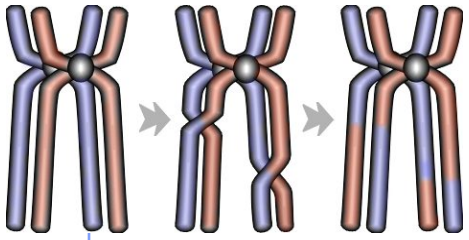
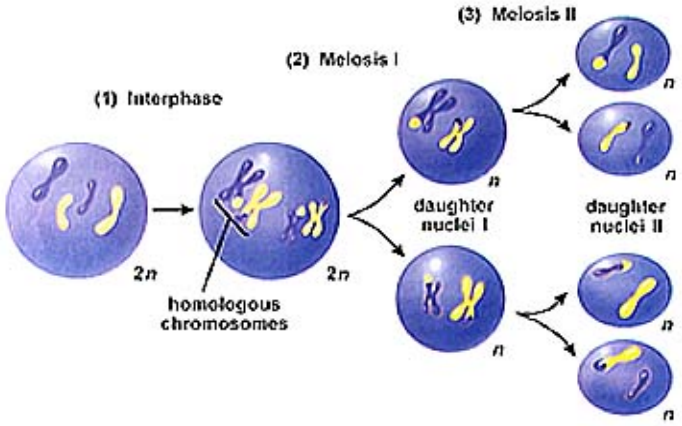
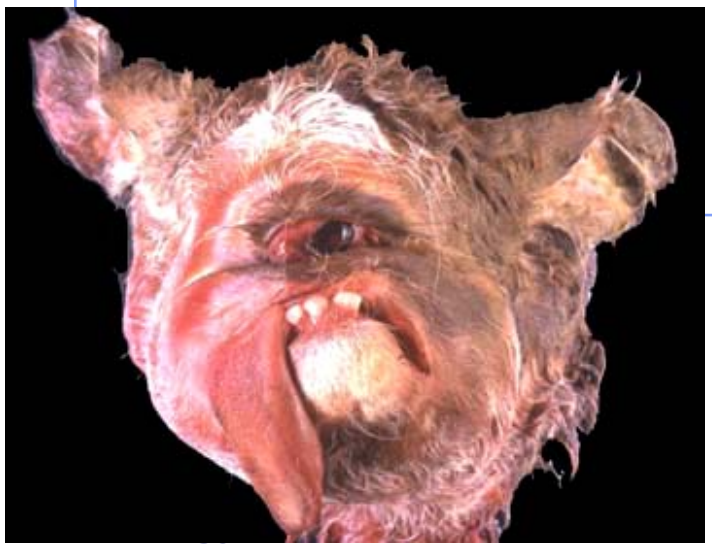




Errors of Meiosis
Chromosomal Abnormalities



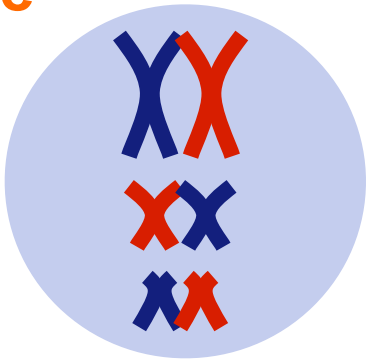
Calf with cyclopia (single eye in middle of forehead). In spite of this calf's resemblance to someone you may have once dated, the most likely explanation of sporadic cases like this (it was born at the WSVL) is probably a major chromosomal abnormality.

Causes of Chromosomal abnormalities

- **Incorrect number of chromosomes in cells can result from an erroneous process known as:**
  - **nondisjunction**
    - **when chromosomes don't separate properly during meiosis (failure during anaphase I or II)**

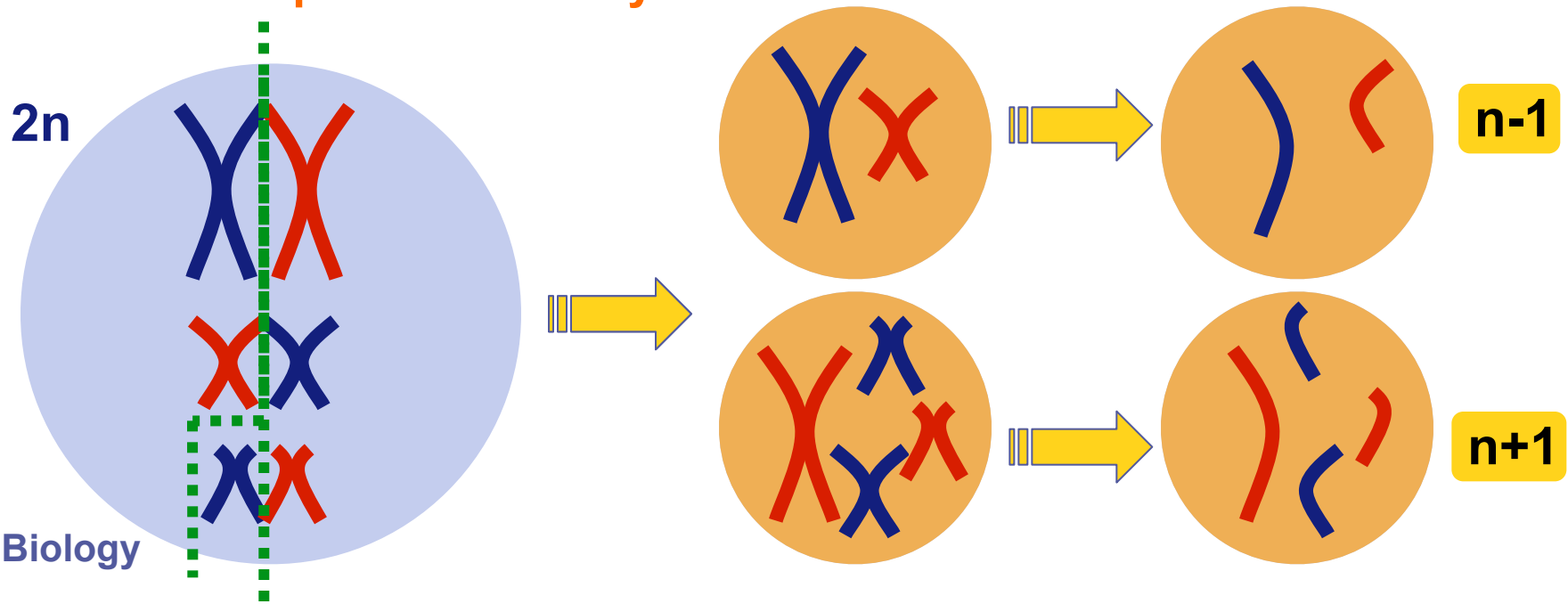
- **Incorrect structure of chromosomes leaders to gross (large-scale) mutations**
  - **breakage of chromosomes can lead to four major changes in chromosome structure**

