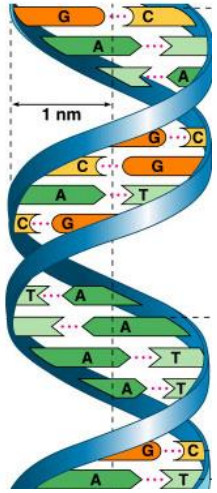
# Genetic Testing & Chromosomal Disorders



# Genetic Testing

## Blood Tests

### Genetic Carrier Screening

- DNA test to determine if a person carries a gene for an inherited disorder
- Before or during pregnancy

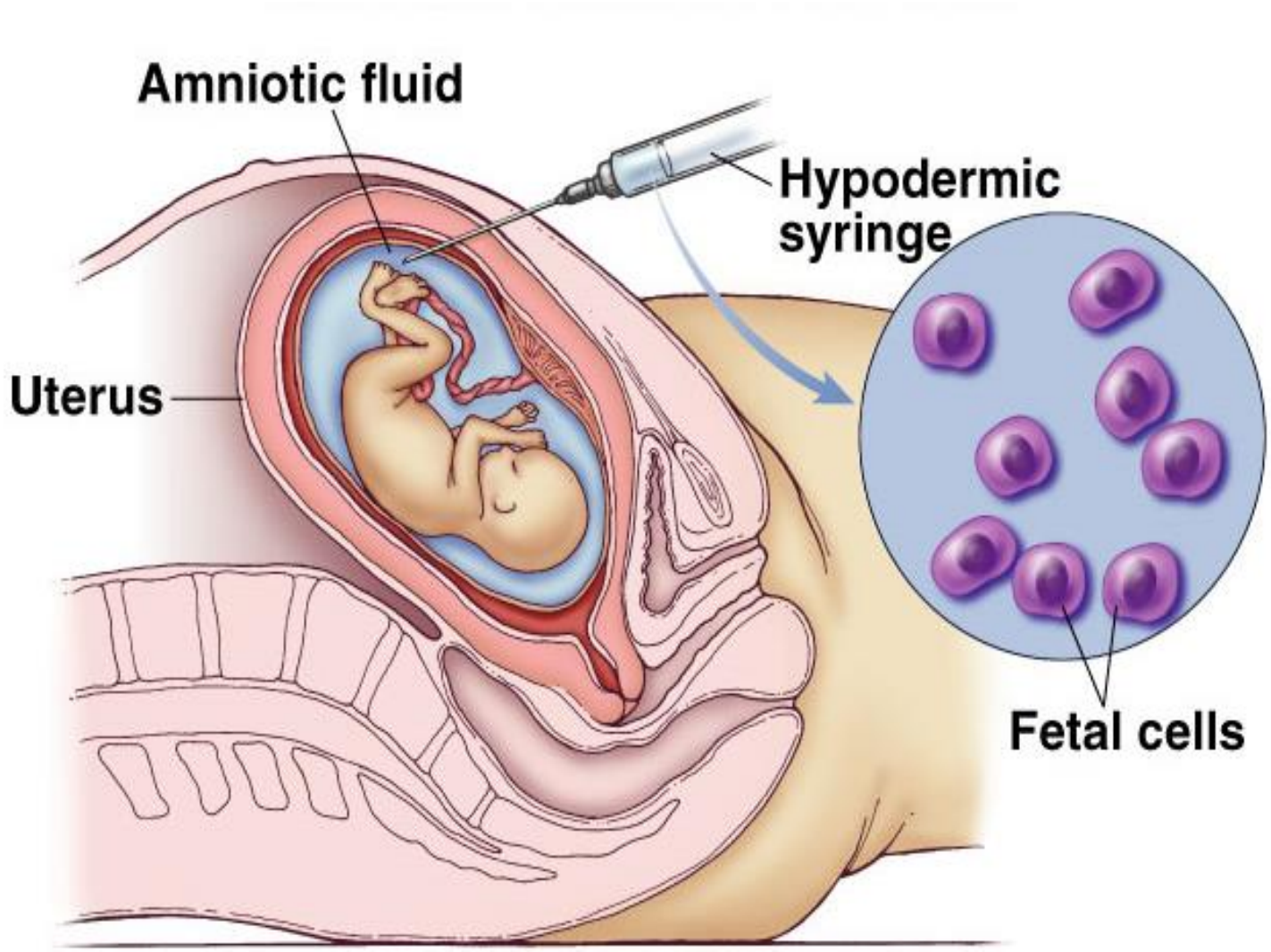
### Non-Invasive Prenatal Screening (NIPT)

- Checks the baby's DNA in the mother's blood
- Screens for specific chromosomal abnormalities
- Can also tell the gender
- During 1st trimester of pregnancy

CBS News - Iceland's Down Syndrome Dilemma

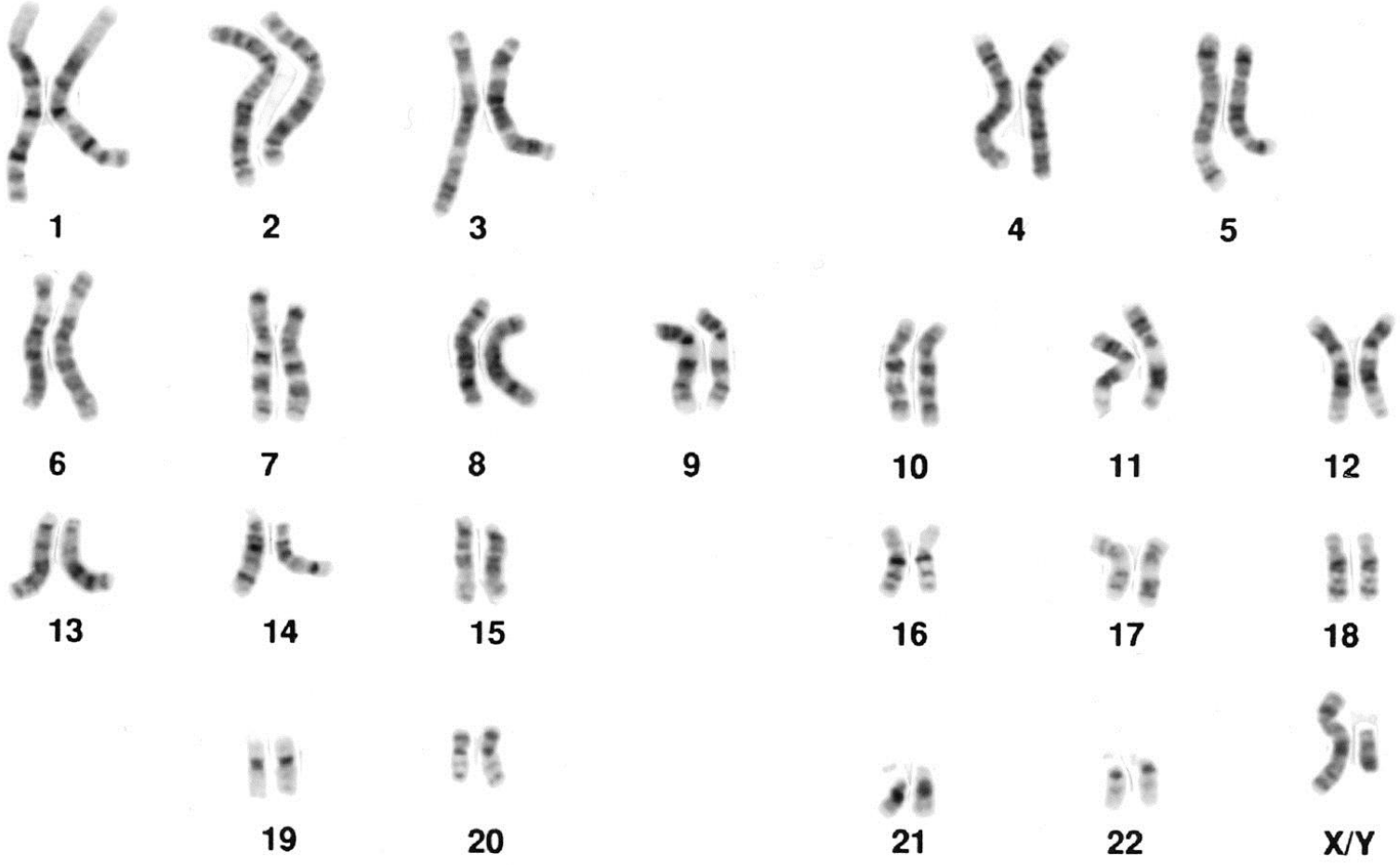
# Amniocentesis

- during 2nd trimester of pregnancy
- sample of embryo cells is obtained by removing amniotic fluid in order to obtain and analyze chromosomes
- invasive, small risk of miscarriage

