L3: Chromosomal Abnormalities

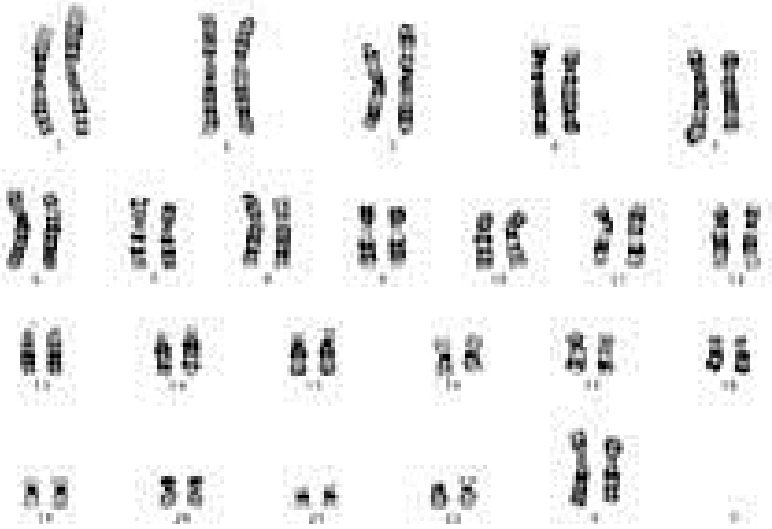
Medical Genetics

Stage :3

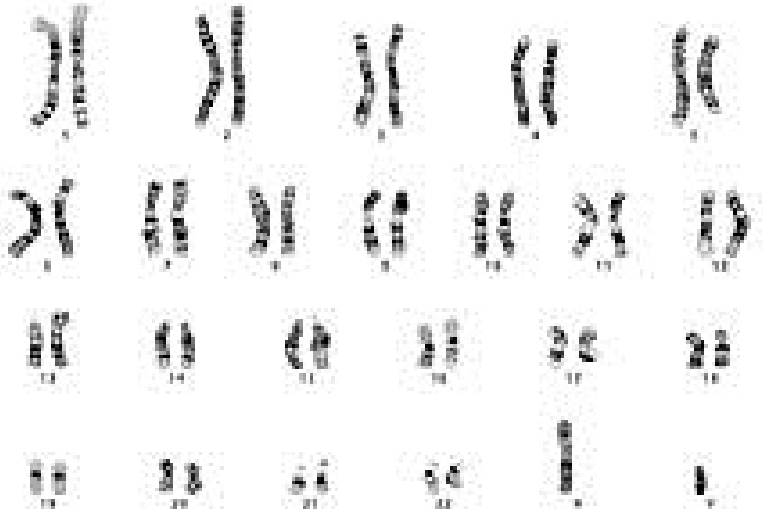
By:

Dr. NOOR MAJID

Let's See some Normal Karyotypes!



Female



Male

What is a chromosomal mutation?

- A mutation that involves the
  - ***Addition***
  - ***Deletion***
  - ***Translocation***
  - ***Non-disjunction***

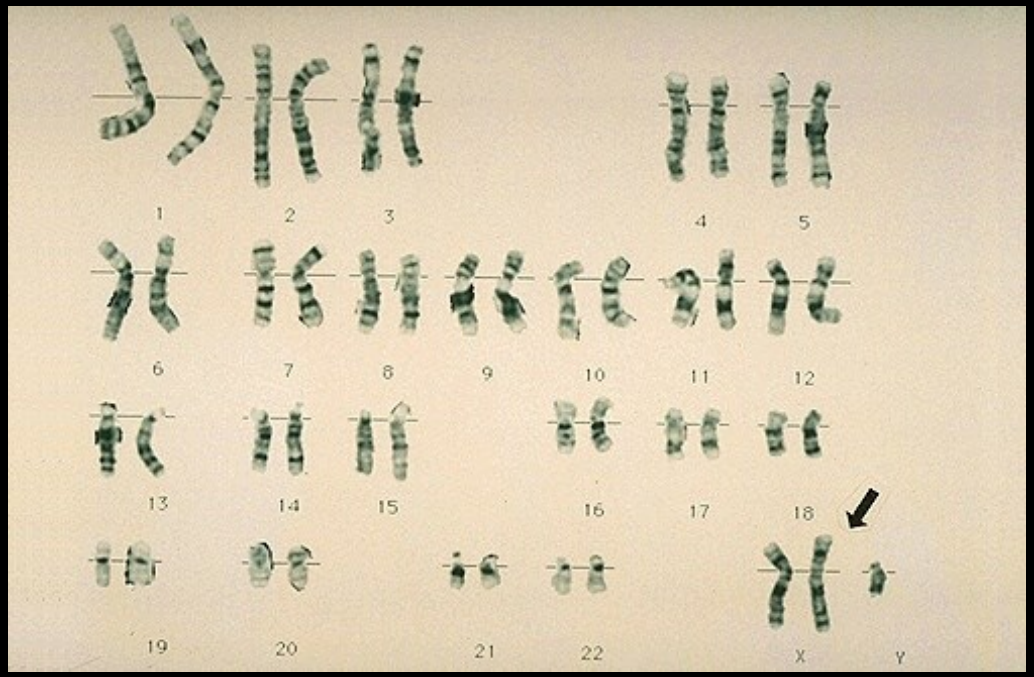
Of a piece or a whole *chromosomes*.

MUTATIONS

What type of mutation involves the presence of extra chromosomes or the deletion of chromosomes?

Nondisjunction!!!!!