1. deletion
2. duplication
3. inversion
4. translocation

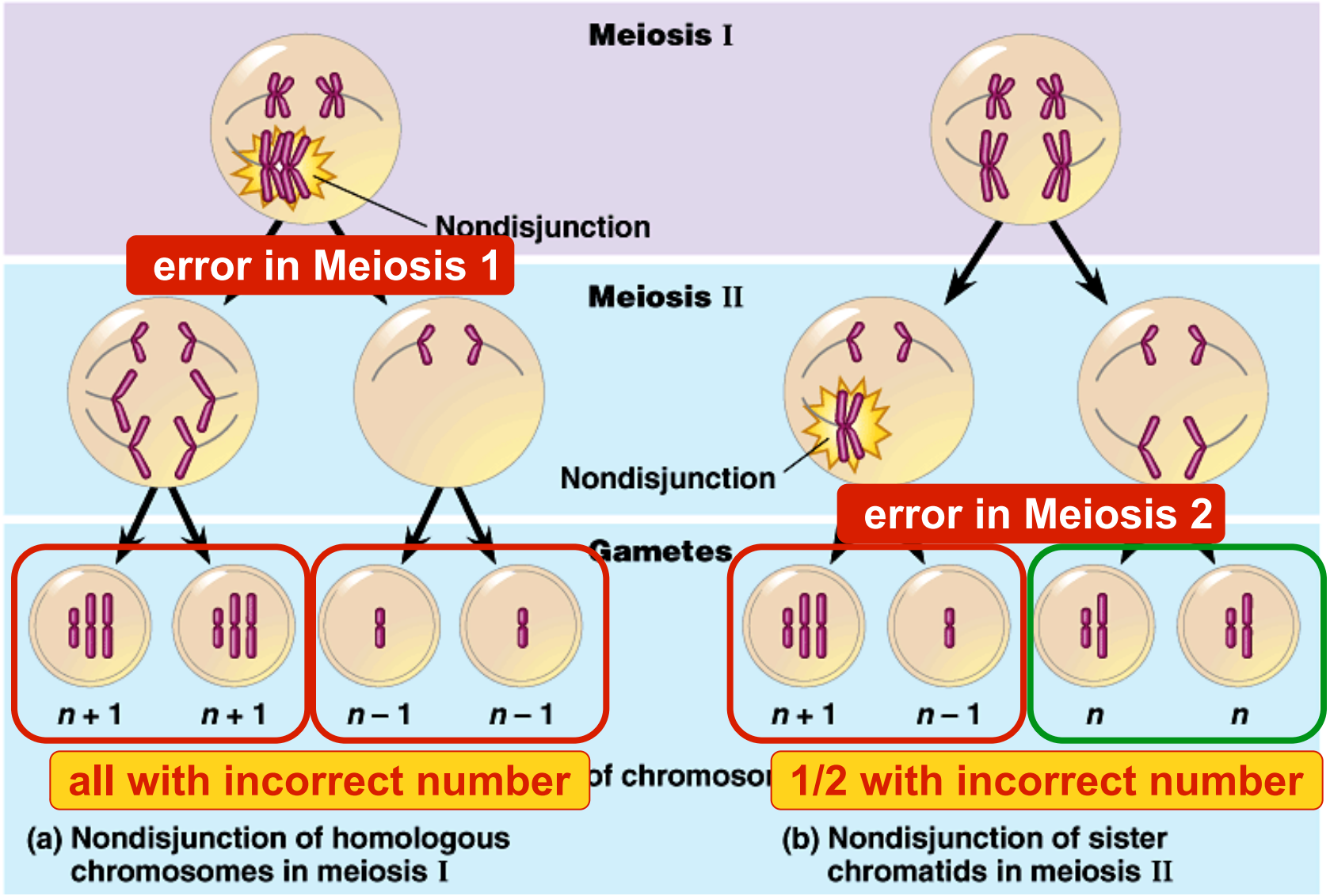


Nondisjunction during Meiosis & Gamete Formation

- Problems with attachment of chromosomes to the meiotic spindle or problems cleaving the proteins that hold homologous chromosomes and/or sister chromatids together can cause errors in daughter cells
  - homologous chromosomes do not separate properly during Meiosis 1
  - sister chromatids fail to separate during Meiosis 2
    - End up with too many or too few chromosomes

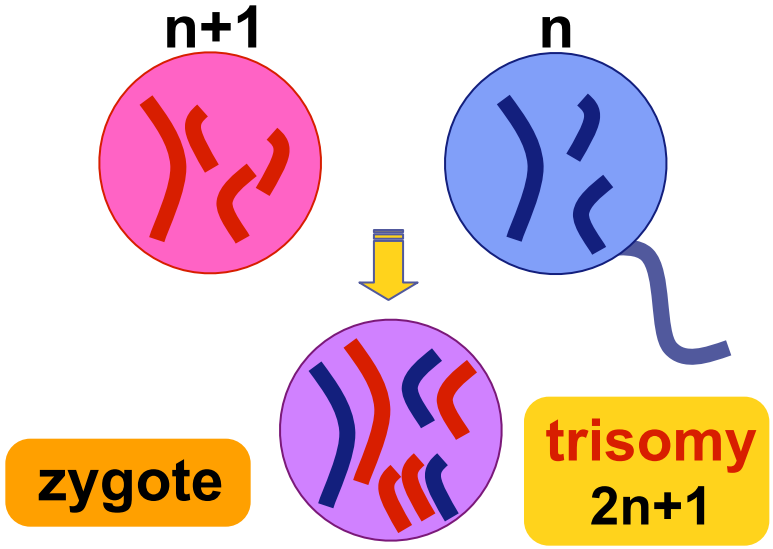


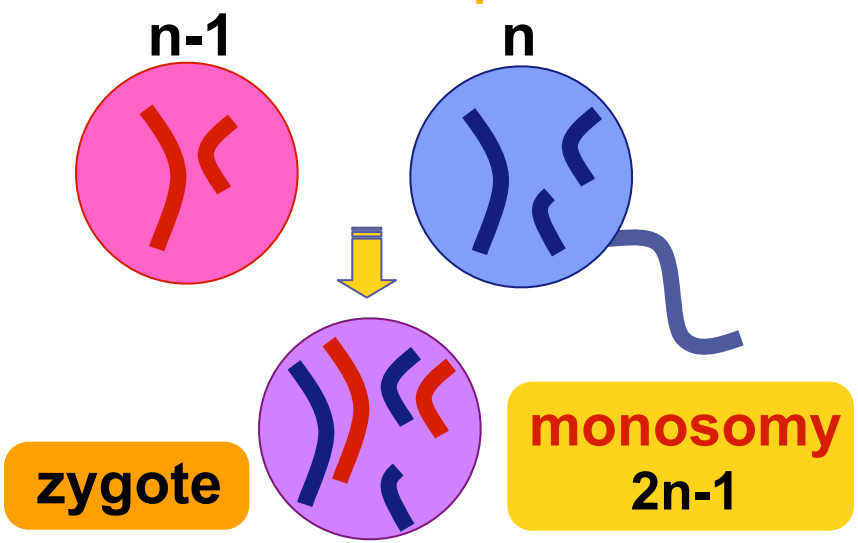
Nondisjunction causes an alteration of chromosome number in the gametes.



