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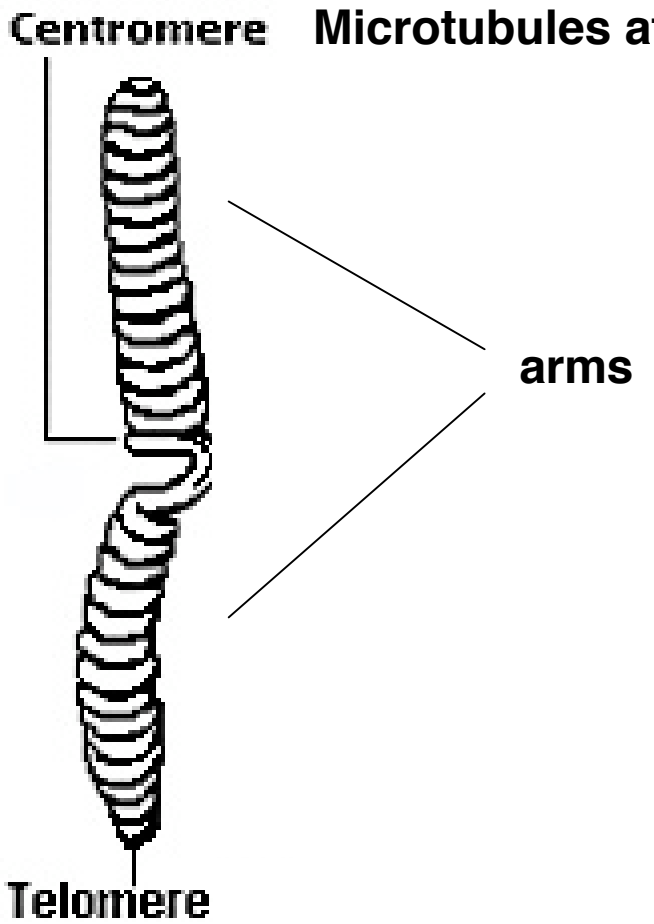
Outline

1. Chromosomes
-Structure
-Karyotype

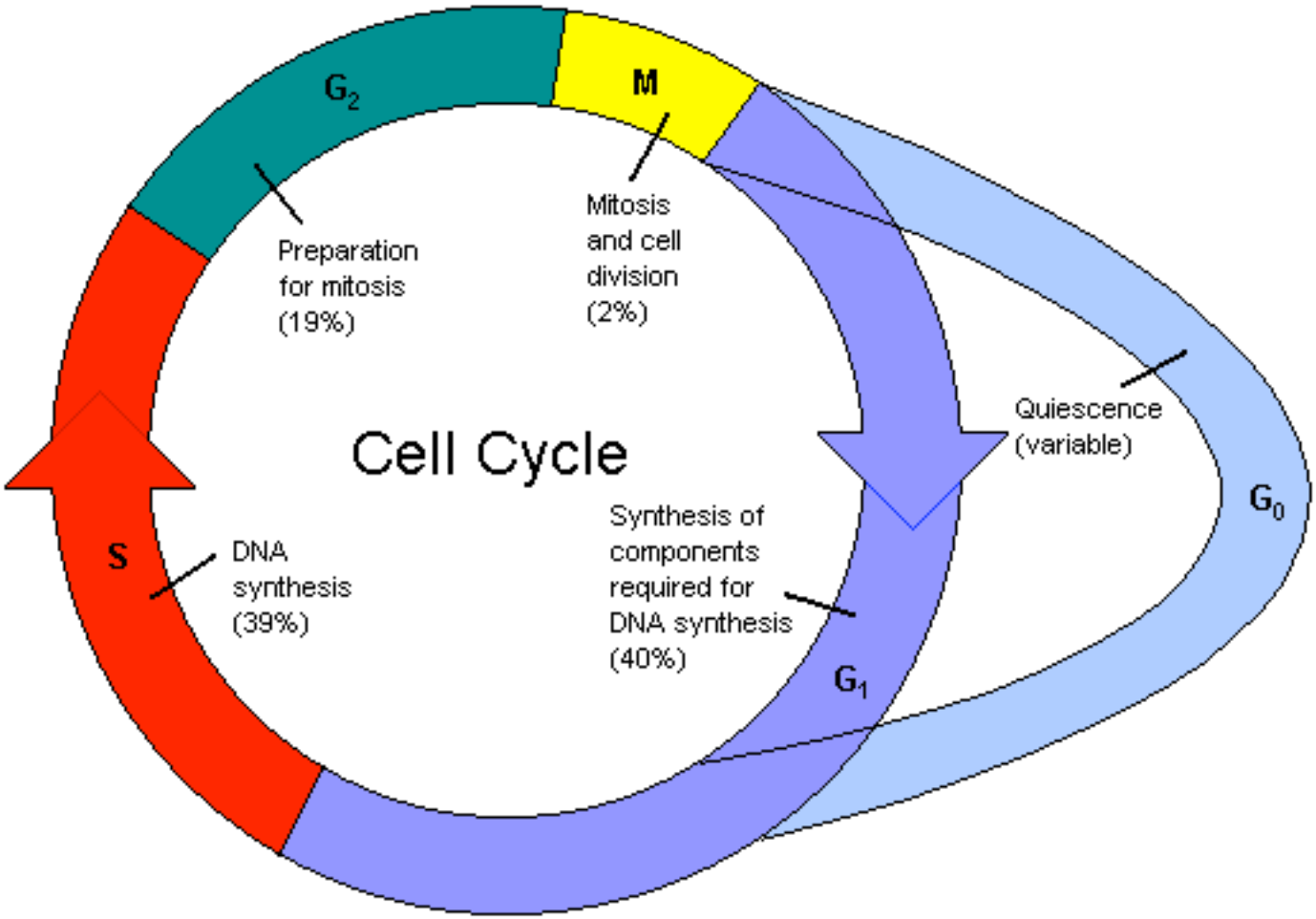
2. Meiosis
-Normal
-Nondisjunction
-Consequences

3. Dosage compensation
-Phenomenon
-Mechanism

We can observe mitotic chromosomes using light microscopy



We can see chromosomes during mitosis!



Chromosomes condense during mitosis

(that's why we can see them with the microscope)

