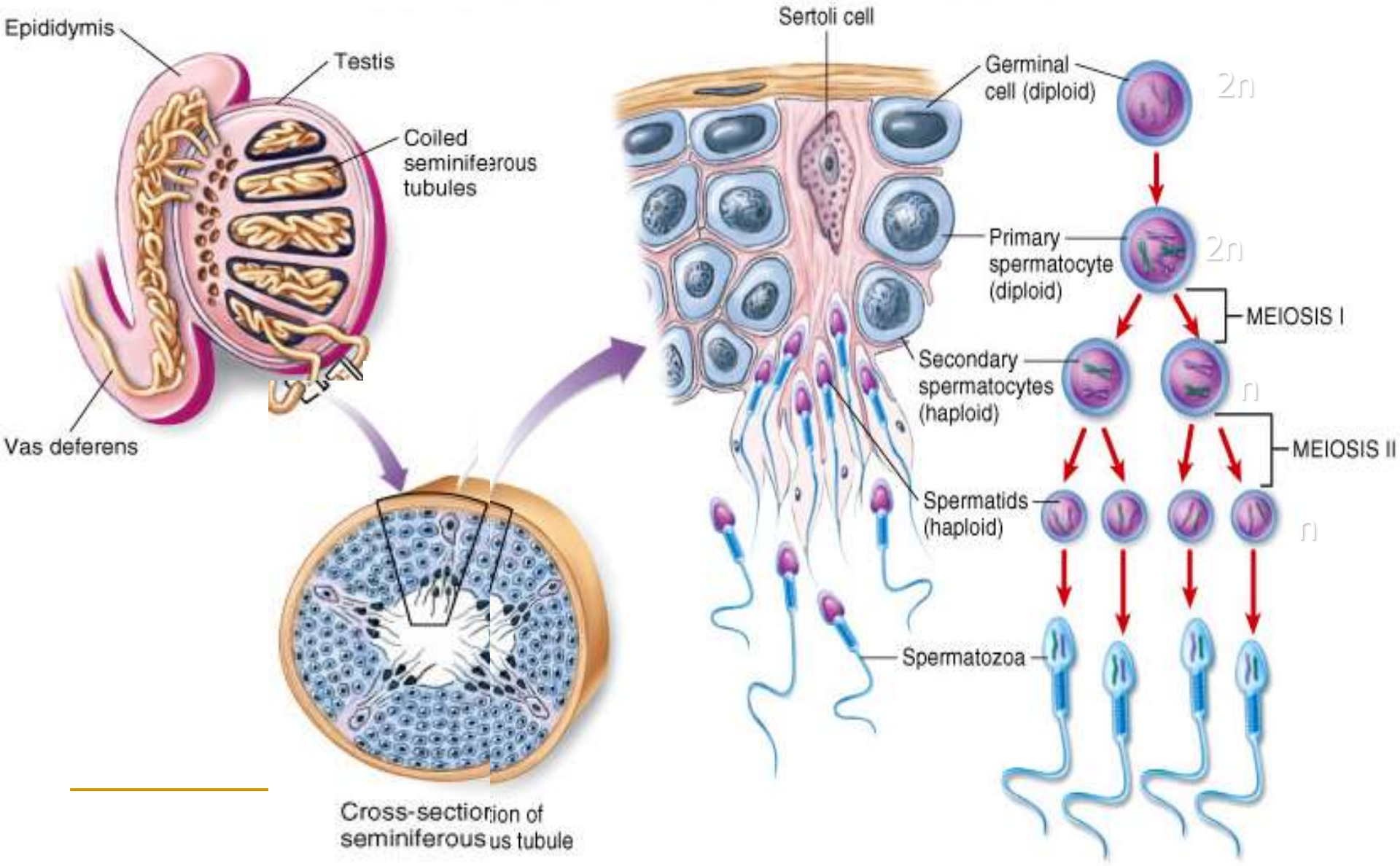


Dr. Thontowi Djauhari NS, MKes

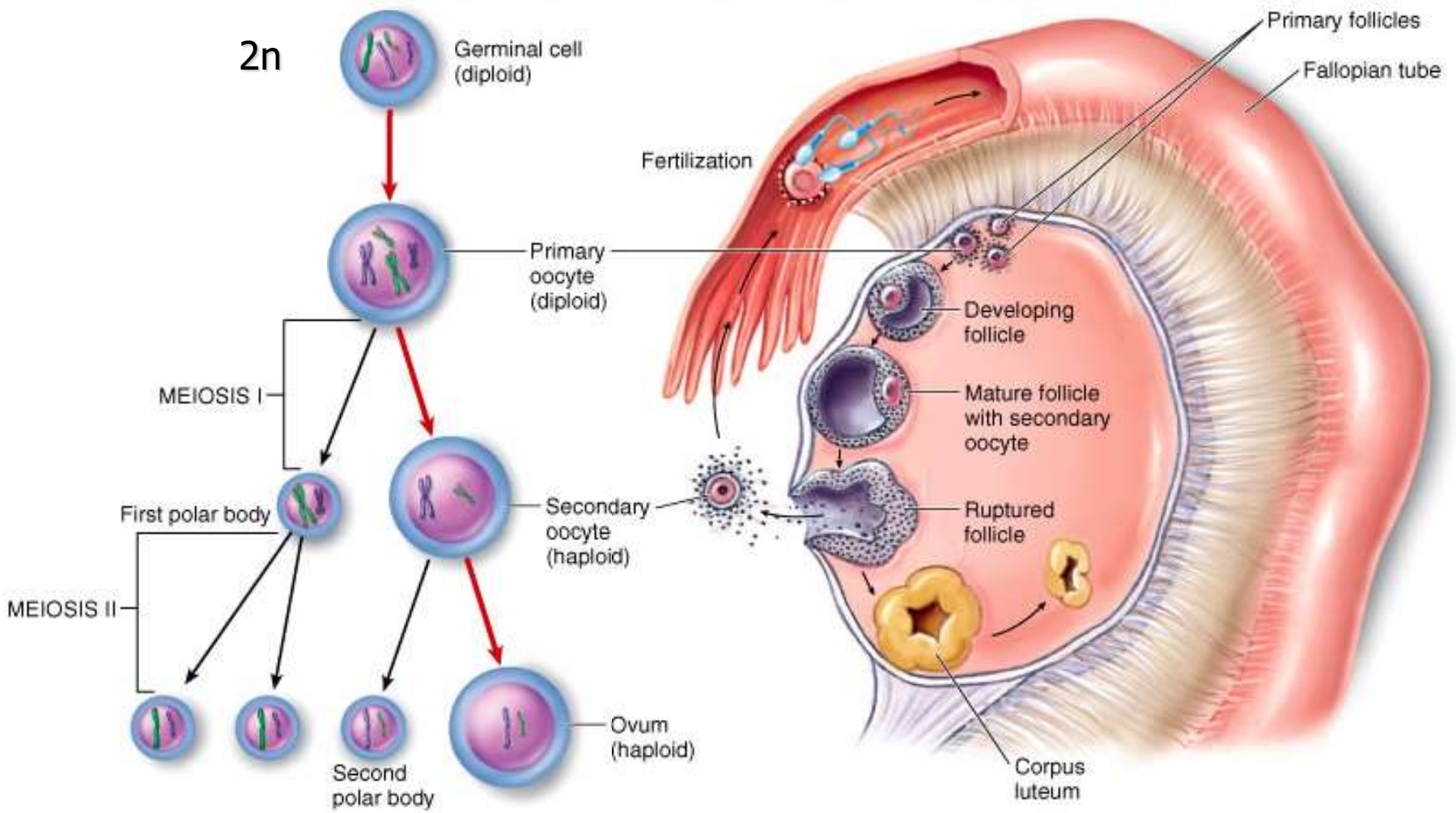
- Awalnya manusia mempunyai 46 kromos (diploid)
- Proses Meiosis akan mengurangi jumlah sel menjadi 23 kromosom (haploid)
- Penyatuan ovum + sperma akan menghasilkan 46 kromosom

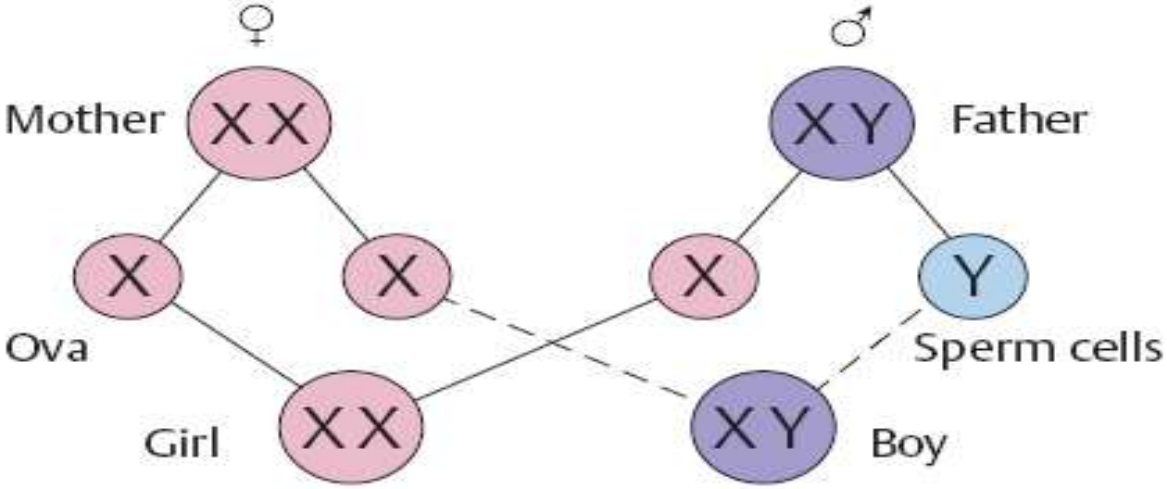


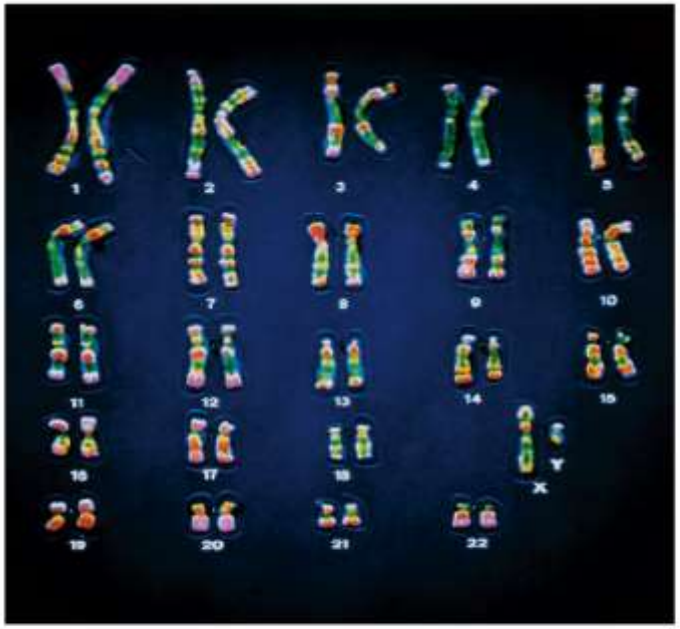
Testis and Formation of Sperm



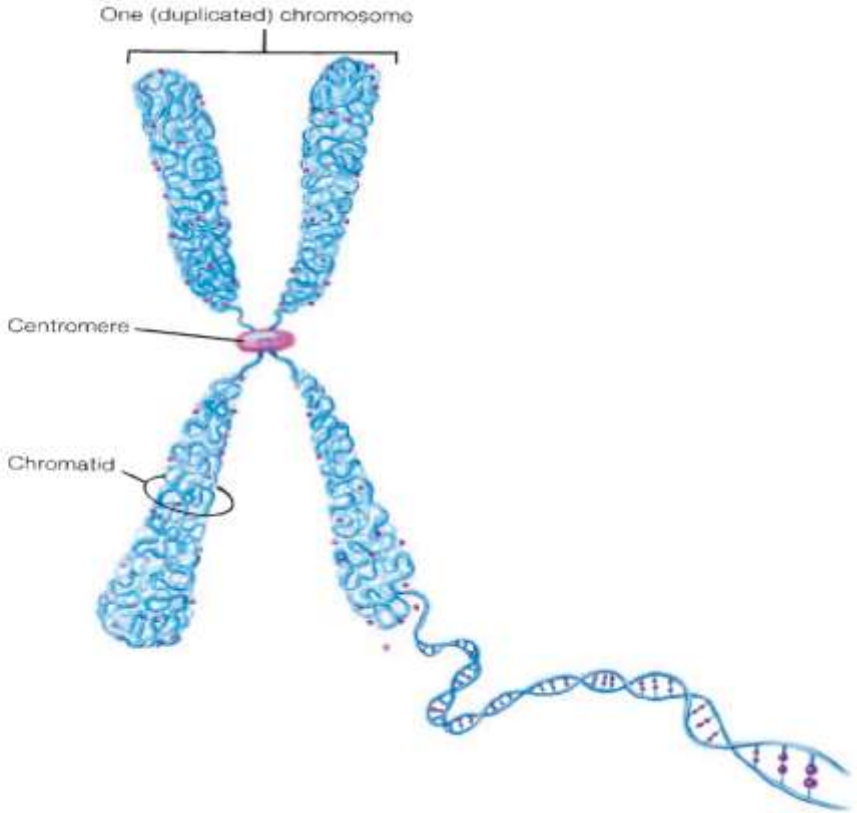
The Ovary and Formation of an Ovum

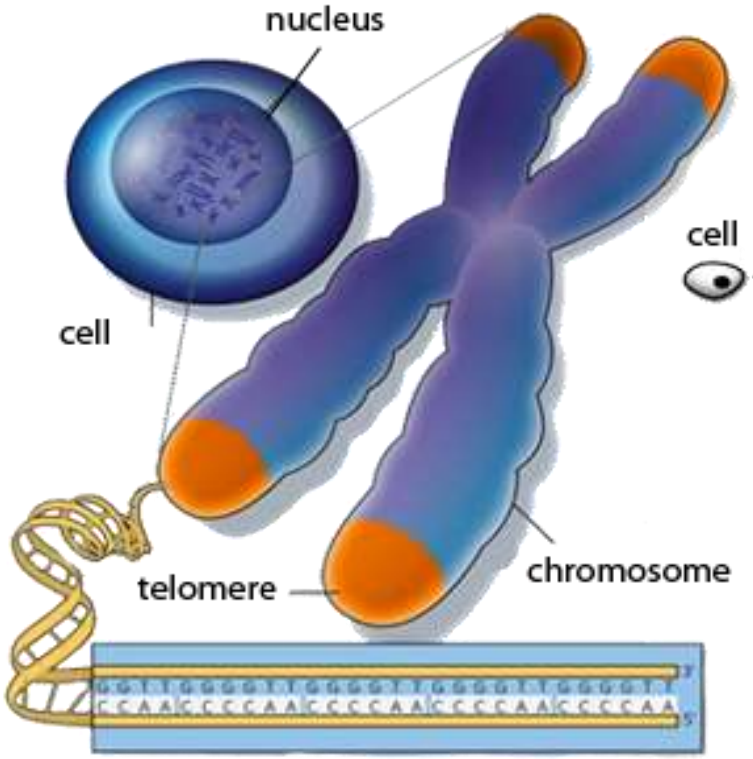


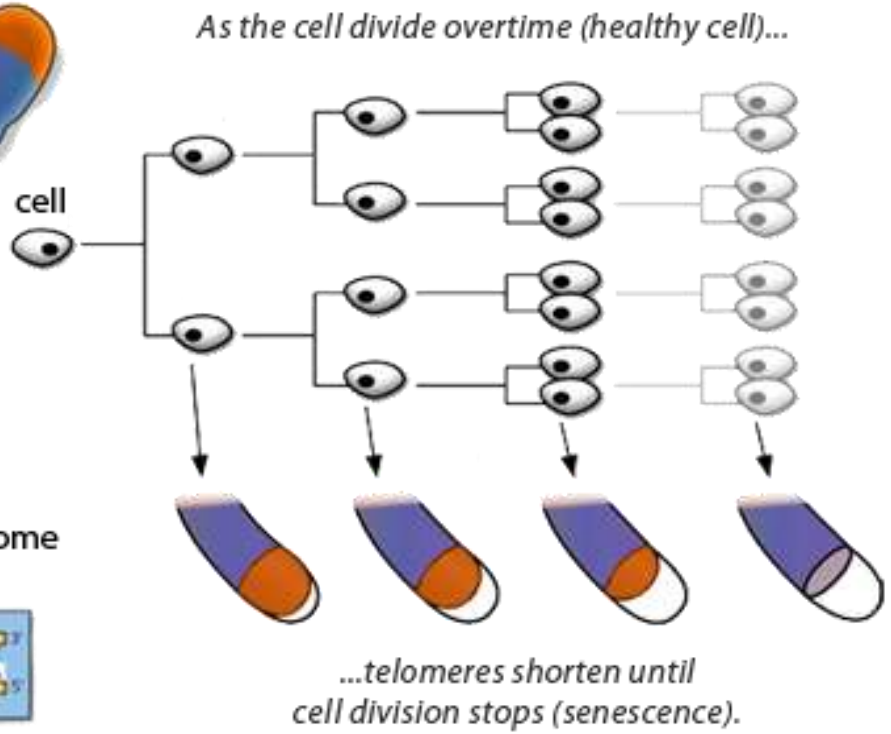


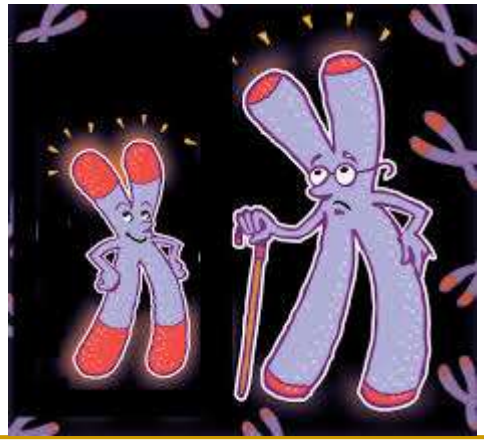


URE 3.17 A color-enhanced light micrograph showing the full plement of male chromosomes arranged in numbered homolo- pairs.




nucleus
cell
telomere
chromosome


As the cell divide overtime (healthy cell)...
cell
...telomeres shorten until
cell division stops (senescence).