Trisomy: any extra chromosome

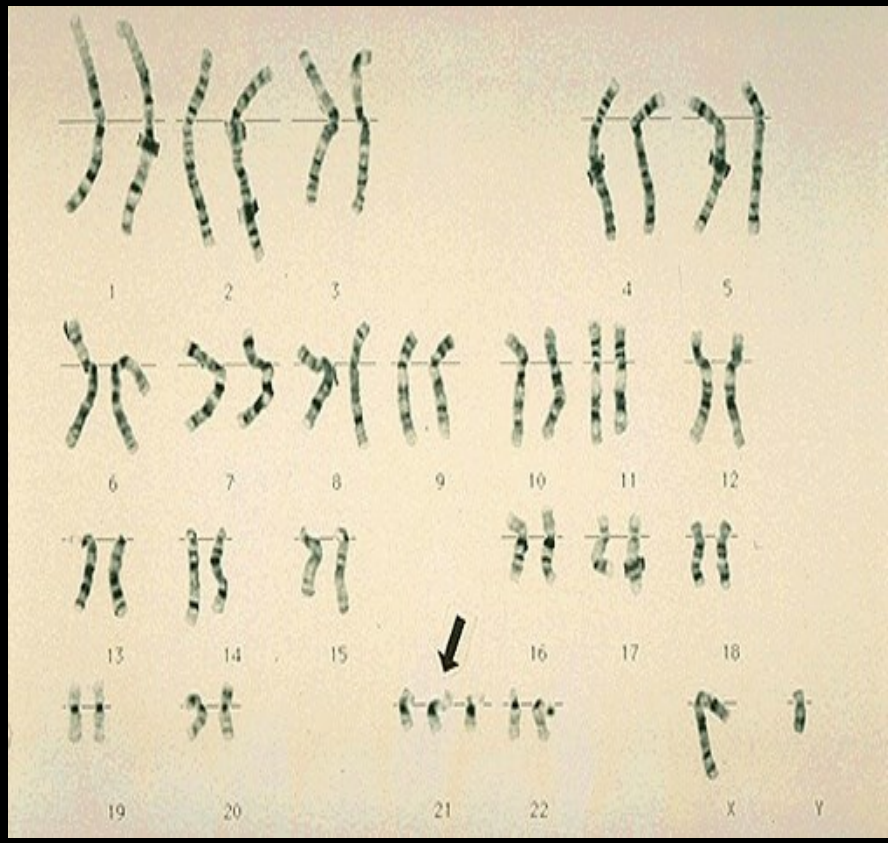


In trisomy cases, you end up with *47* chromosomes instead of *46*

Klinefelter's syndrome has the genotype XXY

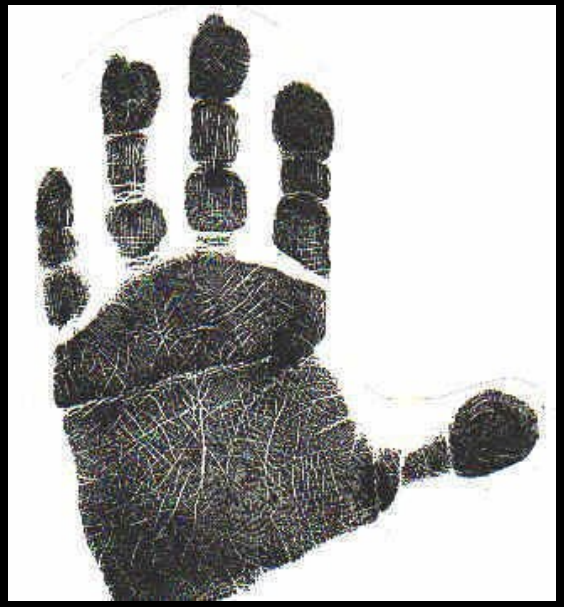
An Example of Trisomy

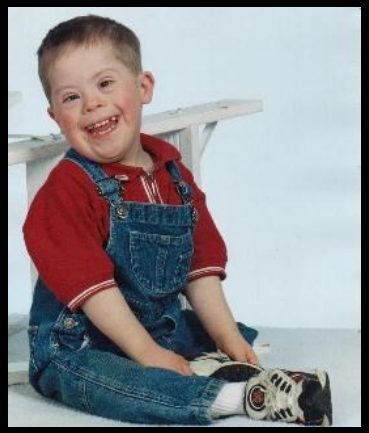
- Down's Syndrome
  - A.k.a- *trisomy 21*
  - Shorthand:
    - *47, XY or XX, +21*
    - *XY is male*
    - *XX is female*
  - Survival rate is very *high* for this non-disjunction!



What is It?????

- The non-disjunction rate increases with **Mom's age**
- Trisomy 21 is one of the most common causes of mental retardation (IQ between ***25-74***).
  - An average person has an IQ between ***90-110***.
- This results in a number of characteristic features:
  - Short stature, broad hands, stubby fingers and toes, a ***wide rounded*** **face**, a large protruding ***tongue*** that makes speech difficult. Individuals with this syndrome have a high incidence of respiratory infections, heart defects, and leukemia.
- Incidence:
  - 1/750 live births.
  - Mothers in their early twenties have a risk of ***1/1,500***.
  - Women over 35 have a risk factor of 1/70, which jumps to ***1/25*** for women 45 and over.



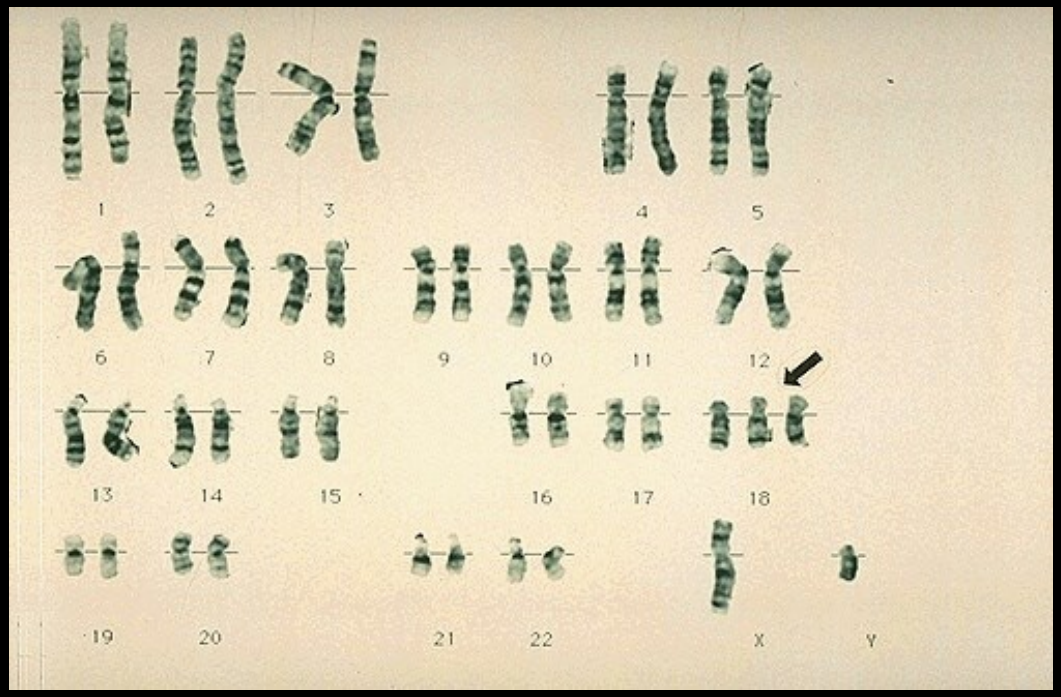


Edward's Syndrome

- This karyotype demonstrates *trisomy 18*
- Shorthand: (47, XY, +18).
- If the genotype is XY, what is the gender of this individual?
  - male