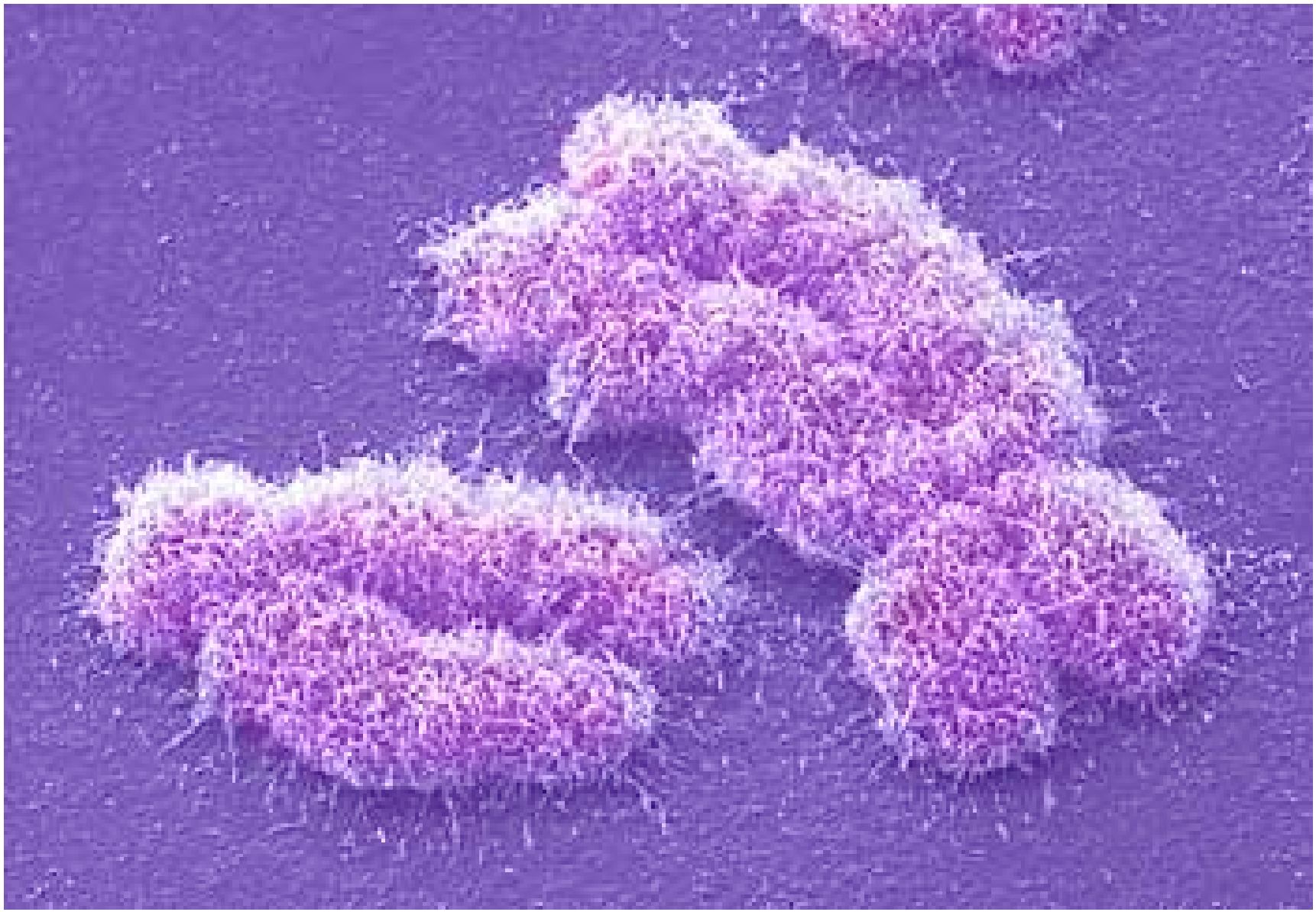
Smallest human chromosome

1.4 cm long stretched out

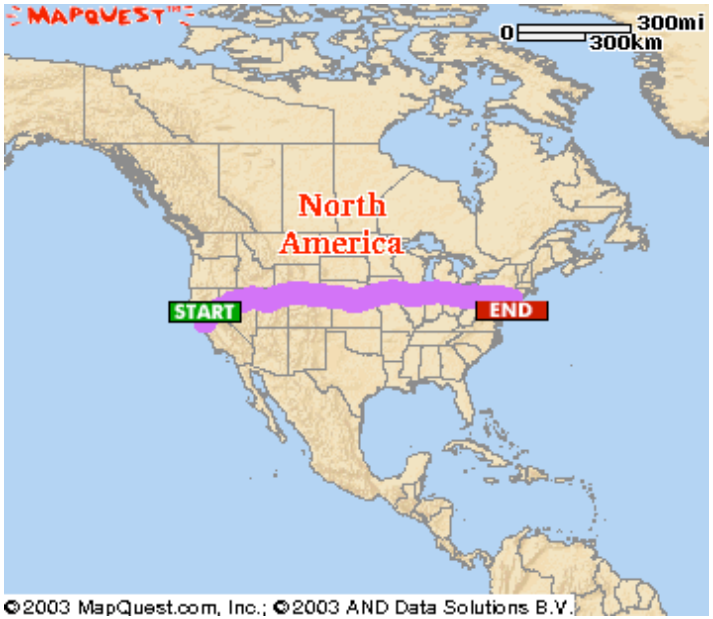
2 microns in mitosis

Compacted 7000 fold

Chromosomes



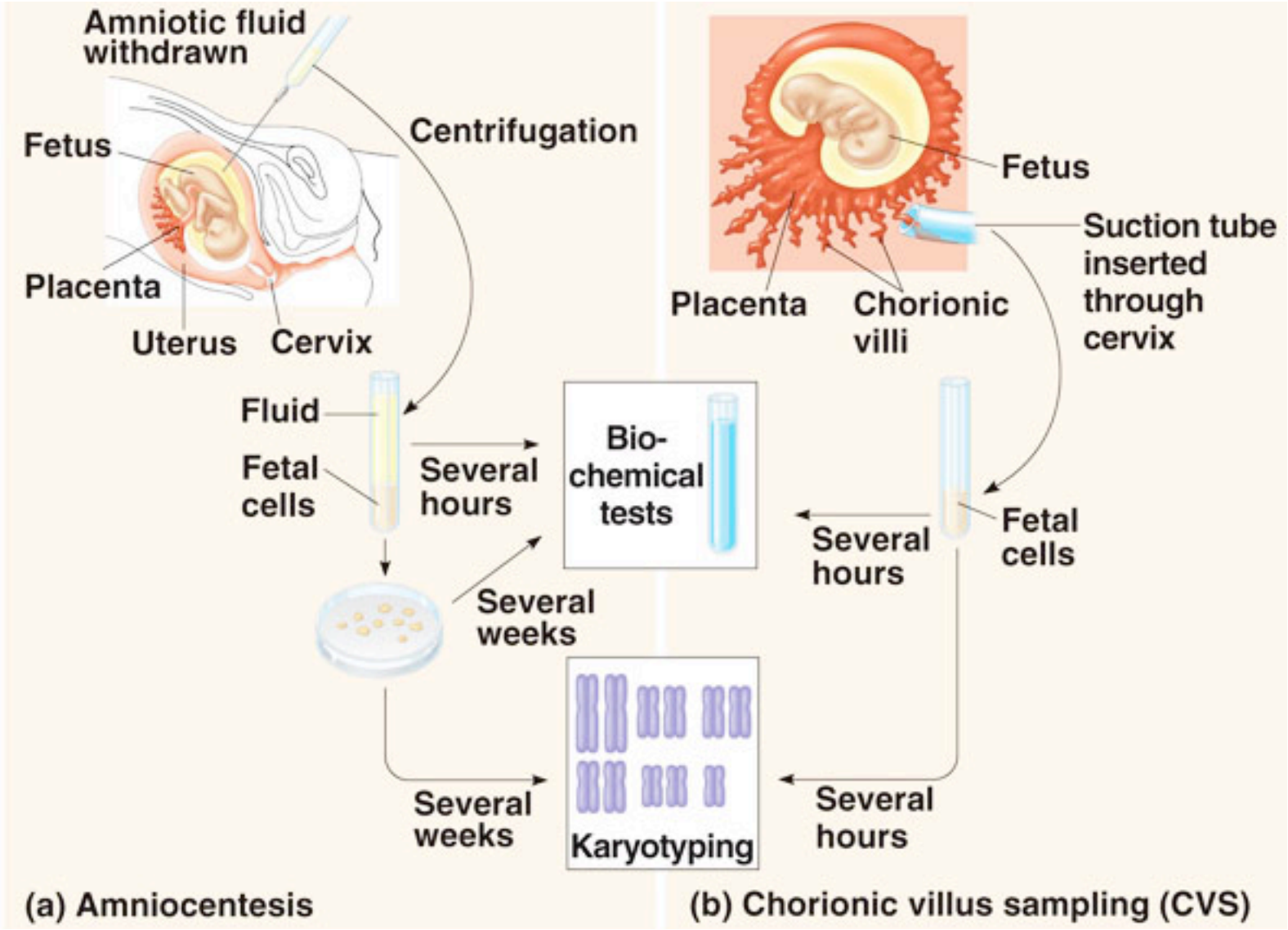
What is 7000 fold compaction?



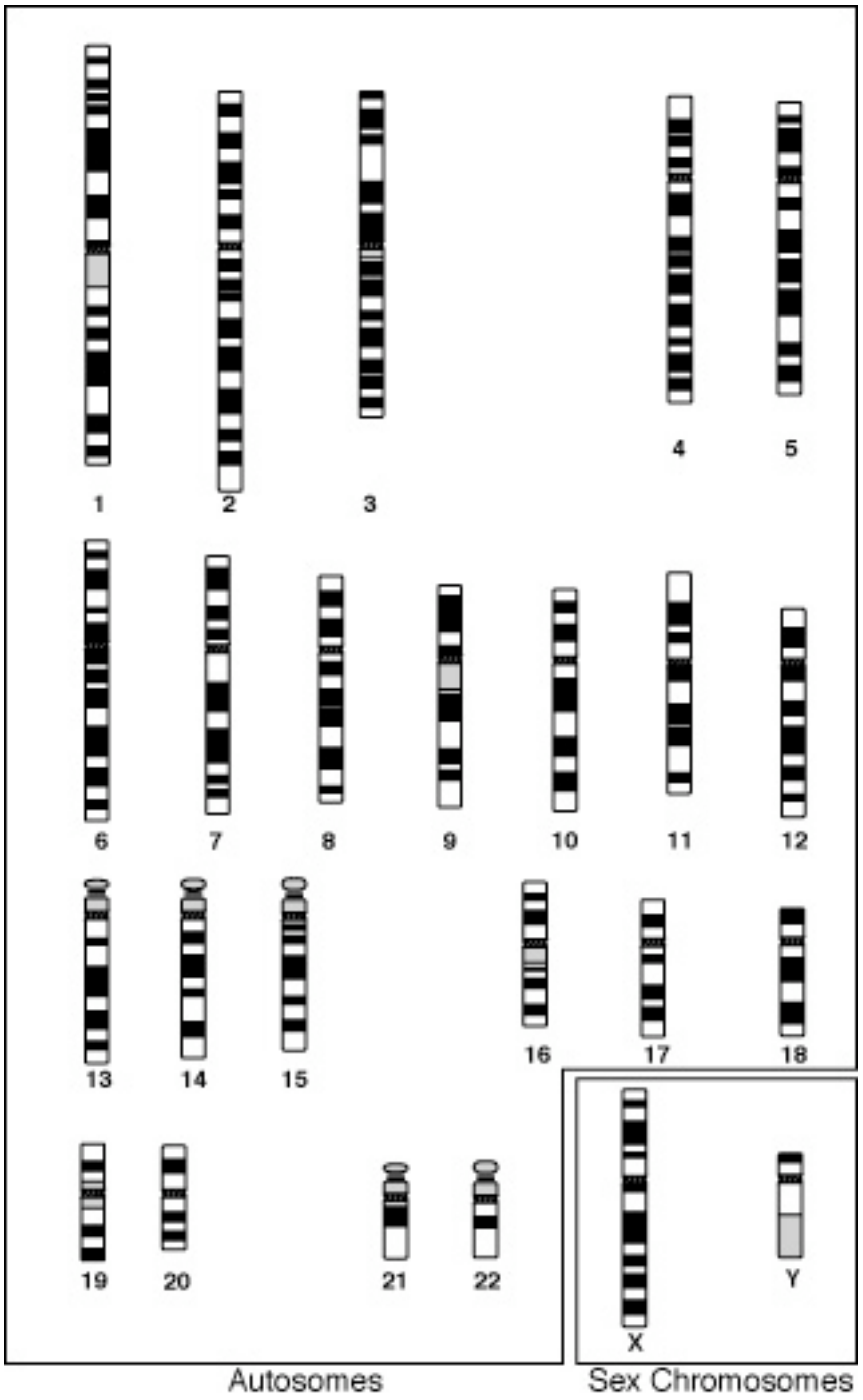
I80 runs 2916 miles from San Francisco, CA to Teaneck, NJ