Fertilization of gamete after nondisjunction

- Zygote now too has erroneous number of chromosomes, a condition called aneuploidy
  - Leads to abnormal dosage of gene product
    - Trisomy: cells have 3 copies of a certain chromosome
    - Monosomy: cells have only 1 copy of a certain chromosome
- Polyploidy = when organisms have more than two complete chromosomal sets in all somatic cells.
  - Ex: Triploidy (3n) & tetraploidy (4n)
    - Common in plants
      - Ex: bananas are triploids and wheat is hexaploid



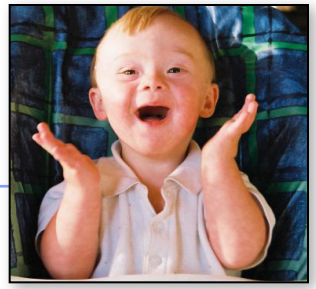


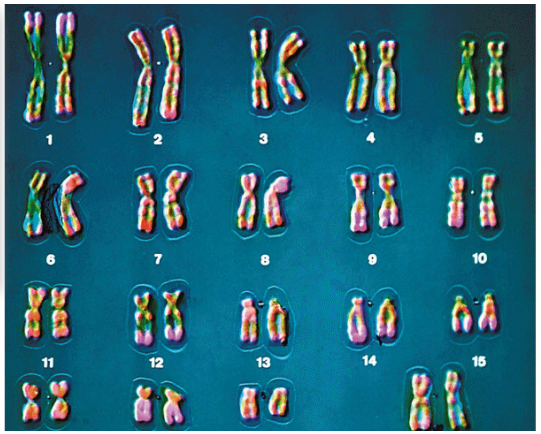
Human gross chromosome disorders

- High frequency in humans
  - most embryos are spontaneously aborted
  - alterations are often too disastrous - gene dosage altered greatly
  - developmental problems result from biochemical imbalances and abnormal cellular functioning
    - imbalance in key proteins
      - Ex: imbalances in regulatory molecules
        - hormones
        - transcription factors

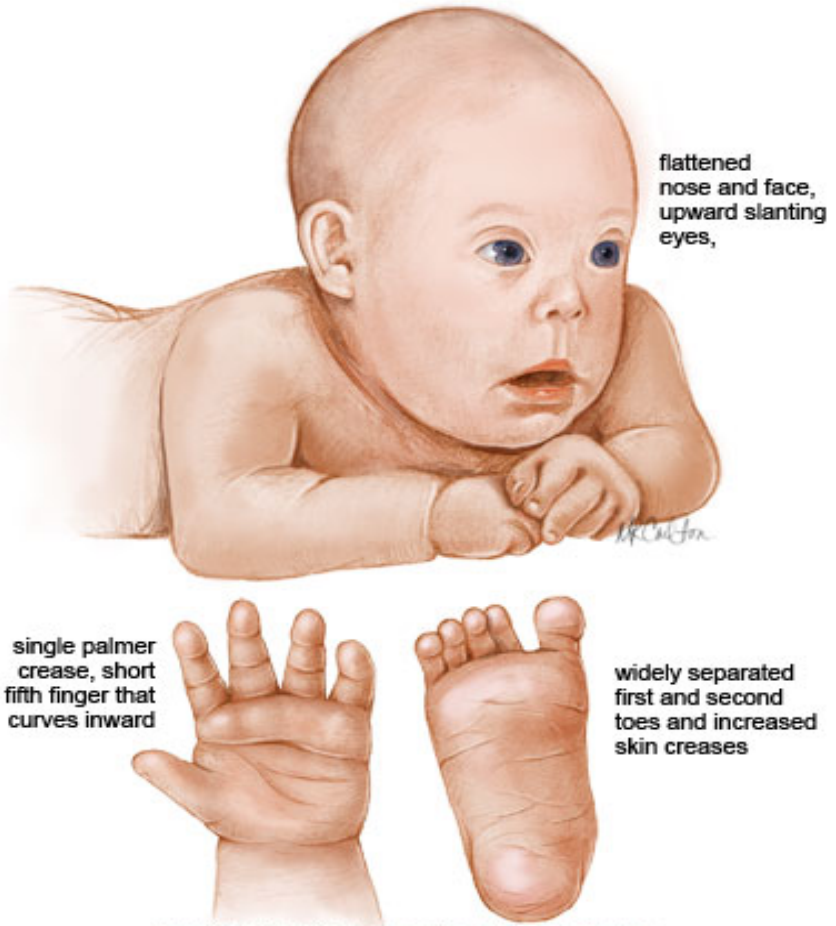
- Certain conditions are tolerated though
  - If abnormal protein concentrations upset the balance less = survivable
    - But baby still develops a characteristic set of symptoms = syndrome

Down syndrome



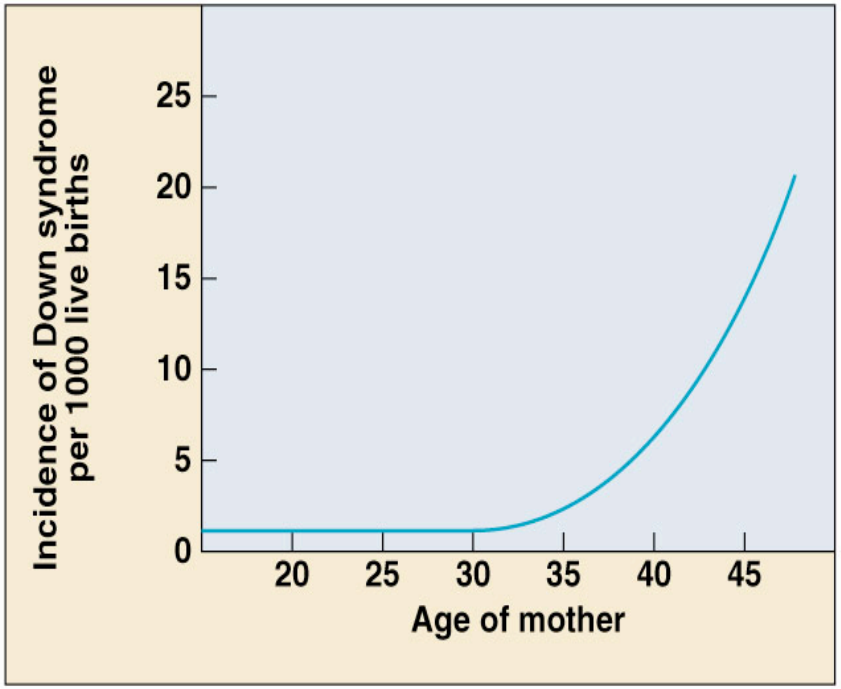


- Trisomy 21
  - 3 copies of chromosome 21
  - 1 in 700 children born in U.S.
- Chromosome 21 is the smallest human chromosome
  - but still severe effects
    - Short neck and flat face, upwar slanting eyes, low muscle tone and a single crease across the palm of the hand.
    - Congenital heart defects accompany Down syndrome in about 40% of the cases.
    - Vision and hearing problems are also common.
- Frequency of Down syndrome correlates with the age of the mother