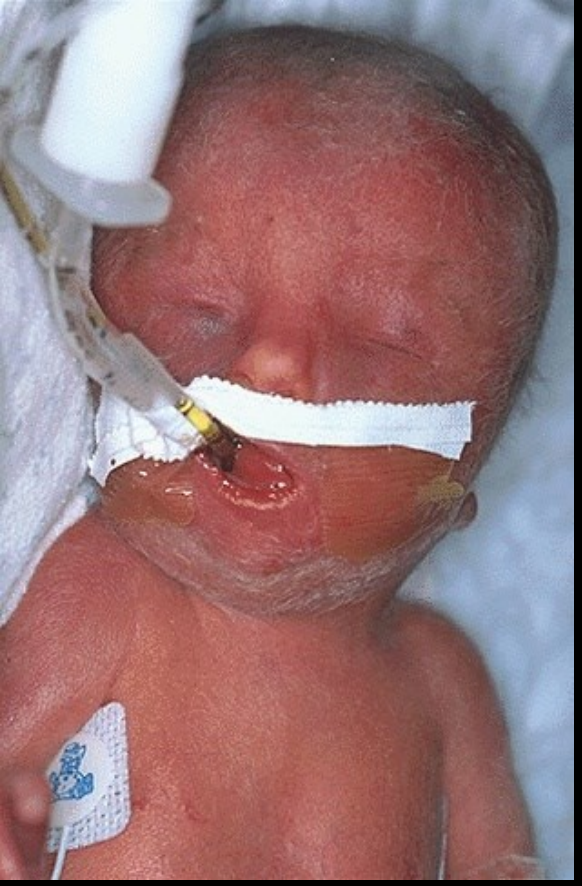
- Incidence is only *1 in 8000* live births

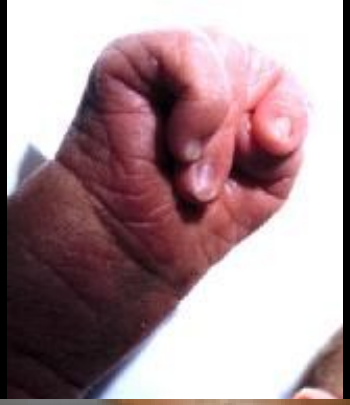
- It is uncommon for fetuses with this condition to survive

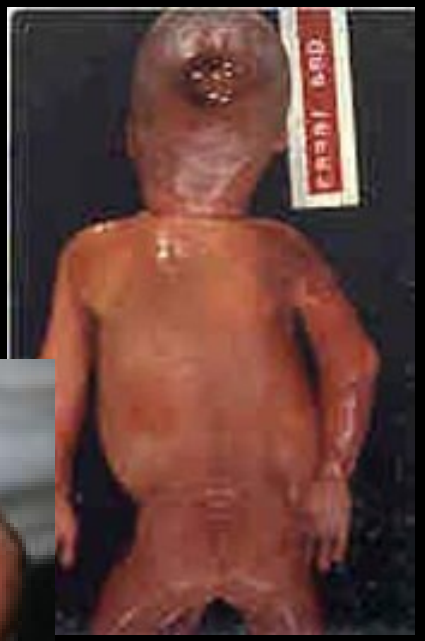


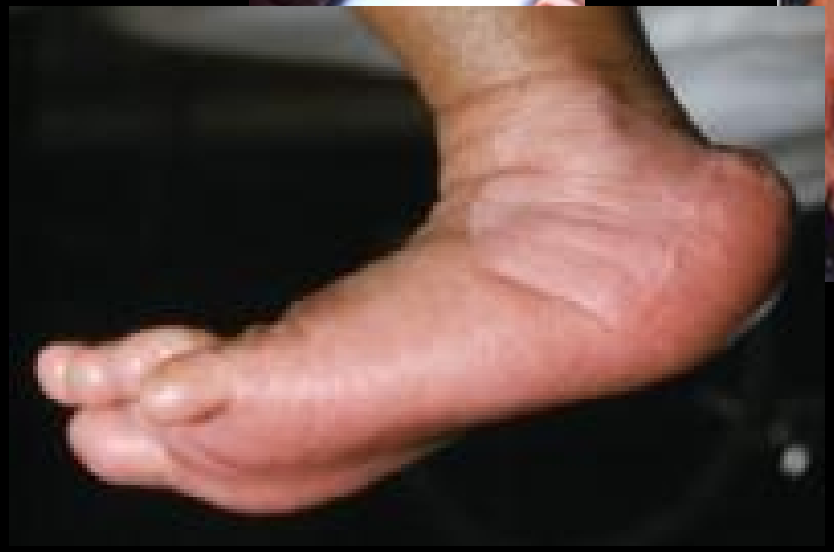
What can a survivor expect?

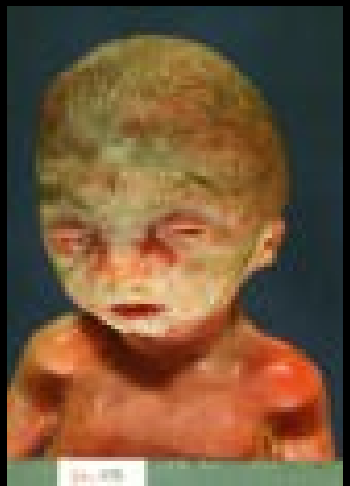
- 30% of these children *die* within the *first* month and only 10% survive one year.
- There is *severe mental retardation*.
- Other characteristics:
  - elongated skull, a very narrow pelvis, rocker bottom feet.
  - the ears are often low set and the mouth and teeth are small.
  - nearly all babies born with this condition die in early infancy.