I80 compacted 7000 fold--0.42 miles <1/10th Bay Bridge

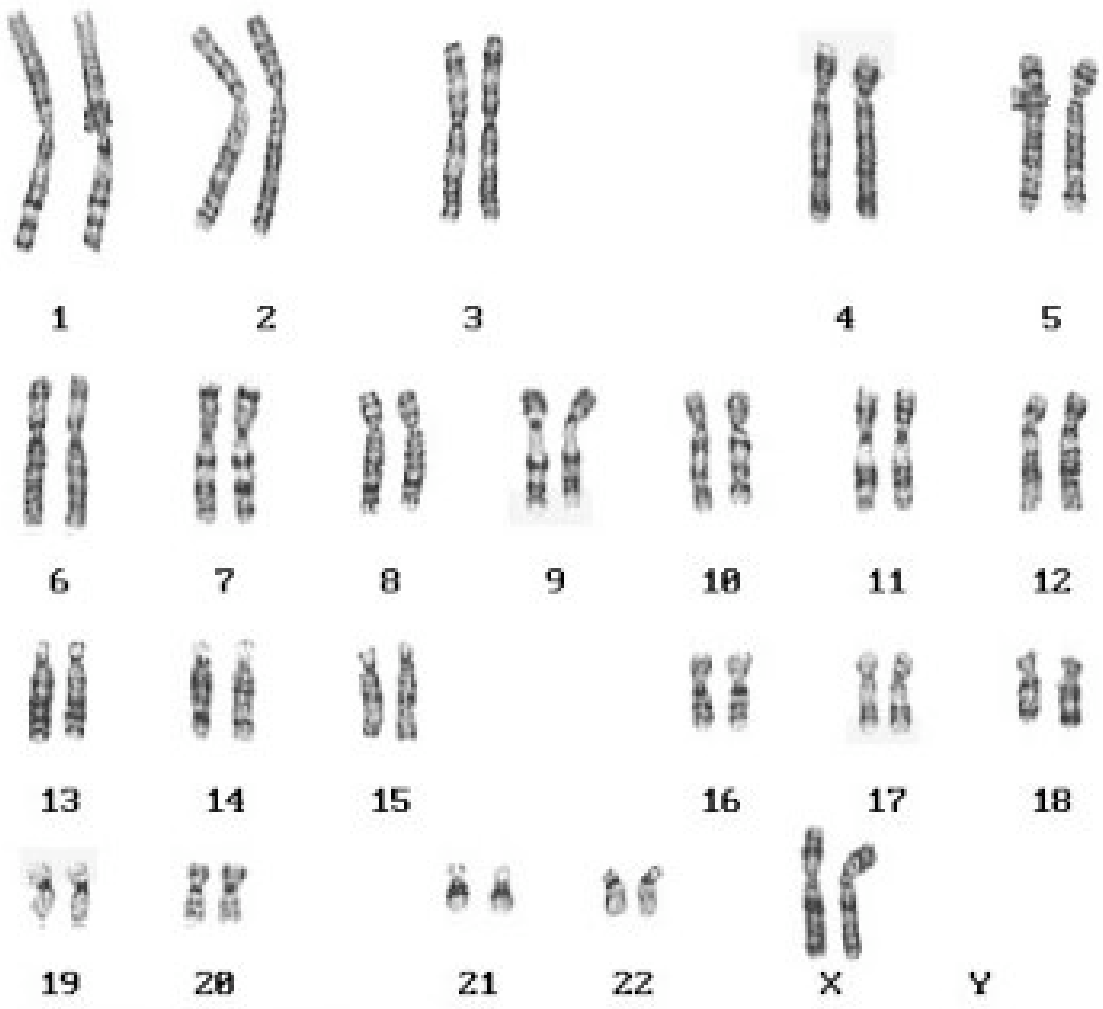
Amniocentesis



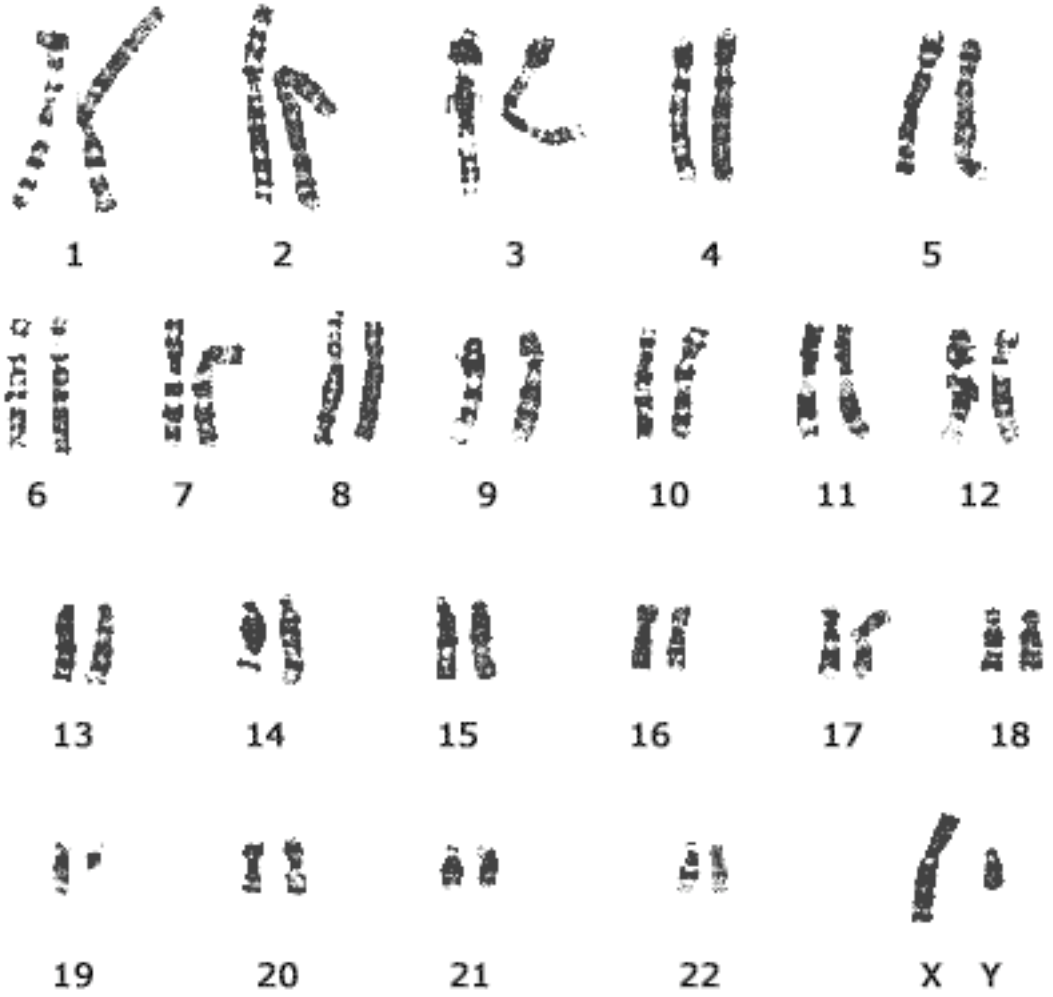
Chromosomes can be identified by their size and banding pattern.


1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y
Autosomes
Sex Chromosomes

Normal female, XX



Normal male, XY



Why amniocentesis and karyotyping?

