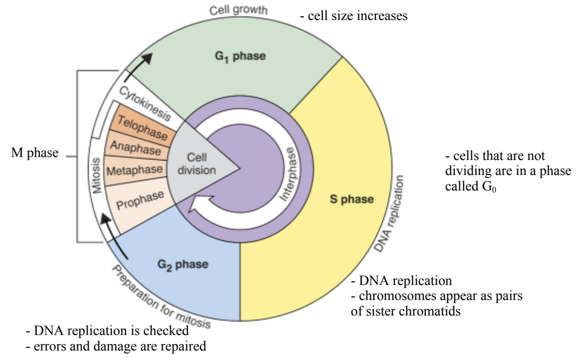
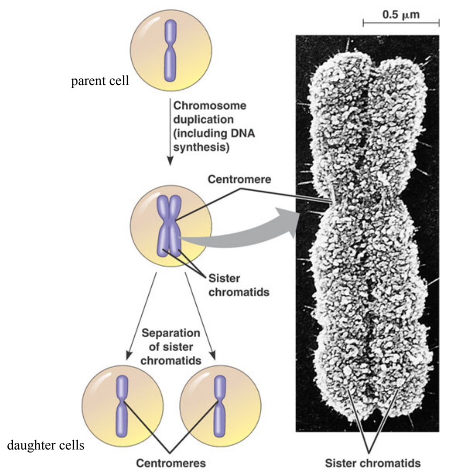
Why might it be important for cells to divide at a specific rate and time?
Normal Growth
Normal Development
Maintenance

Different cells types divide at different frequencies
What types of cell might divide more frequently?
Some cells can divide, but don't divide often.
Some cells do not appear to divide after maturity.



1. What functions does cell division accomplish?

2. Do all of the cells in your body divide at the same rate? Explain.



3. State the phase that is described by each of the following events during mitosis.
a) The chromosomes move apart and go to opposite poles of the cell.
b) The nucleolus and nuclear envelope reappear.
c) The centrioles complete their own replication.
d) The cell grows in size.
e) The spindle has reached its full development.
f) Chromosomes becomes shorter and thicker strands.

4. Looking under a microscope, you notice that some cells have several nuclei within the cytoplasm of a single cell. Which phase of the cell cycle is not operating correctly to form such cells?

5. Why must cytokinesis occur after, rather than before, anaphase?

6. Identify the difference between cytokinesis in animal cells and plant cells.

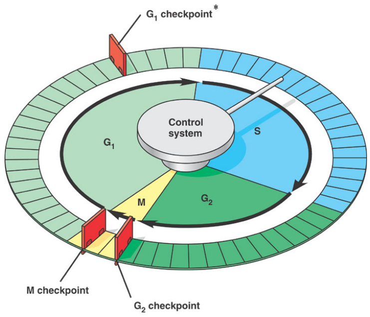
7. A drug interferes with the construction of the mitotic spindle. What effect would this drug have on cells?

8. Why is the replication process during interphase so important to cell division?

Cell cycle is driven by molecular signals

- Internal (*e.g.*, the cell can't enter mitosis until all of the chromosomes are replicated)
- External (*e.g.*, growth factors that stimulate the growth and division of cells)

Signals indicate if key cellular processes have been completed correctly
- *e.g.*, can DNA synthesis begin?
- has DNA synthesis been completed correctly?
- has the spindle been constructed?
- are all chromosomes attached to spindle?



- a checkpoint is a time when the cell decides to either stop or proceed
- normally, the cycle is stopped at a checkpoint until it is overridden
- the cell checks that certain things have been completed before proceeding
- most cells are actually permanently in G_0 and never divide

* G_1 checkpoint (late G_1 phase)
- called the restriction point because it is the point of no return
- if the cell passes this checkpoint it MUST divide
- if all signals are not satisfactory, the cell enters G_0

Density-dependent inhibition

Anchorage dependence

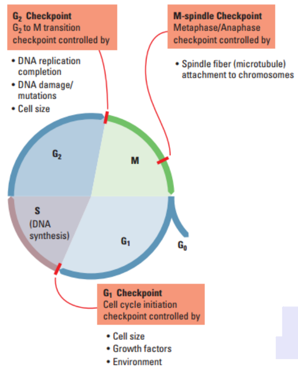
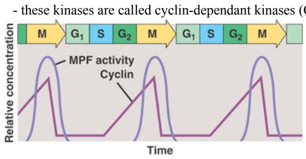


Figure 4. Diagram of the Cell Cycle Indicating the Checkpoints

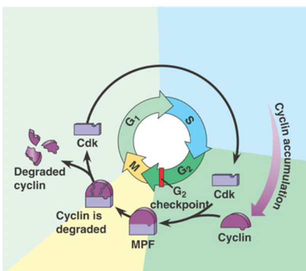
So, what molecules are involved in regulating the cycle?