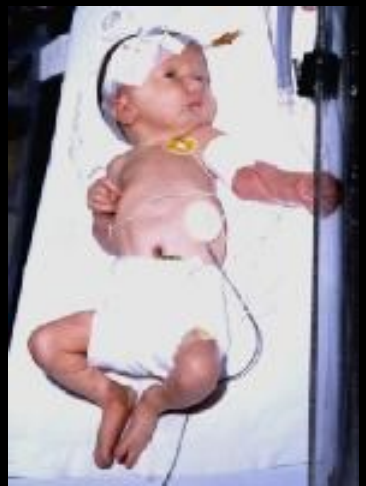






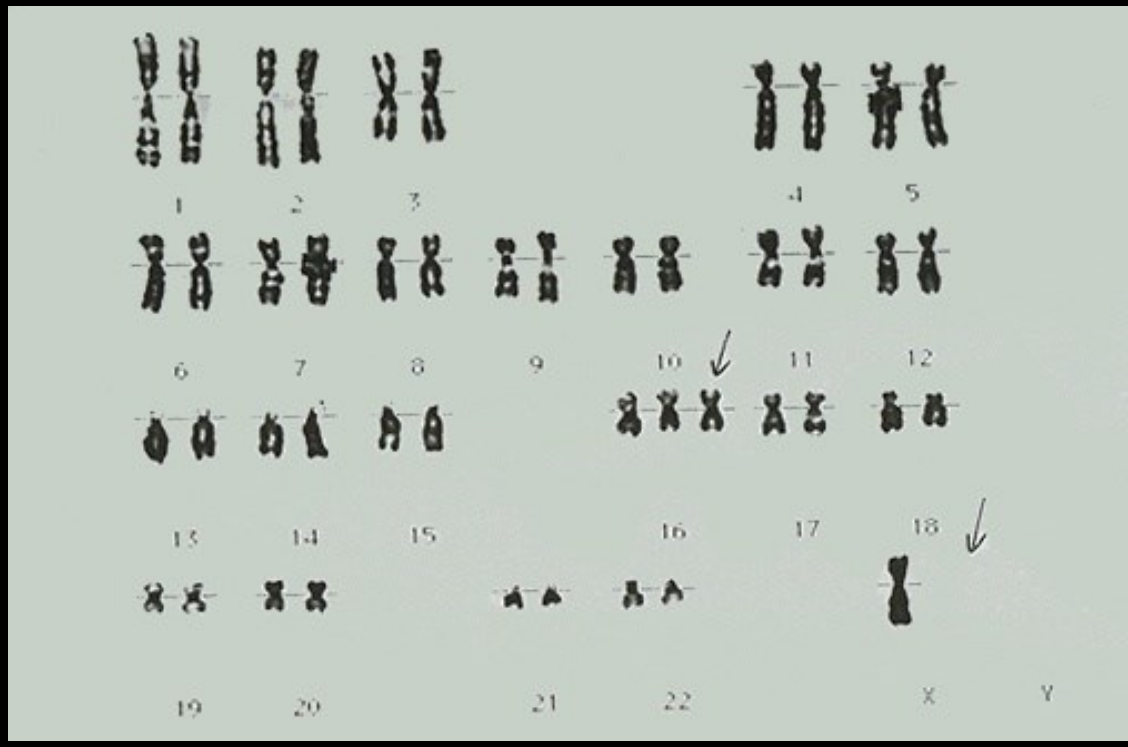






Other Trisomies of Interest:

- Here is an example of trisomy 16.
- This is the most common chromosomal abnormality, but the fetuses ***NEVER*** survive past the first trimester

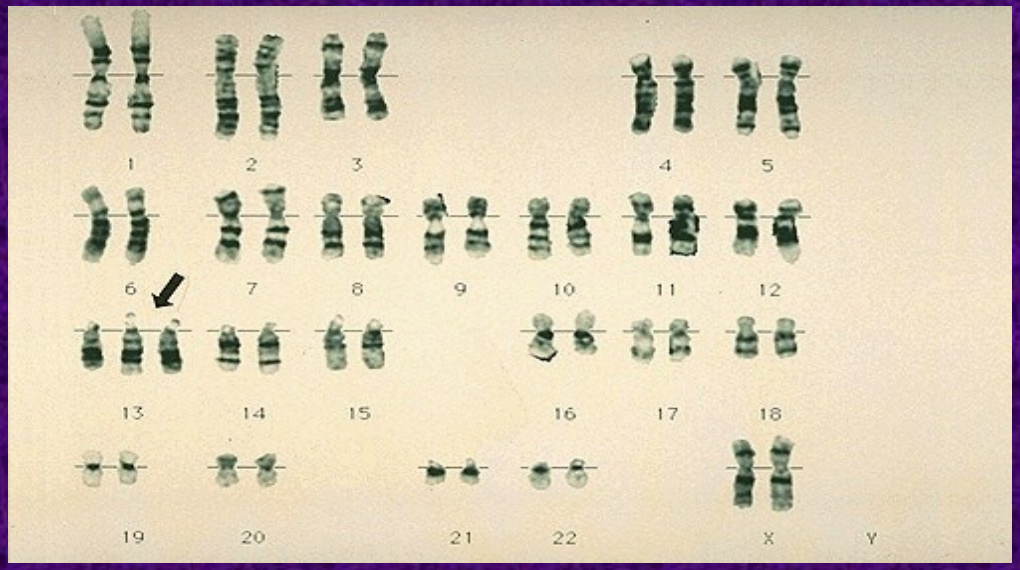


Many first trimester fetuses are lost in this fashion (many are "***silent***" abortions).