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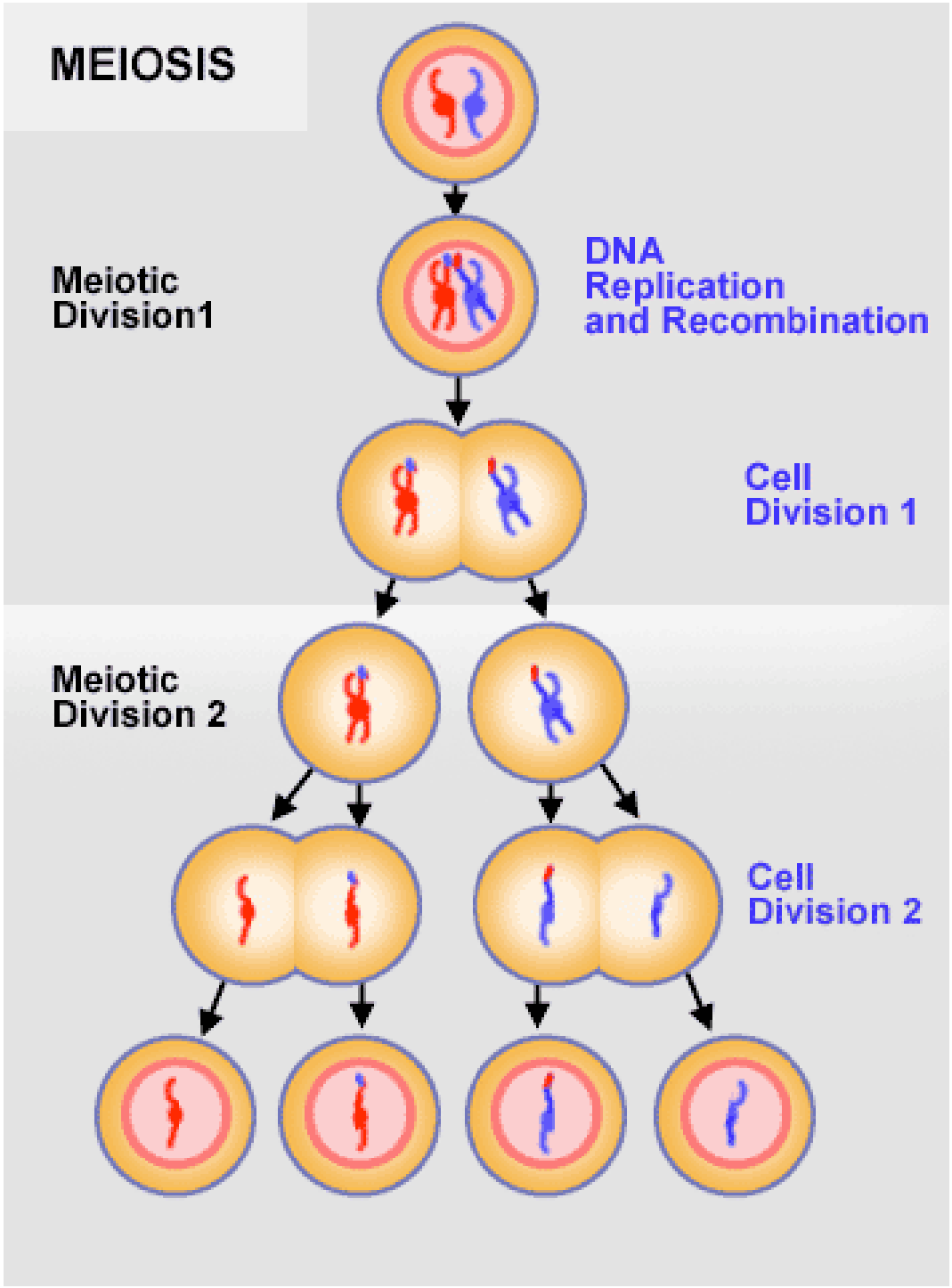
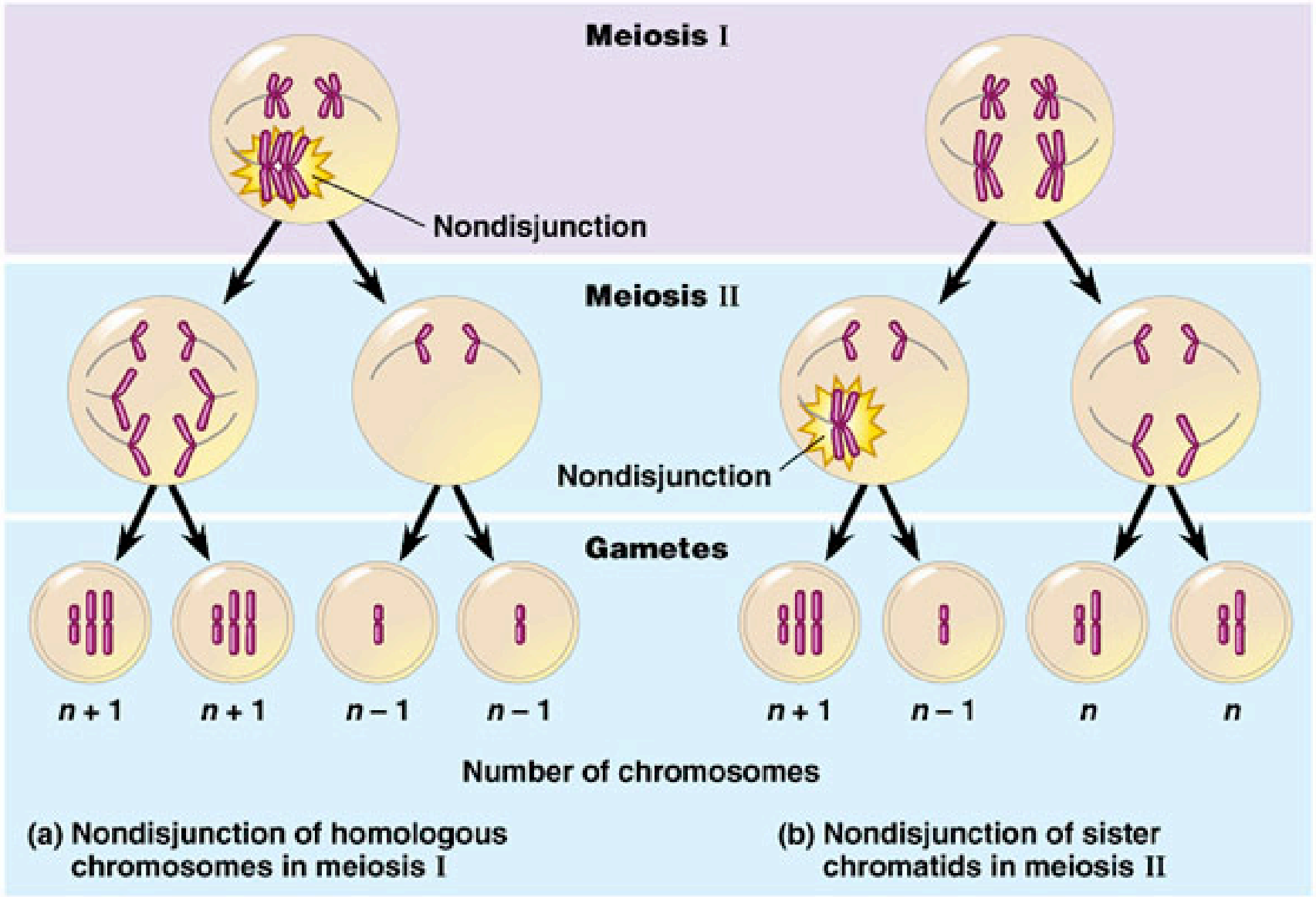
Meiosis usually results in gametes with a single set of chromosomes!


MEIOSIS
Meiotic
Division1
DNA
Replication
and Recombination
Cell
Division 1
Meiotic
Division 2
Cell
Division 2

Nondisjunction



Nondisjunction in meiosis I or II results in gametes with an extra or missing chromosome.

When these gametes fuse, the fusion results in zygotes with an extra or missing chromosome, a situation termed aneuploidy!

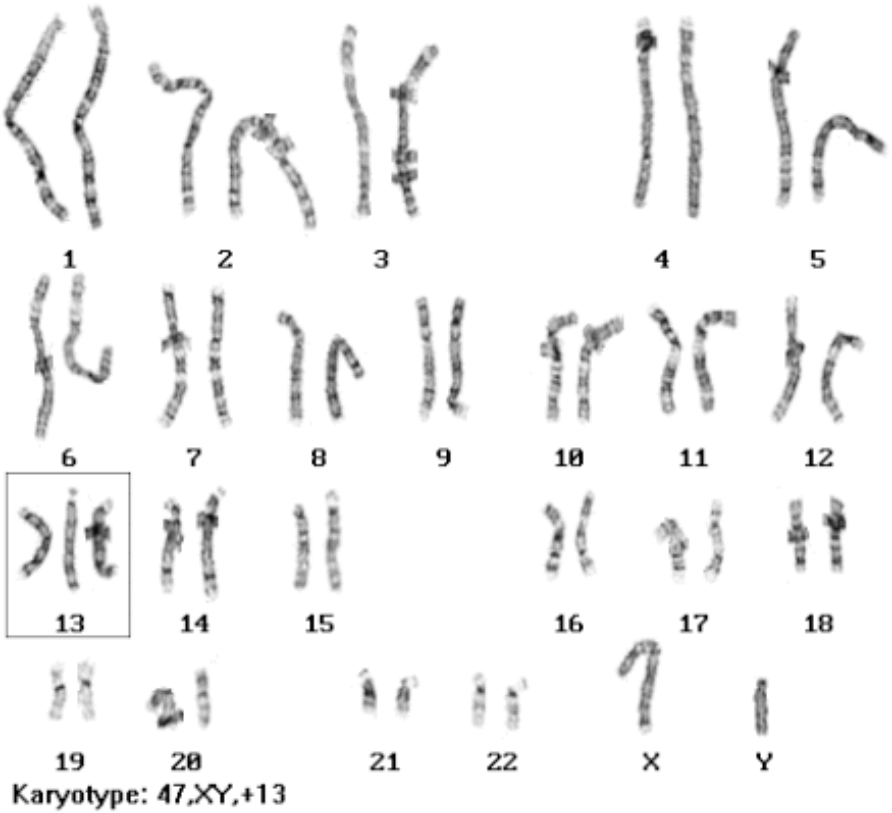
What are the consequences of aneuploidy in humans?

Autosomes first!

All monosomic (43 autosomes; missing an autosome) spontaneously abort!

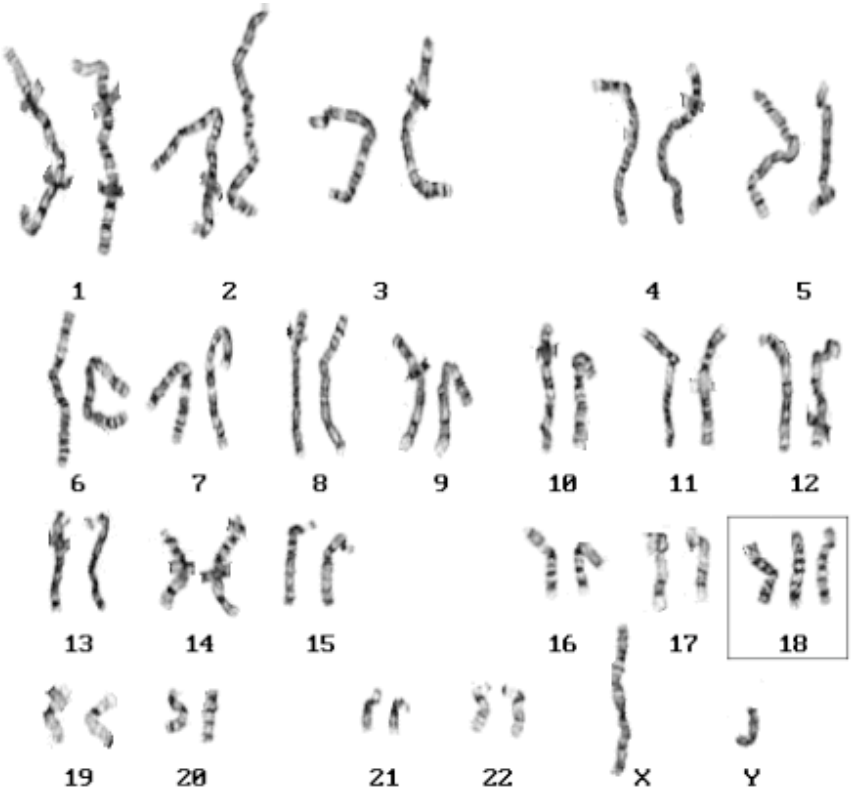
Almost all trisomic (45 autosomes; an extra autosome) fetuses spontaneously abort! There are three exceptions.