- proteins called cyclins and kinases
- the kinases are usually inactive and only become active when attached to a cyclin
- these kinases are called cyclin-dependant kinases (Cdks)



(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle

- cyclin binds with Cdk to form a complex called MPF



(b) Molecular mechanisms that help regulate the cell cycle

1. cyclin begins to accumulate

2. cyclin molecules combine with Cdk to produce an enzyme that activates other proteins by phosphorylation (MPF)

- growth factors can be proteins which turn on the production of Cdk or cyclin
- the cell monitors the number of these and when there are enough it moves past the G_2 checkpoint
- the G_2 checkpoint also checks that all chromatids are aligned at the metaphase plate

3. MPF phosphorylates various proteins, triggering mitosis

4. During anaphase, MPF triggers a pathway that destroys cyclin, moving the cell into G_1 phase

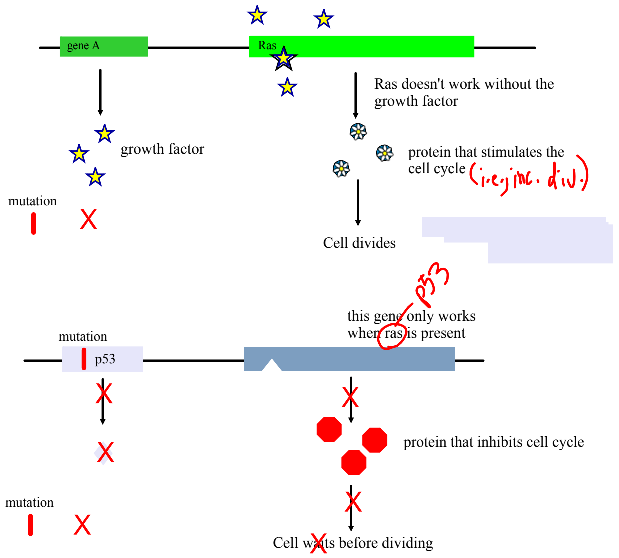
- the genes are basically the same in yeast, insects, plants & animals (including humans)

9. a) Imagine that a drug is developed that forces cells to remain in G1 of the cell cycle. What would be the effect on the cell?
b) On the individual?

10. What signals control the growth and division of normal cells?

Some genes stimulate cell division while others inhibit it.

- proto-oncogenes
  - normally stimulate cell division
  - they become "oncogenes" (cancer-causing) by mutation or increased expression
    - *e.g.*, ras is mutated in 30% of human cancers
- tumor-suppressor genes
  - normally inhibit cell division
  - can cause cancer by decreased expression or mutation
    - *e.g.*, p53 is mutated in 50% of human cancers
  - if they are moved to another location they can become active, causing cells to continue dividing



How do cancerous cells form?

What has to go wrong?	How does it happen?
unlimited growth	turn on growth promoter genes (*e.g.*, ras)
ignore checkpoints	turn off tumor suppressor genes (*e.g.*, p53)
escape apoptosis	turn off suicide genes
immortality (*i.e.*, unlimited divisions)	turn on chromosome maintenance genes
promote blood vessel growth	turn on blood vessel growth genes
overcome anchorage & ~~contact~~ inhibition	turn off touch-sensor gene

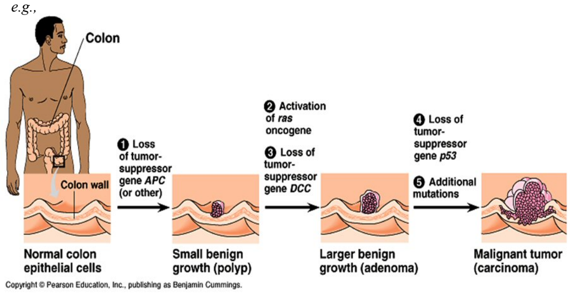
density depend.

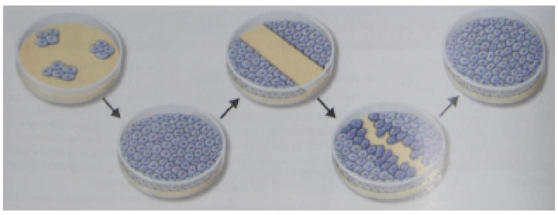
What triggers the changes?
- exposure to UV and other radiation
- chemical exposure
- genetics

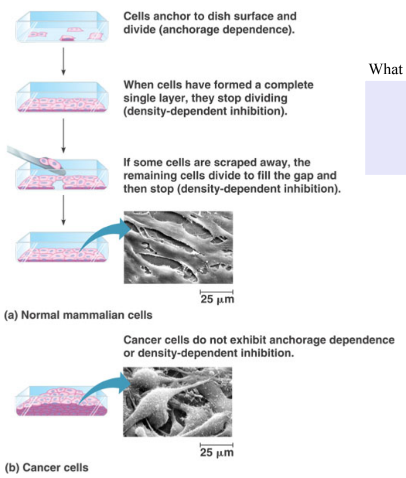
That's why the risk increases with age.