MUTASI → Perubahan materi genetik (DNA) yang dapat diwariskan secara genetis kepada keturunannya

menghasilkan ↓

MUTAN

TEMPAT TERJADINYA MUTASI

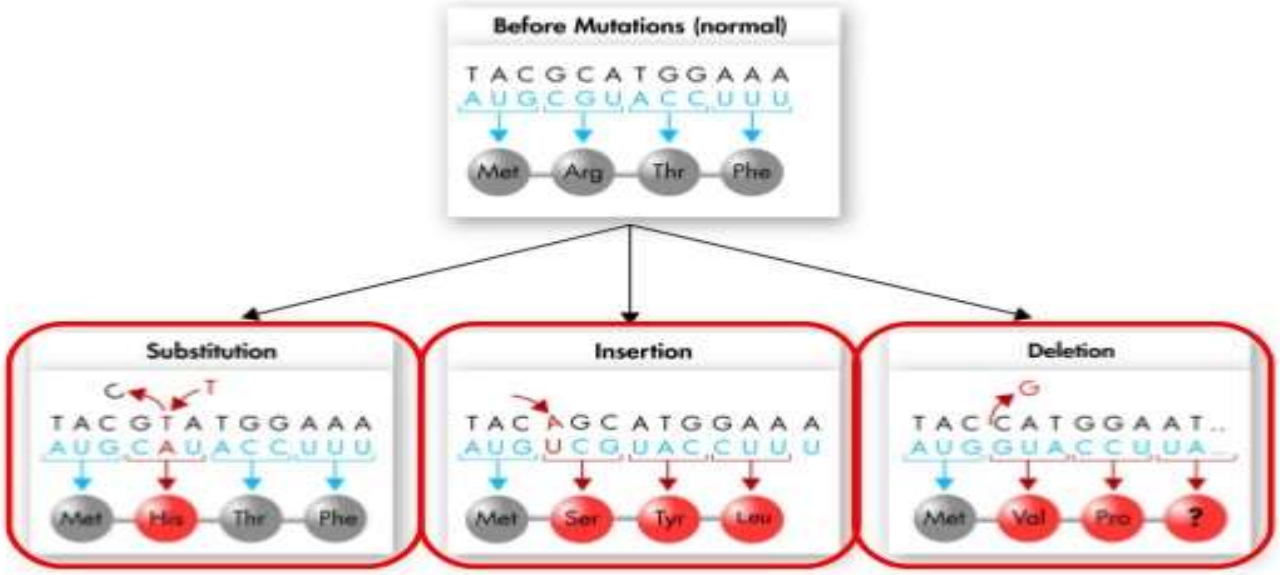
- → Mutasi Gametik — Pada sel kelamin
- → Mutasi Somatik — Pada sel tubuh

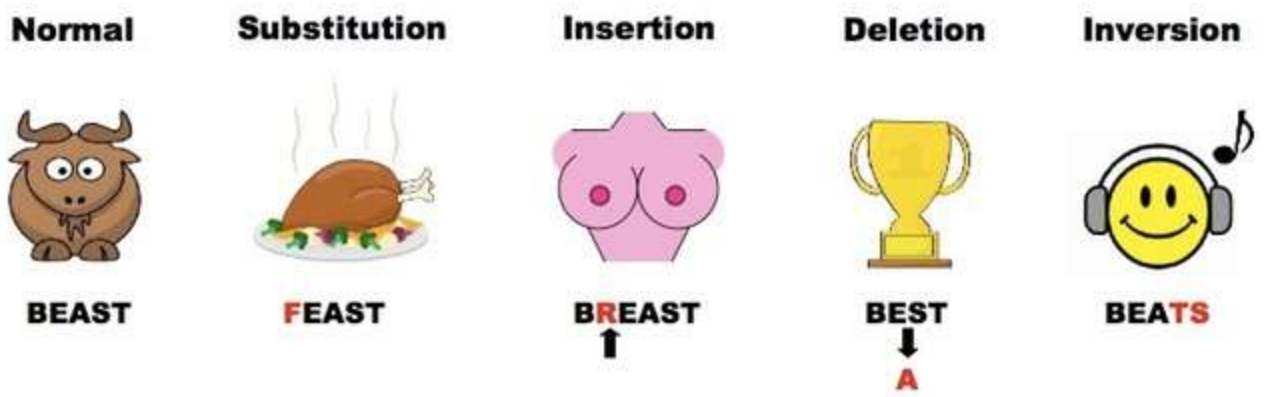

JENIS MUTASI
Berdasarkan
TINGKATAN MUTASI
PENYEBAB
FENOTIF MUTAN
Mutasi Gen
Mutasi Kromosom
Mutasi Spontan
Akibat Rangsang Luar
Alami
Buatan
Mutasi Morfologi
Mutasi Letal
Mutasi Biokimia
Mutasi Kondisional
Mutasi Resisten

Gene Mutations: Point Mutations

A point mutation is a change in a single nucleotide.

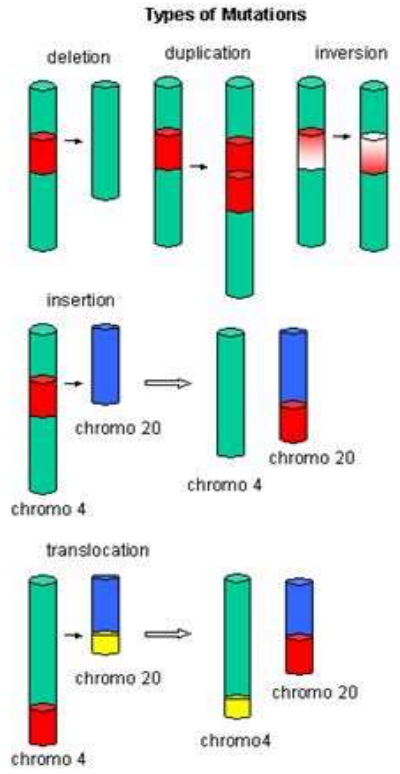
There are three types of point mutations:

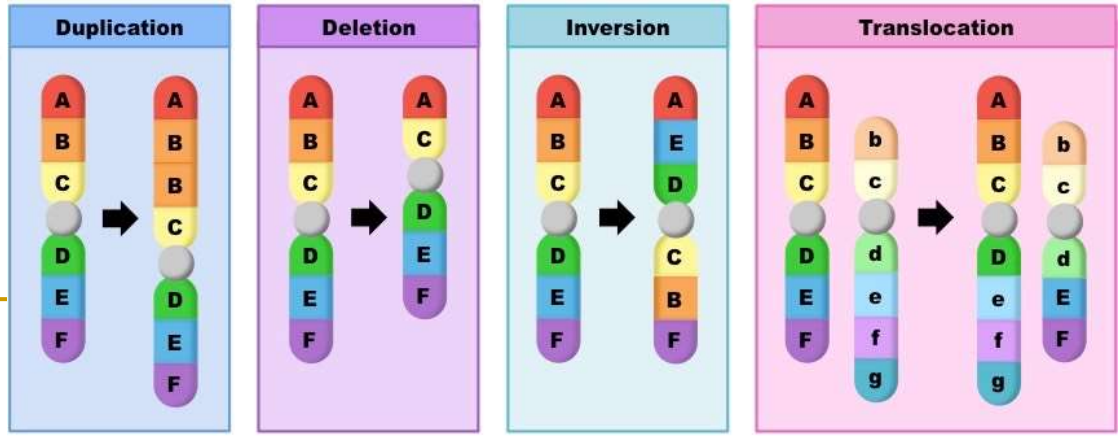




Chromosomal mutations

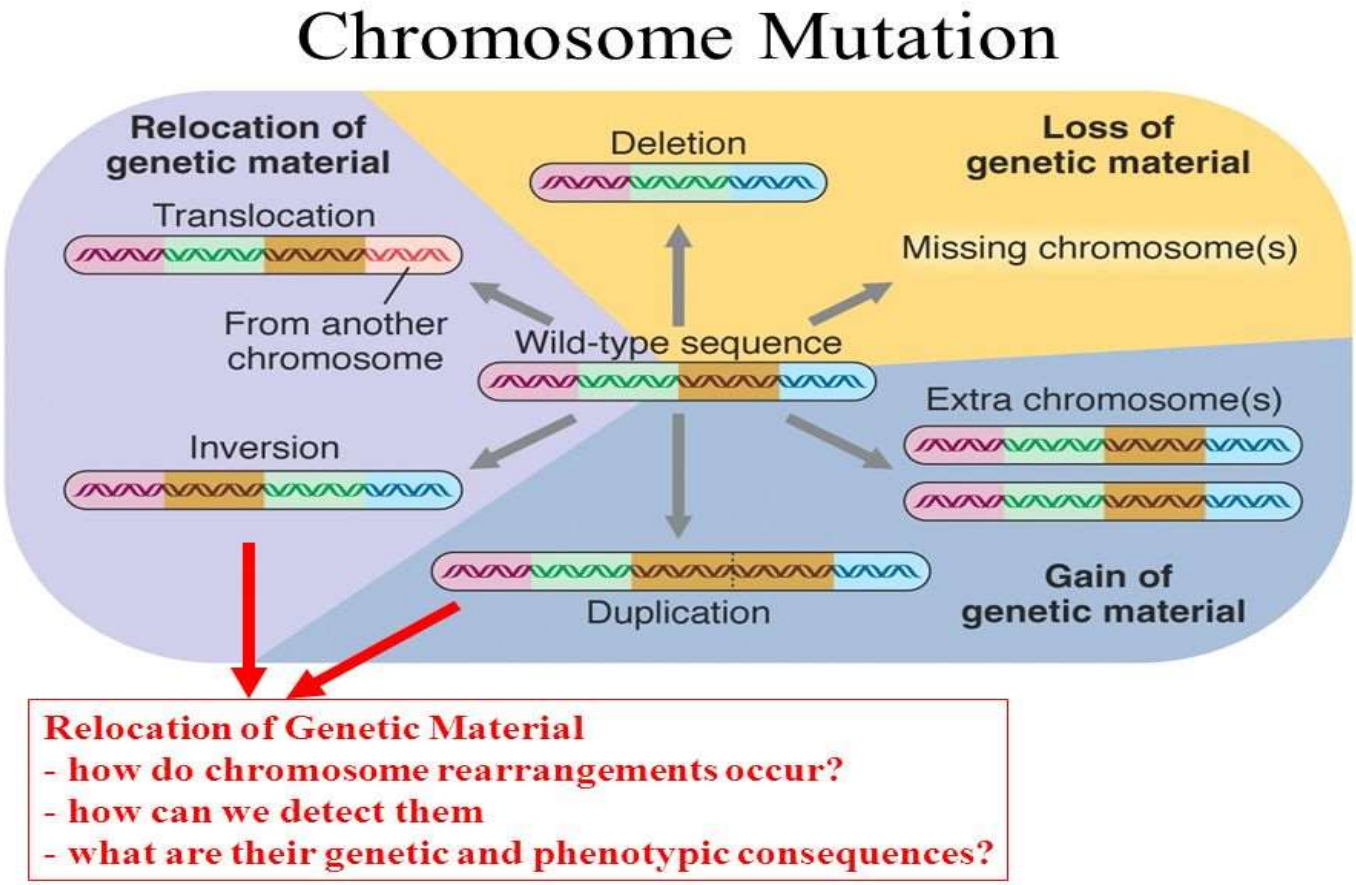
- Involve the chromosomal changes in the number or structure of chromosomes
- Can change the locations of genes on chromosomes, and the number of copies of some genes
- Four types:
  - Deletions
  - Duplications
  - Inversions
  - Translocations





Perbedaan Utama – Mutasi Gen vs Mutasi Kromosom.

Perbedaan utama antara mutasi gen dan mutasi kromosom adalah **mutasi gen merupakan perubahan urutan nukleotida gen** sedangkan **mutasi kromosom adalah perubahan struktur atau jumlah kromosom**. Pengaruh mutasi kromosom lebih tinggi daripada mutasi gen karena besarnya mutasi pada mutasi kromosom adalah tinggi..



Mutasi kromosom	Mutasi gen
Terjadi apabila perubahan berlaku pada struktur atau bilangan kromosom	Terjadi apabila perubahan berlaku pada gen
Contoh: Sindrom Down, Sindrom Klinefelter, Sindrom Turner.	Contoh : buta warna, albinism, haemophilia
Tidak diwarisi	Boleh diwarisi

GAMETOGENESIS

- MITOSIS: MENJADI 2 SEL YANG SAMA

- MEIOSIS :
  - I : - PAIRING KROMOSOM HOMOLOG
    - CROSS OVER (PERTUKARAN SEGMEN)
  - II: - SINTESIS DNA TIDAK TERJADI
    - PEMISAHAN KROMOSOM GANDA MENJADI TUNGGAL

MITOSIS

- **Mitosis is a continuum but biologists distinguish 4 stages**
  - **Prophase**
  - **Metaphase**
  - **Anaphase**
  - **Telophase**

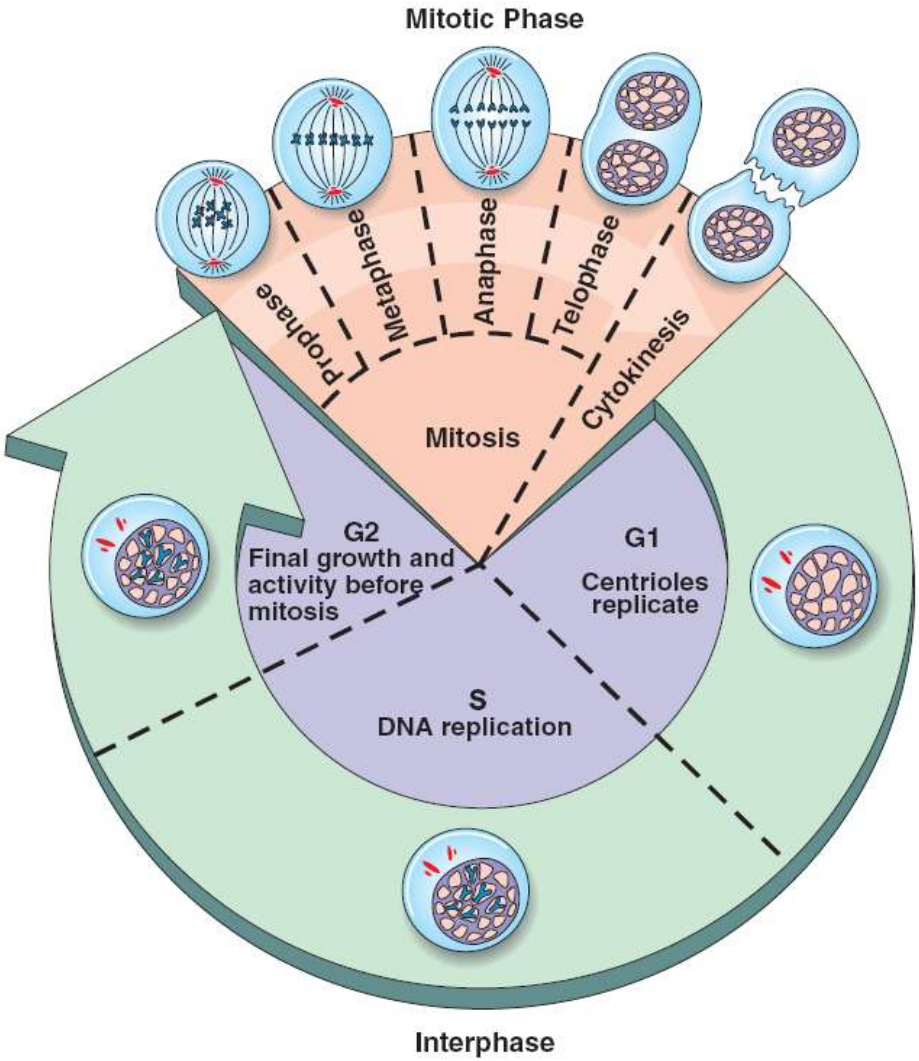
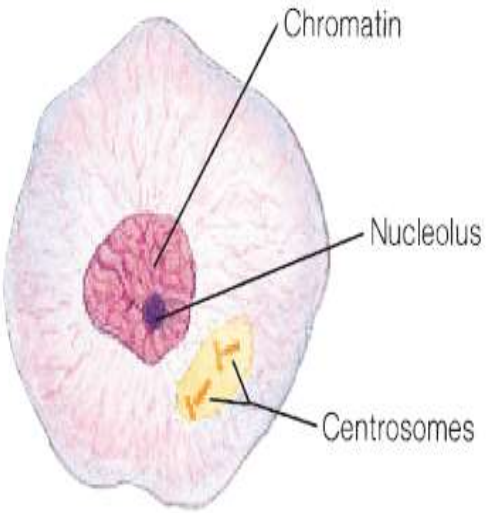
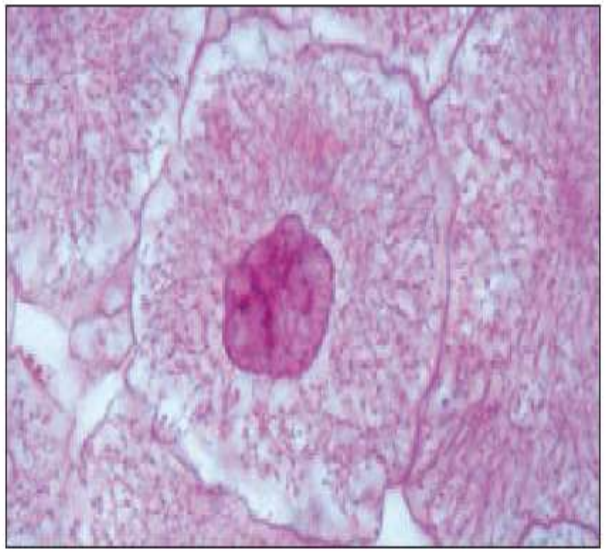


FIGURE 3.25 Interphase and the mitotic phase are the two principal divisions of the cell cycle. During the mitotic phase, nuclear division is followed by cytoplasmic division and the formation of two daughter cells.