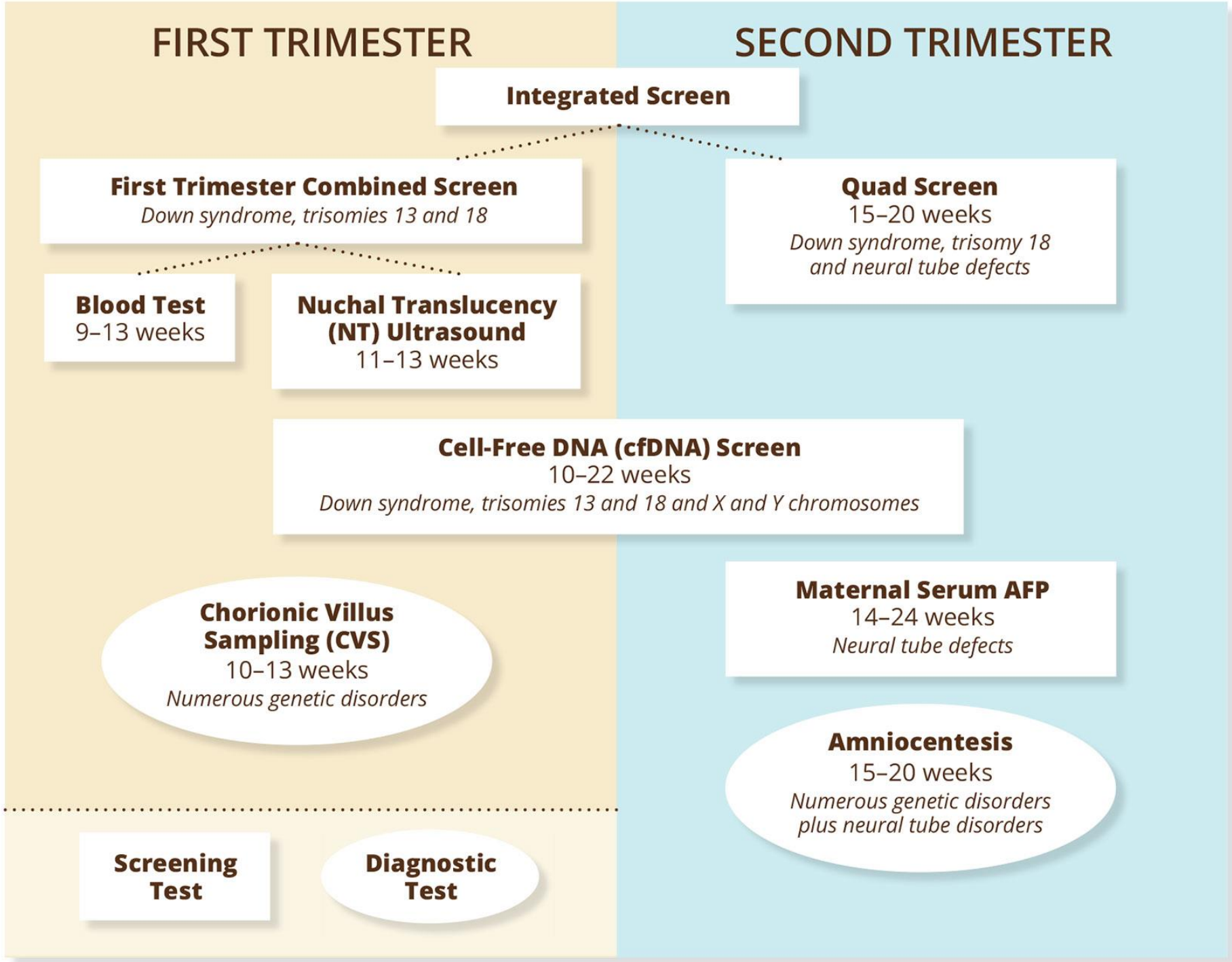


## Karyotype

- stain & photograph complete set of chromosomes
- organized in homologous pairs in order
- analyzed for chromosomal abnormalities



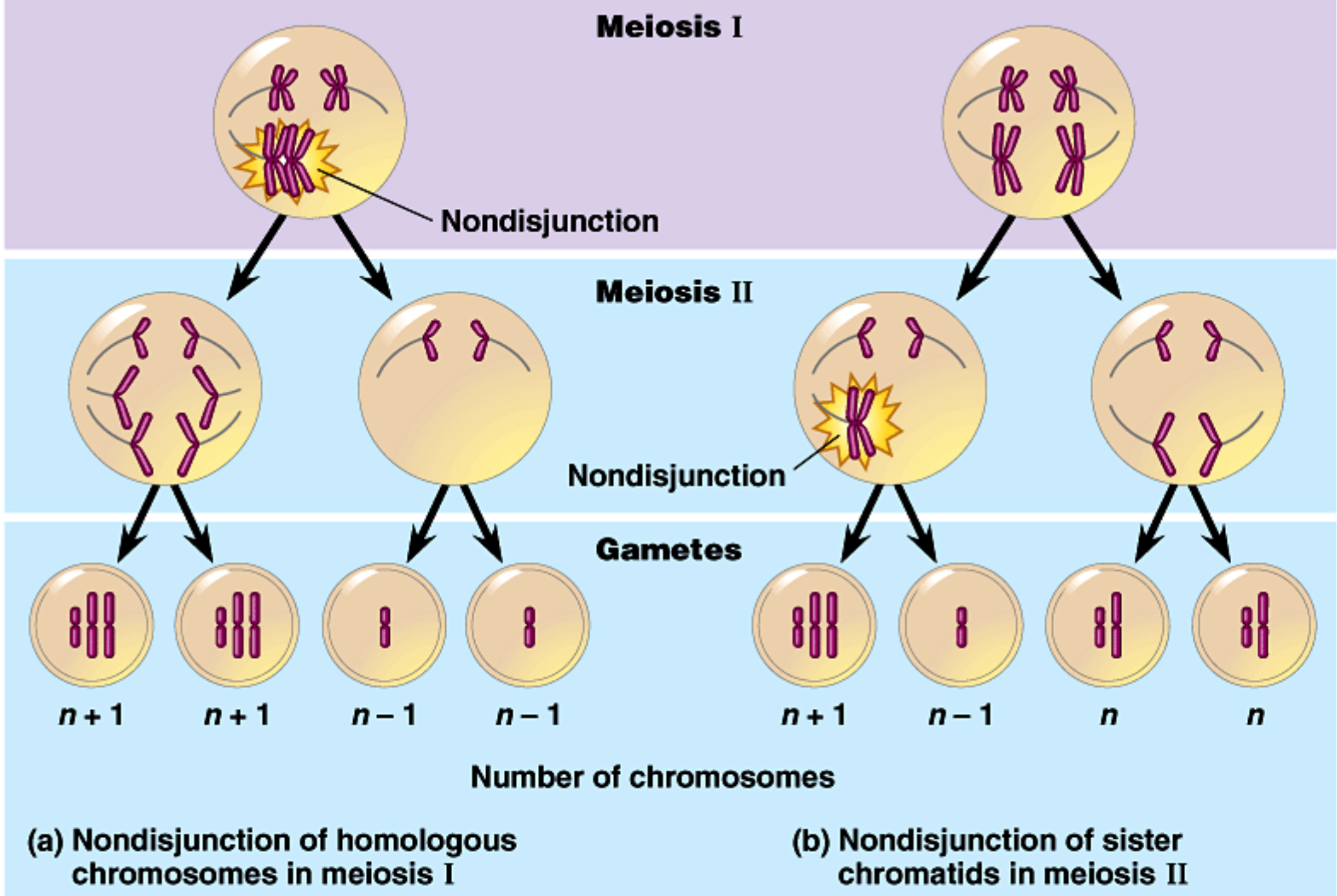

Normal Karyotype


FIRST TRIMESTER
SECOND TRIMESTER
Integrated Screen
First Trimester Combined Screen
Down syndrome, trisomies 13 and 18
Quad Screen
15–20 weeks
Down syndrome, trisomy 18 and neural tube defects
Blood Test
9–13 weeks
Nuchal Translucency (NT) Ultrasound
11–13 weeks
Cell-Free DNA (cfDNA) Screen
10–22 weeks
Down syndrome, trisomies 13 and 18 and X and Y chromosomes
Maternal Serum AFP
14–24 weeks
Neural tube defects
Chorionic Villus Sampling (CVS)
10–13 weeks
Numerous genetic disorders
Amniocentesis
15–20 weeks
Numerous genetic disorders plus neural tube disorders
Screening Test
Diagnostic Test

# Chromosomal Abnormalities

Nondisjunction

- Occurs when chromosomes fail to separate properly (disjunction) during meiosis
- Produces gametes with incorrect number of chromosomes
  - Offspring can have wrong chromosome number
    - trisomy
      - cells have 3 copies of a chromosome
    - monosomy
      - cells have only 1 copy of a chromosome


Meiosis I
Nondisjunction
Meiosis II
Nondisjunction
Gametes
n + 1
n + 1
n – 1
n – 1
n + 1
n – 1
n
n
Number of chromosomes
(a) Nondisjunction of homologous chromosomes in meiosis I
(b) Nondisjunction of sister chromatids in meiosis II

# Human Chromosome Disorders

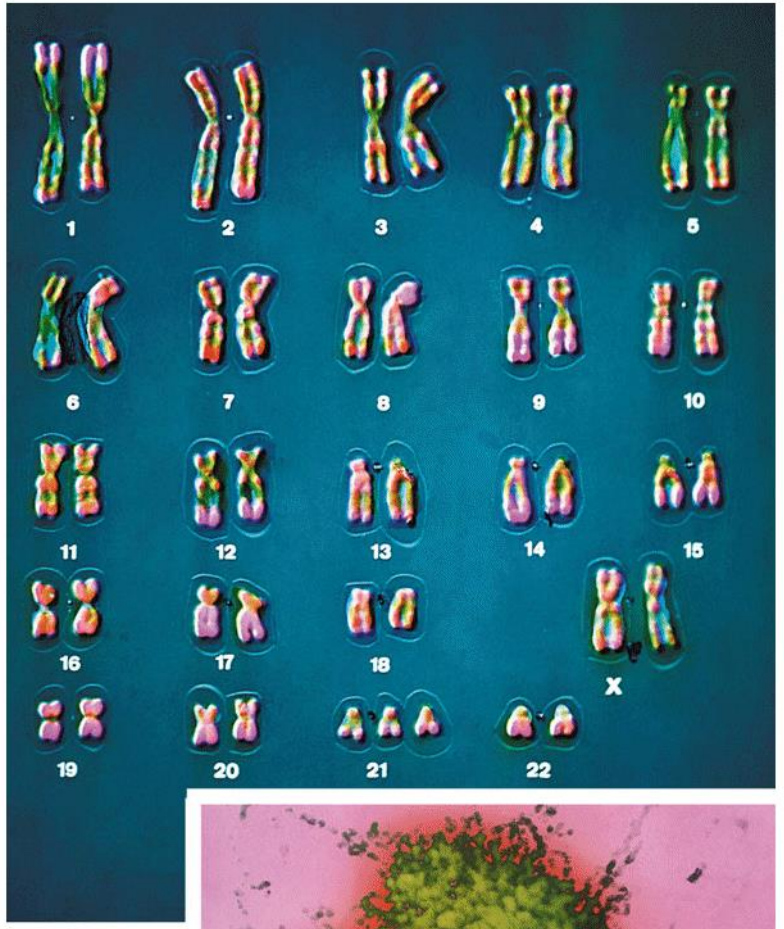
- High frequency in humans
  - most embryos are spontaneously aborted
  - alterations are too disastrous
- Certain conditions are tolerated
  - May affect either autosomes or sex chromosomes

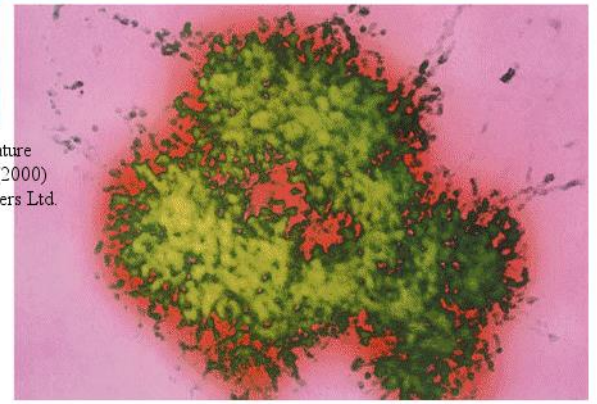
# Examples of **Autosomal** Chromosomal Disorders

## 1. Down Syndrome (Trisomy 21)

- 3 copies of chromosome # 21
- 1 in 700 children born in U.S.