5

e.g.,







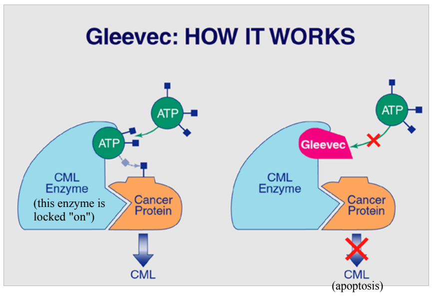
What stops most cells from dividing?

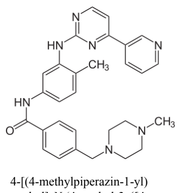
Treatments target rapidly dividing cells.

•	•
•	•
•	•
•	•
•	•

*

- imatinib (Gleevec, approved in 2001) is a treatment for chronic myeloid leukemia (CML), stomach cancer (GIST) and about 10 other cancers
- the drug target is present only in cancer cells
- 1st successful drug targeting only cancer cells (there are now others)

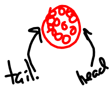




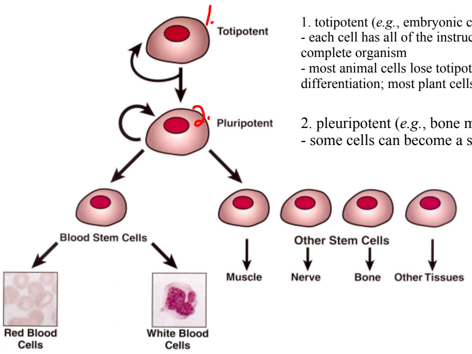
4-[(4-methylpiperazin-1-yl) methyl]-*N*-(4-methyl-3-{[4-(pyridin-3-yl)pyrimidin-2-yl] amino}phenyl)benzamide

- works by preventing a tyrosine kinase enzyme (BCR-Abl) from phosphorylating particular proteins and initiating the sequence of events necessary for cancer development
- prevents the growth of cancer cells and leads to their death by apoptosis
- BCR-Abl tyrosine kinase enzyme exists only in cancer cells so imatinib targeted therapy

- each cell has all the instructions to produce a whole human
- differentiation allows cells to become specialized
- differentiation is permament



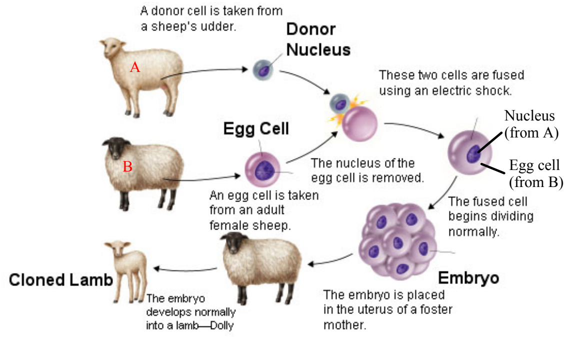
How do cells become different?
- molecules in the cytosol and molecular signals they receive from nearby cells



1. totipotent (*e.g.*, embryonic cells)
- each cell has all of the instructions to produce a complete organism
- most animal cells lose totipotency during differentiation; most plant cells do not

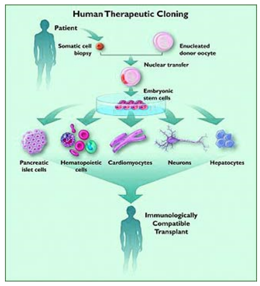
2. pleuripotent (*e.g.*, bone marrow cells)
- some cells can become a small variety of cells

- current research is aimed at learning how to make these cells become the type of cell we want



Nuclear transfer

How can cloning be useful?
- research diseases
- produce genetically identical organisms which carry a useful gene
- create compatible transplants



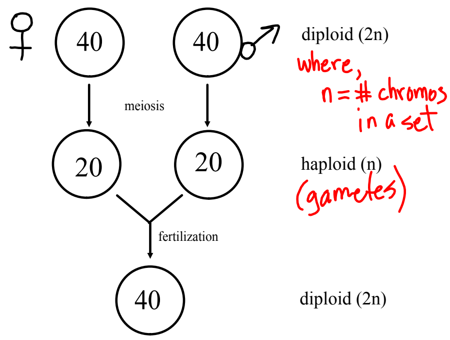
11. How can mutagens cause cancer?