(a) Interphase

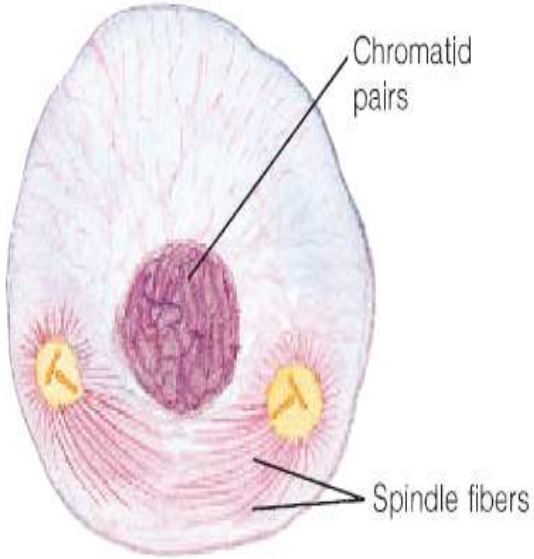
- The chromosomes are in an extended form and seen as chromatin in the electron microscope.
- The nucleus is visible.

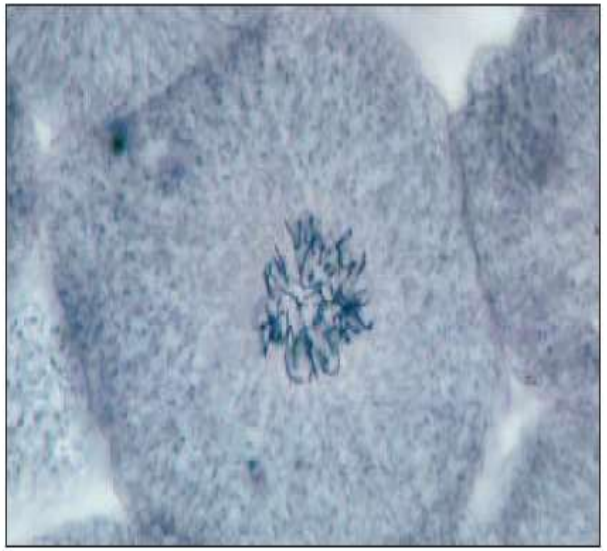




(b) Prophase

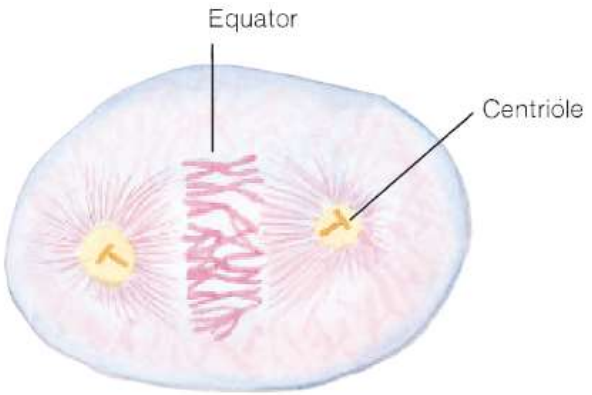
- The chromosomes are seen to consist of two chromatids joined by a centromere.
- The centrioles move apart toward opposite poles of the cell.
- Spindle fibers are produced and extended from each centrosome.
- The nuclear membrane starts to disappear.
- The nucleolus is no longer visible.

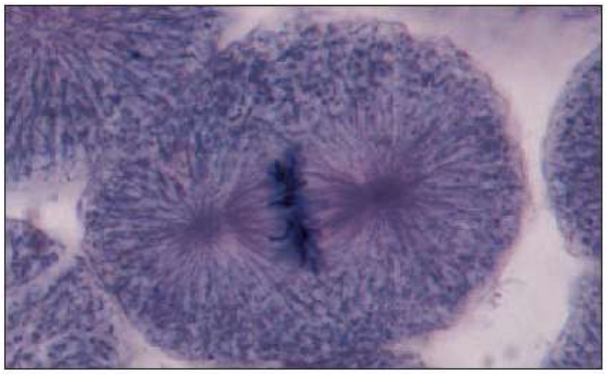




(c) Metaphase

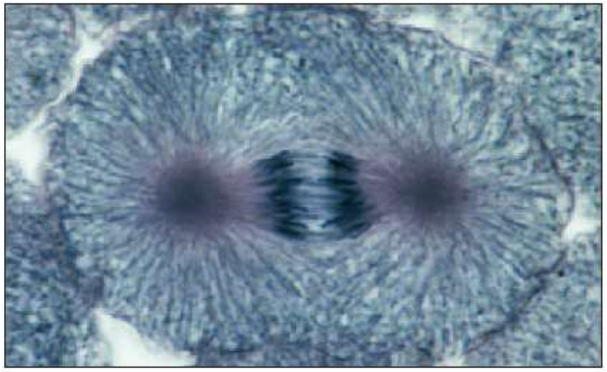
- The chromosomes are lined up at the equator of the cell.
- The spindle fibers from each centriole are attached to the centromeres of the chromosomes.
- The nuclear membrane has disappeared.

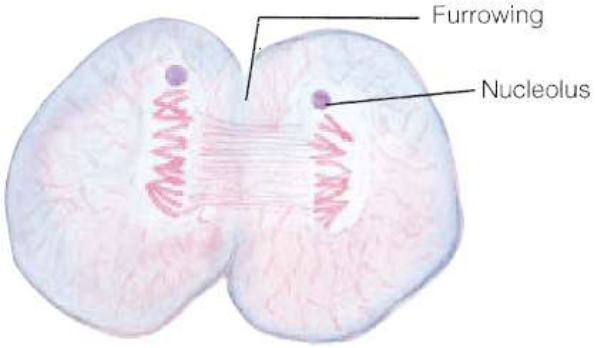




(d) Anaphase

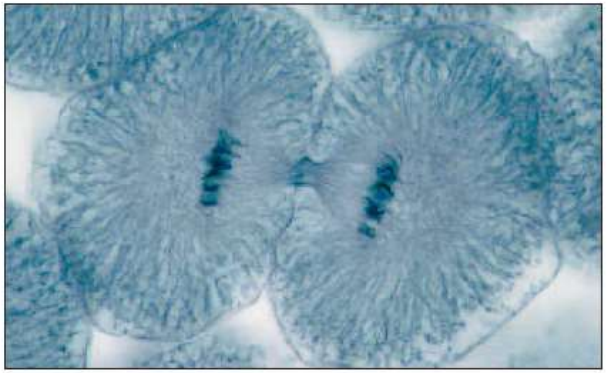
- The centromeres split, and the sister chromatids separate as each is pulled to an opposite pole.





(e) Telophase

- The chromosomes become longer, thinner and less distance.
- New nuclear membranes form.
- The nucleolus reappears.
- Cell division is nearly complete.



MEIOSIS

- Percampuran materi genetis pada waktu cross over sehingga dapat terjadi variasi genetis
- Supaya sel kelamin menjadi kromosom haploid dengan jumlah DNA ½ dari jumlah DNA sel somatis (meiosis 2)