- Chromosome 21 is one of the smallest human chromosomes but still produces severe effects



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, R. Nature 405, 283-284 (2000)
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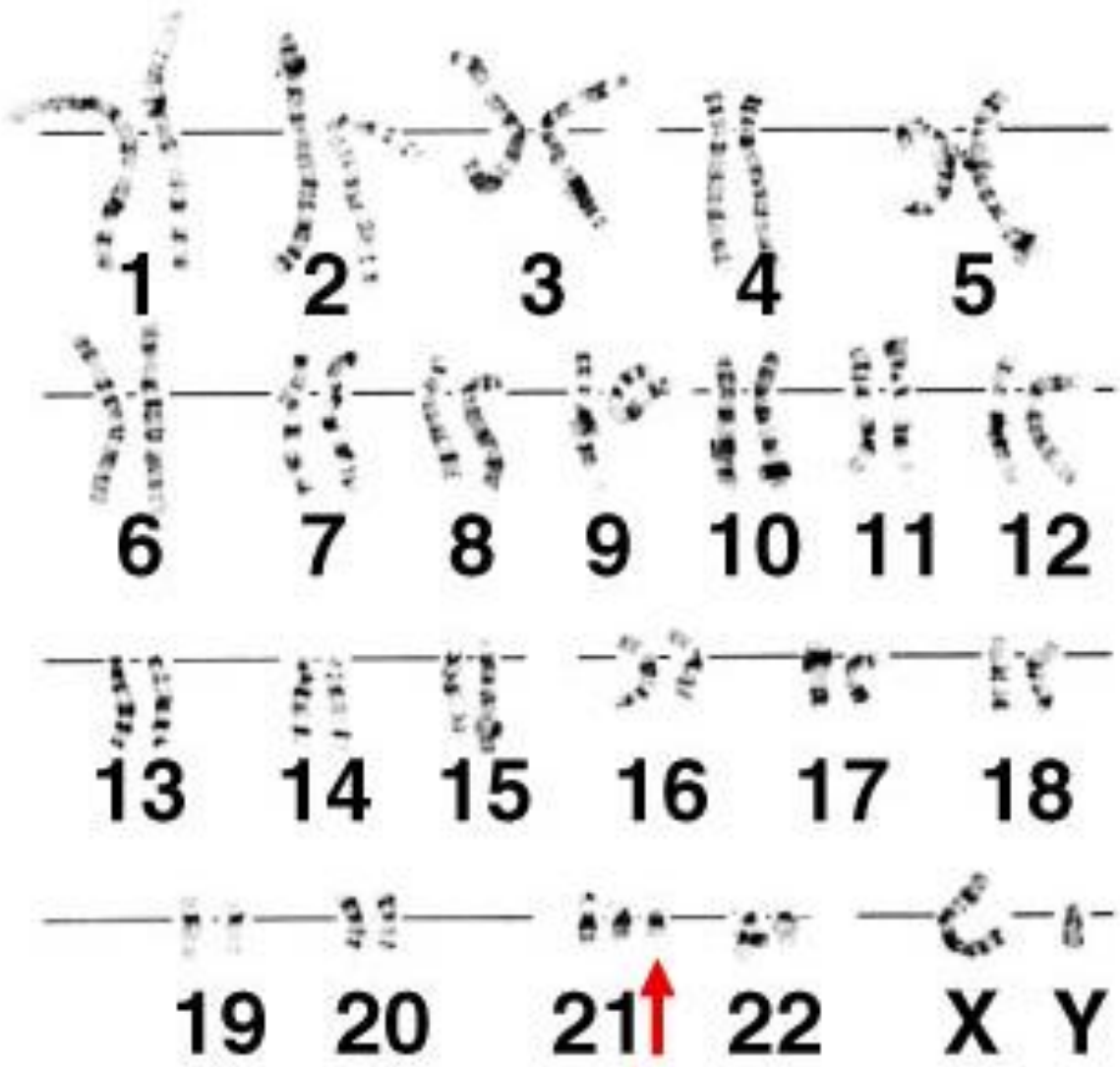
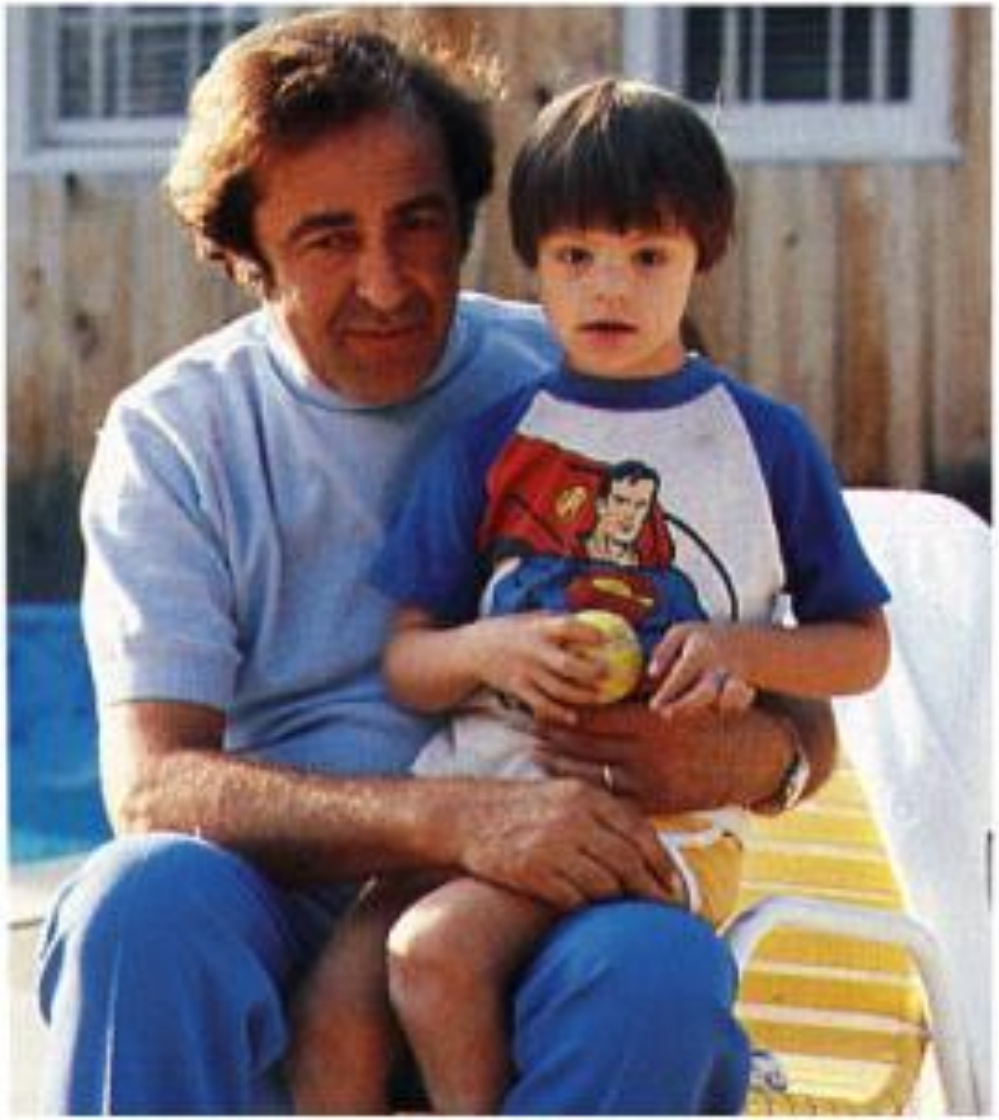
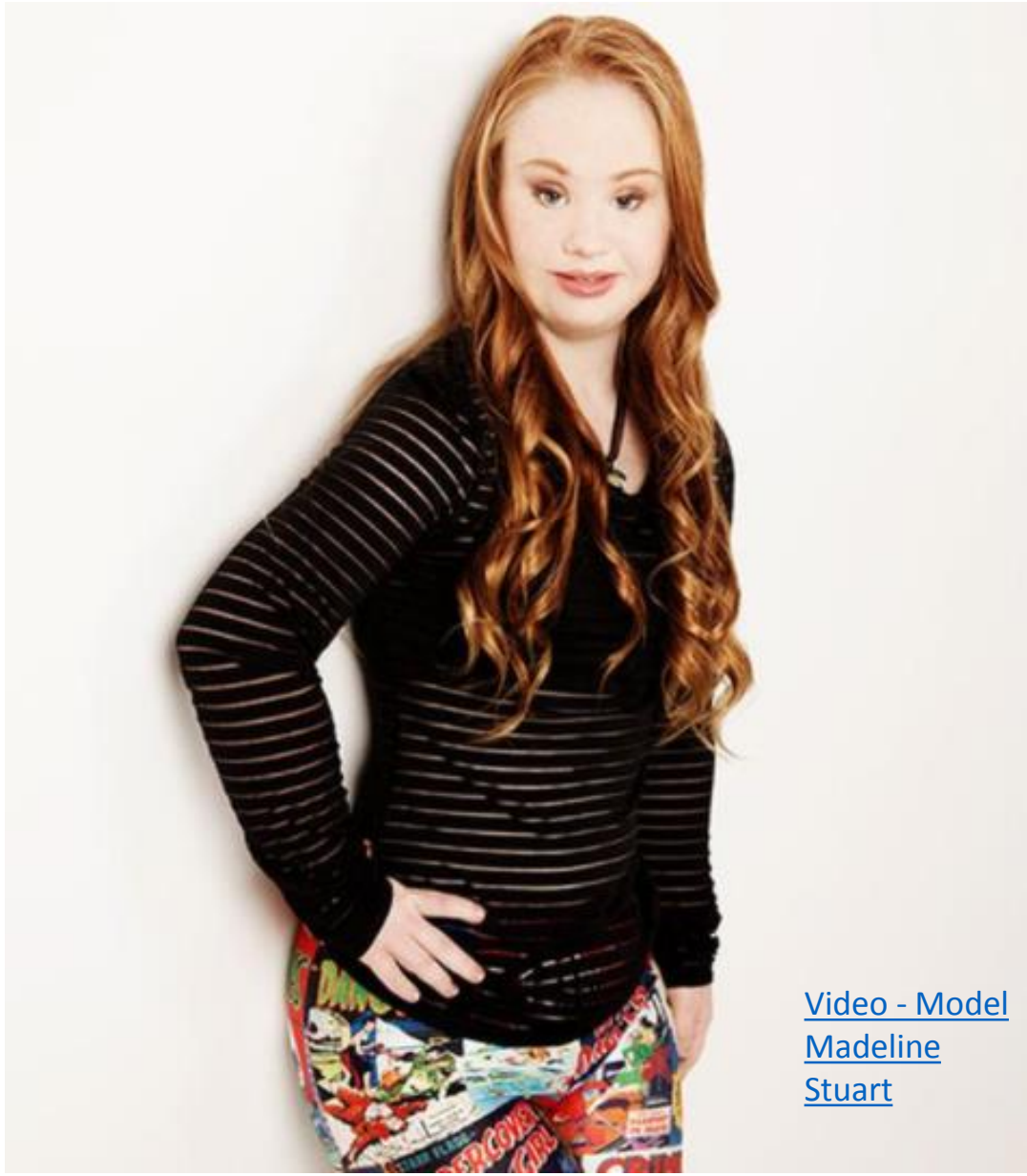
# Trisomy 21