Down syndrome & age of mother

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



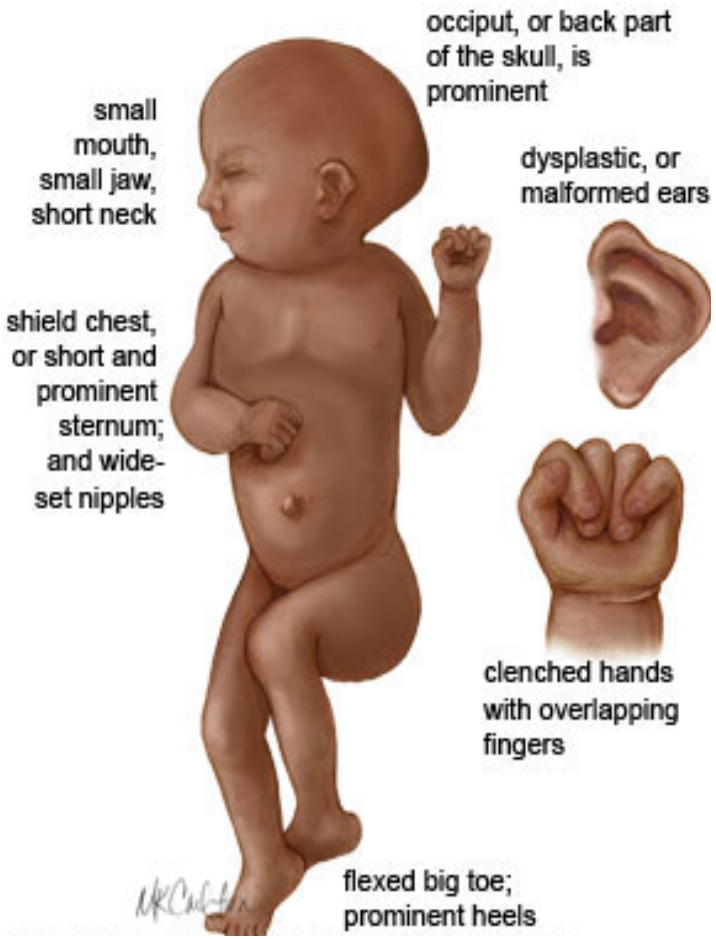
Rate of miscarriage due to amniocentesis:

- **1970s data**
  0.5%, or 1 in 200 pregnancies
- **2006 data**
  <0.1%, or 1 in 1600 pregnancies

Edward syndrome

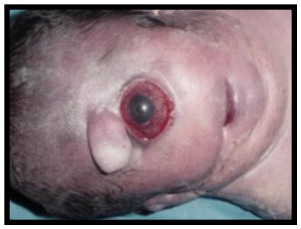
Trisomy 18 is a relatively common syndrome affecting approximately 1 out of 3,000 live births

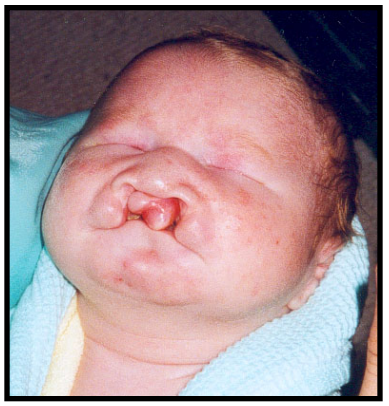
- Affecting girls more than three times as often as boys.
- The presence of an extra number 18 chromosome leads to multiple abnormalities.
- Many of these abnormalities make it hard for infants to live longer than a few months.
  - microcephaly, a high forehead, profound psycho-motor retardation, and serious heart malformations including ventral atrial septal defects and patent ductus arteriosus, a persistent opening between the heart chambers that prevents efficient blood flow.
- Life expectancy is typically very short, with 90% of children dying in the first year.