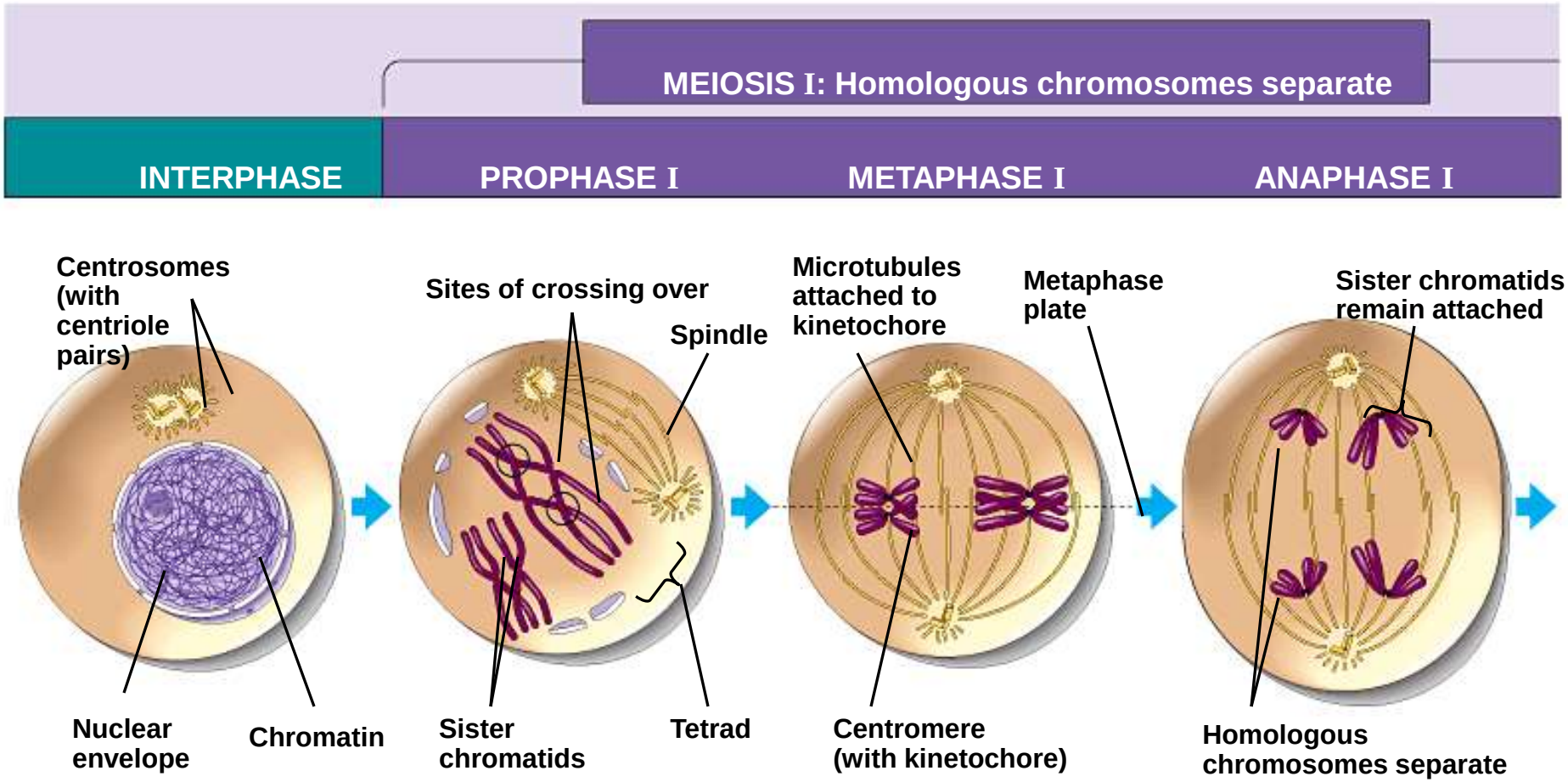


Figure 8.14, part 1

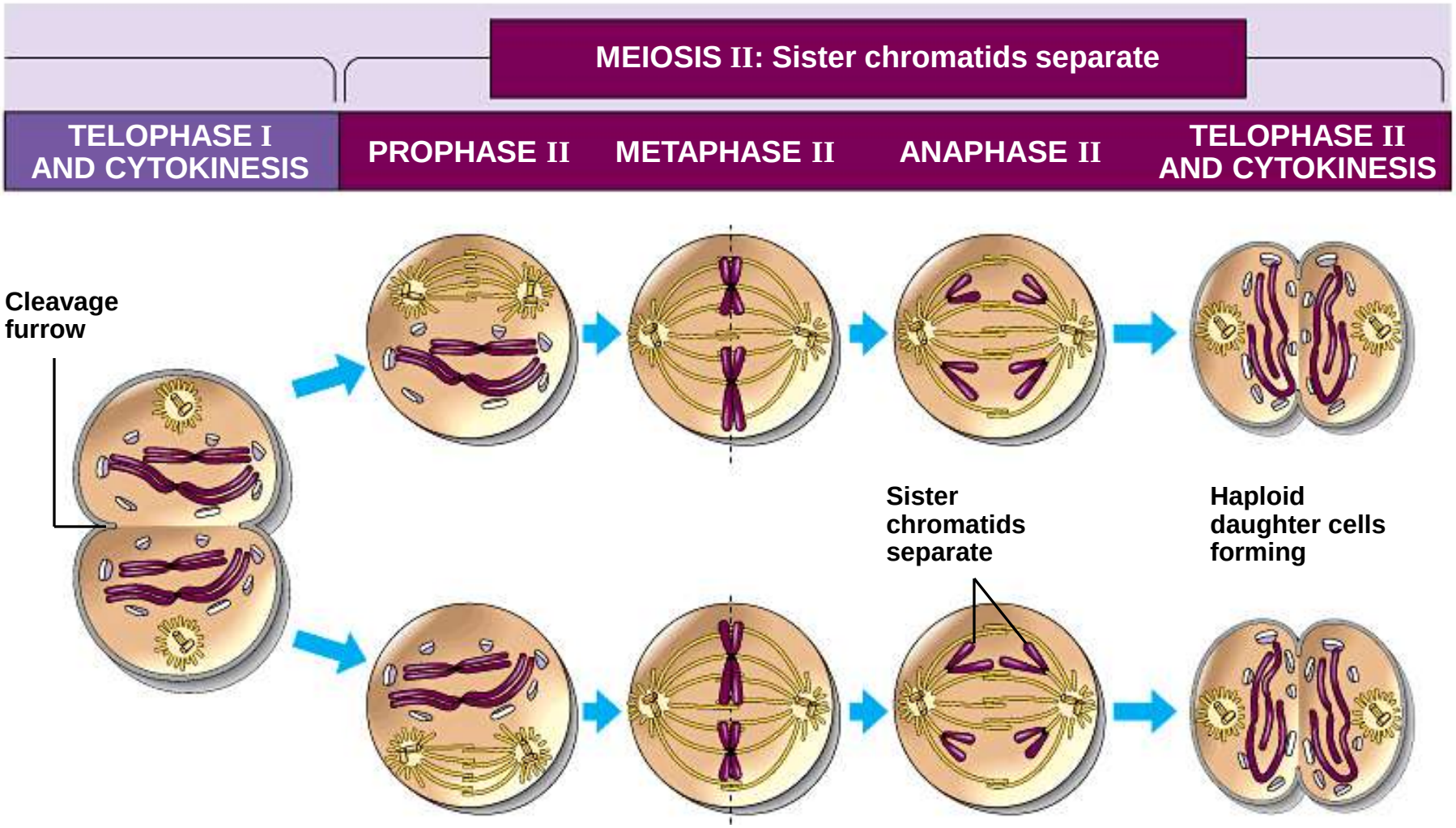


Figure 8.14, part 2

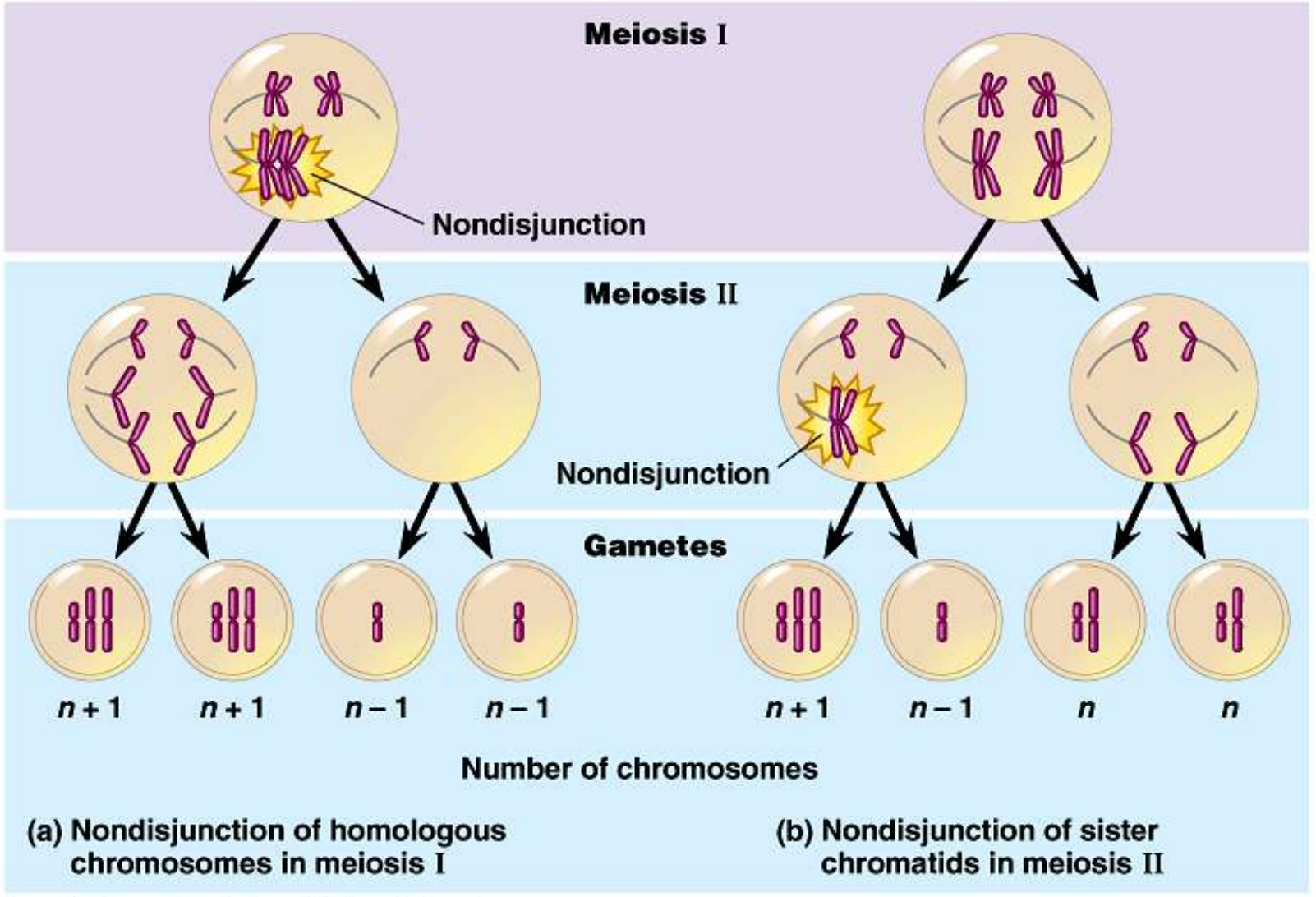
KELAINAN

- NON DYSJUNCTION

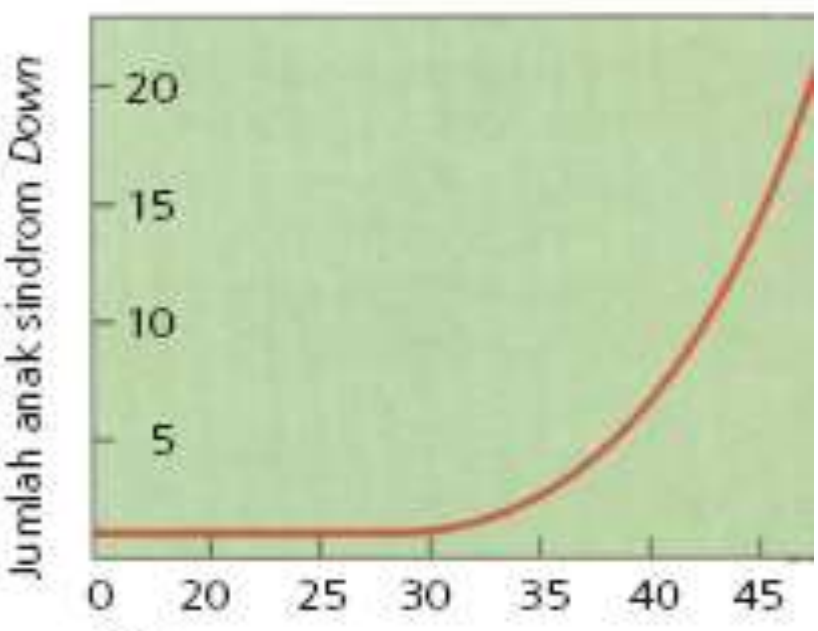
  Non dysjunction dapat terjadi pada waktu meiosis 1 atau meiosis 2

- Turner Syndrome (female) 45,XO
- Trisomy X (female) 47, XXX
- Klinefelter Syndrome (male) 47,XXY
- Extra “Y” chromosome 47,XYY (male)

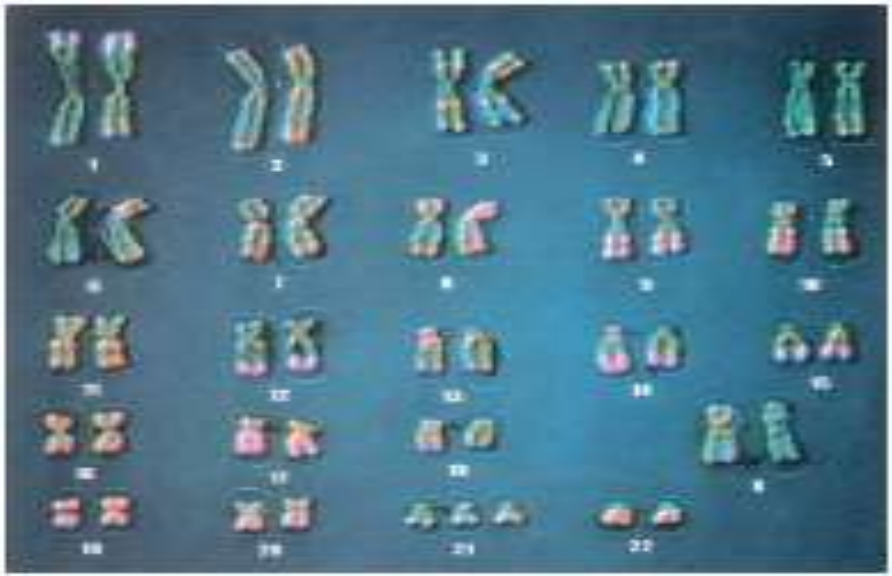
Nondisjuction



Down syndrome: trisomy for Chr 21 (47 Mb)

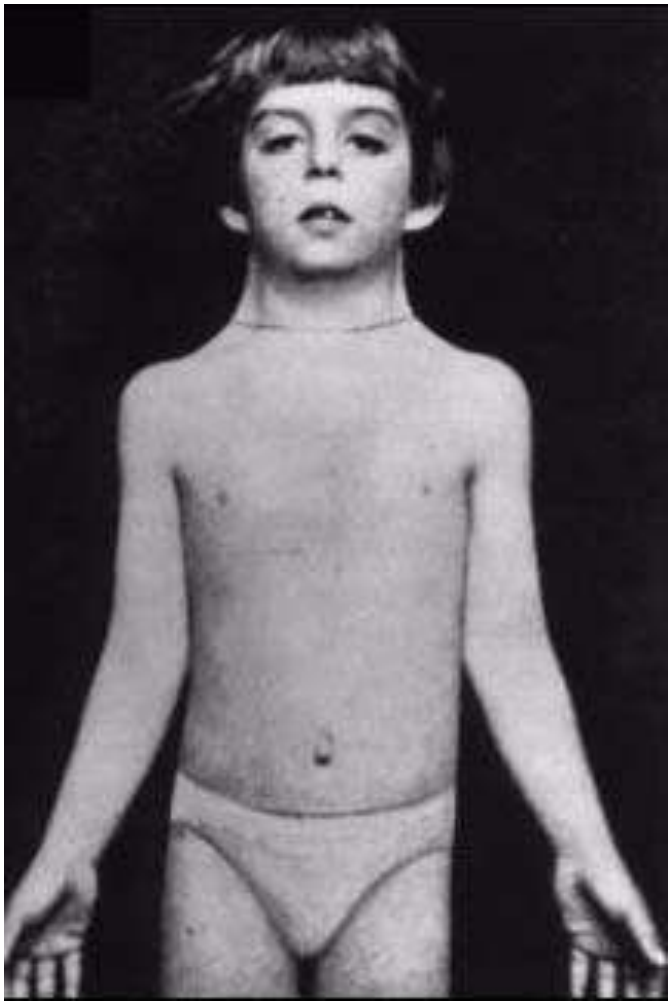


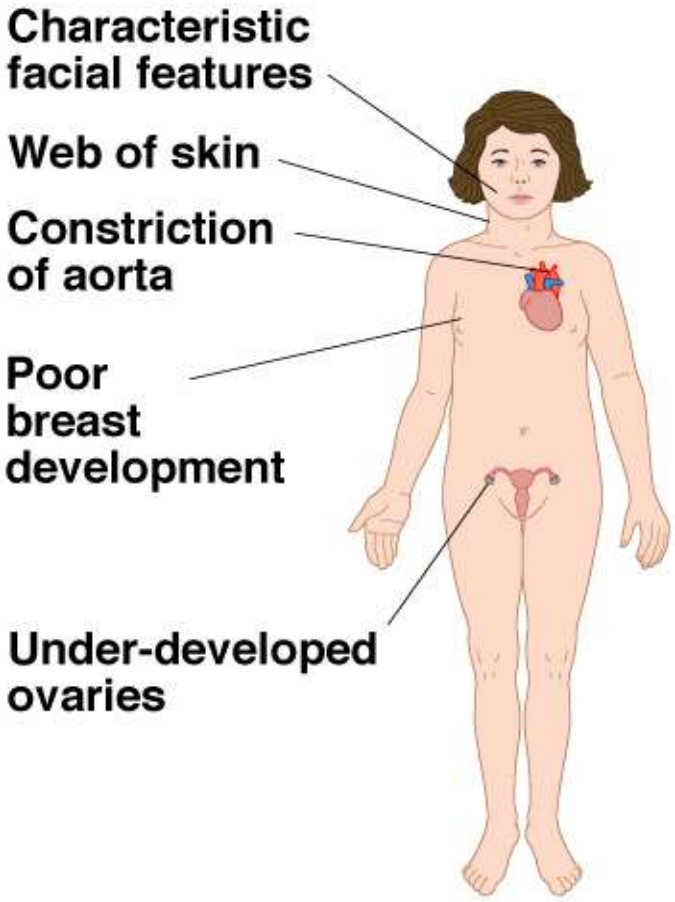
Kurva hubungan antara umur ibu sewaktu melahirkan dengan dilahirkannya anak sindrom Down.



- trisomy of chromosome number 21 (1 in 700 births)—mental retardation, mongoloid features, and heart defects

XO – Turner Syndrome

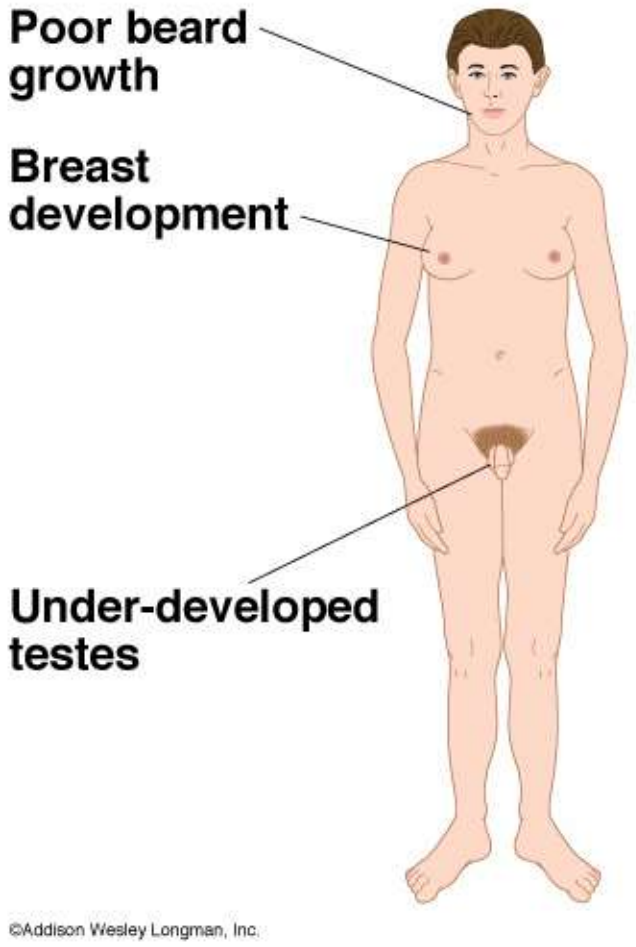


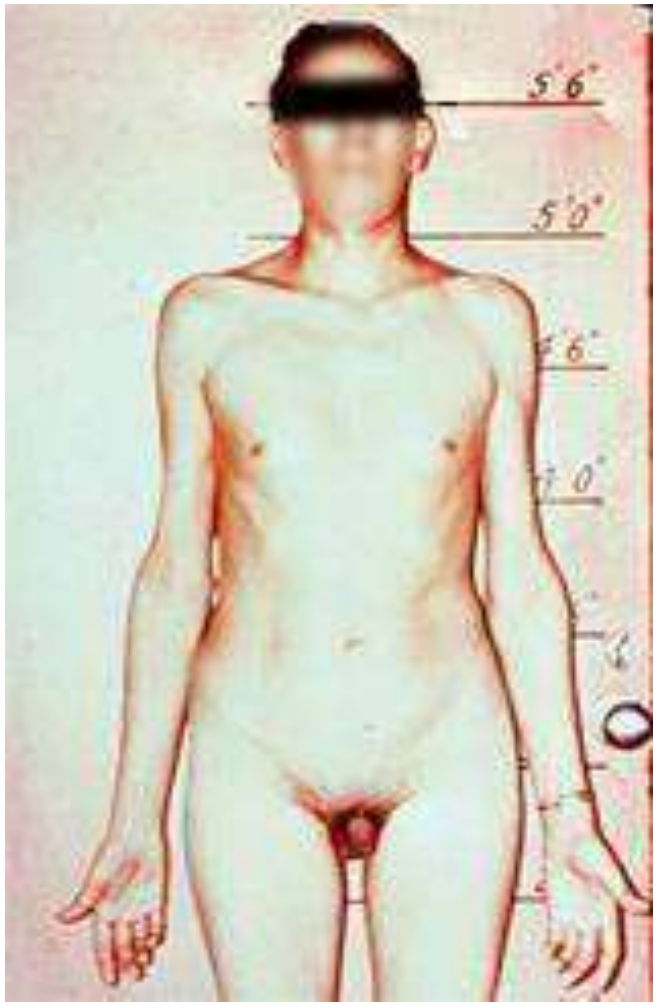


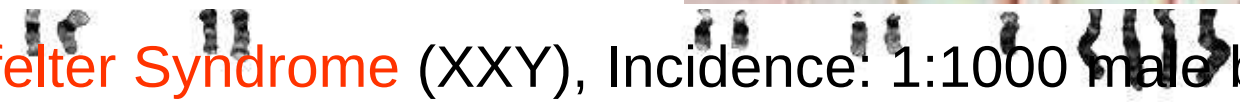
Turner Syndrome (XO), Incidence: 1 in 2500 female births

- **Females missing one X chromosome (XO)**

XXY – Klinefelter Syndrome



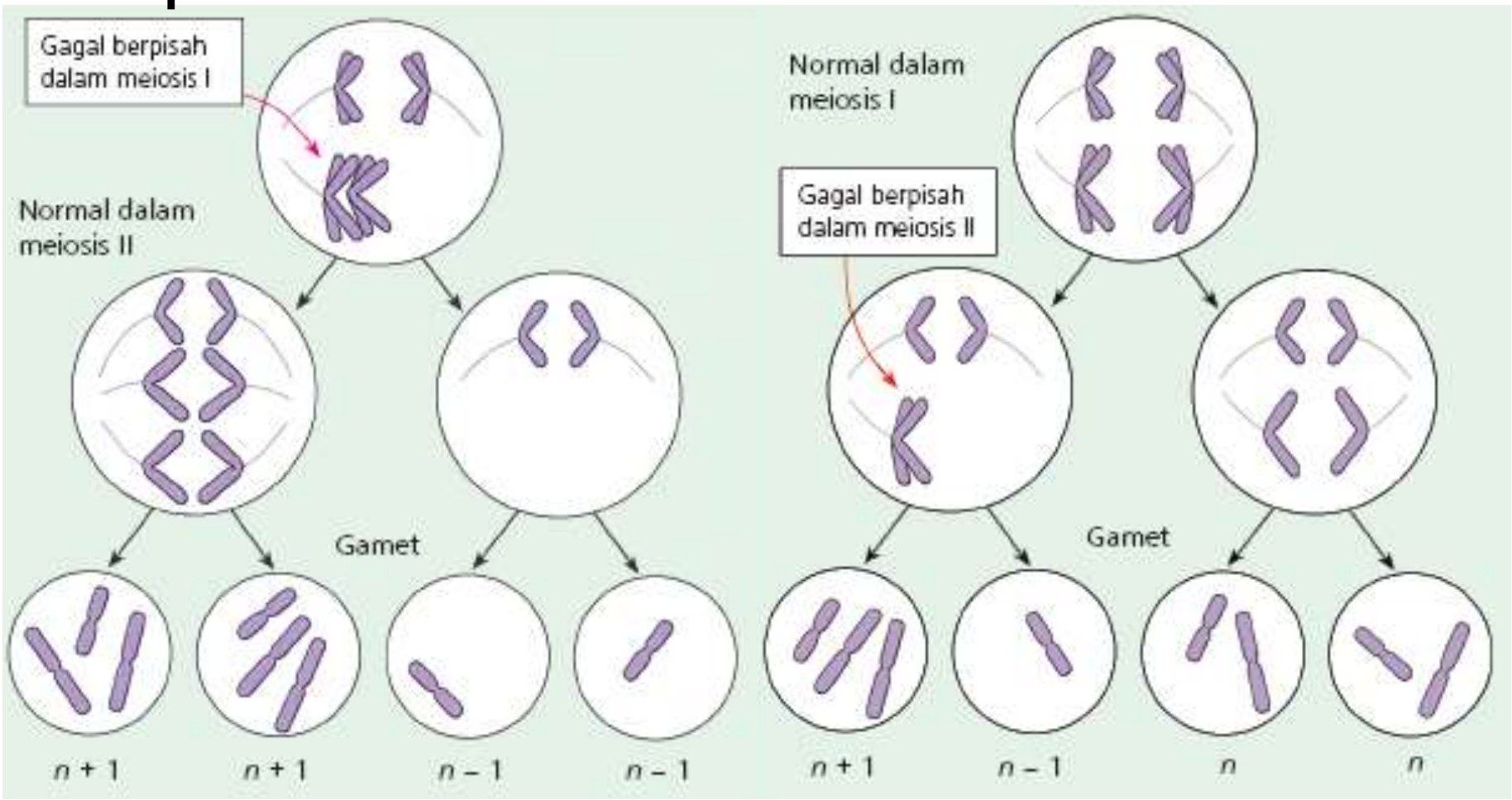




Klinefelter Syndrome (XXY), Incidence: 1:1000 male births

- Males with an extra X chromosome (XXY) (1 in 1000 male births)