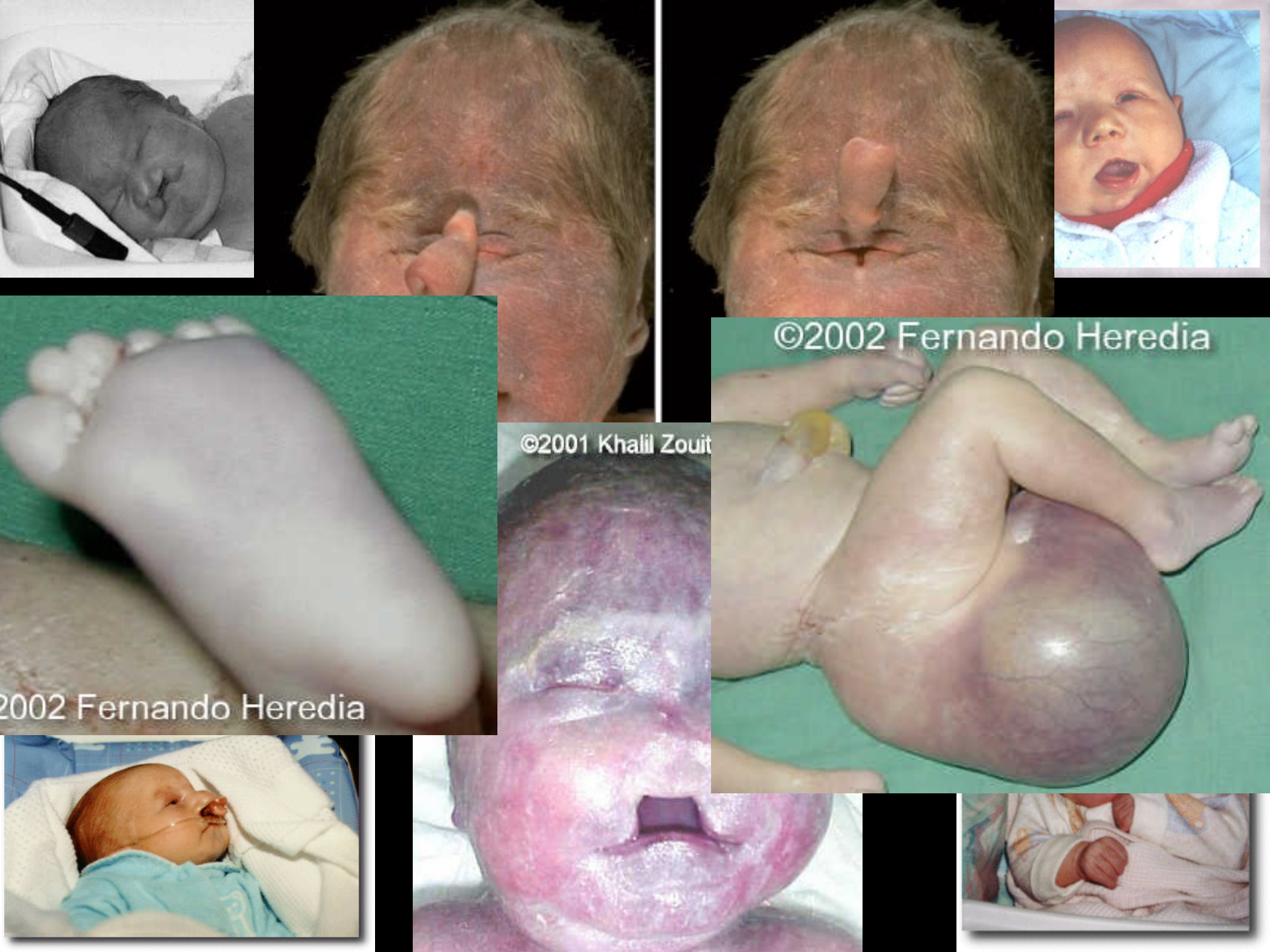
Trisomy 13: Patau Syndrome

- Shorthand: (*47, XX, +13*).
- Occurrence:
  - Only *1 in 15,000* live births. (most aborted naturally)
- Survival:
  - Forty five percent die within the first month
  - *90%* by six months
  - Less than 5% reach *3* years.

Why is death so frequent?



There is severely *abnormal cerebral functions* and virtually always leads to death in early infancy. This baby has: very pronounced ***clefts of the lip*** and palate, broad nose, small cranium, ***polydactyl***, deafness, and nonfunctional eyes. Heart defects and severe mental retardation are also part of the clinical picture.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Trisomy would feel left out without its partner!

Only have 1 X!
This is Turner's syndrome

Monosomy- *having one fewer chromosome in each body cell.*

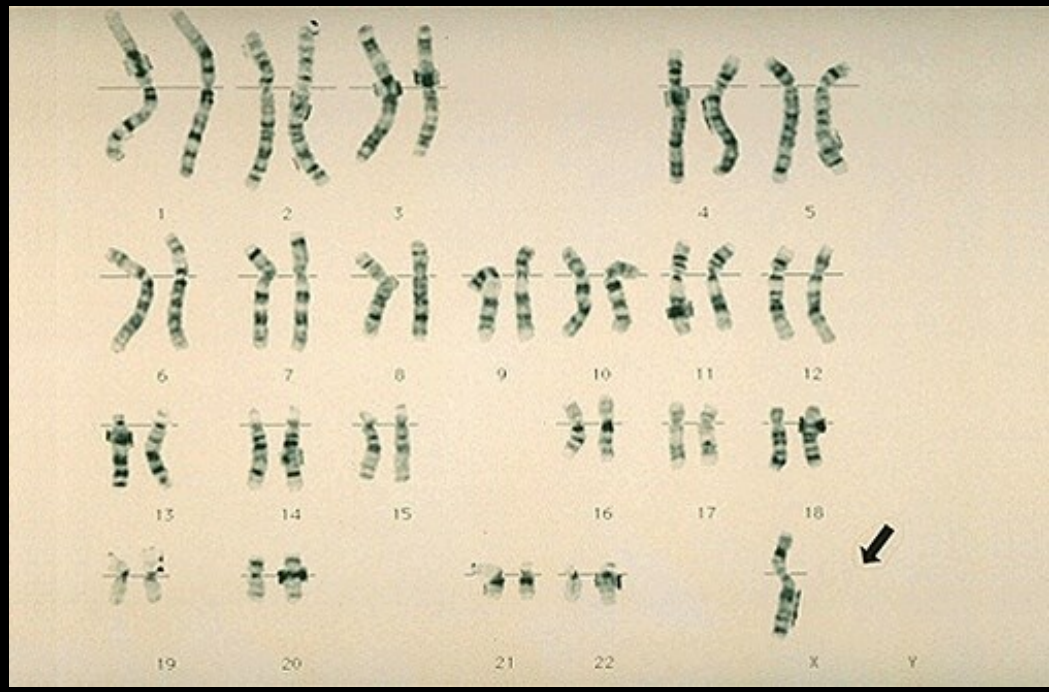
Generally, if a chromosomal mutations occurs during meiosis, one half of the gametes will have monosomy and the other half will have trisomy

Turner's Syndrome

- Gentoype: XO
- It is NOT linked to maternal age.