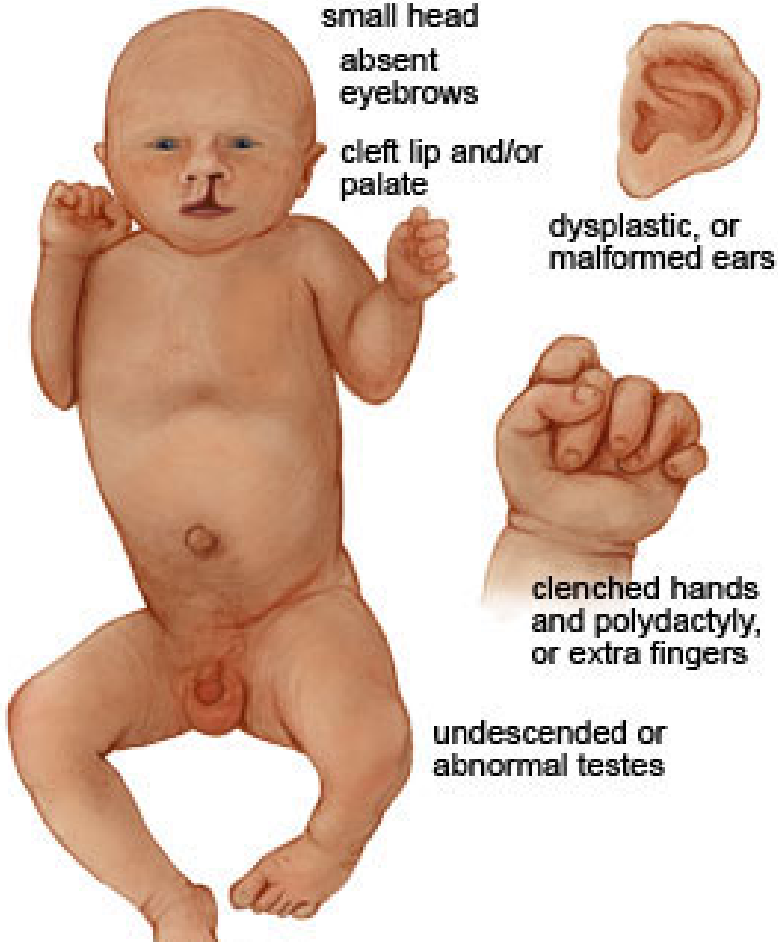


Patau syndrome

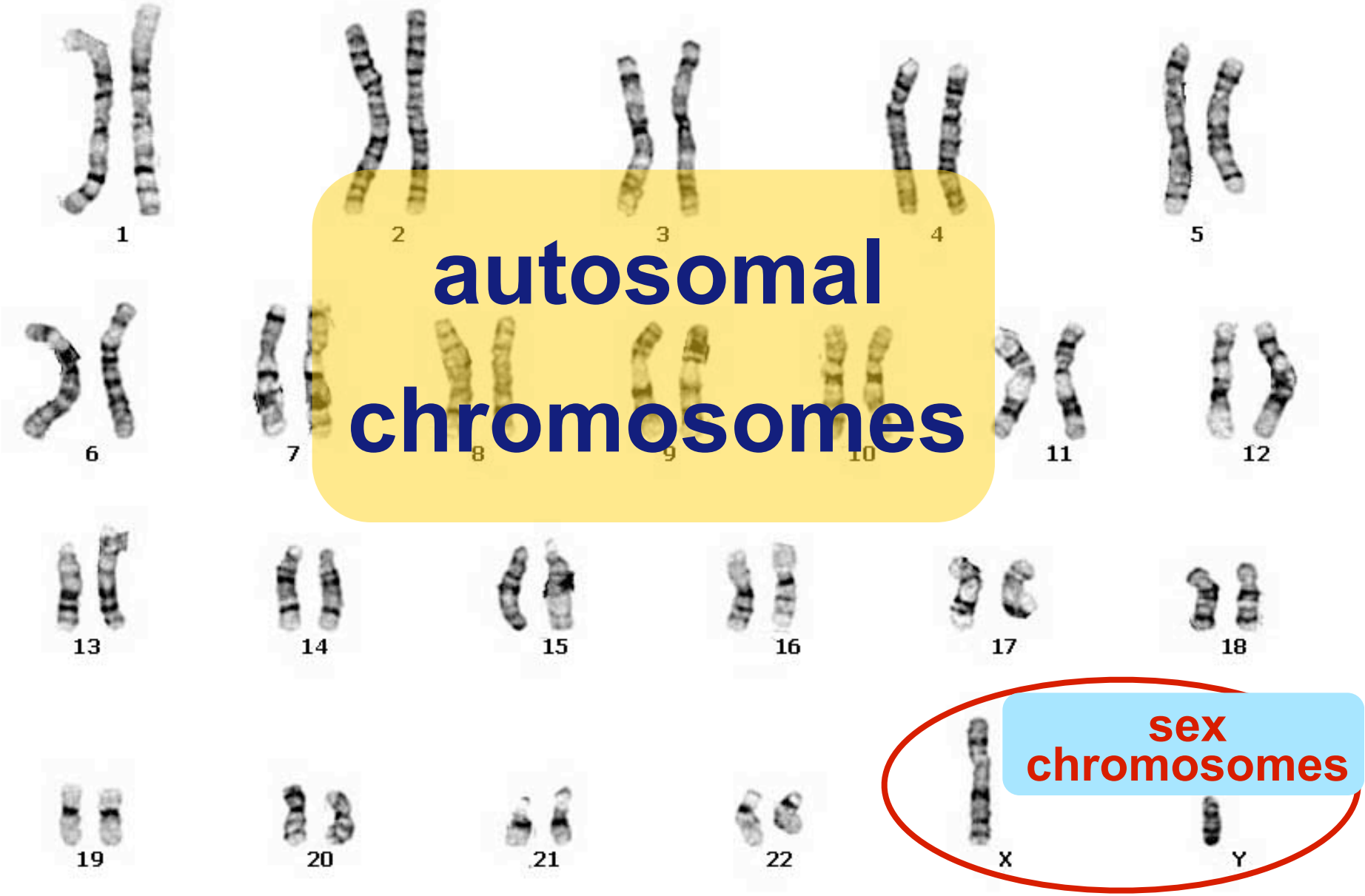
- Trisomy 13 occurs in about 1 out of every 5,000 live births.
  - More than 80% of children with trisomy 13 die in the first month.
    - Trisomy 13 is associated with multiple abnormalities, including defects of the brain that lead to seizures, apnea, deafness, retardation, and eye abnormalities.
    - Most infants have a cleft lip and cleft palate, and low-set ears.
    - Congenital heart disease is present in approximately 80% of affected infants.
    - Hernias and genital abnormalities are common.







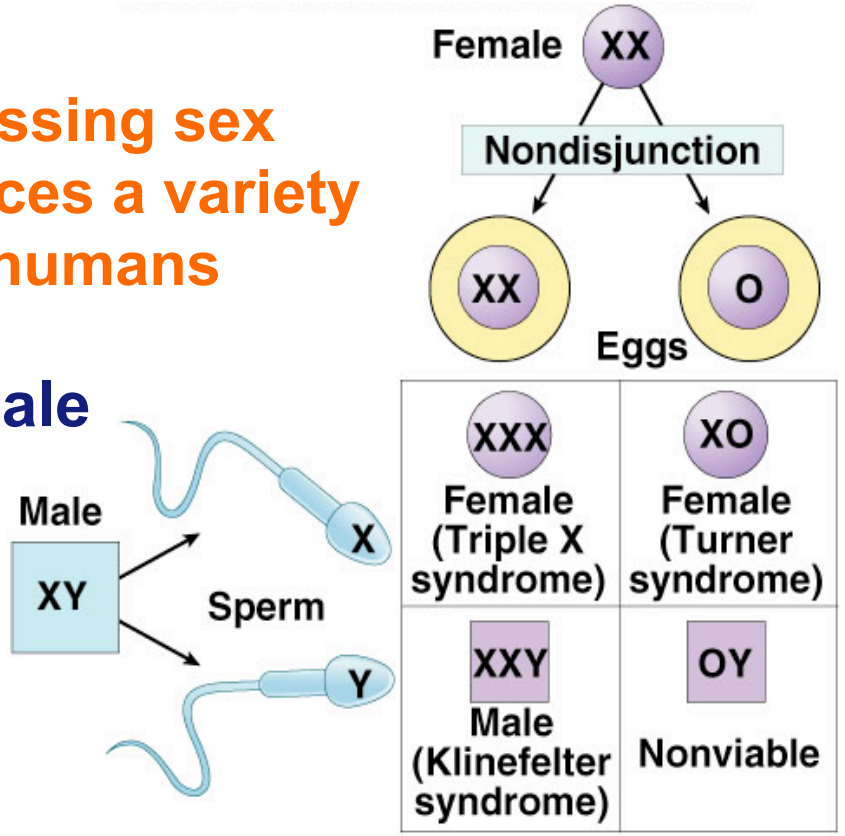
Classes of human chromosomes



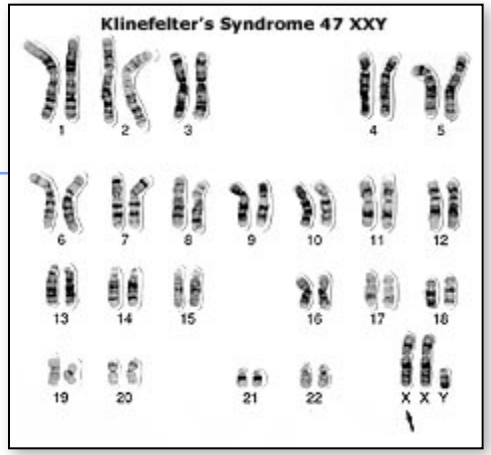
Sex chromosomes abnormalities

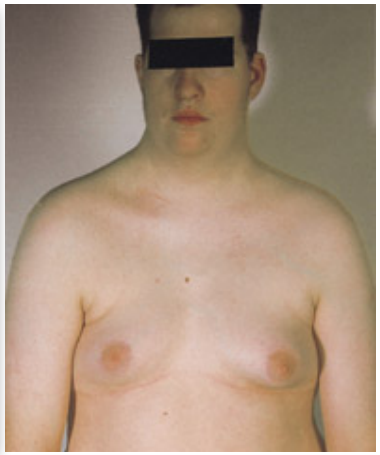
- Human development is more tolerant of wrong numbers in sex chromosome than autosomes
  - But having an extra or missing sex chromosomes still produces a variety of distinct syndromes in humans