Aneuploid



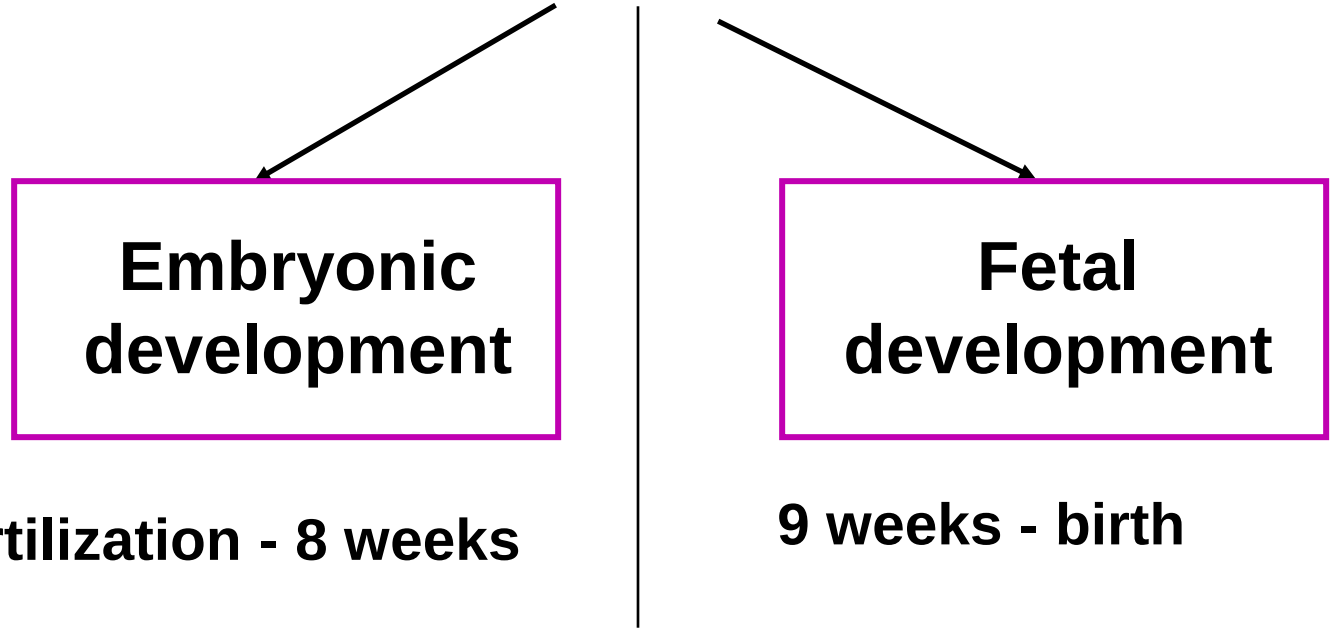
Gagal berpisah saat meiosis I

Gagal berpisah saat meiosis II

Sex Chromosome Aneuploidy

Situation	Oocyte	Sperm	Consequence
Normal	X	Y	46, XY normal male
	X	X	46, XX normal female
Female Nondisjunction	XX	Y	47, XXY Klinefelter syndrome
	XX	X	47, XXX triplo-X
		Y	45, Y nonviable
		X	45, X Turner syndrome
Male Nondisjunction (meiosis I)	X		45, X Turner syndrome
	X	XX	47, XXX triplo-X
Male nondisjunction (meiosis II)	X	YY	47, XYY Jacobs syndrome
	X		45, X Turner syndrome

Prenatal Development



time period from fertilization to birth = gestation

Postnatal Development

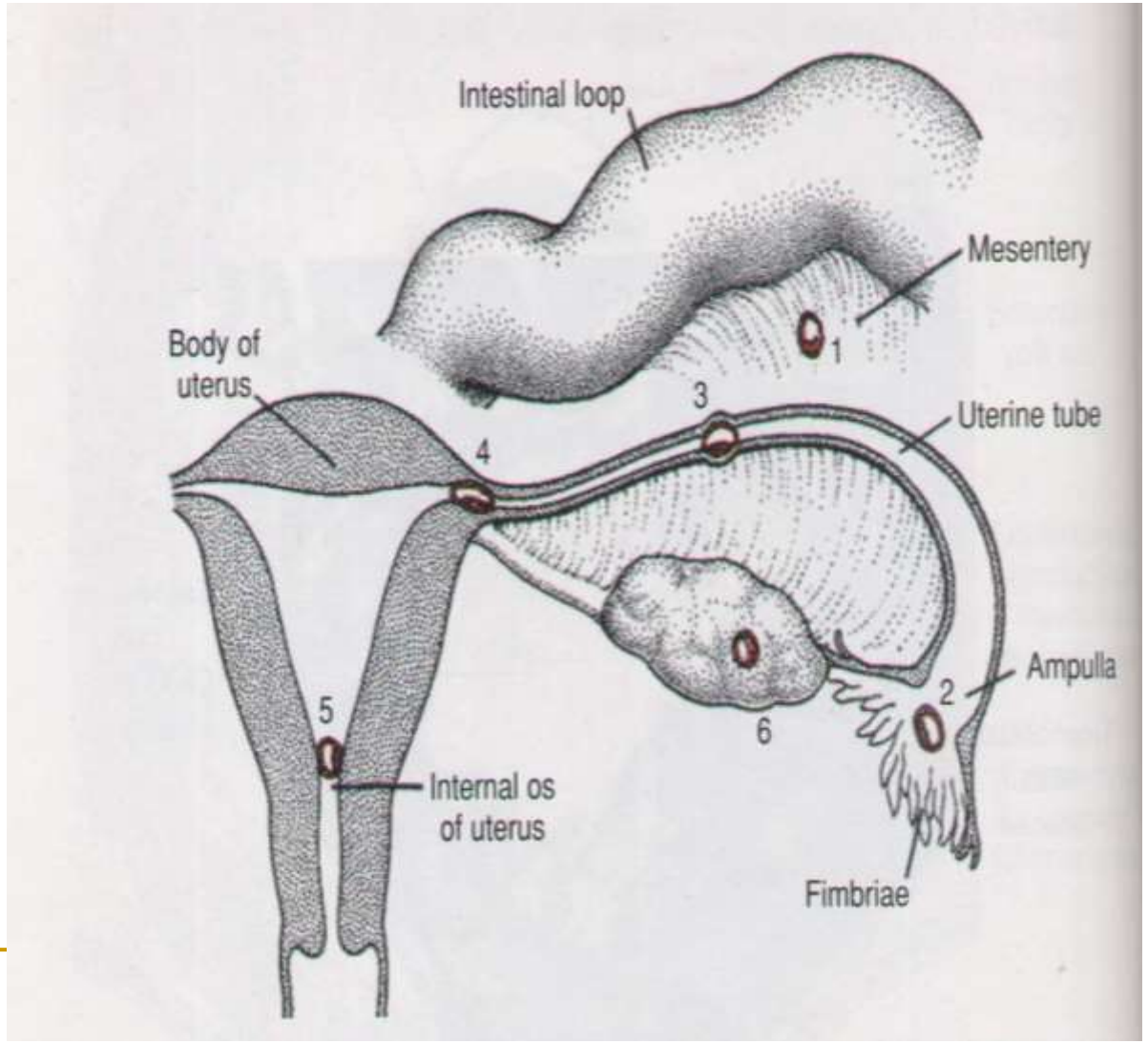
PERKEMBANGAN EMBRIO MINGGU PERTAMA

- Periode ovulasi sampai implantasi
- Berlangsung ± 6 hari
- Sigot mengalami pembelahan sel:

  2 sel → 4 sel → 8 sel → 16 sel (morula)
- Saat nampak lubang (vacuola) pada perkembangan morula : free blastocyst

KELAINAN

- Abortus spontan
- Implantasi yang abnormal
- Mola hydatidosa/ choriocarcinoma

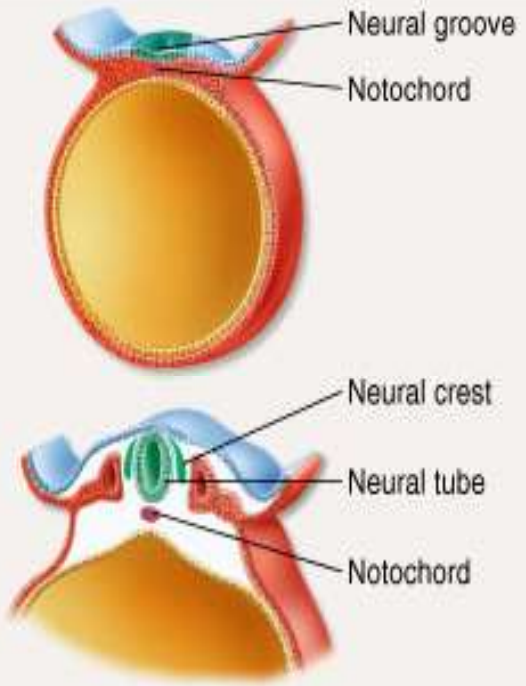


PERKEMBANGAN EMBRIO MINGGU KETIGA

- Intra embryonic mesoderm meluas, bersatu dengan extraembryonic mesoderm
- Pembentukan villi dari trophoblast
- Akhir minggu ke 3 mesoderm berdiferensiasi menjadi pembuluh darah → villous capillary system
- Pembentukan neural plate → neural tube
- Pembentukan neural crest dari ectoderm

Development: Neurulation

Week 3: the primary germ layers begin development into body tissues and organs



Neurulation

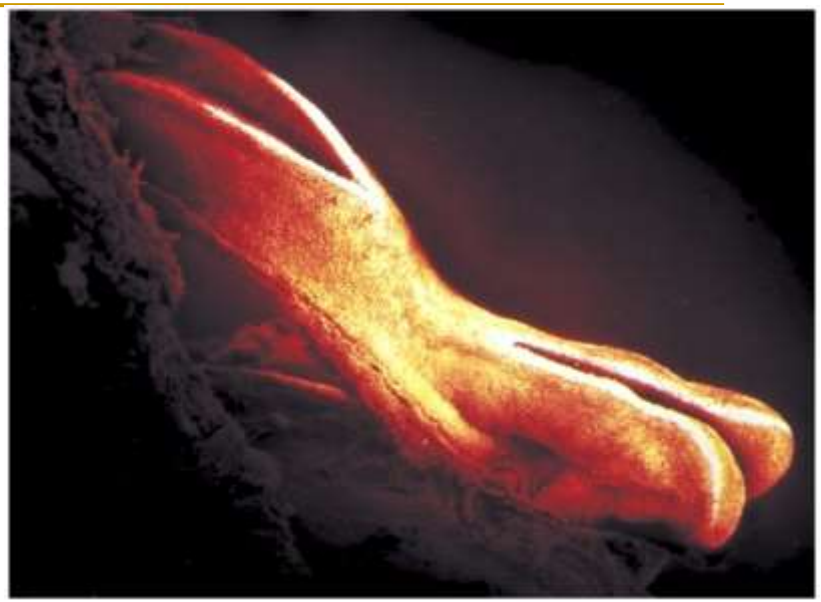
In all chordates, the first organ to form is the notochord; the second is the neural tube.

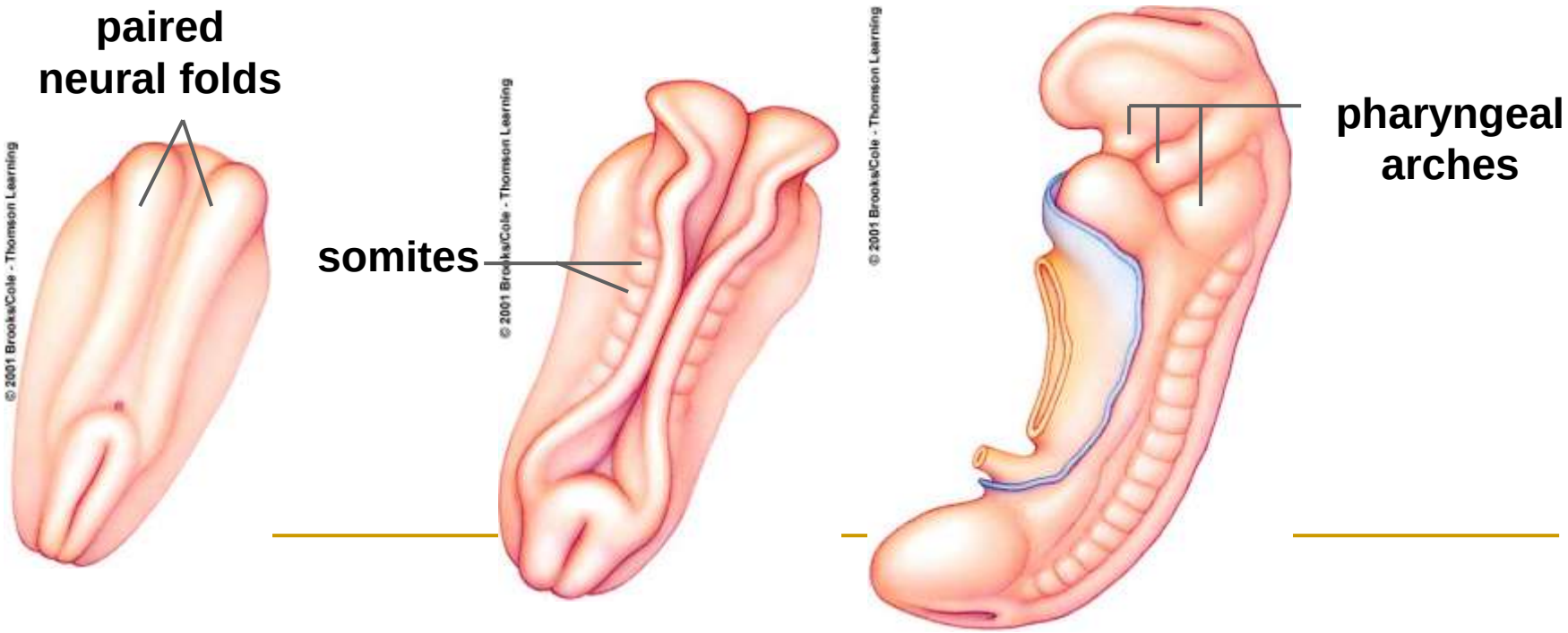
During neurulation, the neural crest is produced as the neural tube is formed. The neural crest gives rise to several uniquely vertebrate structures such as sensory neurons, sympathetic neurons, Schwann cells, and other cell types.

By end of 3rd week, the embryo is ~ 2 mm long

Neurulation

- Development of hollow nerve cord
- Neural groove forms





KELAINAN

Teratoma sacrococcygeal (sisa primitive streak

Neural tube defect (meningocele dll)

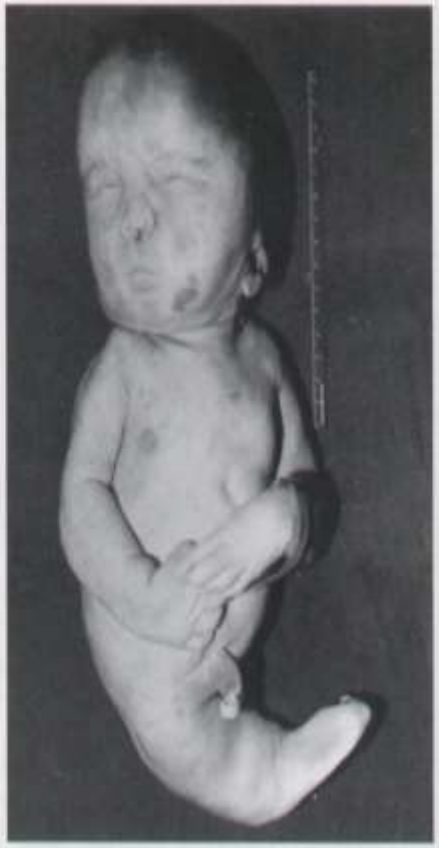


Figure 4.6. Sirenomelia (caudal dysgenesis). Loss of mesoderm in the lumbosacral region has resulted in fusion of the limb buds and other defects.