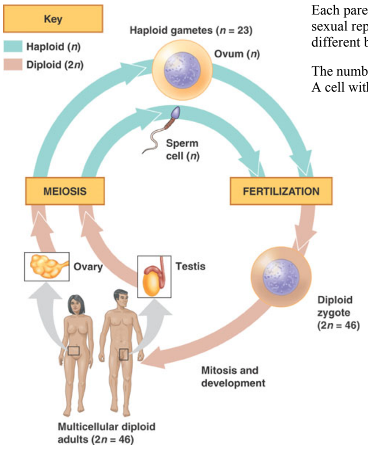
12. Cancer cells are unusual in a variety of ways: they are immortal, they metastasize, don't perform their normal function, and they can form tumors. Explain each of these characteristics at the cell level.

13. a) What evidence suggests that cells contain a biological clock or counter?
b) How might understanding the biological counter help extend human life span?

14. How can stem cells be used in addressing the problems of organ transplantation?

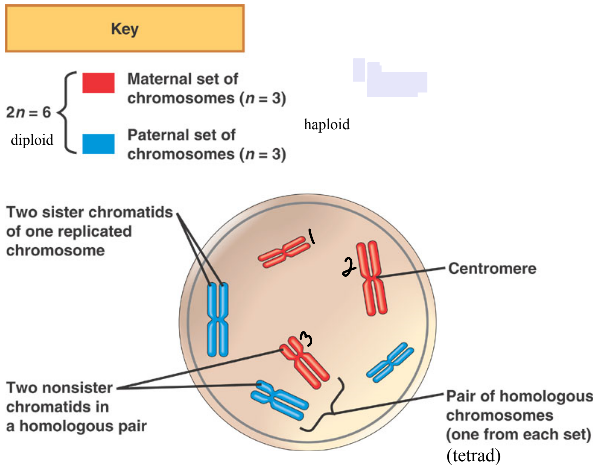
Why is meiosis necessary?



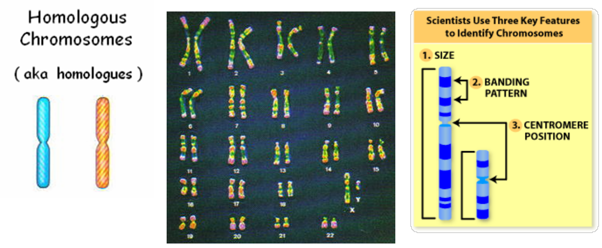


Each parent donates genes to their offspring via sexual reproduction. The genes combine to give different but similar looking offspring.

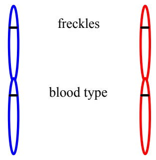
The number of chromosomes in a set = haploid (*n*)
A cell with two sets of chromosomes = diploid (2*n*)



Humans have 46 chromosomes consisting of 23 homologous pairs. Each parent donates one chromosome to each of the 23 homologous pairs.



Homologous chromosomes are the same length and carry the same genes in the same location. Those genes could be different versions.
e.g., the gene on one chromosome could say "freckles" while the other says "no freckles"

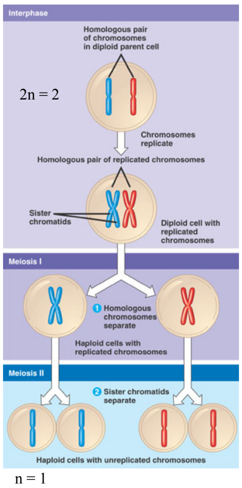


- this is for autosomes only
- for the **sex chromosomes**, females have a homologous pair (XX) while males do not (Xy)

15. What are chromosomes other than sex chromosomes called?

16. Distinguish between haploid and diploid cells in humans. Apply them to the terms "somatic cell" and "sex cell."

17. Do homologous chromosomes have the same number of genes? Do they have identical genes? Explain.



Meiosis animation Back

2n = 6

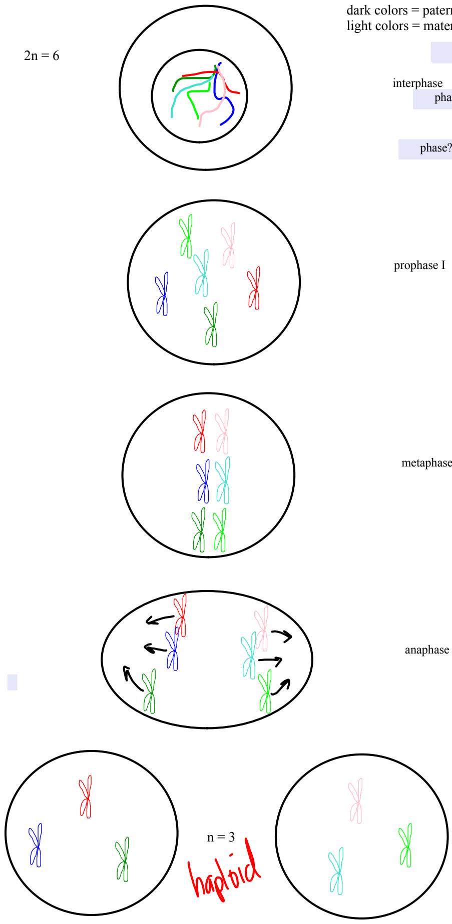
dark colors = paternal
light colors = maternal

phase?

interphase

phase?

phase?