- XXY = Klinefelter's syndrome male
- XXX = Trisomy X female
- XYY = Jacob's syndrome male
- XO = Turner syndrome female

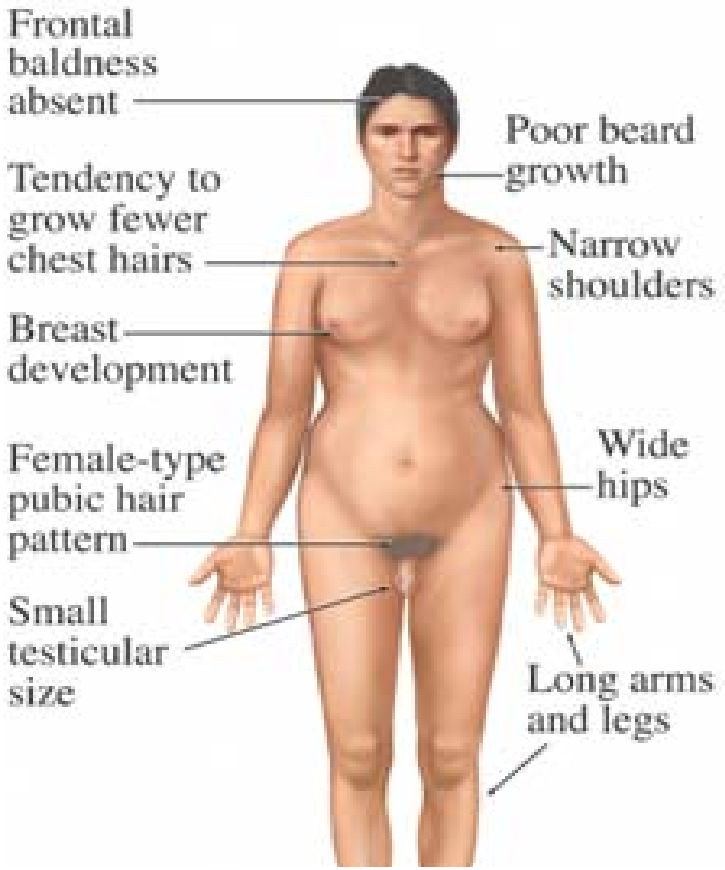


Klinefelter's syndrome



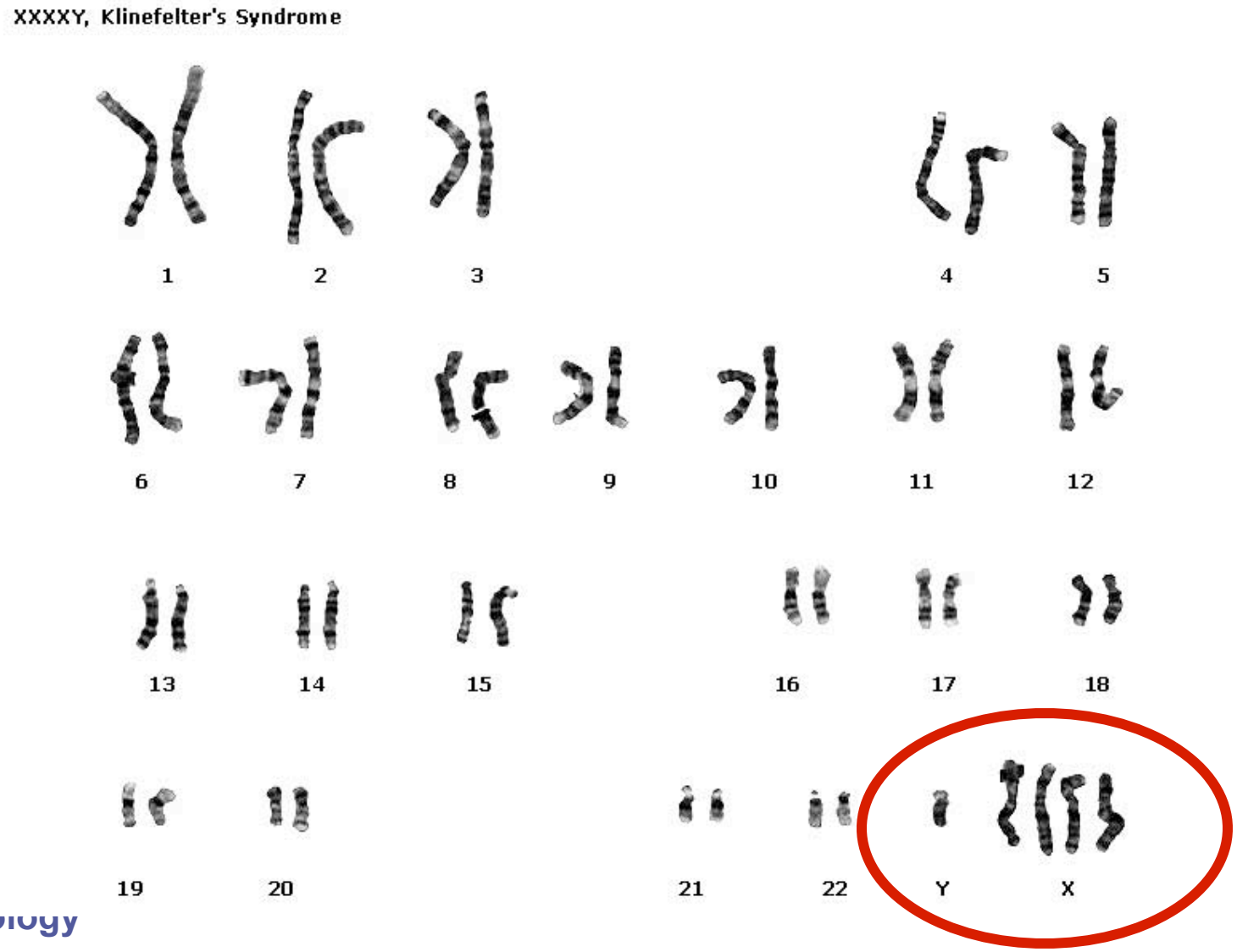


- **XXY male**
  - one in every 2000 live births
  - have male sex organs, but are sterile
  - feminine characteristics
    - some breast development
    - lack of facial hair
  - tall
  - normal intelligence