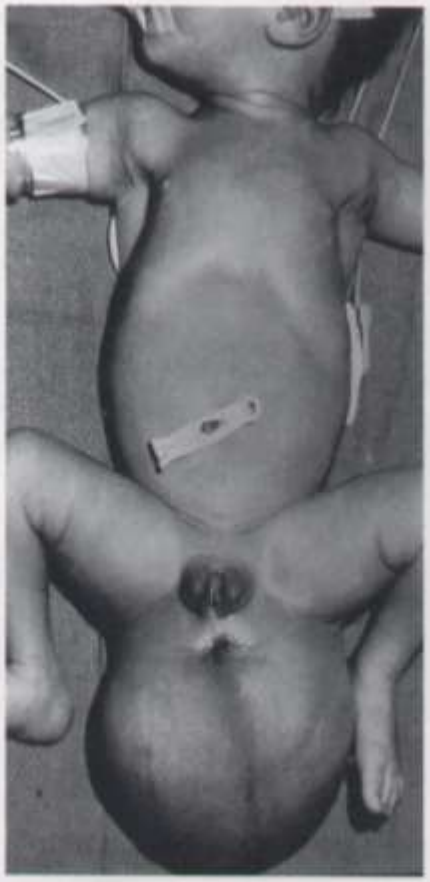
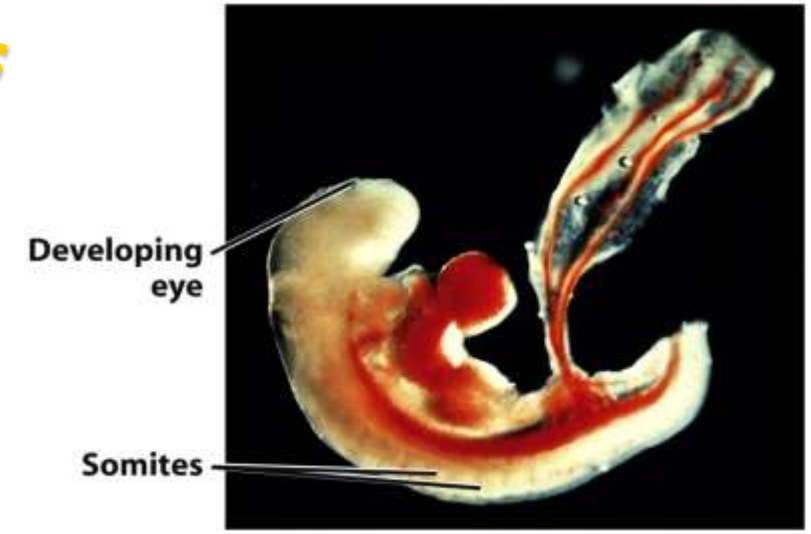


Figure 4.7. Sacrococcygeal teratoma resulting from remnants of the primitive streak. These tumors may become malignant and are more common in females.

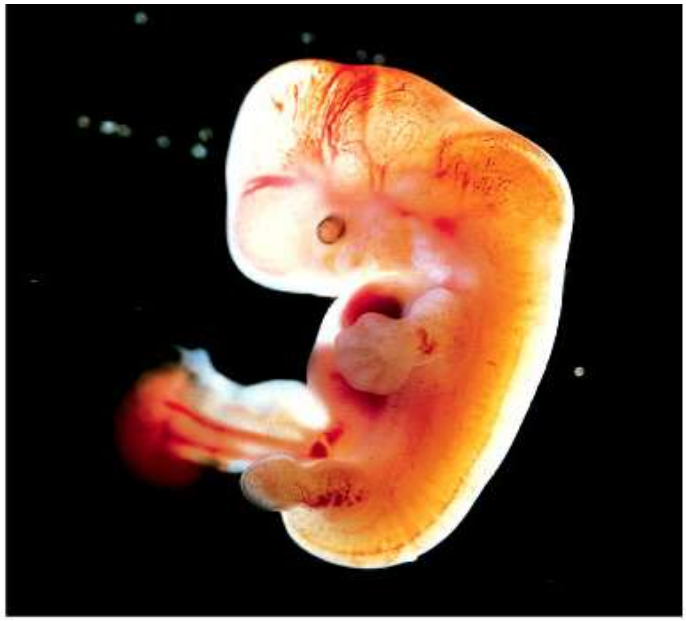
PERIODE FETAL

- **4th week = *organogenesis***
- **Critical time in development**
  - **Embryo ~ 5 mm**



- **Second Month**
- **Embryo ~ 25 mm**

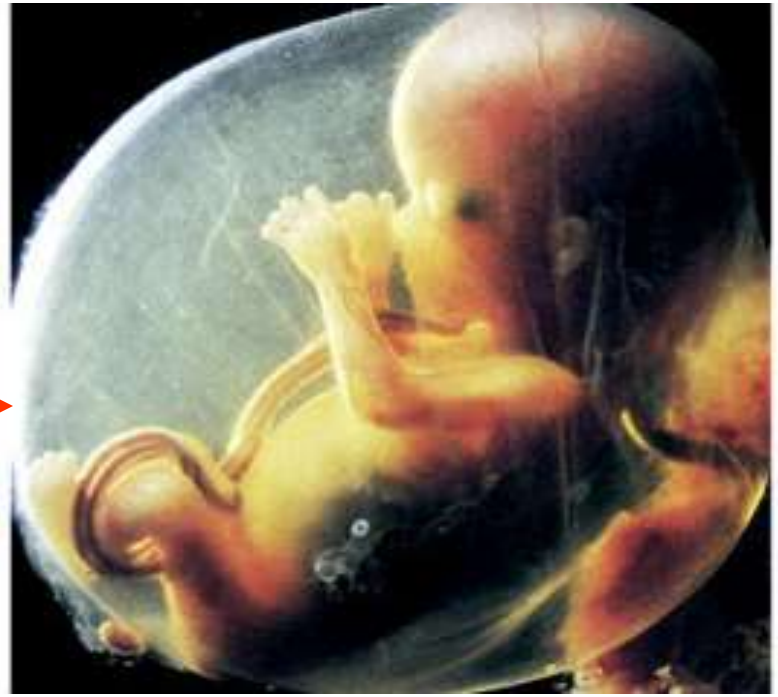
- **Great changes occur in morphology**
  - **Limbs assume adult shape**
  - **Major internal organs evident**



7 weeks

Fetal Development

- **Three Months**
- **Development is essentially complete (except for lungs & brain)**
- ***From 3 months on the developing human embryo is called a fetus***

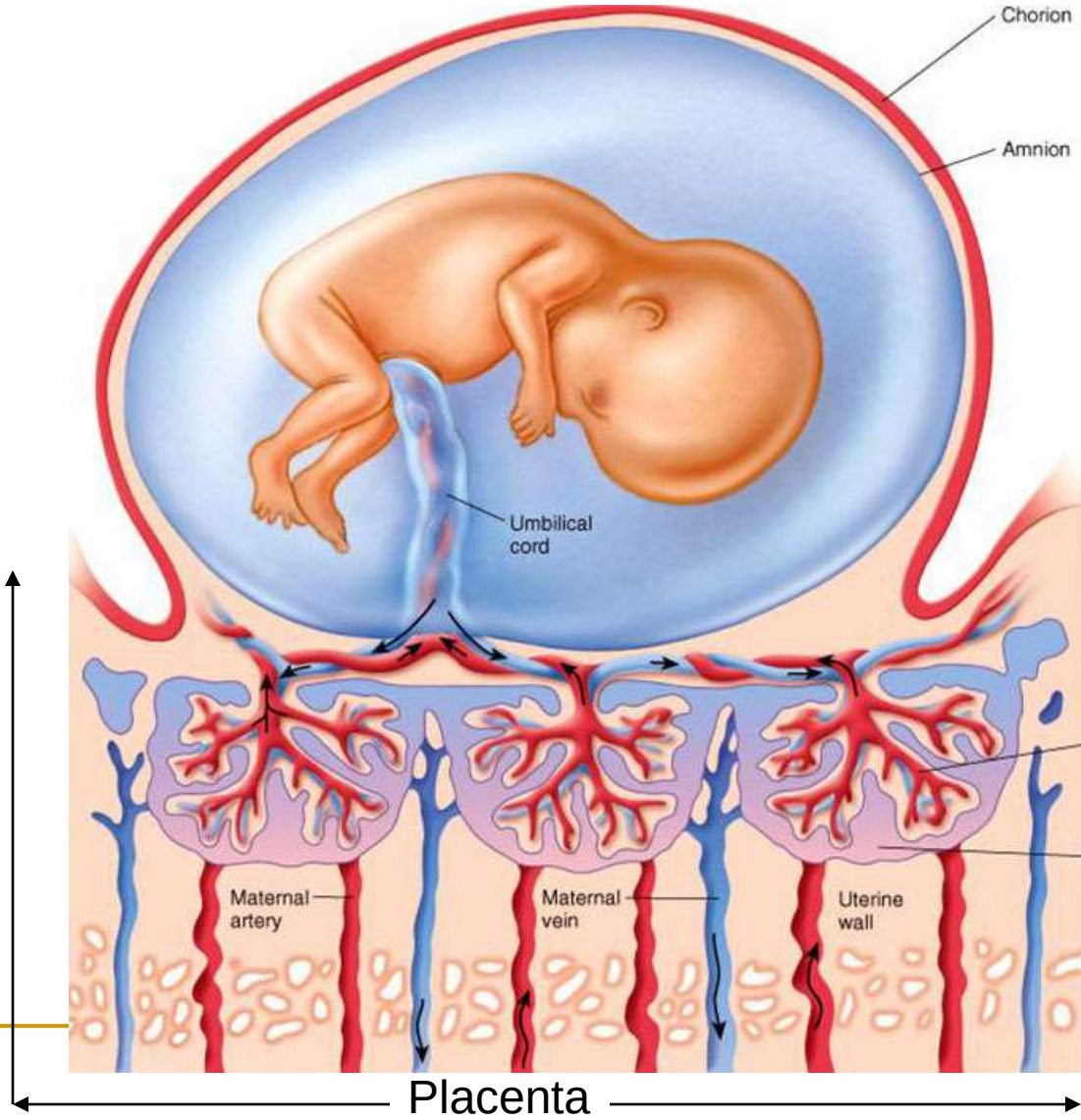


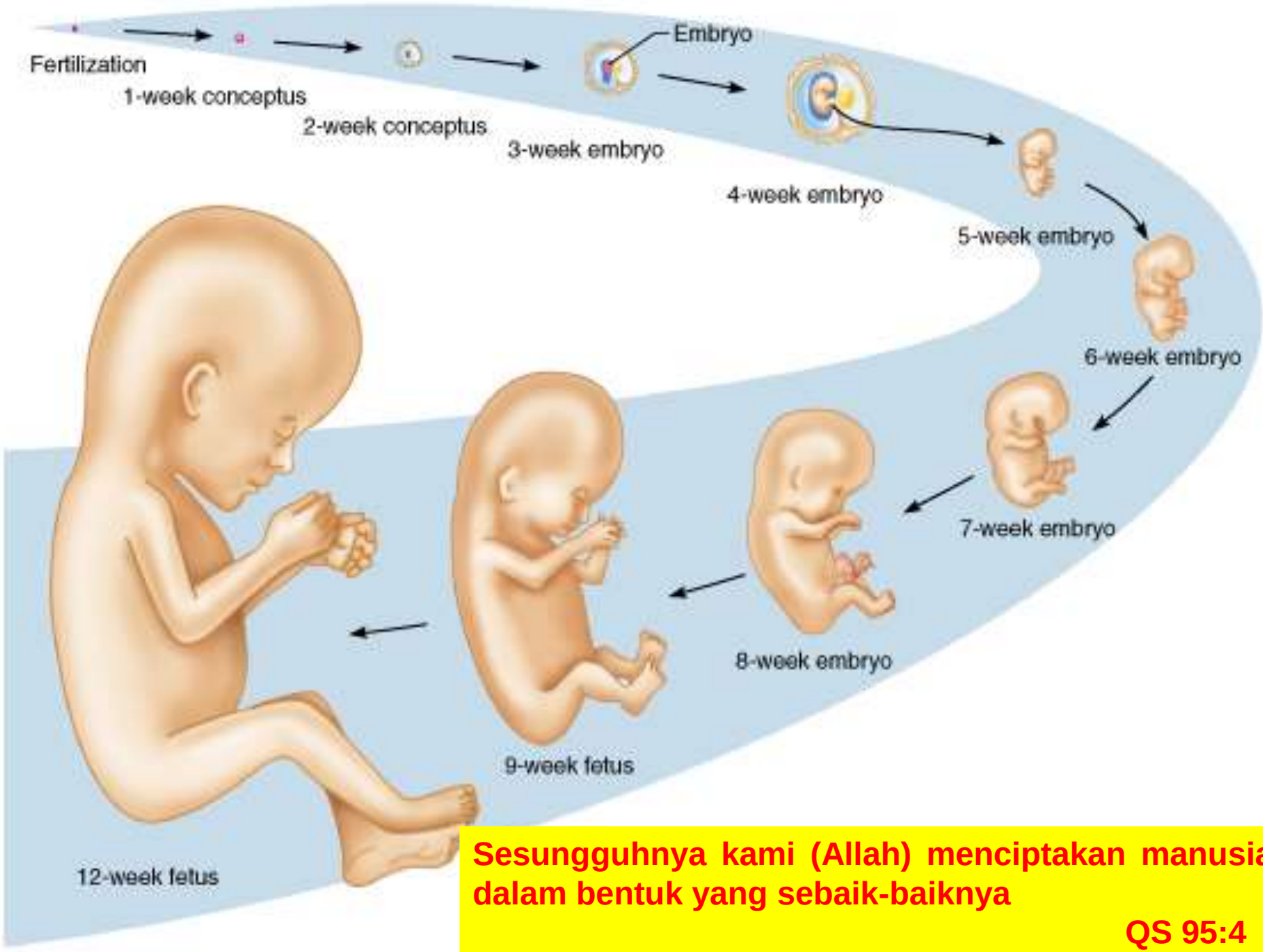
- **Second trimester**
- **Fetus ~ 30 cm long (1 foot, by end of 6th month)** **~ 4 months**

  - **A time of growth!**
    - **Bone formation**
    - **Hair growth**

Fetal Development

- **Third trimester**
- **Weight ~ doubles**
- ***Major change is great increase in size***
  - **Most major nerve tracts formed in brain**
  - **Nutrients from mother's blood via placenta**