# Characteristics of Down Syndrome

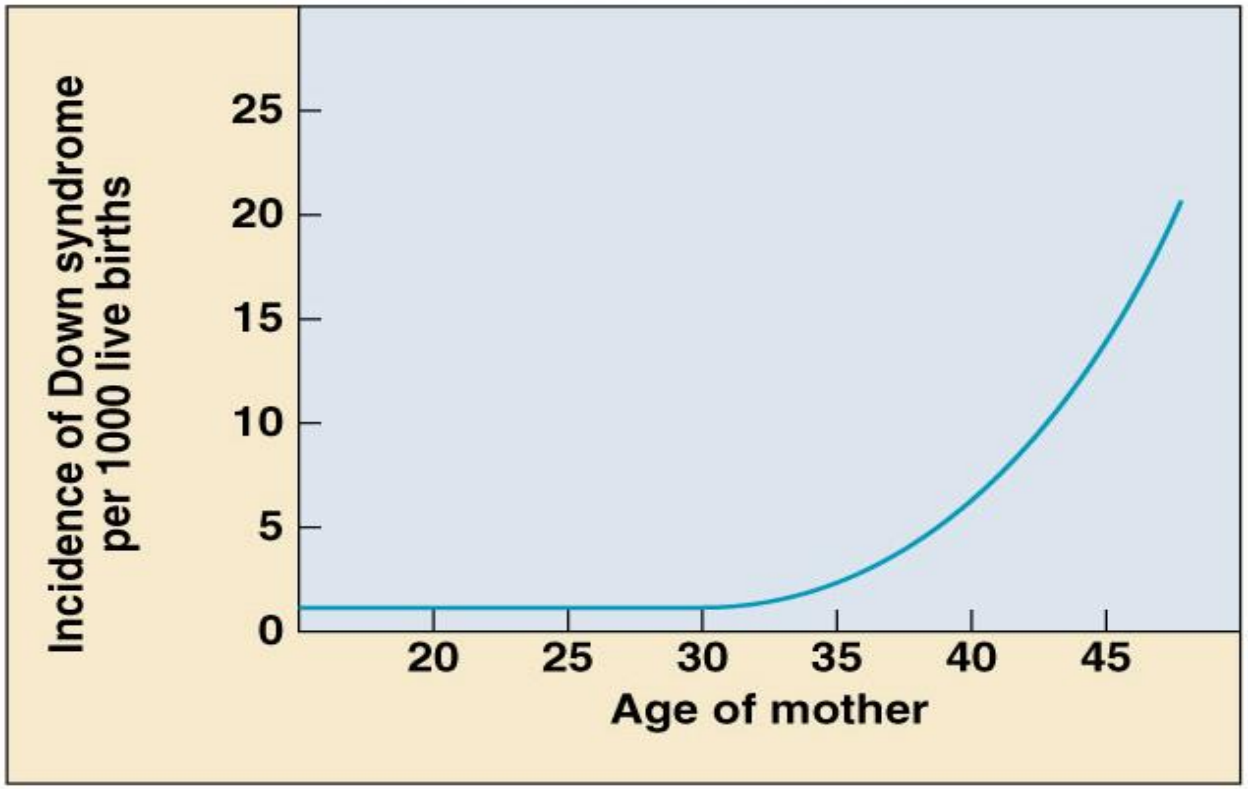
- Upward slant to eyes.
- Small ears that fold over at the top.
- Small, flattened nose.
- Small mouth, making tongue appear large.
- Short neck.
- Small hands with short fingers.
- Life expectancy < 50years.
- Some degree of mental retardation, from mild to severe



Video - Model Madeline Stuart

# Down syndrome & age of mother

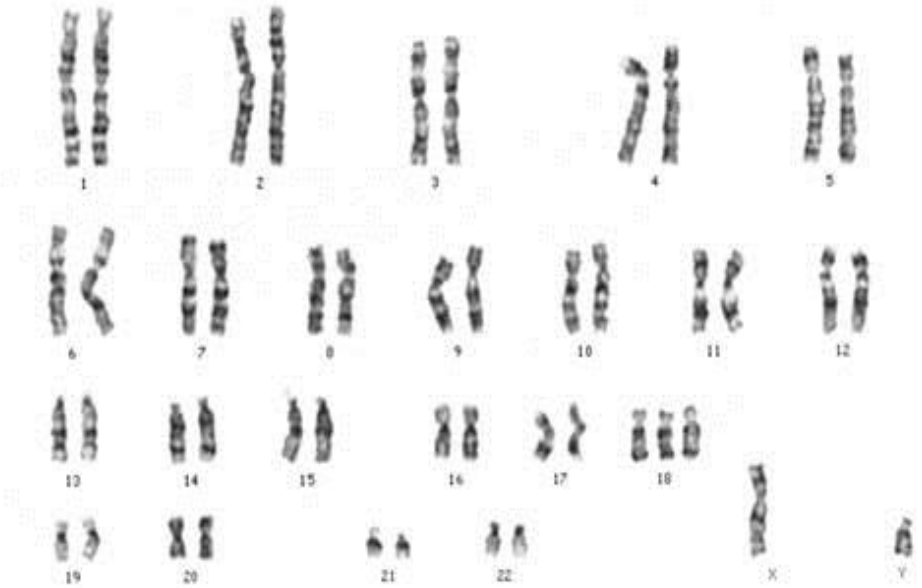
- Frequency of Down syndrome correlates with the age of the mother
- As maternal age increases, risk of Down Syndrome increases




| Mother's age | Incidence of Down Syndrome |
|---|---|
| Under 30 | <1 in 1000 |
| 30 | 1 in 900 |
| 35 | 1 in 400 |
| 36 | 1 in 300 |
| 37 | 1 in 230 |
| 38 | 1 in 180 |
| 39 | 1 in 135 |
| 40 | 1 in 105 |
| 42 | 1 in 60 |
| 44 | 1 in 35 |
| 46 | 1 in 20 |
| 48 | 1 in 16 |
| 49 | 1 in 12 |

**2. Trisomy 18**: Edwards syndrome

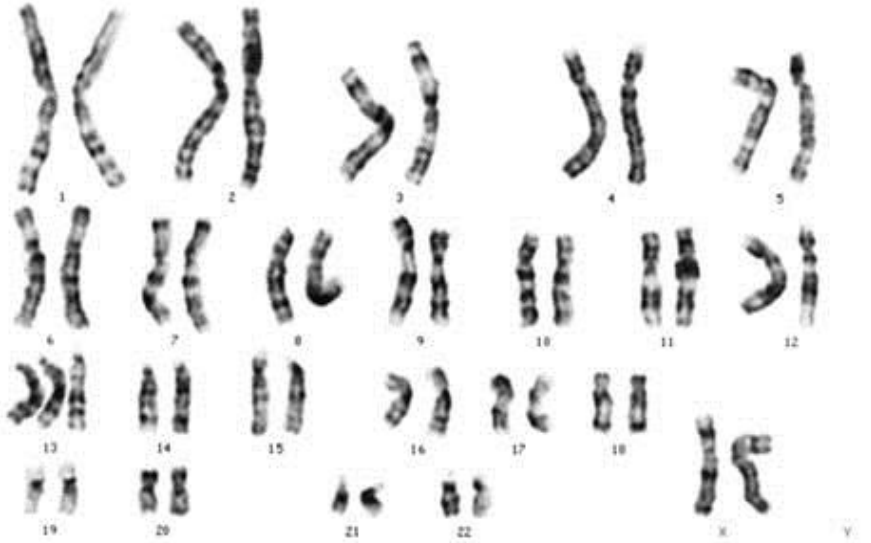
- 1 in every 3,000 live **births**. (2n+1)



**3. Trisomy 13**: Patau syndrome

- 1 in every 5,000 live births. (2n+1)

- Genetic disorders that present a combination of birth defects including severe mental retardation, as well as health problems involving nearly every organ system in the body. Twenty to 30 percent of babies born with trisomy 18 or 13 die in the first month of life, and 90 percent die by age 1.