Trisomy 13; Patau Syndrome



Karyotype: 47,XY,+13

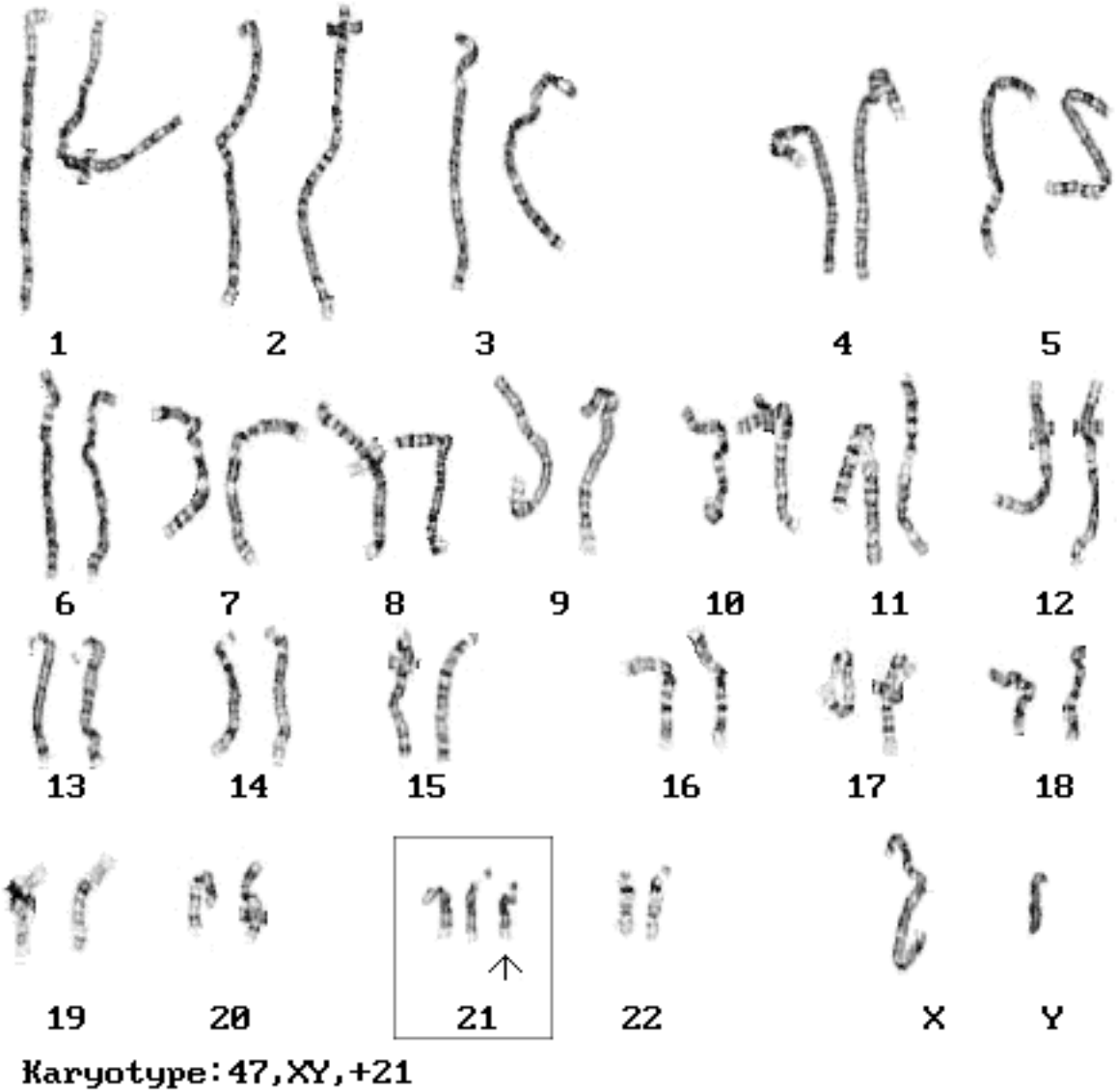
Trisomy 18; Edwards Syndrome



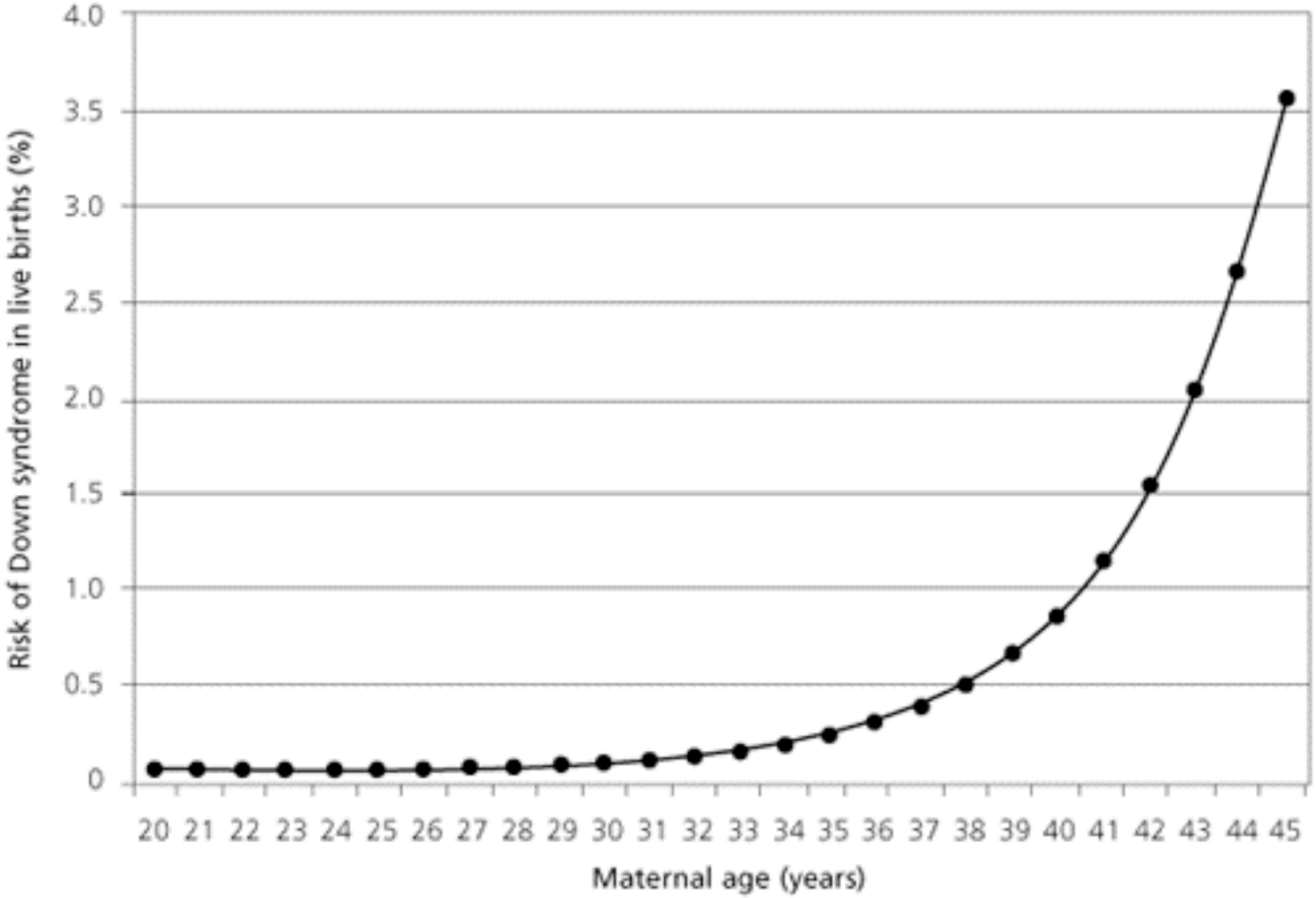
Karyotype: 47,XY,+18

Most fetuses spontaneously abort.
Those that make it die in first year.

Trisomy 21; Down Syndrome



Can survive to age 50
Mental retardation

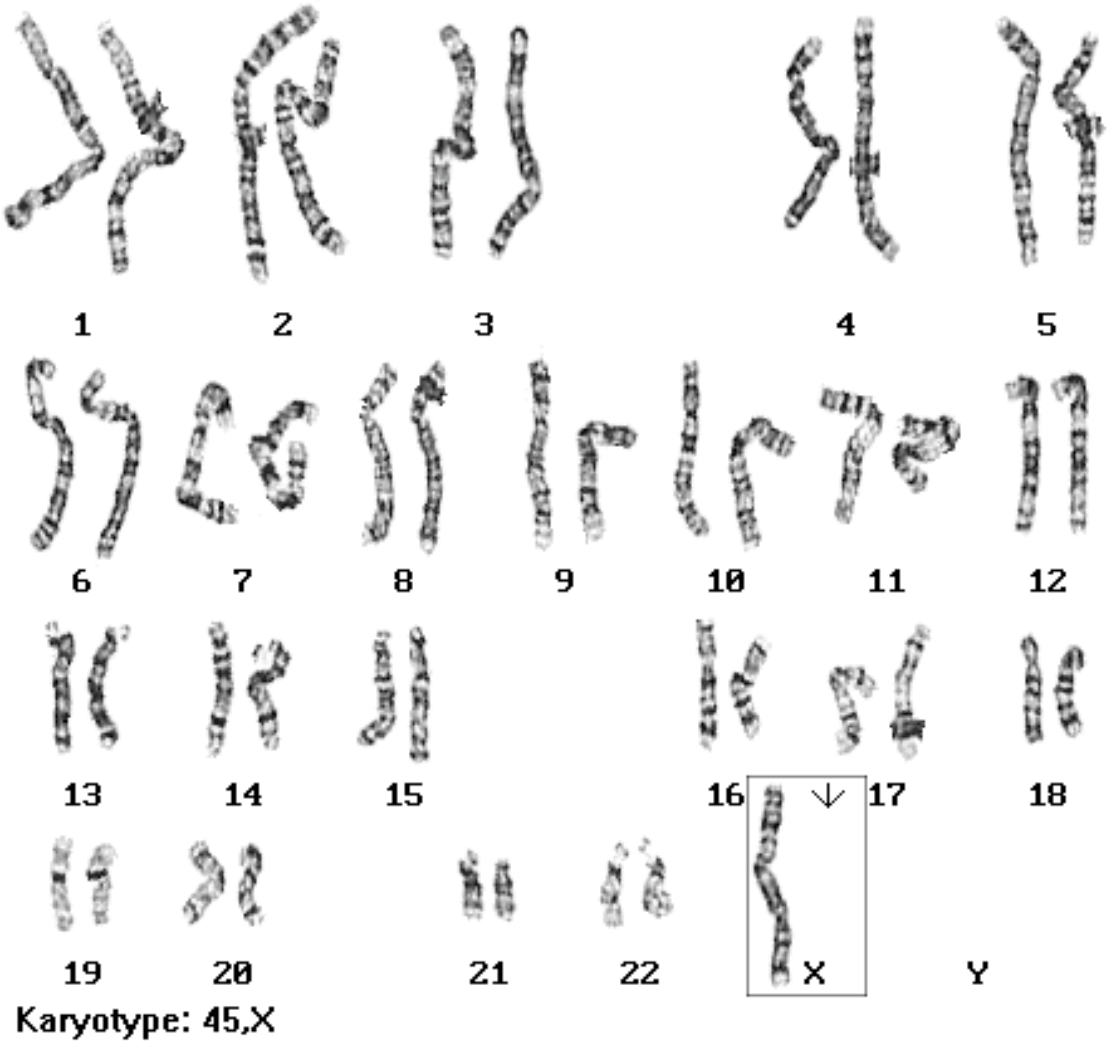

Risk of Down syndrome in live births (%)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45
Maternal age (years)

But, why do aneuploid fetuses die?