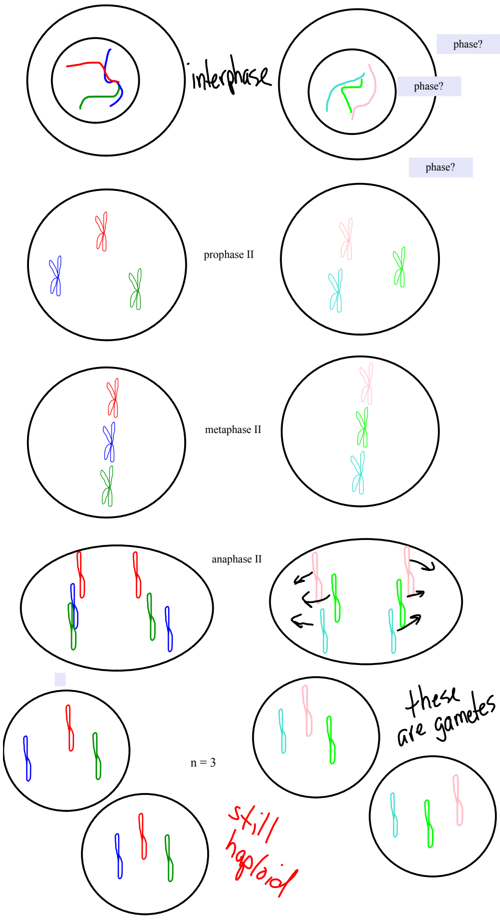
prophase I

metaphase I

anaphase I

n = 3

haploid



interphase

phase?

phase?

phase?

prophase II

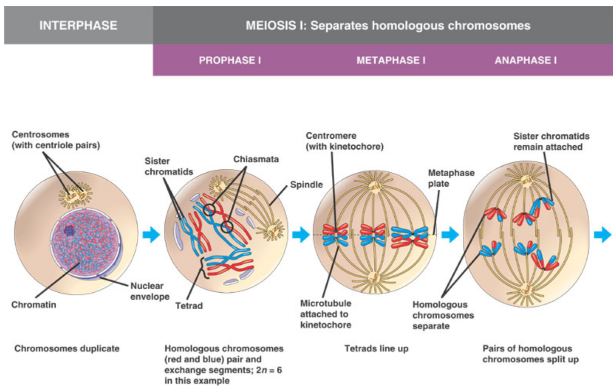
metaphase II

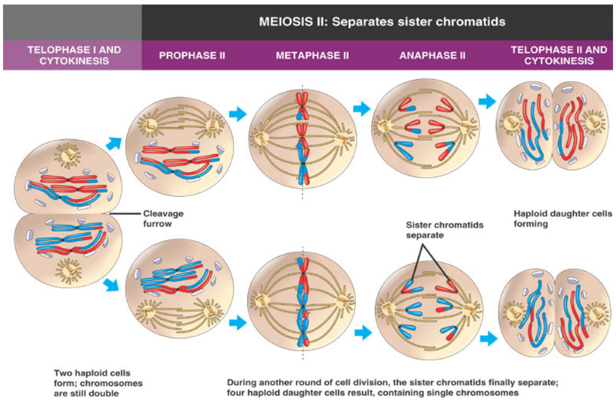
anaphase II

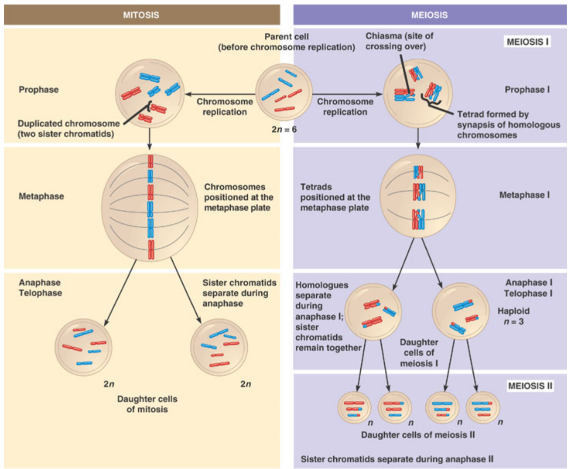
n = 3

these are gametes

still haploid







daughters are clones
daughters are somatic

daughters are different
daughters are sex cells

18. a) A cell with 10 chromosomes undergoes mitosis. Indicate the number of chromosomes you would expect in each of the daughter cells.
b) What about after meiosis?