# Sex Chromosome Disorders

- Human development is more tolerant of wrong numbers in sex chromosomes than autosomes

Male sex chromosome disorders:

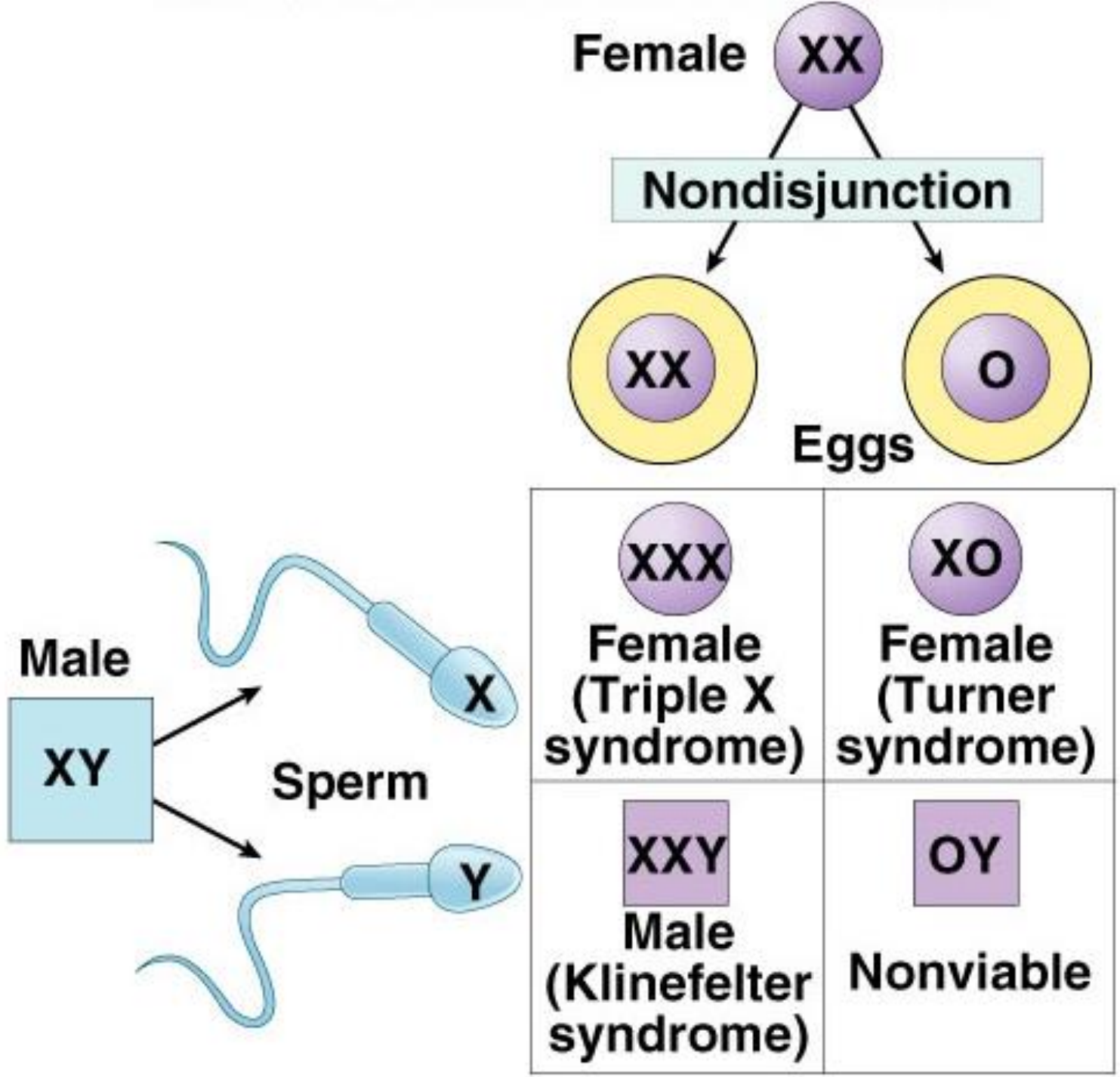
XXY = Klinefelter's syndrome (male w/ extra X)

XYY = Jacob's syndrome (male w/ extra Y)

Female sex chromosome disorders:

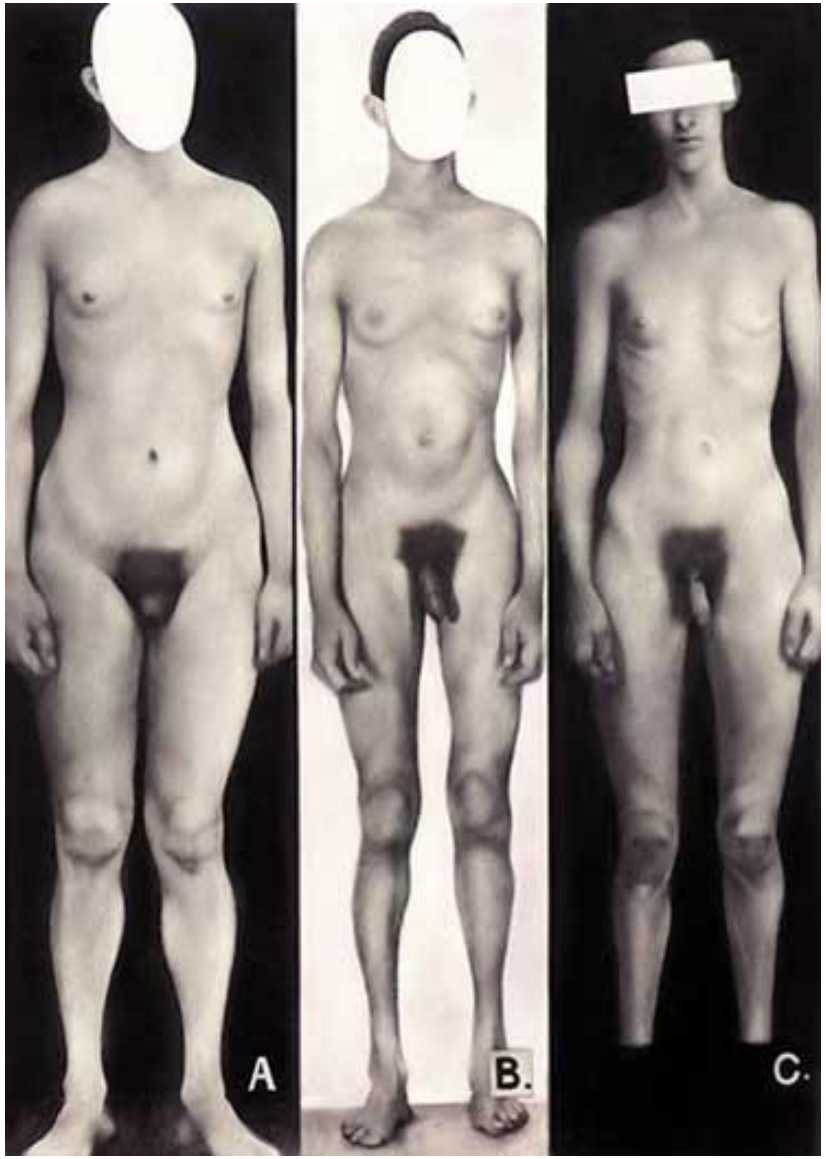
XO = Turner syndrome (female missing X)

XXX = Trisomy X (female w/ extra X)

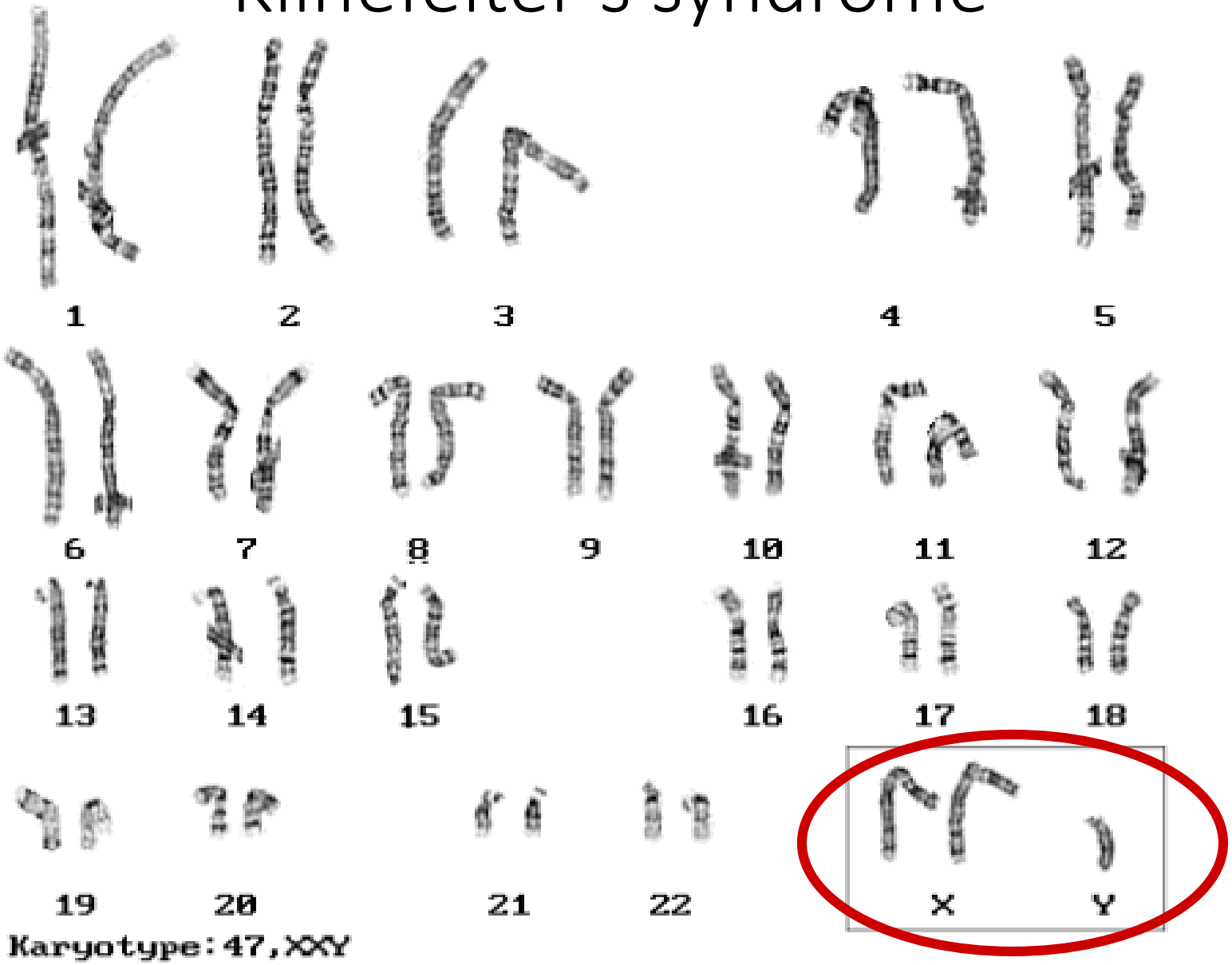

Female
XX
Nondisjunction
XX
O
Eggs
Male
XY
Sperm
X
Y
XXX
Female (Triple X syndrome)
XO
Female (Turner syndrome)
XXY
Male (Klinefelter syndrome)
OY
Nonviable