1000s of genes are over or under expressed!

But the rules are different for the sex chromosomes!

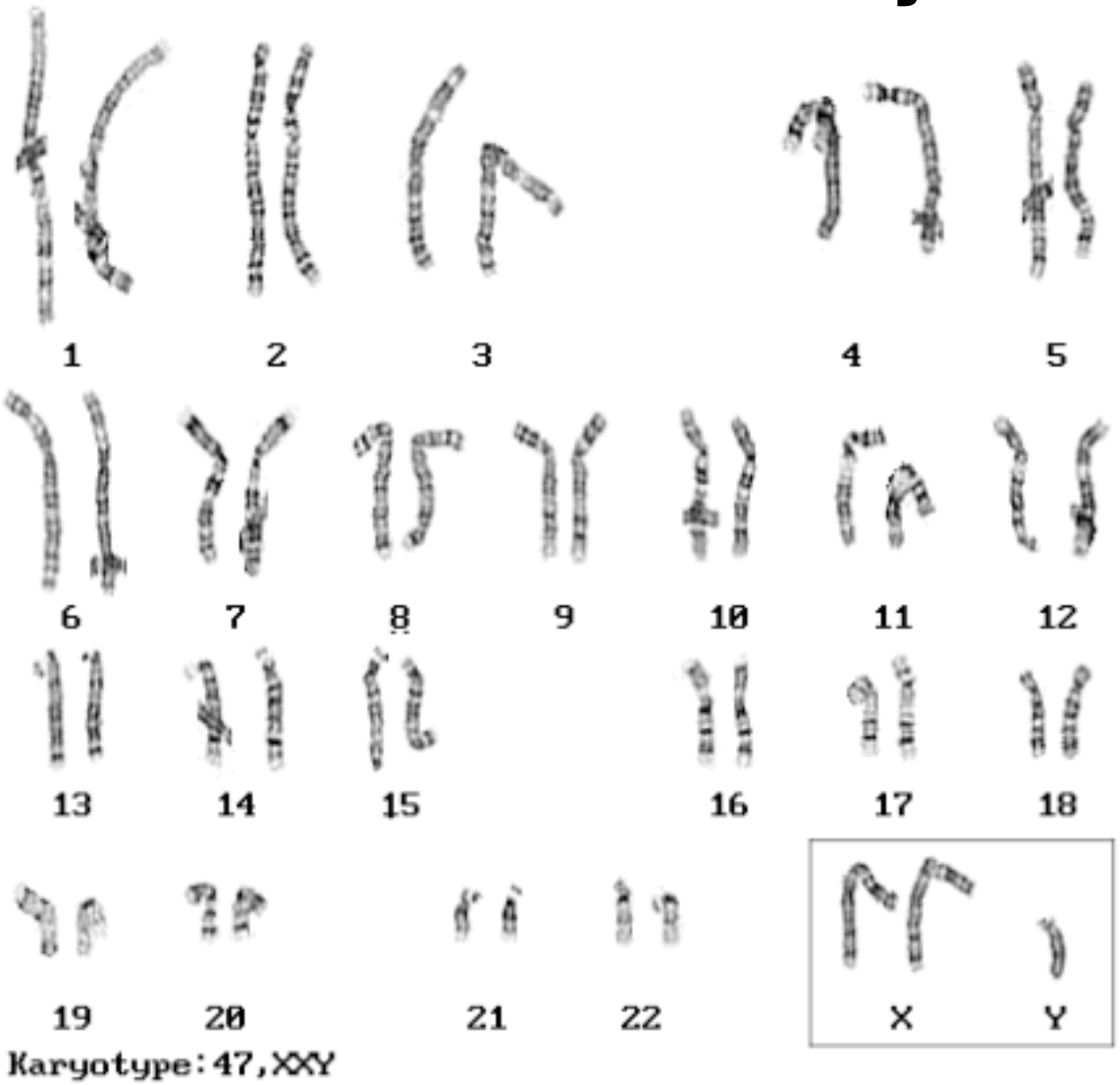
Turner syndrome, XO



Female
Short, wide-chested
Rudimentary ovaries
Sterile
Normal intelligence

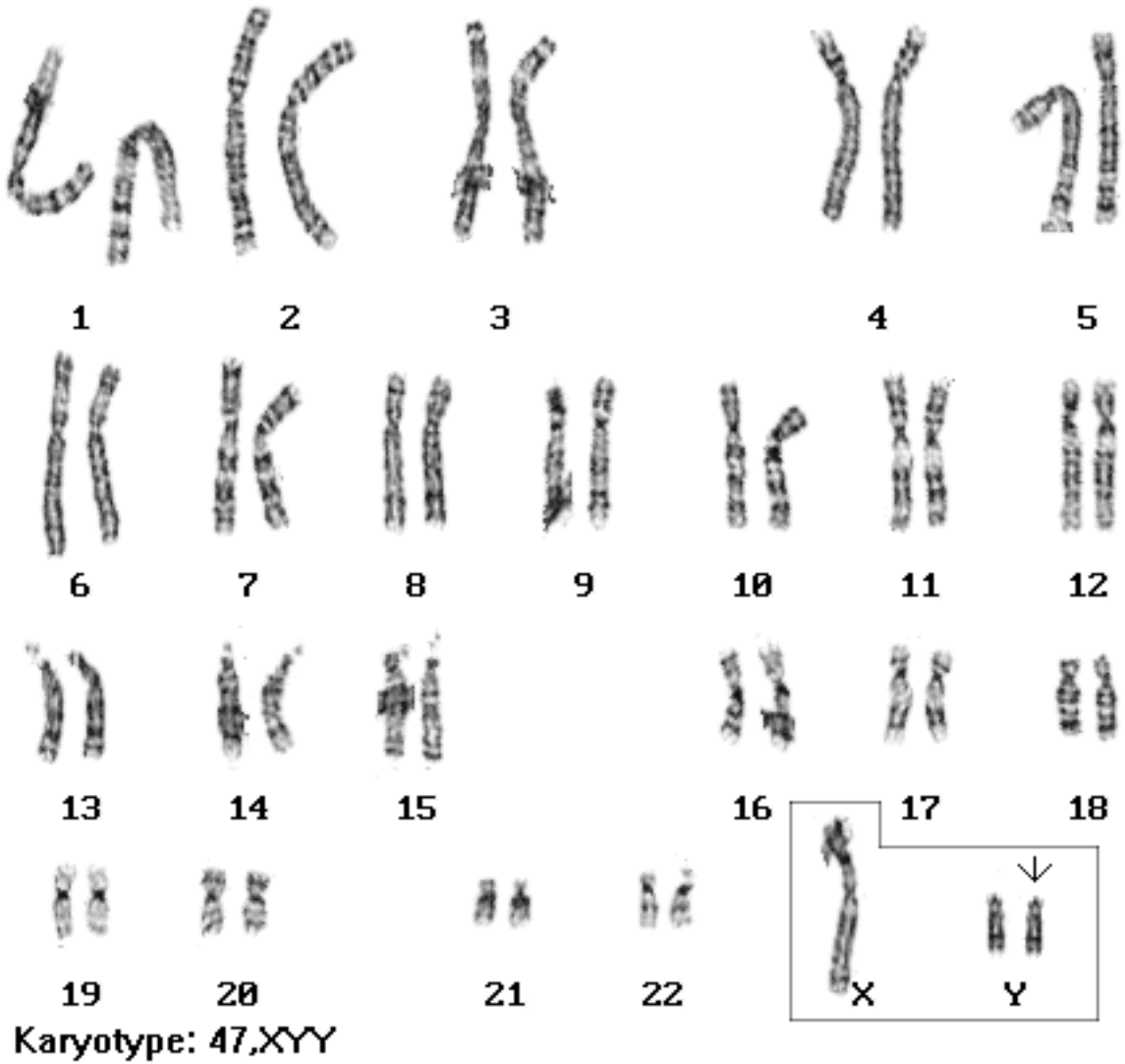
ALL autosomal monosomics die, BUT XO individuals survive and are relatively normal!!!