19. Match the events to the correct phase of meiosis.
a) pairs of homologous chromosomes line up along the equator of the cell
b) synapsis occurs and the four chromatids form a tetrad
c) replication of the genetic material
d) homologous pairs become separated
e) sister chromatids split at the centromere and move toward opposite poles

20. A muscle cell of a mouse has 40 chromosomes. Indicate the number of chromosomes you would expect to find in each of the following cells of the same mouse
a) daughter cell formed after mitosis
b) skin cell
c) egg cell
d) fertilized egg

21. a) If a cell has a diploid number of 32, what would be the chromosome number of a cell in late Prophase I of meiosis?
b) What about at the end of Telophase II?

22. Compare and contrast meiosis and mitosis.

Mutations result in changes in genes. (i.e, genetic diversity)
Genetic diversity leads to evolutionary change.

If an offspring inherits a combination that gives it a better survival advantage, there is an increased chance that combination will be passed on.

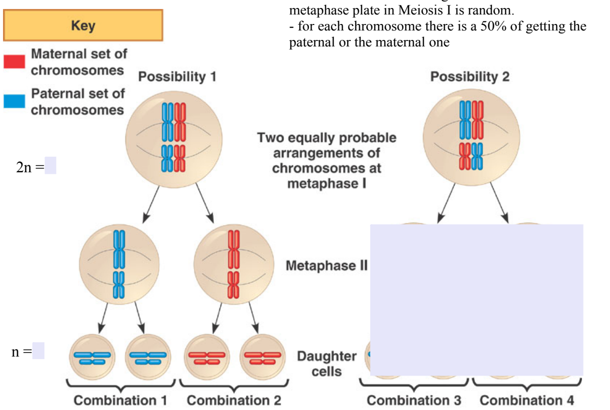
Over time, there will be an accumulation of favorable characteristics.

During meiosis, three things contribute to genetic diversity:
1. Independent assortment of chromosomes
- Random orientation of homologous pairs of chromosomes

2. Random fertilization
- any sperm can fertilize any egg

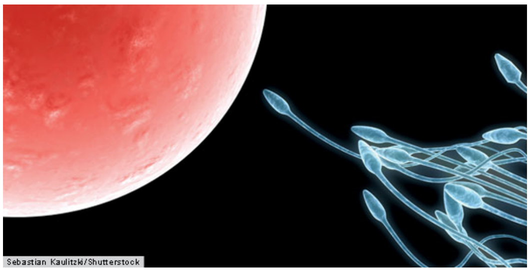
3. Crossing over
- pieces of chromosomes switch places

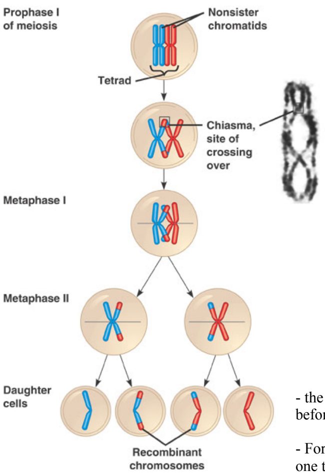
The orientation of homologous chromosomes at the metaphase plate in Meiosis I is random.
- for each chromosome there is a 50% of getting the paternal or the maternal one



The number of possible orientations is 2^n, where n is the haploid number. For humans, th number is

Random fertilization
Any of a male's 8.4 million sperm can fertilize any of a woman's 8.4 million eggs. The total number of combinations is over .





- homologous pairs form tetrads

- pieces of chromosomes get tangled

- small pieces break off and trade places (cross over)

- the result is a combination that did not exist before

- For humans, crossing over occurs, on average, one to three times per chromosome pair.

- When crossing over is considered, the number of combinations is nearly infinite.

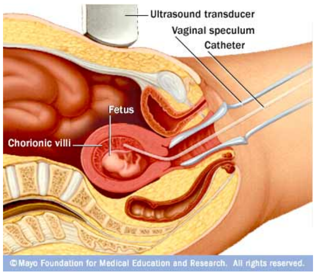
23. Explain how the production of gametes and sexual reproduction increase genetic variation.

24. Explain how synapsis often leads to the exchange of genetic material between chromosomes.

Do chromosomes always separate perfectly, just like they're supposed to?