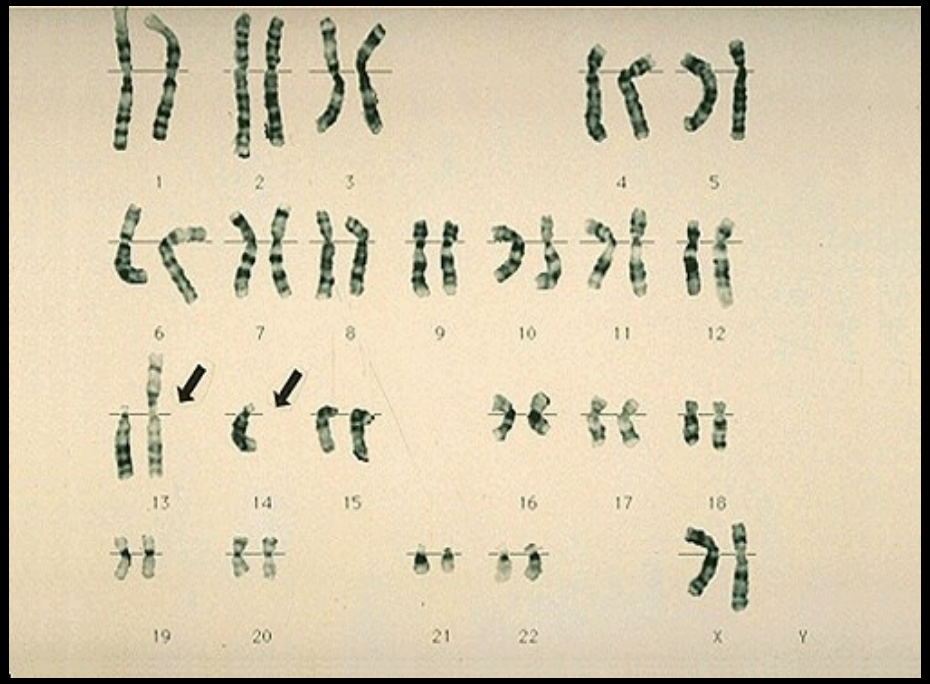
- Women with Turner's syndrome can live relatively normal lives, though they are unable to bear children.

The phenotype of this female includes short stature, short broad neck, and a broad chest. Intelligence does not seem to be affected.