# 1. Klinefelter syndrome

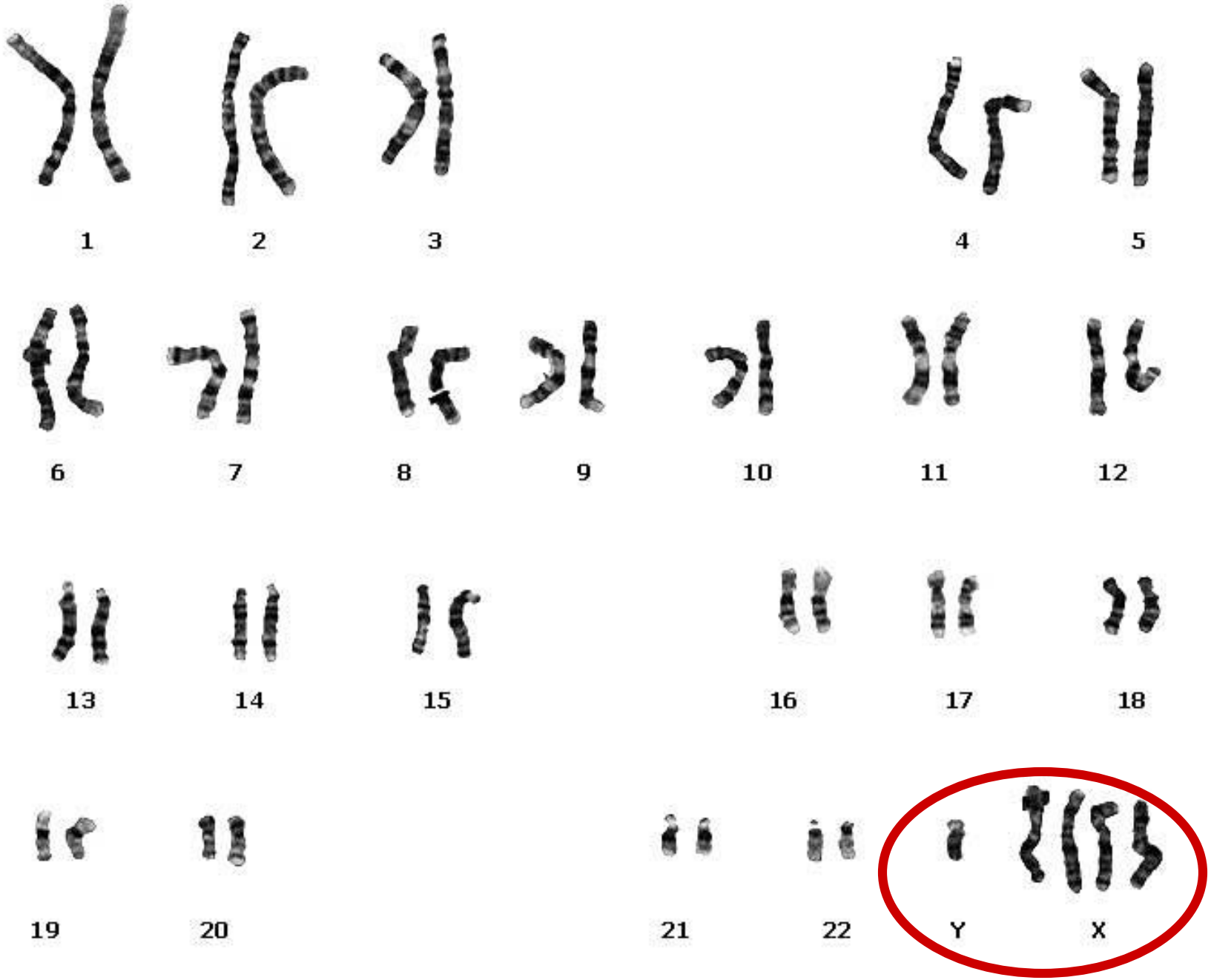
- XXY male
  - 1 in every 2000 live births
  - have male sex organs, but are sterile (cannot reproduce)
  - feminine characteristics (breast development)
  - tall
  - normal intelligence