Amniocentesis
- 15 to 20 weeks pregnant but can be done as early as 11
- amniotic fluid is tested for chromosomal abnormalities or for particular alleles
- results are available in 2 weeks
- risk of pregnancy loss is 0.6-0.86% while one study has it at 0.06%

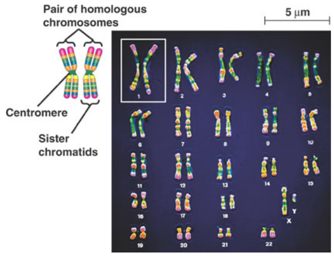
Chorionic villus sampling (CVS)
- can be done at 10-12 weeks pregnant or as early as 8 weeks
- a small piece of tisue is removed from the placenta
- risk of pregnancy loss is 0.5-1%

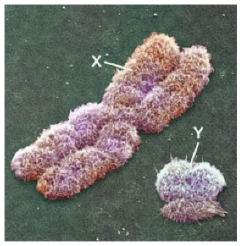


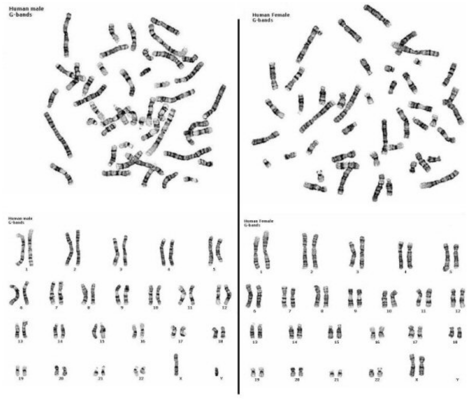
So what if we discover a problem?

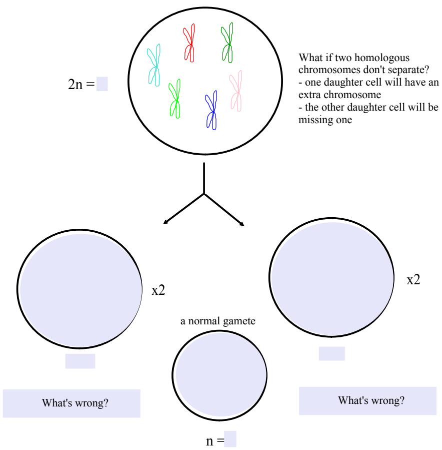
1. Harvest fetal cells.
2. Culture them *in vitro.*
3. Remove the chromosomes and arrange them in pairs to be photographed.

We can detect abnormalities in chromosome number, shape, or size.





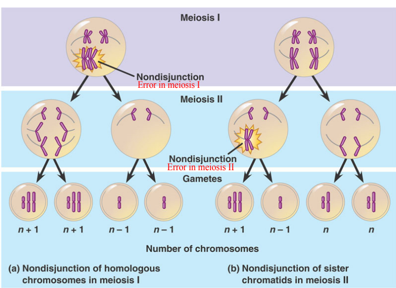




What if two homologous chromosomes don't separate?
- one daughter cell will have an extra chromosome
- the other daughter cell will be missing one

- every cell of the organism will then have the abnormal chromosome number.
- it is believed that many cases of mental retardation are linked to chromosomal defects.

- pieces of chromosomes sometimes get moved to a different place in the genome (this is called a chromosomal translocation) which cause specific cancers.
  - *e.g.*, chronic myelogenous leukemia (CML) occurs when a large fragment of chromosome 22 switches places with a small fragment from the tip of chromosome 9.



(all cells are aneuploid) (half the cells are aneuploid)

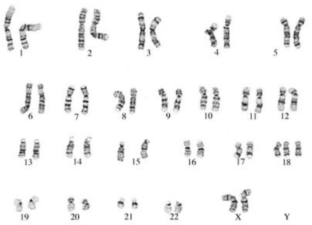
- characteristic facial features
- short stature
- heart defects
- mental retardation
- increased risk of respiratory infection and developing leukemia and Alzheimer's disease
- most are sexually underdeveloped and sterile
- shorter life span (on average)

Frequency
1/750 in Canada

Mother's age	Rate
20	1/1600
25	1/1300
30	1/1000
35	1/365
40	1/90
45	1/30
49	1/12

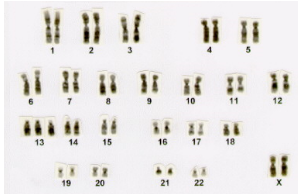
Edward's syndrome

- small, abnormally shaped head, small jaw and mouth
- long fingers that overlap, with underdeveloped thumbs and clenched fists
- cleft lip and palate (a gap or split in the upper lip and/or the roof of the mouth)
- heart, kidney, breathing and feeding problems
- intestines or other organs protruding outside the body (omphalocele)
- severe mental retardation
- life span is usually less than 10 weeks
- frequency is 1 in 3,000 conceptions and approximately 1 in 6,000 live births