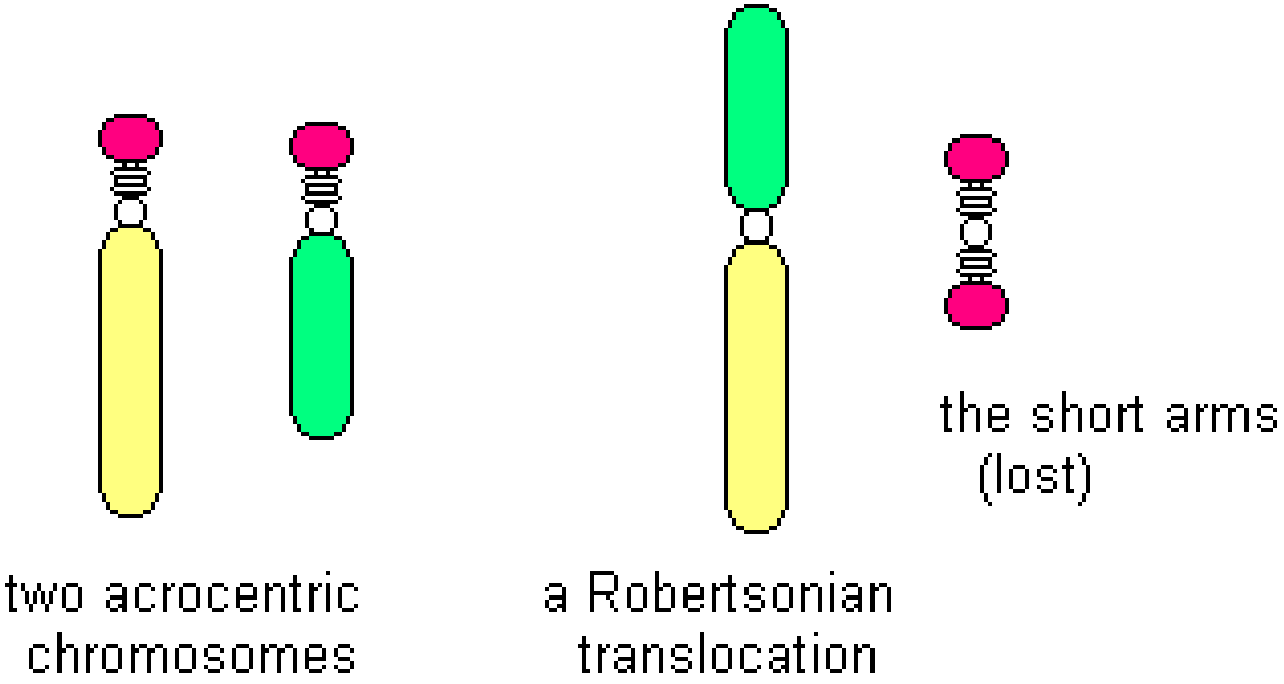
Translocations

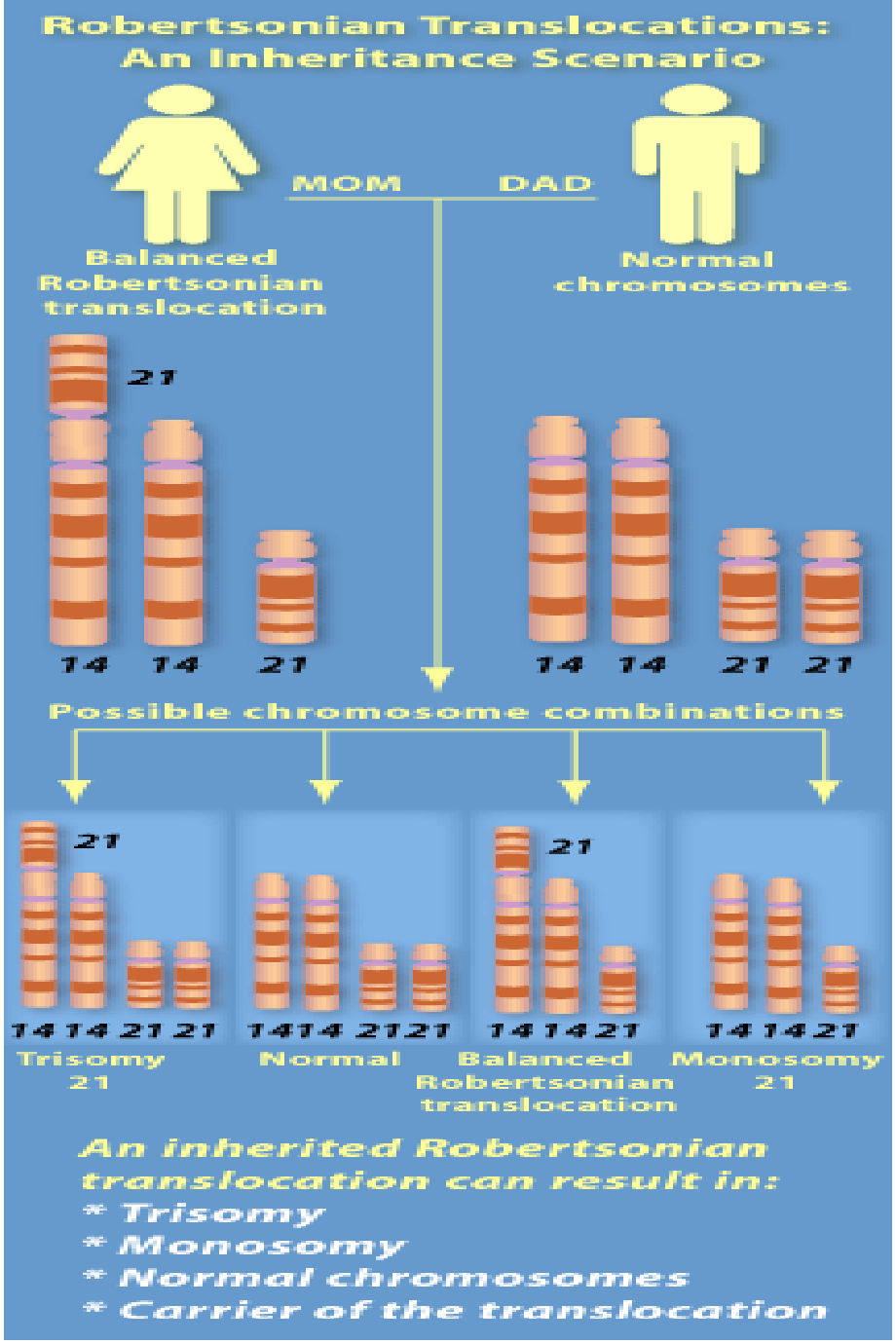
- A section of a chromosome is moved from one chromosome to another!
- The material is not lost, but inserted in a place where it is non-functional



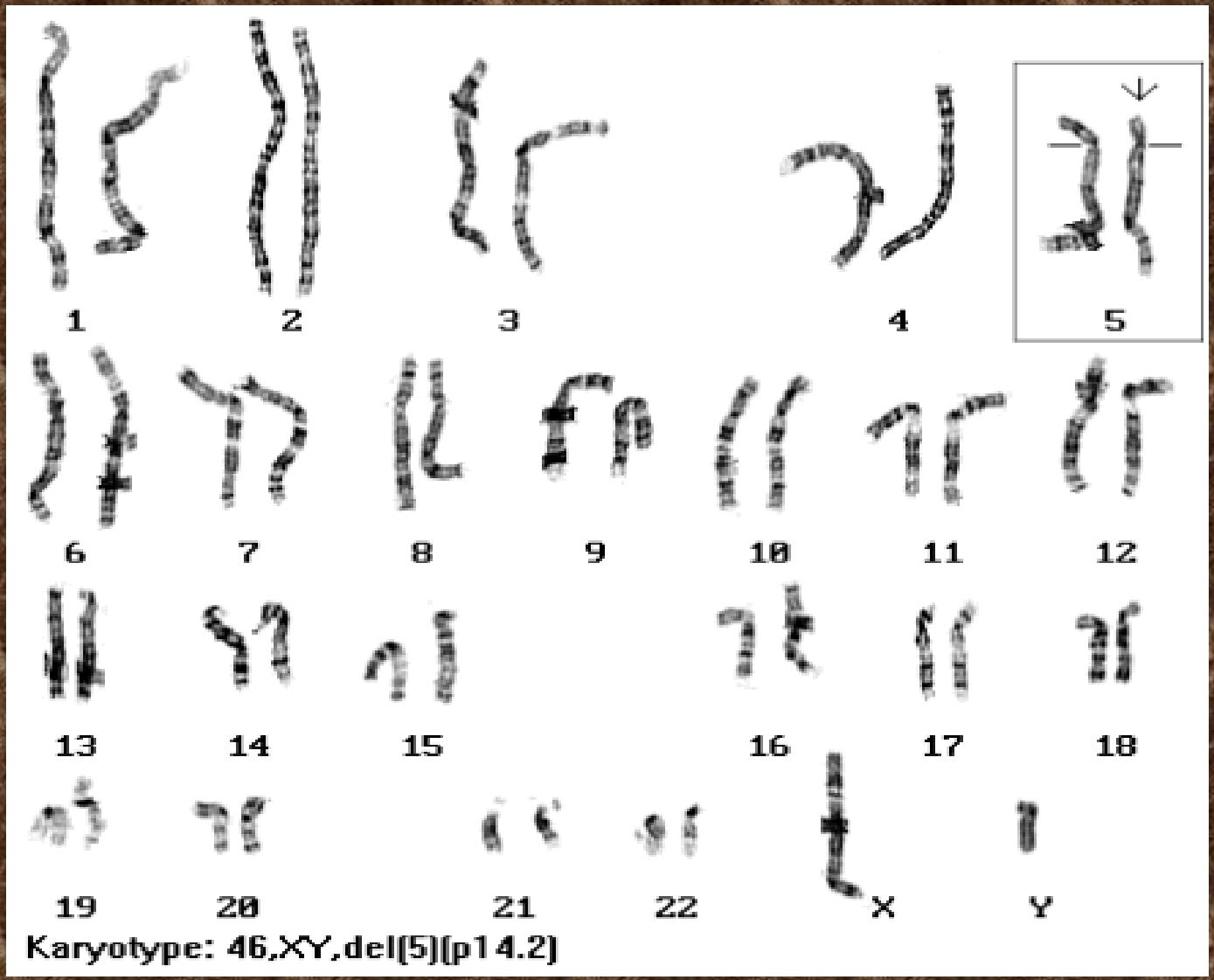
A Robertsonian translocation of chromosomes 13 and 14, an end to end fusion of the two chromosomes

Let's see that up close!