# Klinefelter’s syndrome

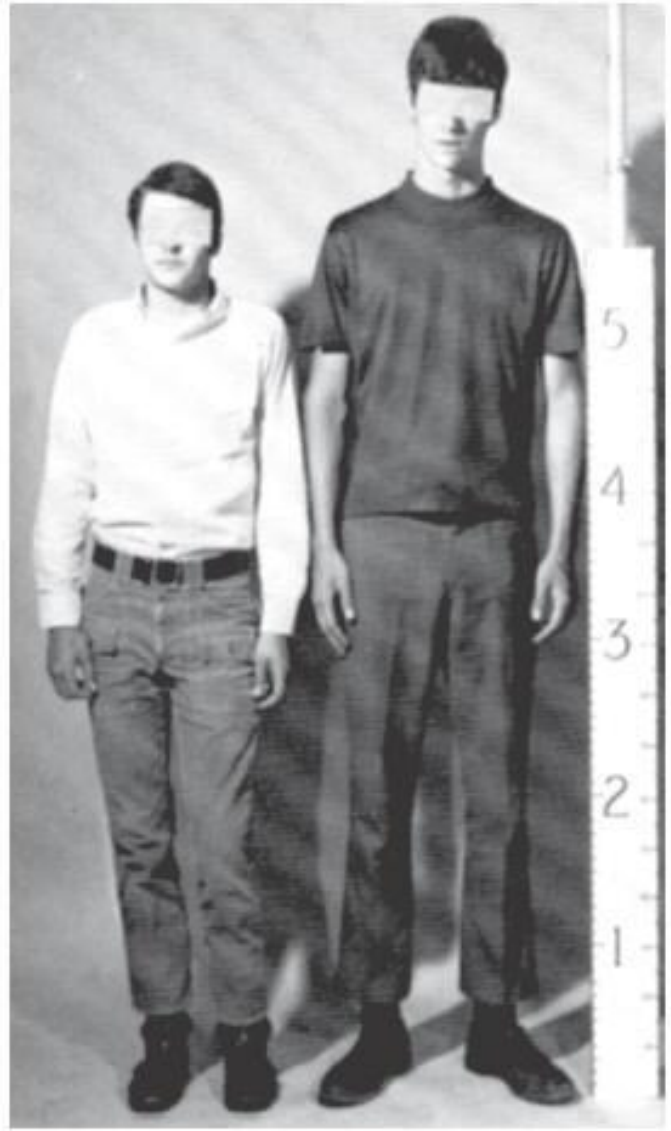


XXXXY, Klinefelter's Syndrome

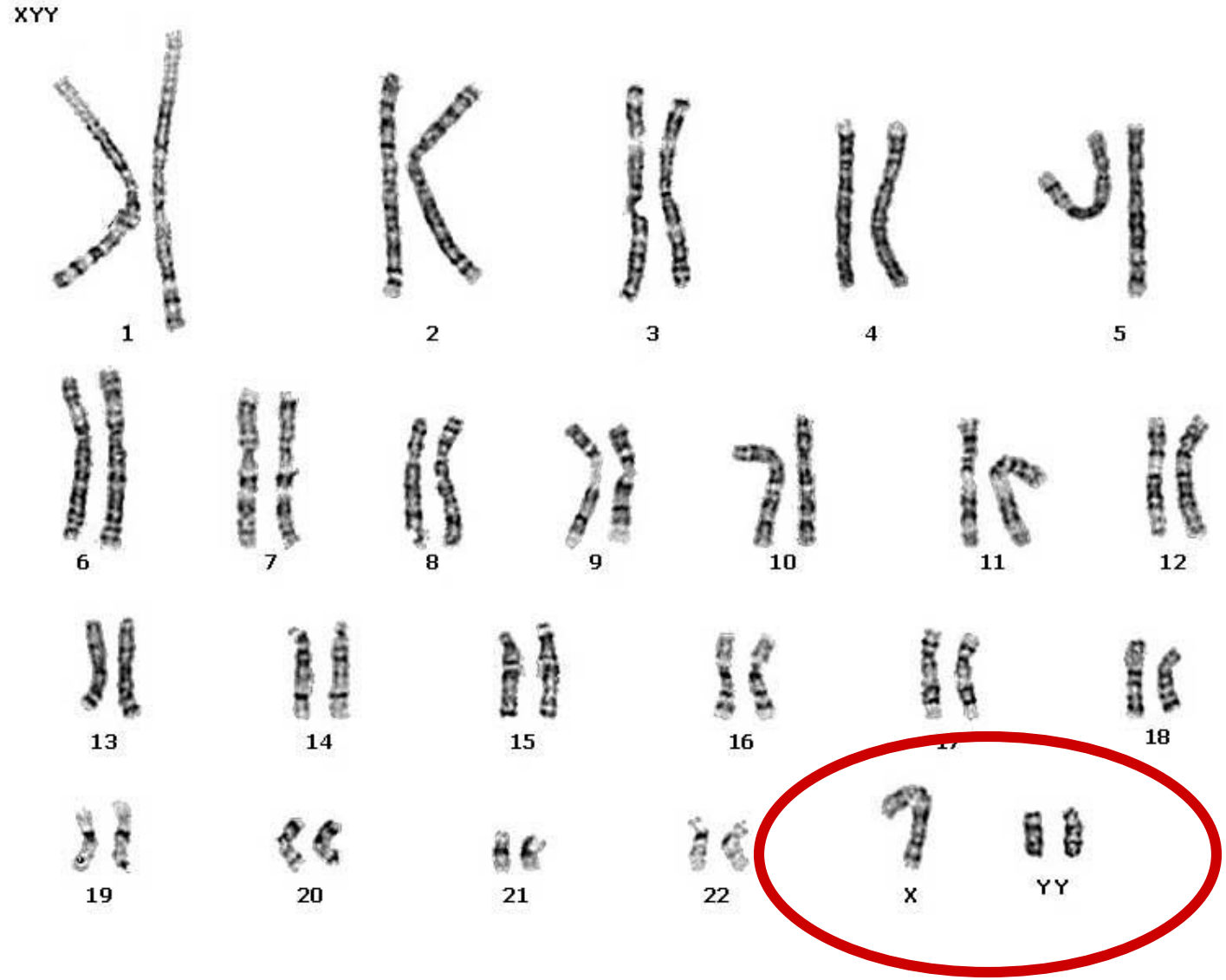


# 2. Jacob's syndrome male

- XYY Males
  - 1 in 1000 live male births
  - somewhat taller than average
  - more active
  - slight learning disabilities
  - delayed emotional maturity
  - higher testosterone levels
  - normal intelligence, normal sexual development



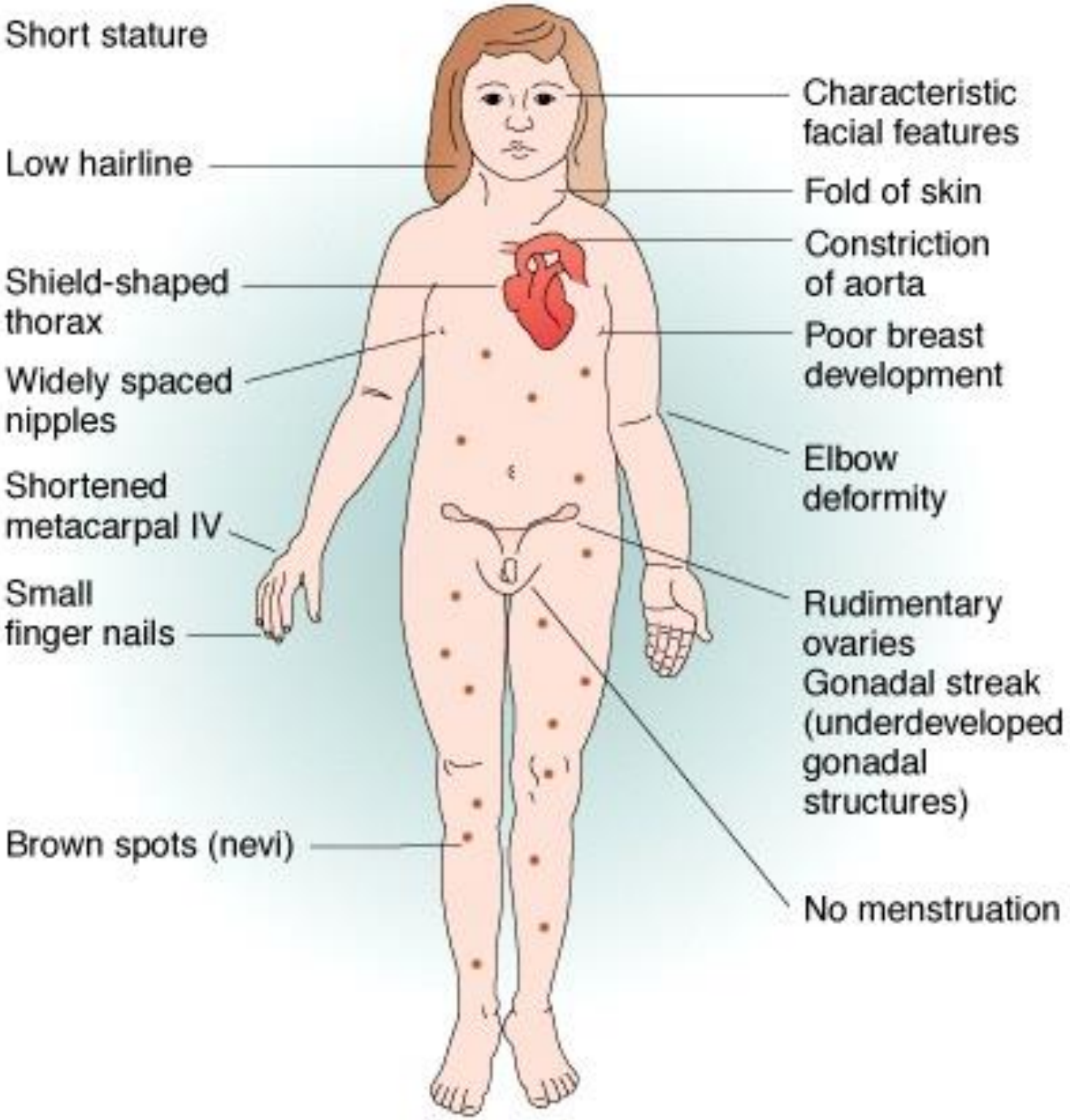
# Jacob's Syndrome XYY Males



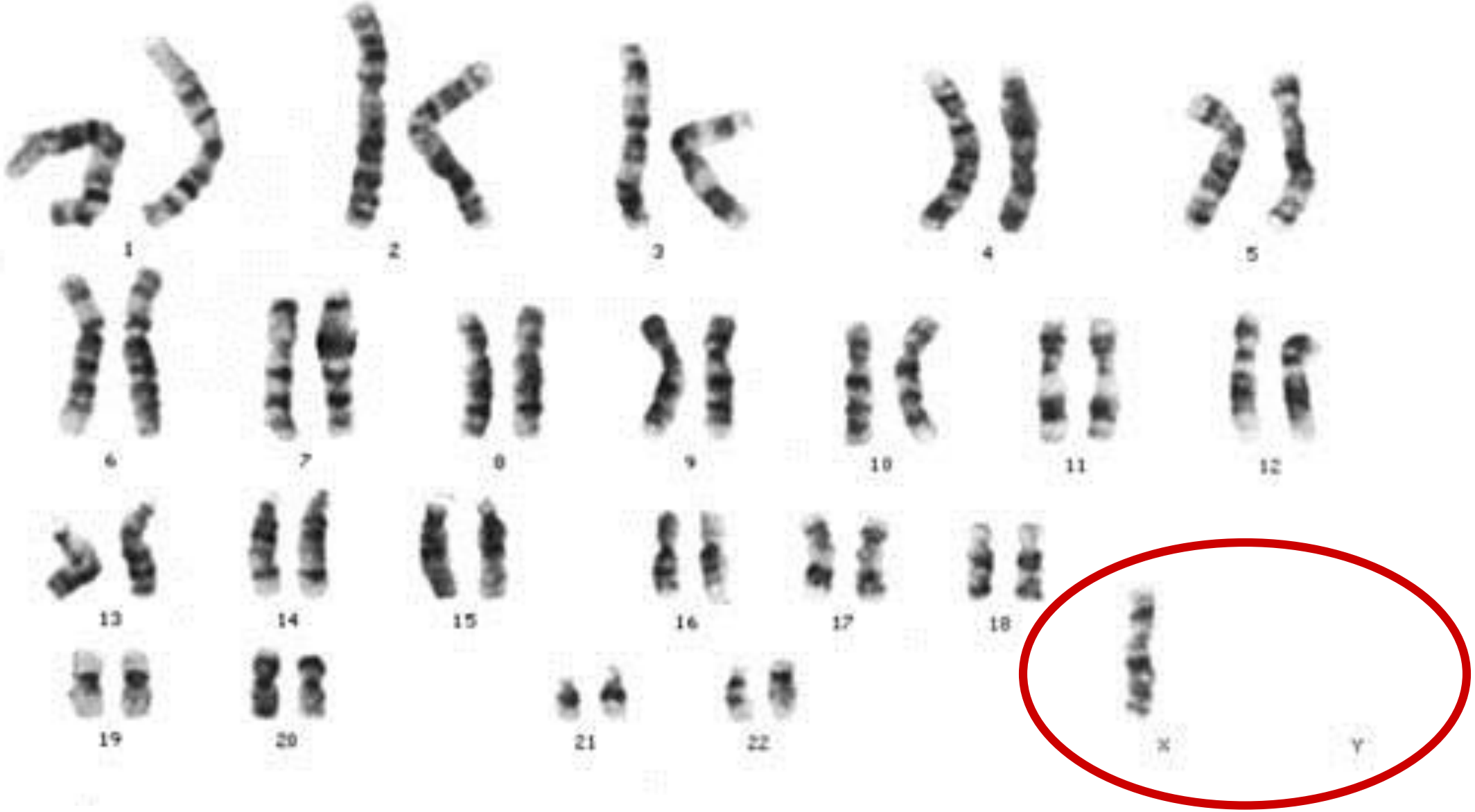
# 3. Turner syndrome

- Monosomy X or X0
  - 1 in every 5000 births
  - varied degree of effects
  - webbed neck
  - short stature
  - sterile, cannot reproduce