Disturbing image

Disturbing image

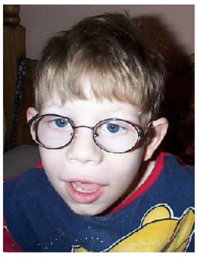


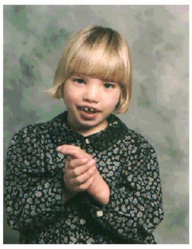
Patau syndrome
- intellectual disability and motor disorder
- microephaly
- spinal defects
- polydactyly (extra digits)
- cyclopia
- proboscis
- omphalocele (abdominal defect)
- overlapping of fingers over thumb
- cutis aplasia (missing portion of the skin/hair)
- cleft palate
- abnormal genitalia
- kidney defects
- heart defects

- life span is rarely more than one year and more than 80% of children die within the first month

Frequency 1/12,000

Disturbing images





- sometimes abnormal crossing over causes pieces of chromosomes to be incorrectly attached or even lost altogether
- usually, these errors cause a variety of cancers but can also cause other disorders
- cri-du-chat is caused by a specific deletion in chromosome 5
- feeding problems because of difficulty swallowing and sucking (the characteristic cry is caused by a defect in the larynx)
- low birth weight and poor growth
- severe cognitive, speech, and motor delays
- behavioral problems such as hyperactivity, aggression, tantrums, and repetitive movements
- unusual facial features (hypertelorism)
- excessive drooling
- constipation
- microcephaly
- 1/50,000 births

- it is possible that nondisjunction occurs in other chromosomes but the consequences are lethal

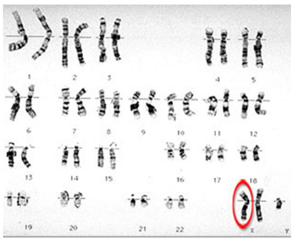
- nondisjunction of the sex chromosomes is also possible
- produces many combinations of sex chromosomes

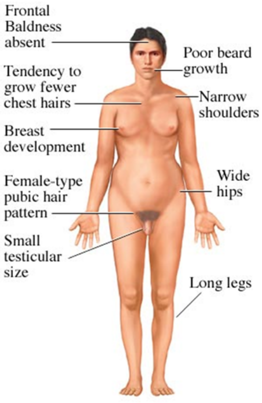
XXX females
- trisomic X females are indistinguishable from normal females
- frequency is estimated at 1/1000
- unsure because not usually diagnosed unless genetic screening for some other purpose

Xyy males
- indistinguishable from normal males (although might be slightly taller)
- estimated at 1/1000

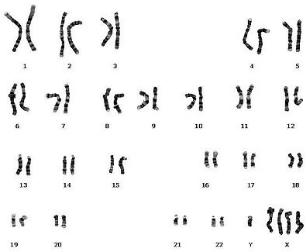
Why are aneuploid conditions of the sex chromosomes less serious?

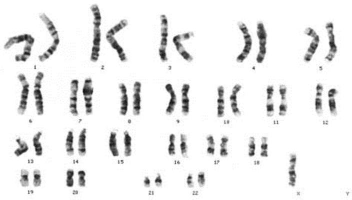
- individuals are anatomically male but have abnormally small testes that fail to descend
- usually sterile
- female secondary sex characteristics develop
- normal intelligence
- condition exists in roughly 1 out of every 1,000 males. One in every 500 males has an extra X chromosome but does not have the syndrome





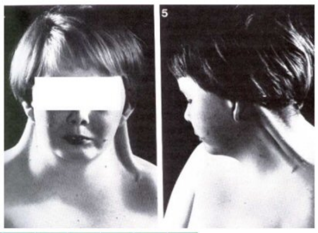
XXXXY, Klinefelter's Syndrome

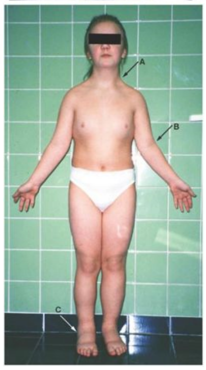




Frequency 1/2000 - 1/5000

- phenotypically female
- short stature, swelling, broad chest, low hairline, low-set ears, and webbed necks, congenital heart disease, hypothyroidism, diabetes, vision problems, hearing concerns, many autoimmune diseases, a specific pattern of cognitive deficits
- usually sterile as the sex organs do not mature
- estrogen replacement therapy helps with the development of female secondary sex characteristics





25. What is a karyotype and where would one get the cells to make one?

26. Describe nondisjunction and its effect on the chromosomal composition of a cell.

27. As any pair of chromatids can fail to separate during meiosis, theoretically there are 23 possible kinds of monosomy and trisomy. However, monosomies and trisomies for most of the 23 chromosome pairs are quite rare (or unheard of). Why do you think this is so?

Attachments

Cri Du Chat.mp4