Klinefelter syndrome, XXY



Male
Phenotype of syndrome not apparent until puberty
Breast development
Low fertility
Subnormal intelligence

XYY Syndrome



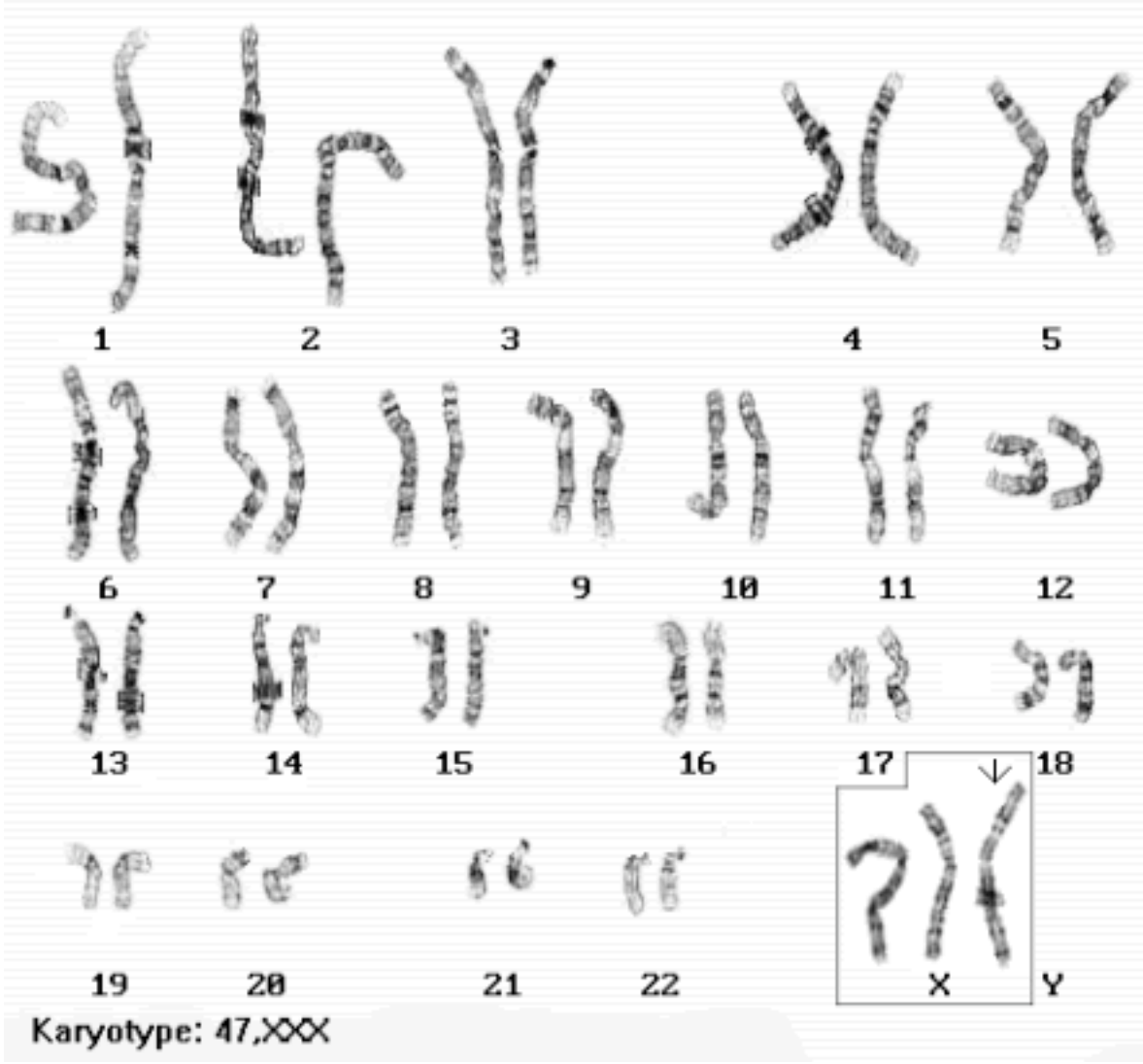
XYY Individuals

~5% criminals with violent and antisocial behavior are XYY, but only 0.1% of males in population XYY

Does this syndrome cause violent behavior?

Should this syndrome be used as a defense in criminal trials?

XXX Females are normal



XXXX and XXXXX females also exist

AHA!! Yet another difference between sex chromosomes and autosomes.

Autosomal trisomies die, but XXY, XYY, XXX, and XXXX can survive.

Two conclusions

Y associated with maleness

Abnormal # sex chromosomes tolerated

Why do individuals lacking an autosome or having an extra autosome die?

1000s of genes under or over expressed!!!

OK, but then why do XO, XXX, XXXX and XXXXX individuals survive?

X inactivation/dosage compensation

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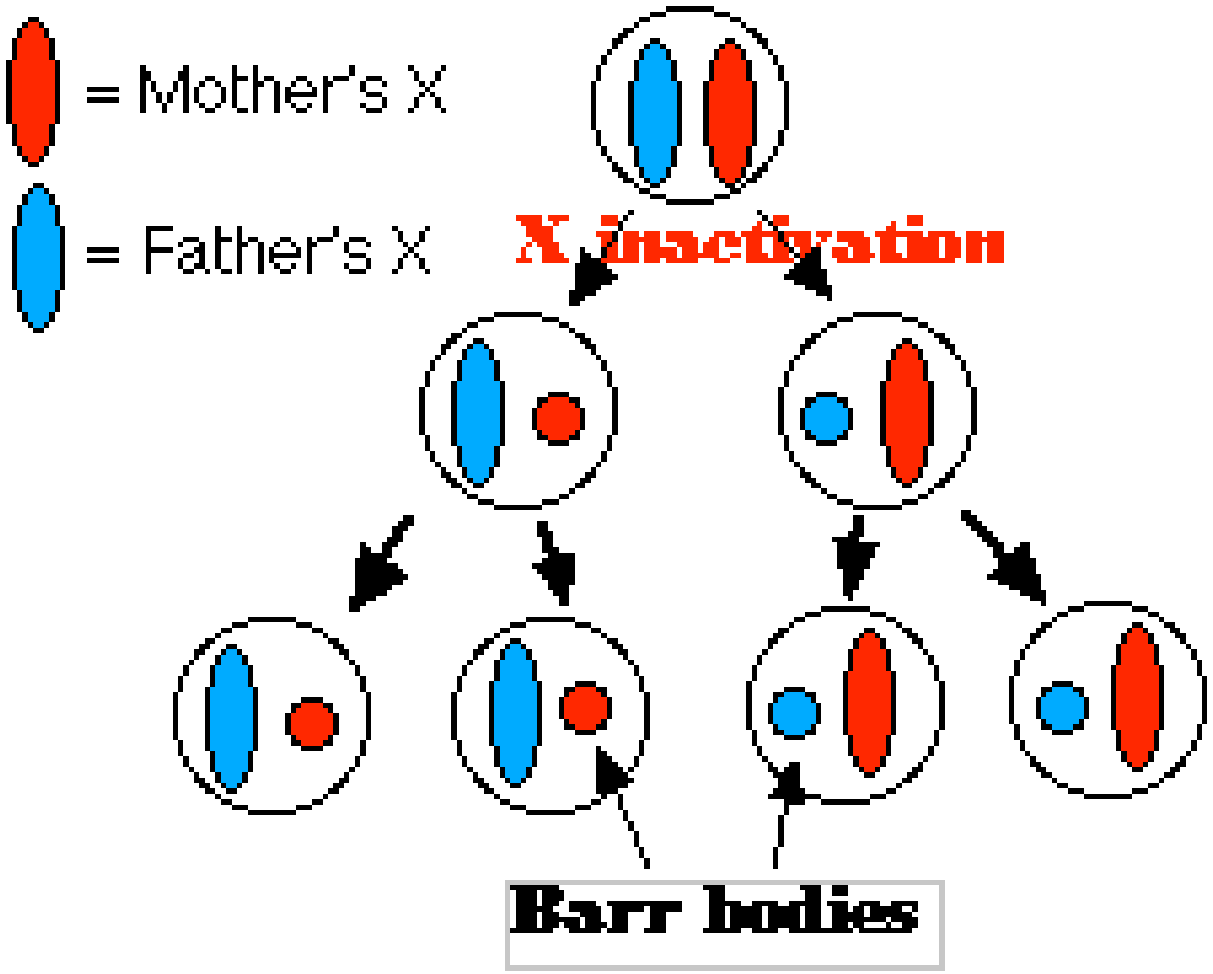
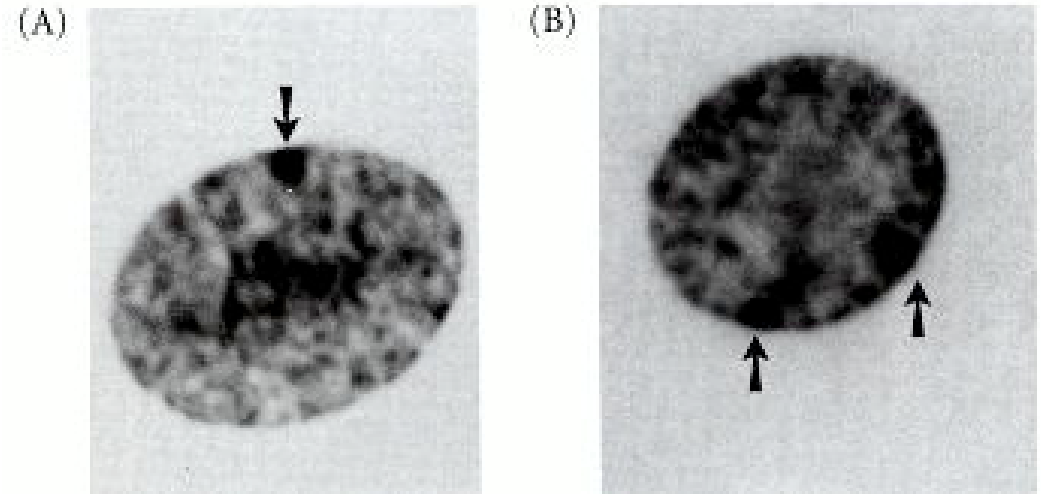
Males have one X chromosome and females have two.