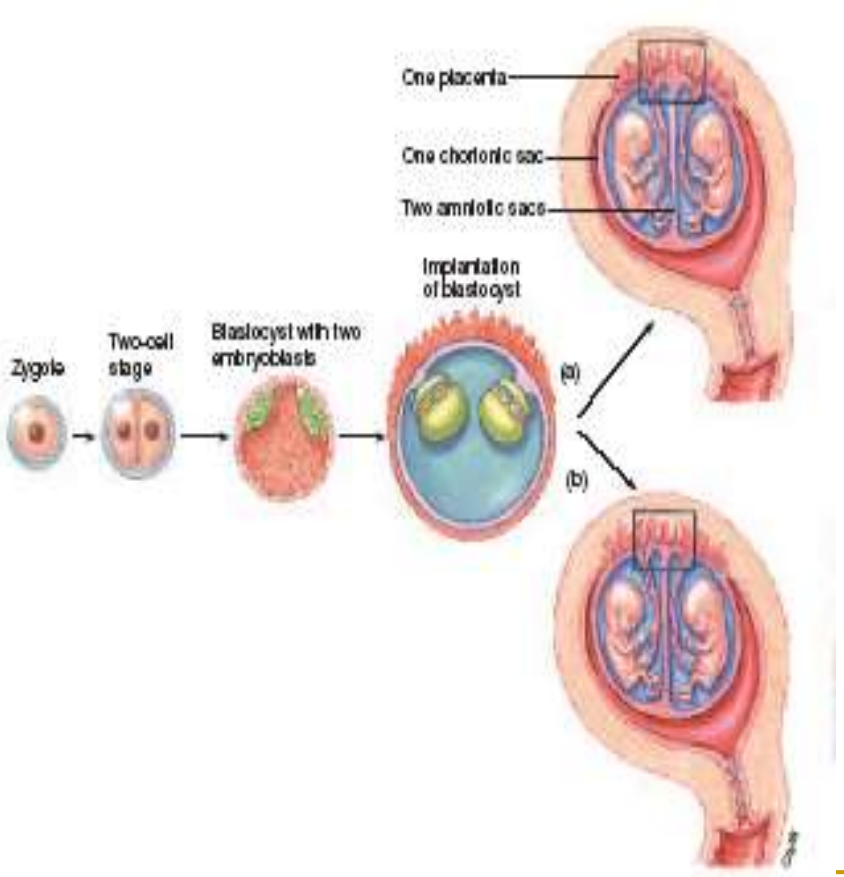


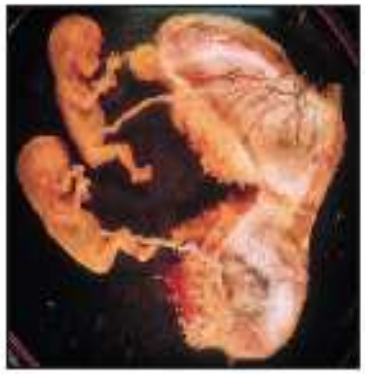


Sesungguhnya kami (Allah) menciptakan manusia dalam bentuk yang sebaik-baiknya

QS 95:4

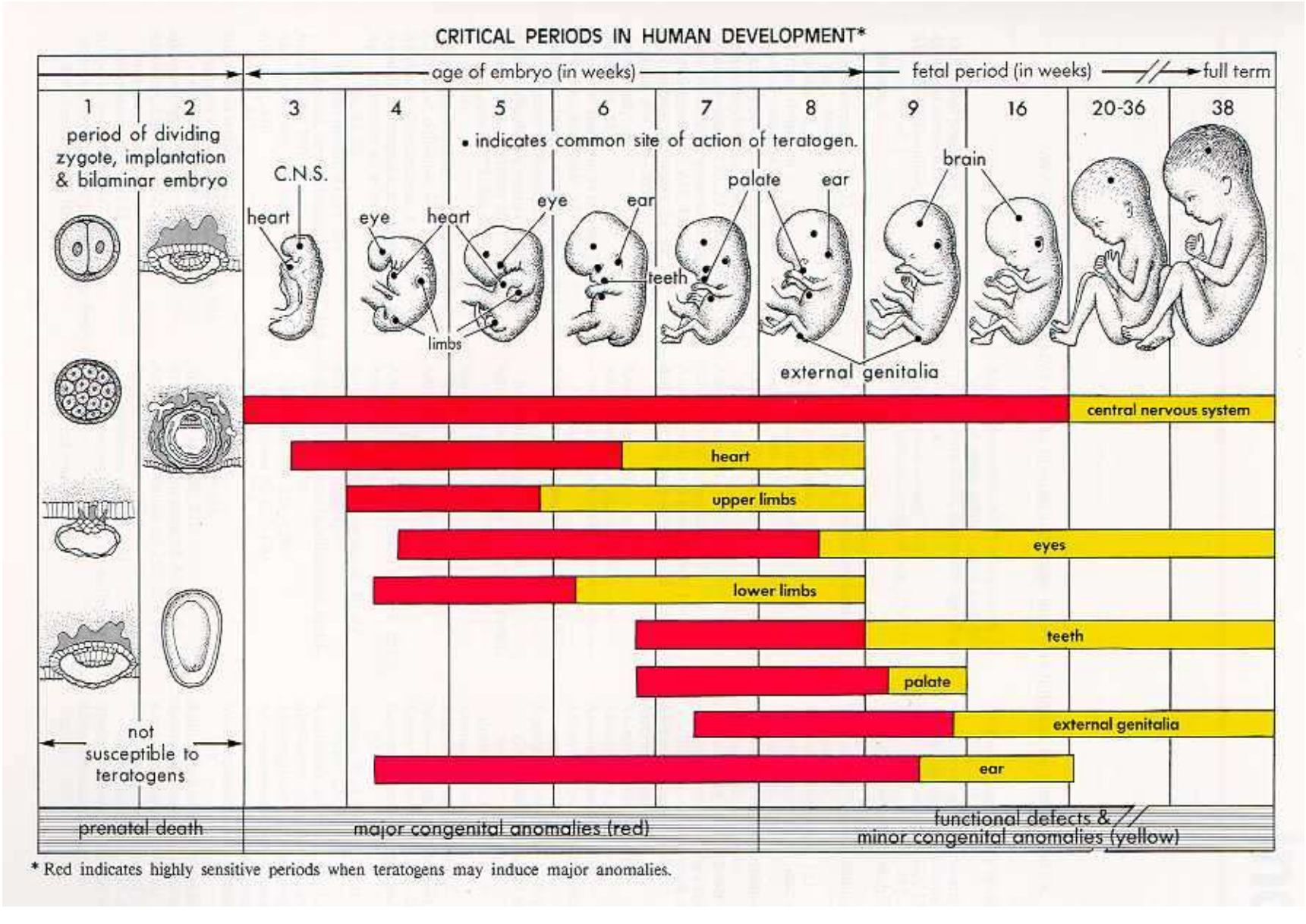
TWIN


One placenta
One chorionic sac
Two amniotic sacs
Implantation of blastocyst
Zygote
Two-cell stage
Blastocyst with two embryoblasts
(a)
(b)



Two zygotes
Two-cell stage
Blastocysts
Implantation of blastocysts
Separate chorionic sacs
(a)
(b)
Fused chorionic sacs

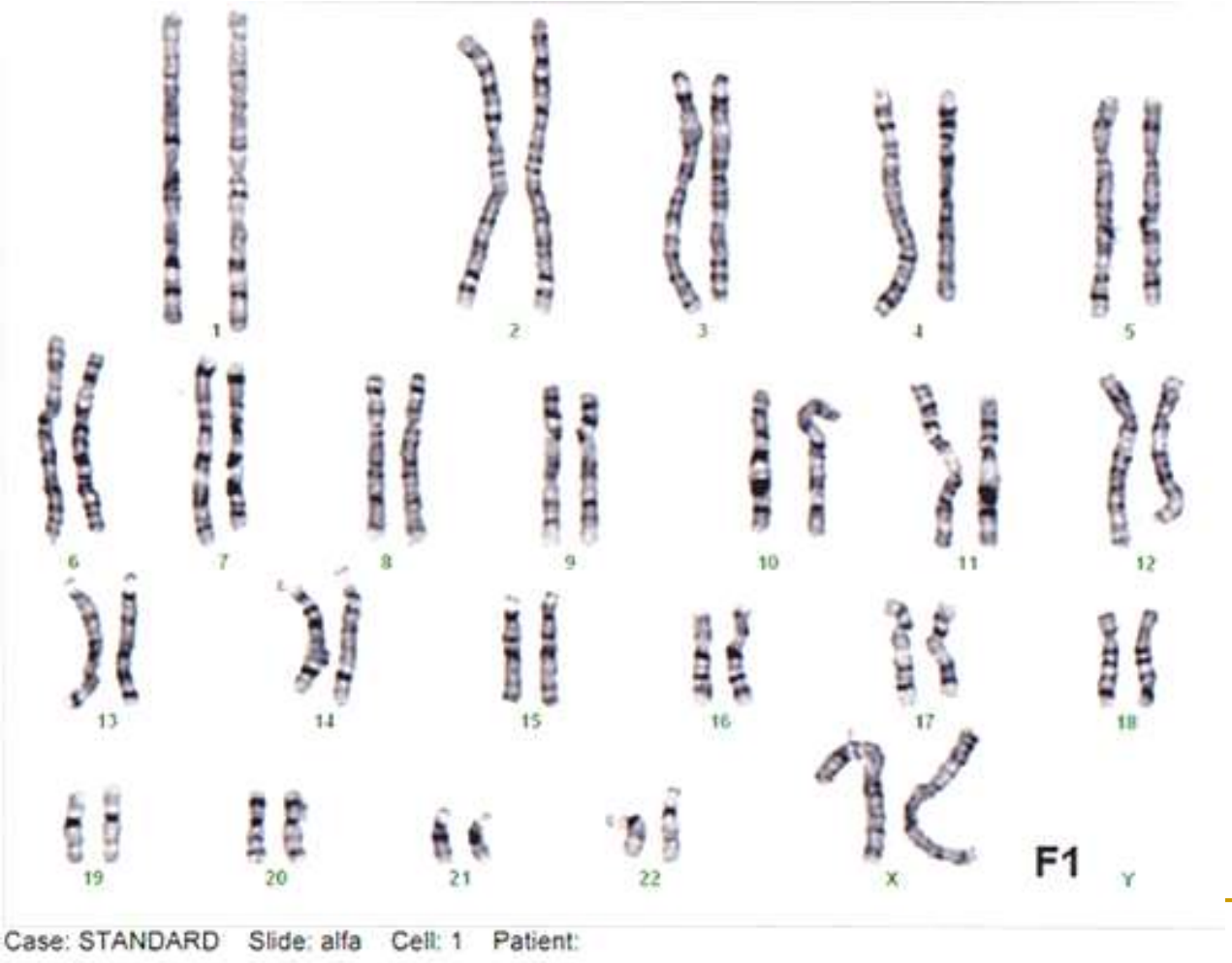

A



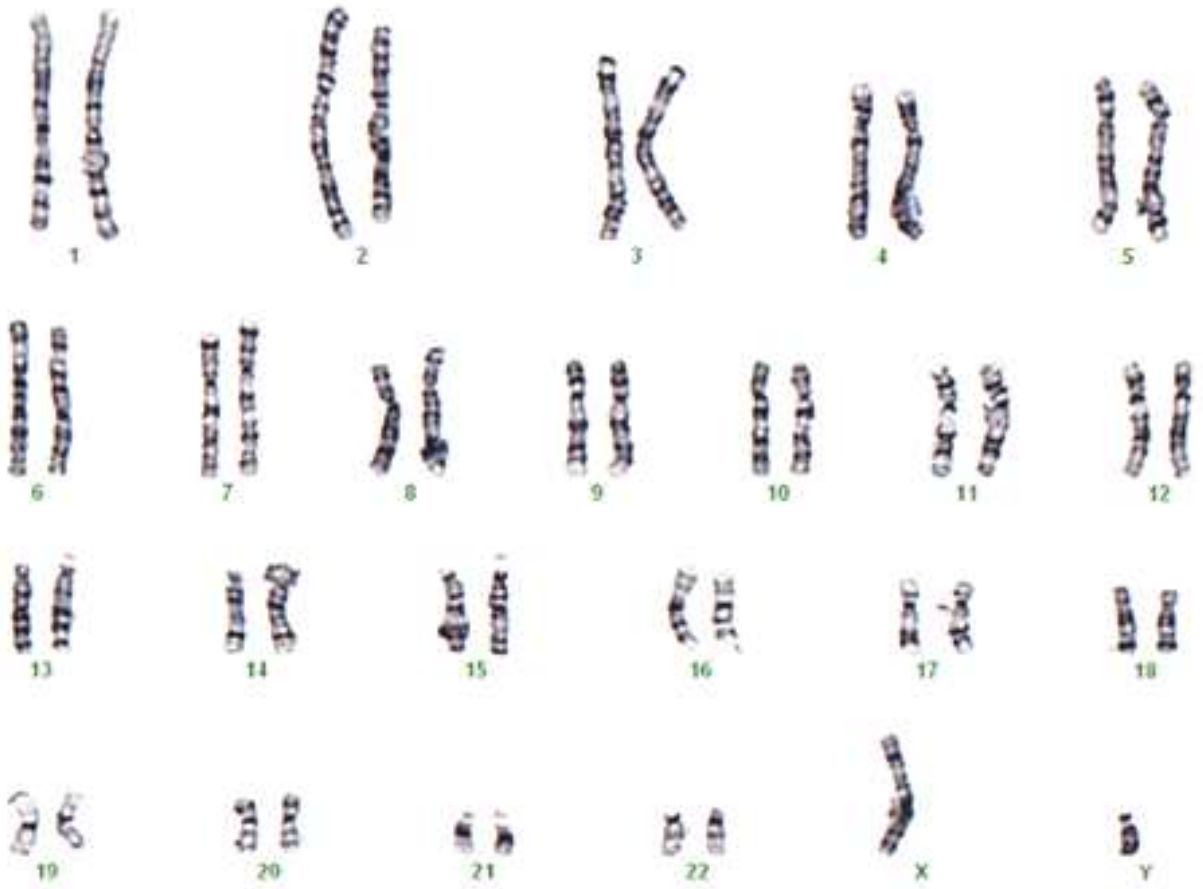
* Red indicates highly sensitive periods when teratogens may induce major anomalies.

TERIMA KASIH

Normal Female: 46,XX



Normal Male: 46,XY

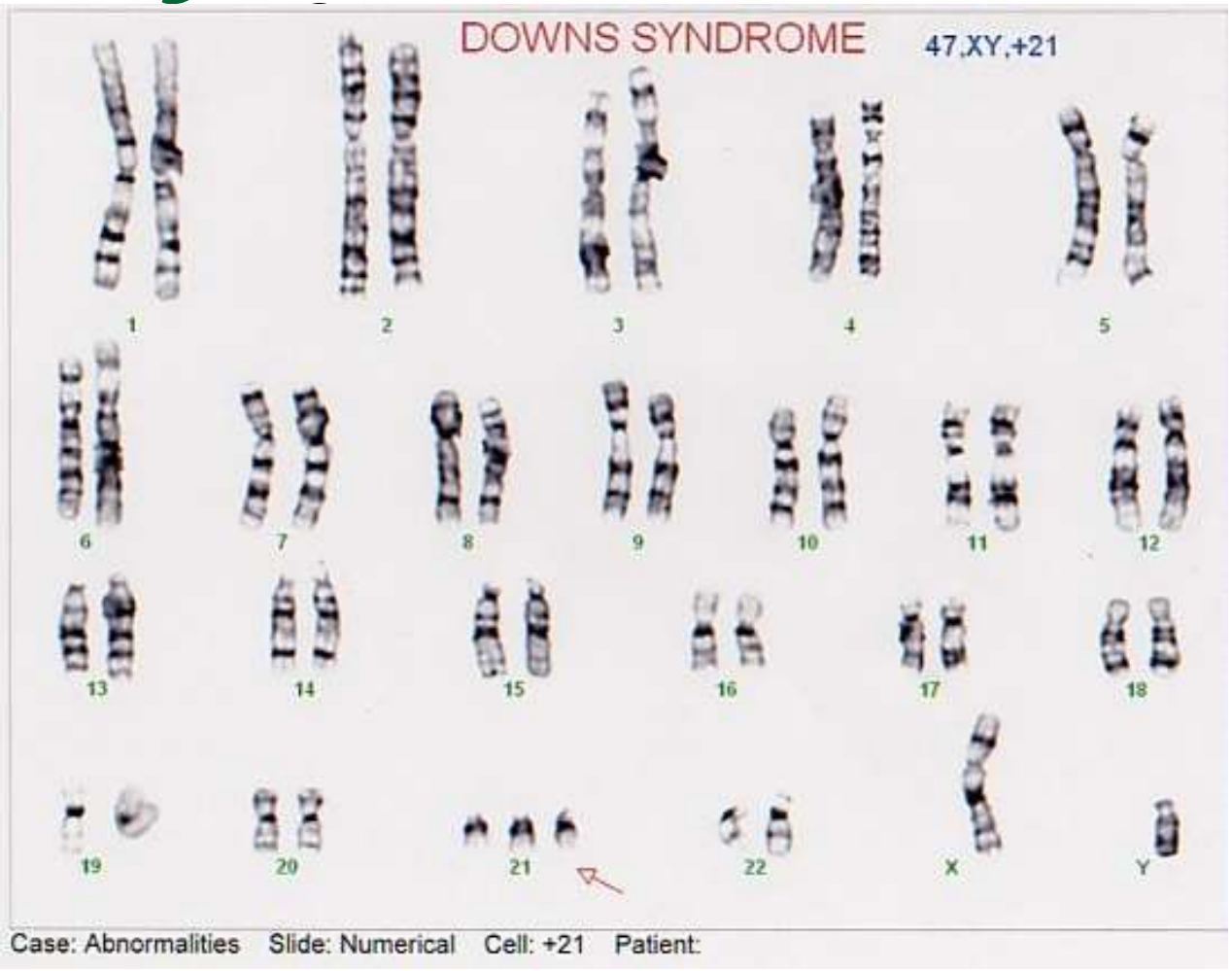


Case: New Slide: Kathleen Cell: 1 Patient:

Autosomal Abnormalities

Trisomy 21

Dow



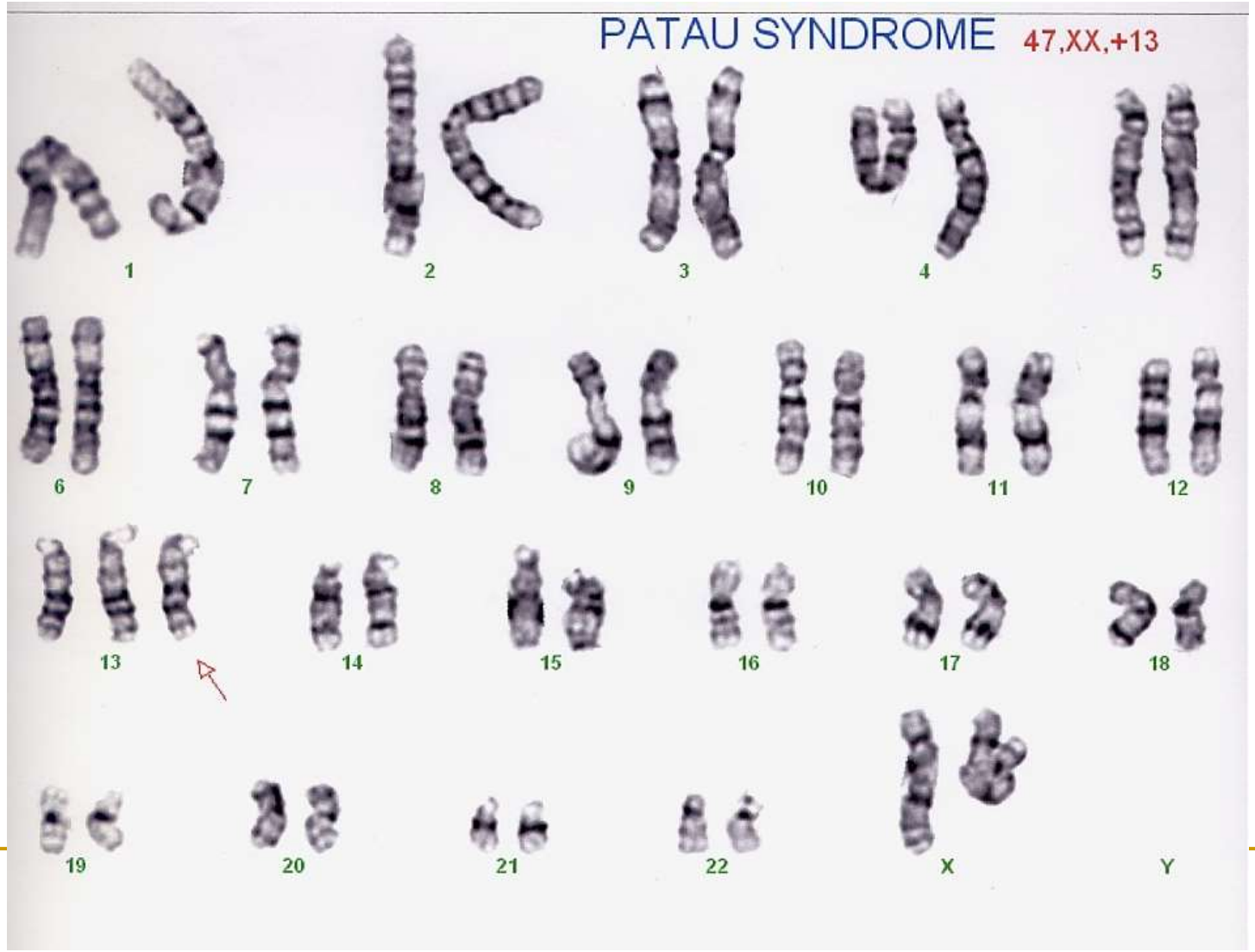
47, XX, 21+ Female with Down Syndrome

47, XY, 21+ Male with Down Syndrome

Trisomy 21
Major Clinical Features

- mental retardation
- slanted palpebral fissures
- epicanthal folds
- small, round, flat face
- small mouth, protruding tongue
- congenital heart problems
- Brushfield spots (iris)
- small, hypoplastic ears
- simian creases
- hypotonia, lax joints, hyperextensive