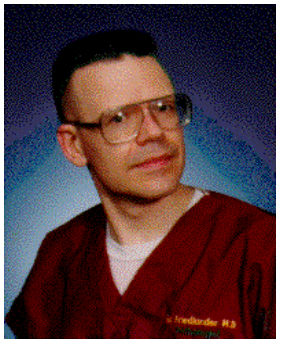


Klinefelter's syndrome

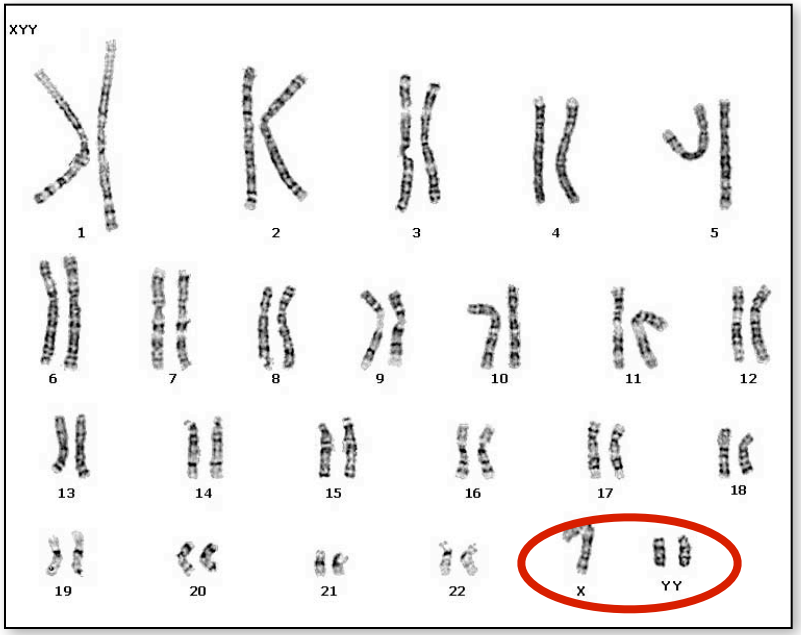
(extra X chromosomes often supercoil into barr bodies)



Jacob's syndrome male

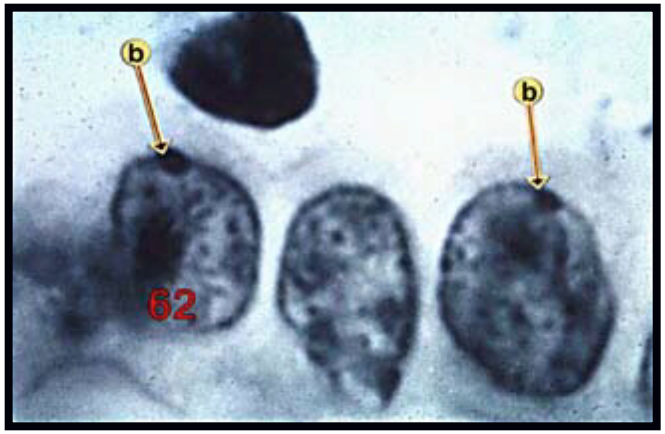


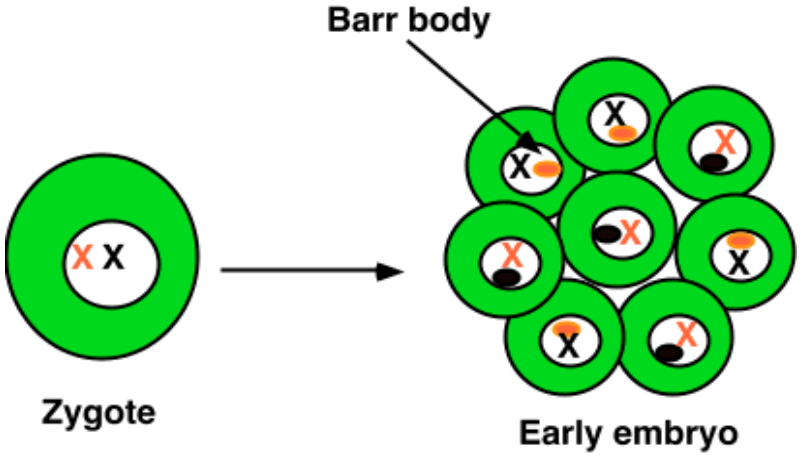
- **XYY Males**
  - 1 in 1000 live male births
  - extra Y chromosome
    - slightly taller than average
    - more active
    - more acne
    - normal intelligence, slight learning disabilities
    - delayed emotional maturity
    - normal sexual development



Trisomy X

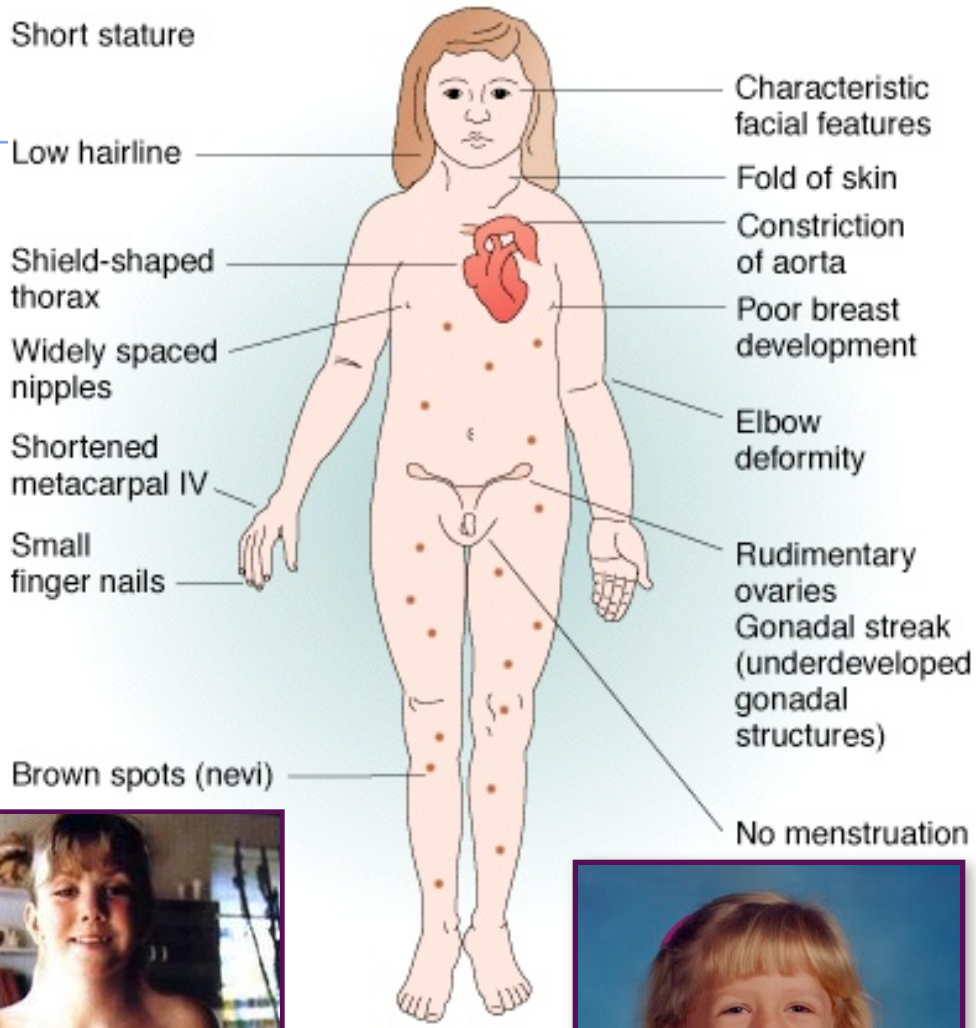
- XXX
  - 1 in every 2000 live births
  - produces healthy females
    - Some wide spread eyes
    - Poor muscle tone
    - Small chin
    - May have some developmental delays
  - Why?
    - Barr bodies
      - all but one X chromosome is inactivated