In mammalian females, early in embryonic development <u>each cell</u> inactivates one X chromosome



Barr bodies are inactivated X chromosomes



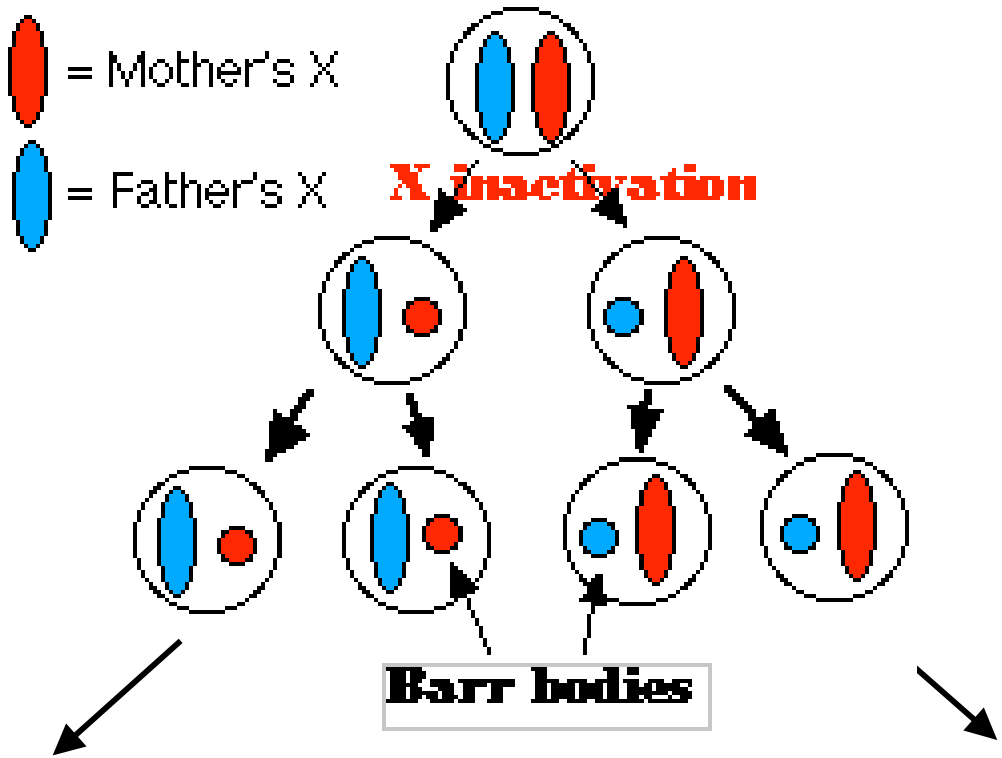
XX **XXX**

One Barr body **Two Barr bodies**

XXX, XXXX and XXXXX individuals survive because only one X chromosome is expressed!

Karyotype	# Barr bodies
XY	0
XO	0
XX	1
XXX	2
XXXX	3
XXXXX	4

Whoa!!! All mammalian females are mosaic!!!

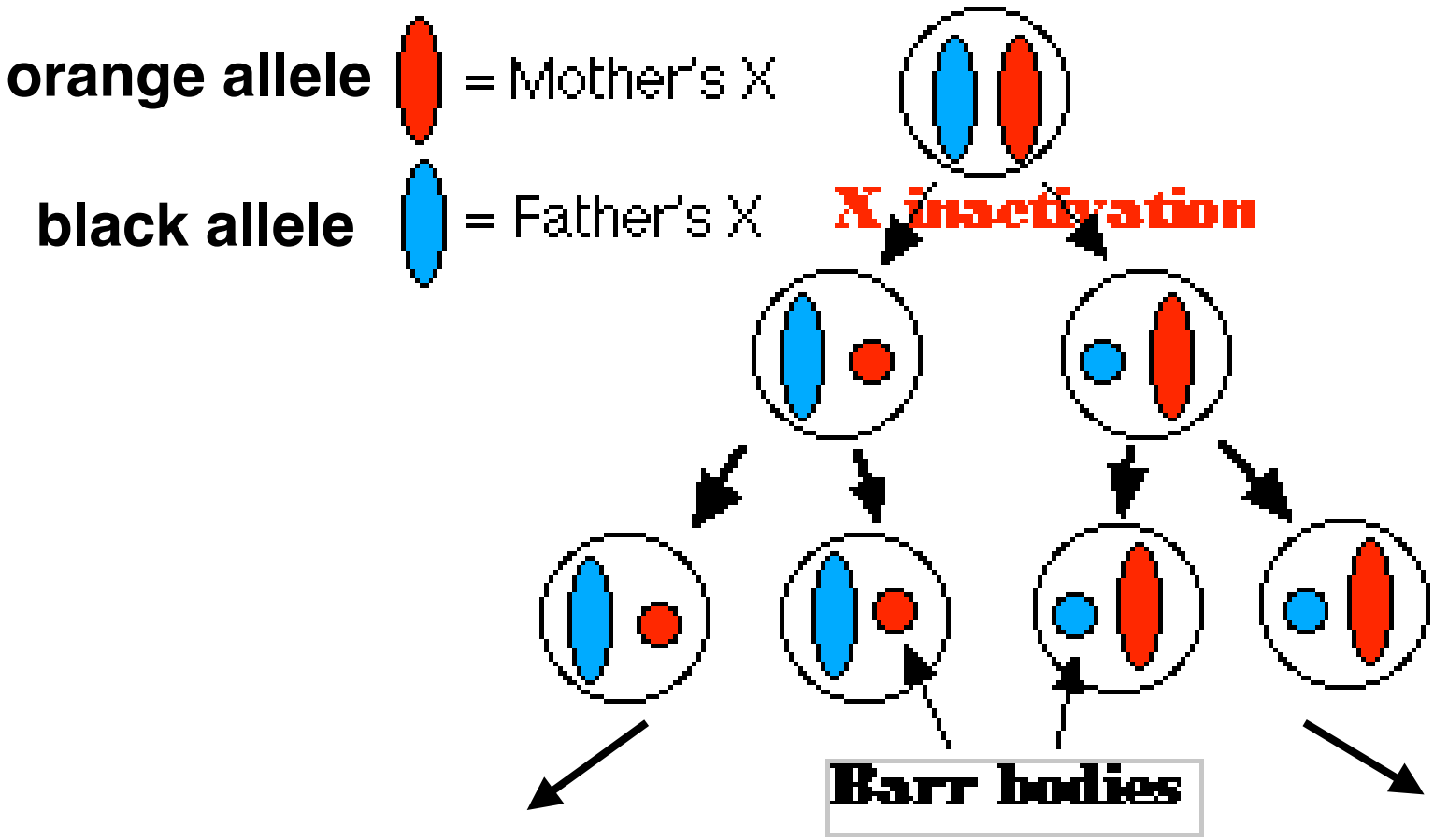


These cells express only paternal X chromosome genes.

These cells express only maternal X chromosome genes.

X inactivation results in black and orange patches on Calico cats.

Female Calico cats have black and orange alleles of an X-linked gene.



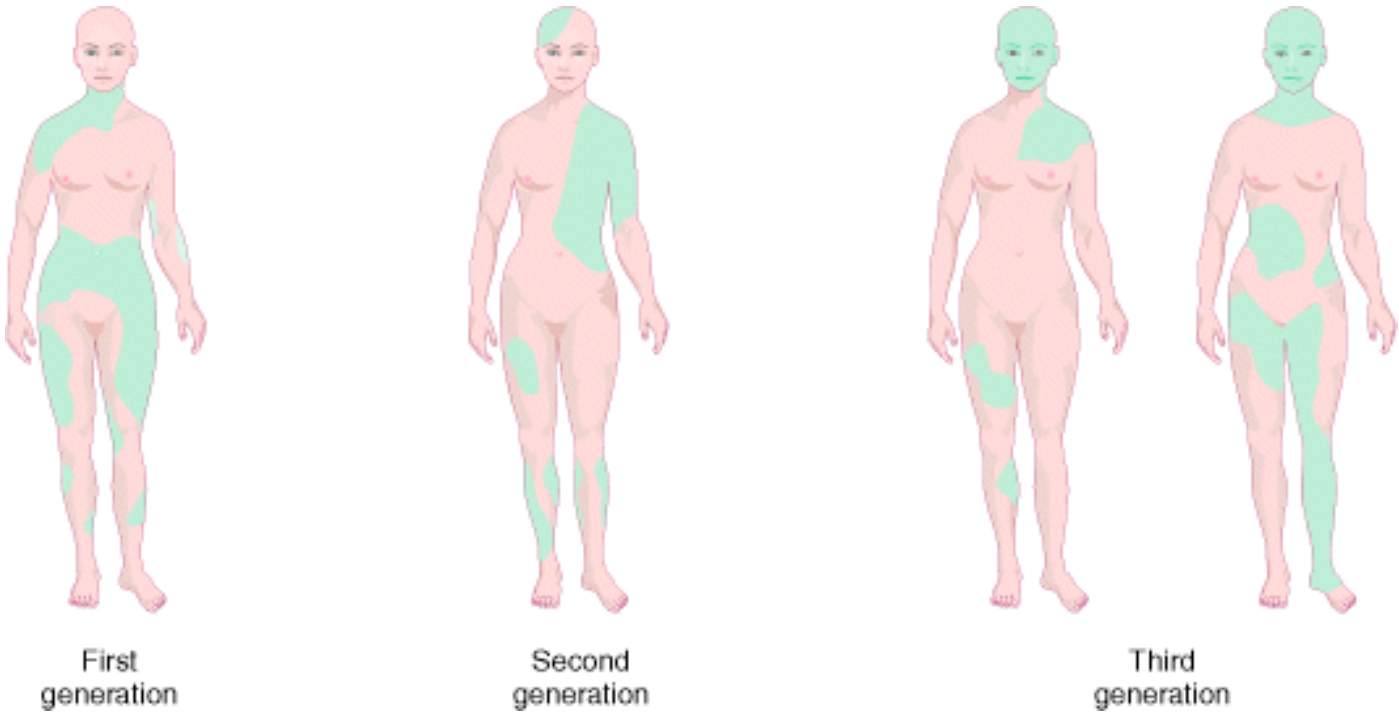
These cells express only paternal black allele.

These cells express only maternal orange allele.

Other consequences of X inactivation

X-linked genetic diseases can be mosaic in females

anhidrotic ectodermal dysplasia



Three generations of females heterozygous for X linked anhidrotic ectodermal dysplasia (absence of sweat glands). Areas without sweat glands are shown in green.