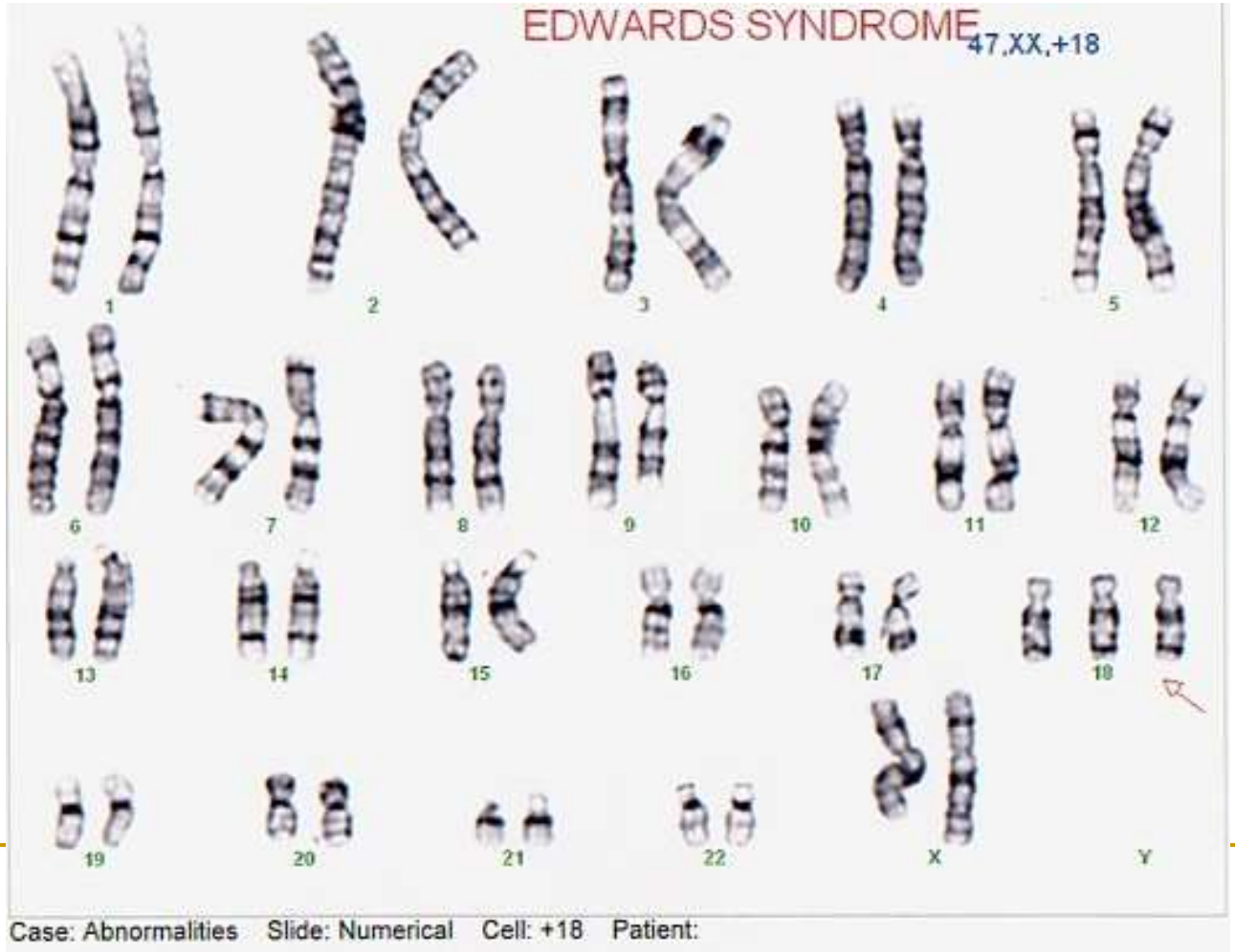
Trisomy 13
Patau Syndrome 47,XY,13+



Trisomy 13
Major Clinical Features

- mental retardation
- growth retardation
- microcephaly
- cleft lip/palate
- small jaw (micrognathia)
- deformed, low-set ears
- polydactyly
- congenital heart defects
- rocker bottom feet
- seizures
- low birth weight

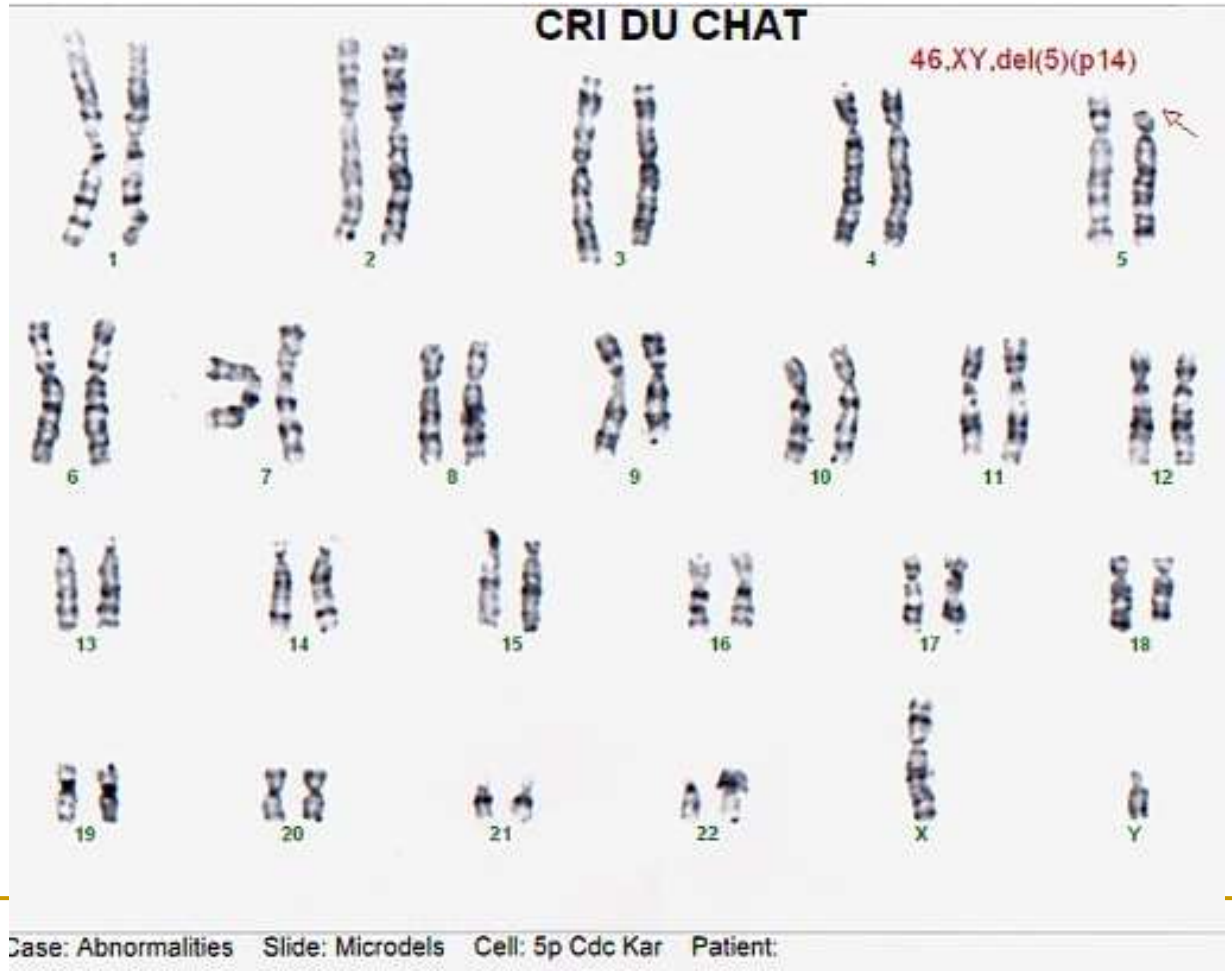
Trisomy 18
Edward' Syndrome 47,XX,+18



Trisomy 18
Major Clinical Features

- mental retardation
- growth retardation
- short neck
- cleft lip/palate
- dislocated hips/abnormal pelvis
- deformed, low-set ears
- hypertonia
- congenital heart disease
- horseshoe kidneys
- hydronephrosis
- short sternum
- pyloric stenosis

Cri du chat Syndrome (5p-)



Cri du chat
Major Clinical Features

- distinctive cat-like cry
- profound developmental retardation
- severe mental retardation
- microcephaly
- hypotonia
- hypertelorism
- congenital heart disease
- round, moon-shaped face
- large mouth, short philtrum
- low set ears
- hand and foot abnormalities

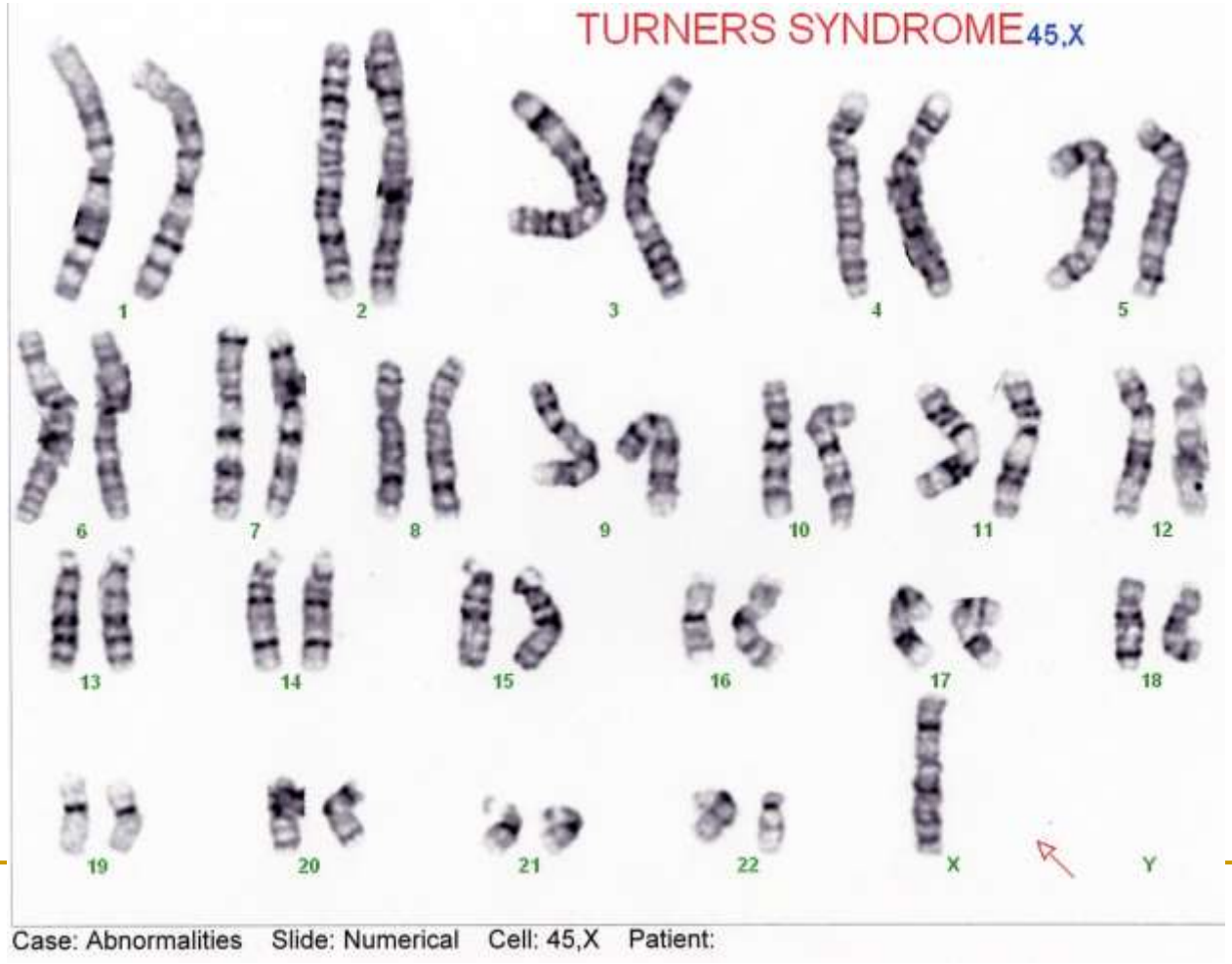
Sex Chromosome Anomalies

- General features:
  - Some growth retardation (GR)
  - Reproductive anomalies/problems
  - Good viability
  - Prenatally diagnosable
  - Associated with spontaneous abortion (Sab)

Sex Chromosome Anomalies

- Monosomy X: Turner's Syndrome (45, X)
- Trisomy X: Triplo-X Syndrome (47, XXX)
- Trisomy (47, XXY): Klinefelter's Syndrome
- Trisomy (47, XYY): XYY Syndrome

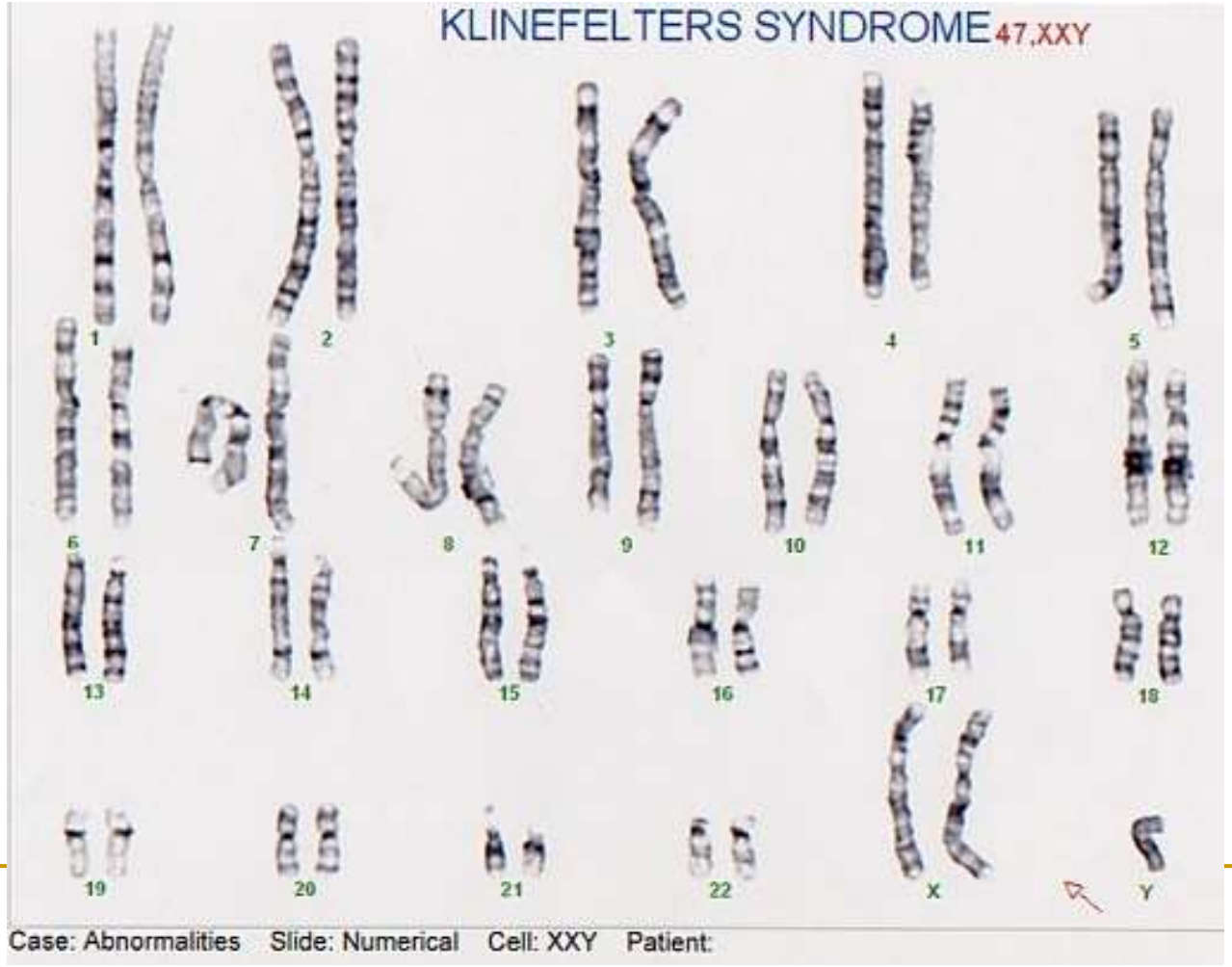
Turner's Syndrome 45,X



Turner's Syndrome
Major Clinical Features

- female phenotype
- short (less than 5 feet)
- primary amenorrhea
- low estrogen levels
- maldevelopment of the ovaries
- sterility
- webbing of the skin of the neck
- wide-spaced nipples
- edema at birth
- cardiovascular problems

Klinefelter's Syndrome 47,XXY



Klinefelter's Syndrome
Major Clinical Features

- small testes
- aspermia

(little to no sperm production)

- gynecomastia
- long limbs
- large hands & feet
- retardation in some
- fertility in some
- social limitations in some