# Turner syndrome

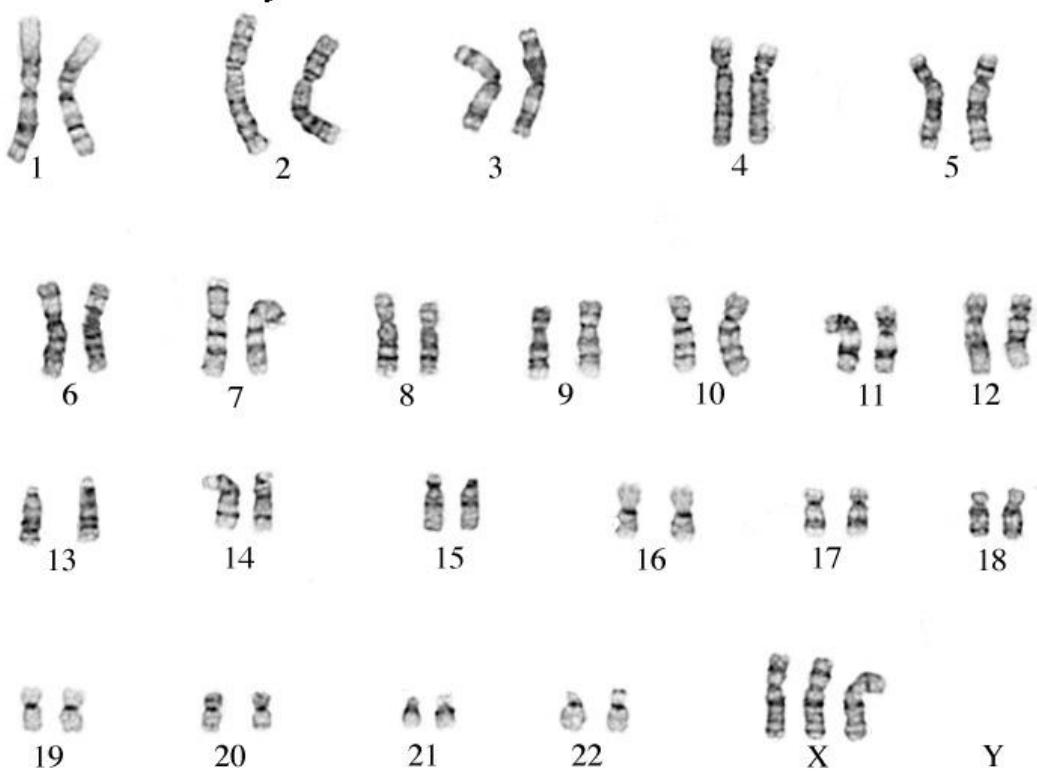


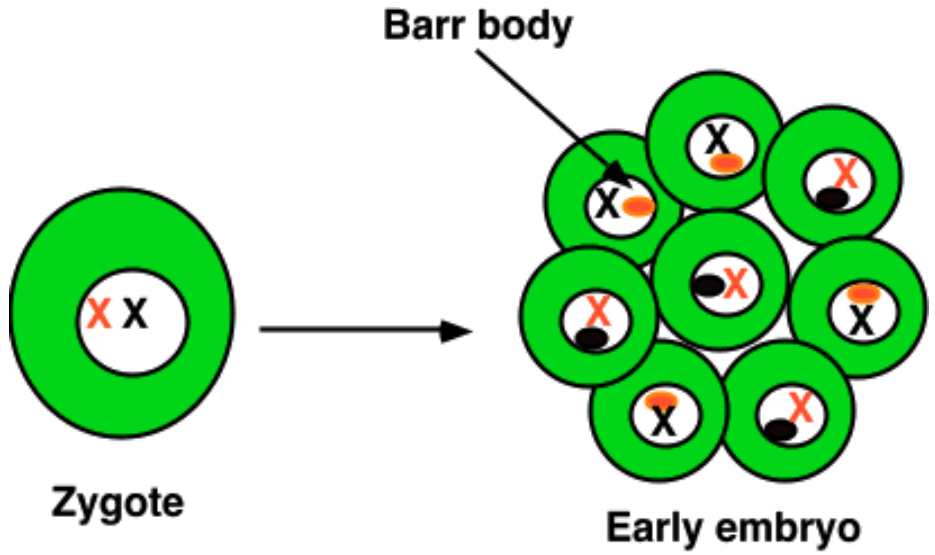
# Turner's Syndrome



# 4. Trisomy X

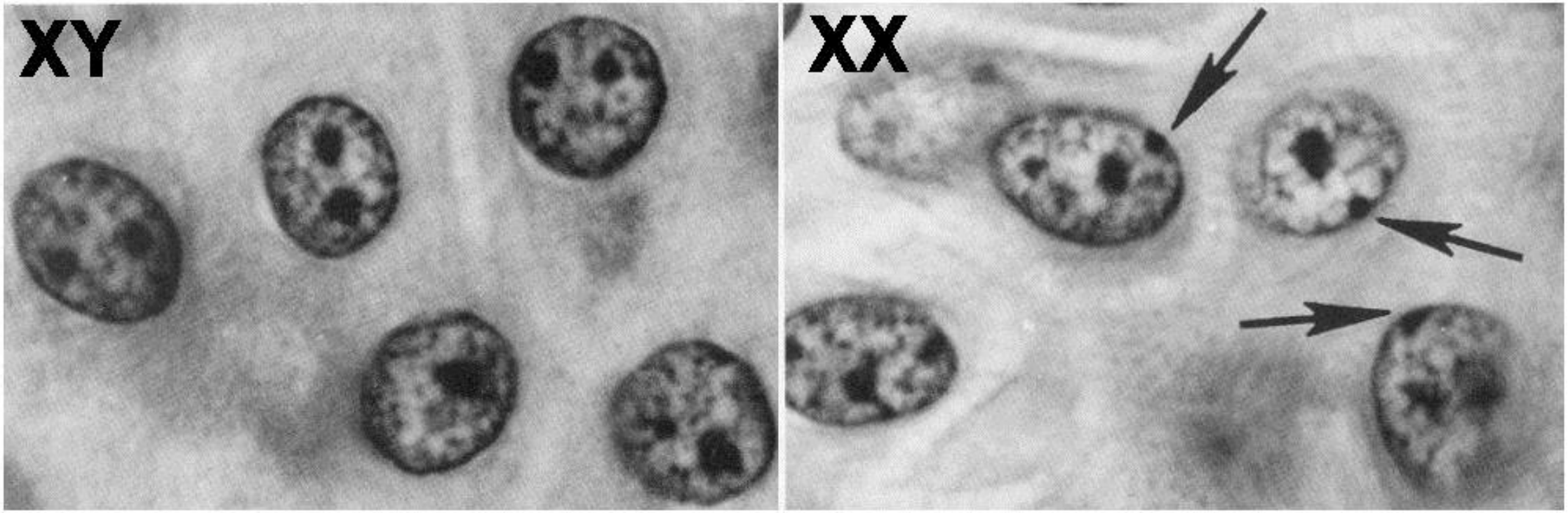
- XXX (female)
  - 1 in every 2000 live births
  - produces healthy females
  - WHY?
    - Only one X chromosome is activated in each cell
    - Others are inactive, called Barr bodies



# X inactivation in Female Mammals

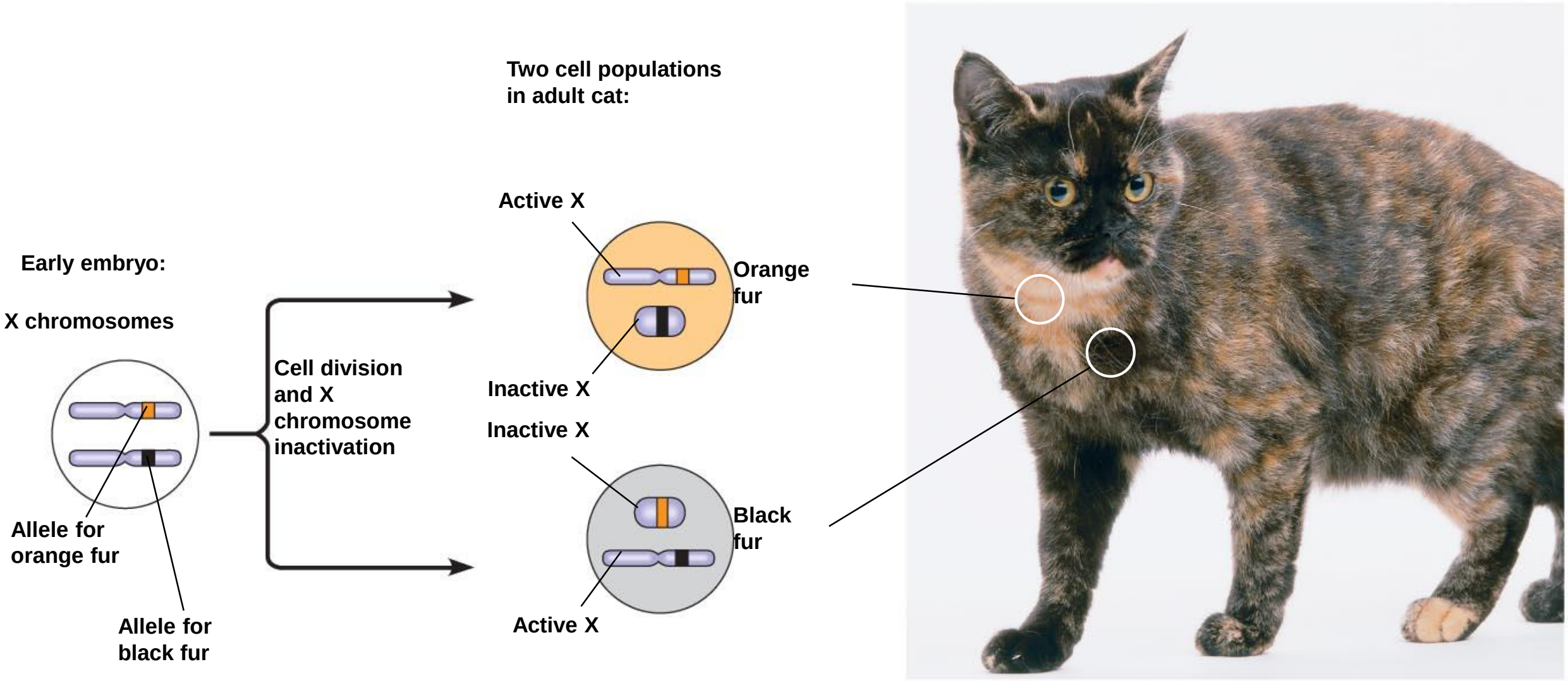
- In mammalian females, one of the two X chromosomes in each cell is randomly inactivated, known as a barr body, during embryonic development




HHMI X-Inactivation (short clip)

# X inactivation in Female Mammals

- If a female is heterozygous for a particular gene located on the X chromosome, she will be a mosaic for that character
  - Ex. Calico and tortoiseshell cats

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