Robertsonian Translocations:
An Inheritance Scenario
MOM
DAD
Balanced Robertsonian translocation
Normal chromosomes
21
14 14 21
14 14 21 21
Possible chromosome combinations
21
14 14 21 21
Trisomy 21
14 14 21 21
Normal
21
14 14 21
Balanced Robertsonian translocation
14 14 21
Monosomy 21
An inherited Robertsonian translocation can result in:
* Trisomy
* Monosomy
* Normal chromosomes
* Carrier of the translocation

Onto Deletions!

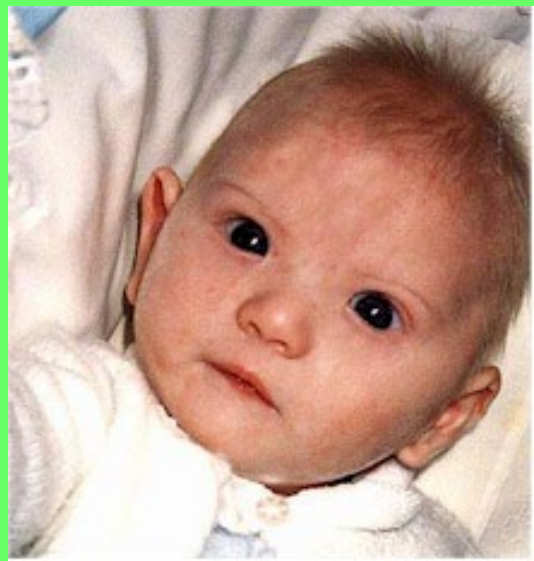


Cri du Chat

Cry of the Cat individuals sound like cats crying.
Why?
The larynx of the child is improperly developed.

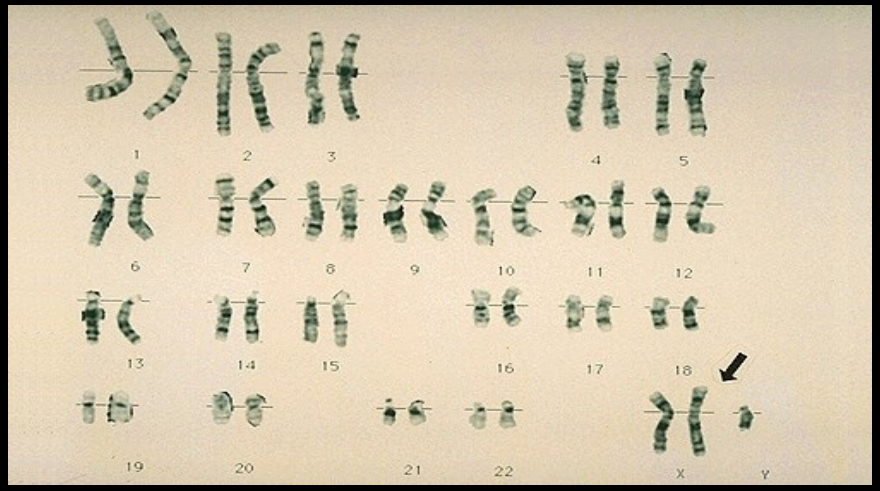
Fun Facts About "The Cat"

- The cause of this condition is a deletion of about half of the short arm of chromosome 5.
- Cri-du-chat babies are severely mentally retarded, round face, low set ears, heart disease, and have a small cranium.
- Occurrence:
  - 1/1,000,000 live births.
  - Karyotype:
    46XX or 46 XY with chromosome #5 upper arm deletion.

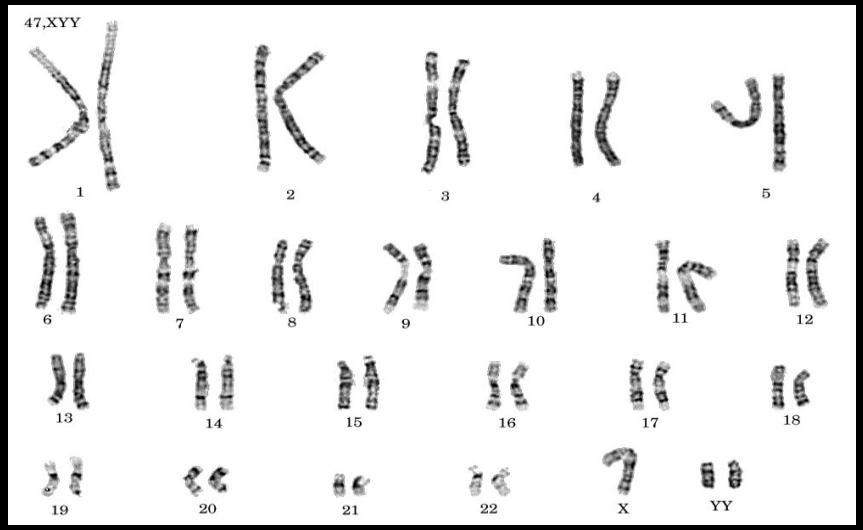


The Sex-linked Trisomies!

- Klinefelter's Syndrome
  - Shorthand: 47, XXY
  - "Supermale"



- Jacobs Syndrome
  - Shorthand: 47, XYY
  - The not so "supermale"



Klinefelter's Syndrome

- What type of mutation would cause a person to have an extra X chromosome?
  - NONDISJUNCTION!!!!
- Occurrence:
  - about 1 in 500 males
- Affected persons being relatively normal.
  - Abnormality includes: tall stature, sterility, enlarged breasts.

The not so "superman"- Jacobs Syndrome

- What type of mutation would cause an individual to have one less chromosome than normal?
  - NONDISJUCTION!!!
- Occurrence:
  - 1/1000 live male births.
- Apperence:
  - Men with this karyotype are tall and have low mental ability.

The End!