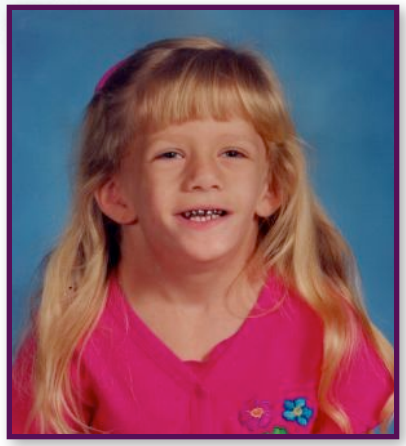




Turner syndrome

- **Monosomy X or X0**
  - 1 in every 5000 births
  - varied degree of effects
    - Absent or incomplete development at puberty, including sparse pubic hair and small breasts
    - Broad, flat chest shaped like a shield
    - Drooping eyelids
    - Dry eyes
    - Infertility
    - No periods (absent menstruation)
    - Short height
  - webbed neck
  - short stature
  - sterile

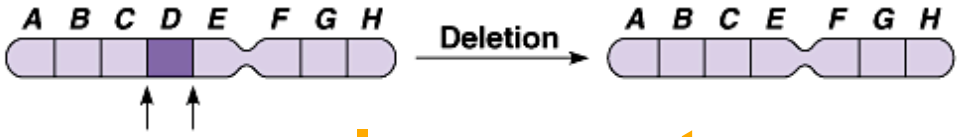




Large-scale mutations - *Changes in chromosome structure involving one or more genes/large sections of DNA*

Often these are errors made during **crossing over** during gamete formation

- **deletion**
  - loss of a chromosomal segment (unequal crossing over of DNA between non-sister chromatids)



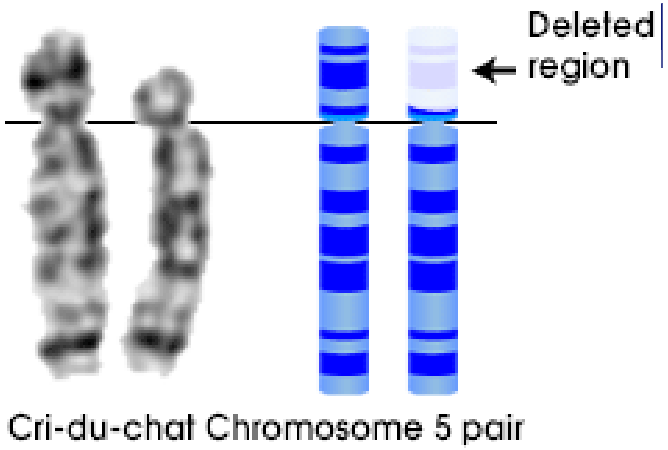
- **duplication**
  - repeat of a segment (unequal crossing over of DNA between non-sister chromatids)

- **inversion**
  - reverses the orientation of a segment of a chromosome

- **translocation**
  - move segment from one chromosome to another type of chromosomes

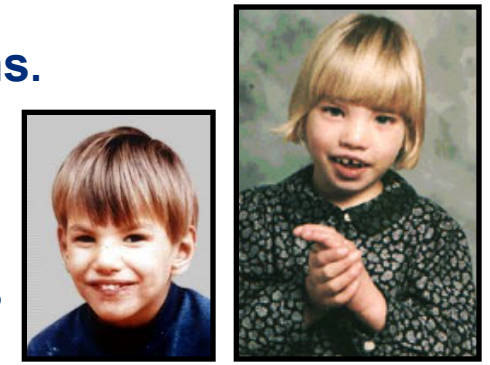
iology

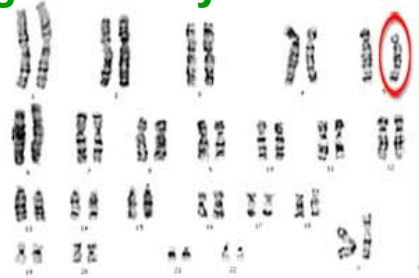
Cri-du-Chat Syndrome

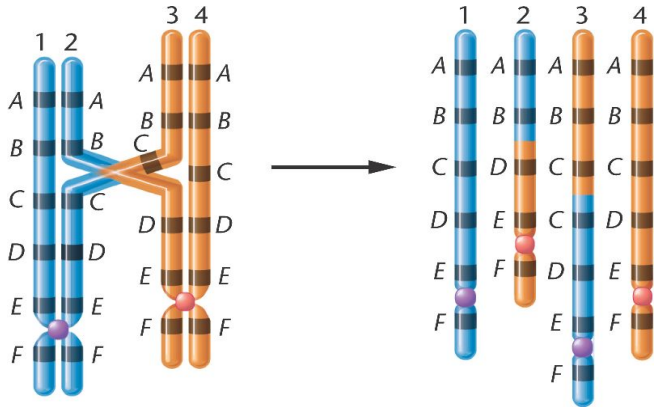


Cri-du-chat Chromosome 5 pair

- Caused by a chromosomal deletion.
  - Deletions occurs during the formation of an egg or sperm
  - Caused by unequal recombination/crossing over during meiosis, resulting in missing chromatid DNA
- Babies are small at birth & may have respiratory problems.
  - Often, the larynx doesn't develop correctly, which causes the signature cat-like cry.
- People may have a small head (microcephaly), an unusually round face, a small chin, widely set eyes, folds of skin over their eyes, and a small bridge of the nose.
- Several problems occur inside the body, as well.
  - May have heart defects, muscular or skeletal problems, hearing or sight problems, or poor muscle tone.
  - Difficulty walking and talking correctly.
  - Behavior problems (such as hyperactivity or aggression)
  - Severe mental retardation.







Unequal Crossing Over

Don’t hide…

Ask Questions*!!*