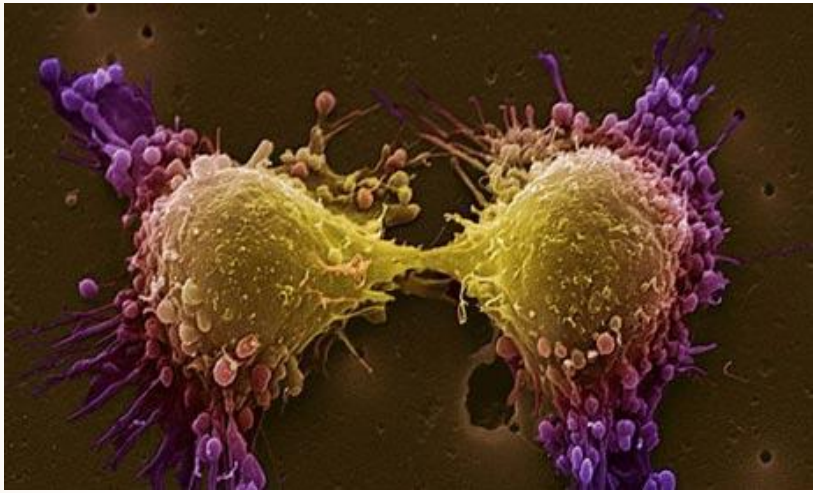
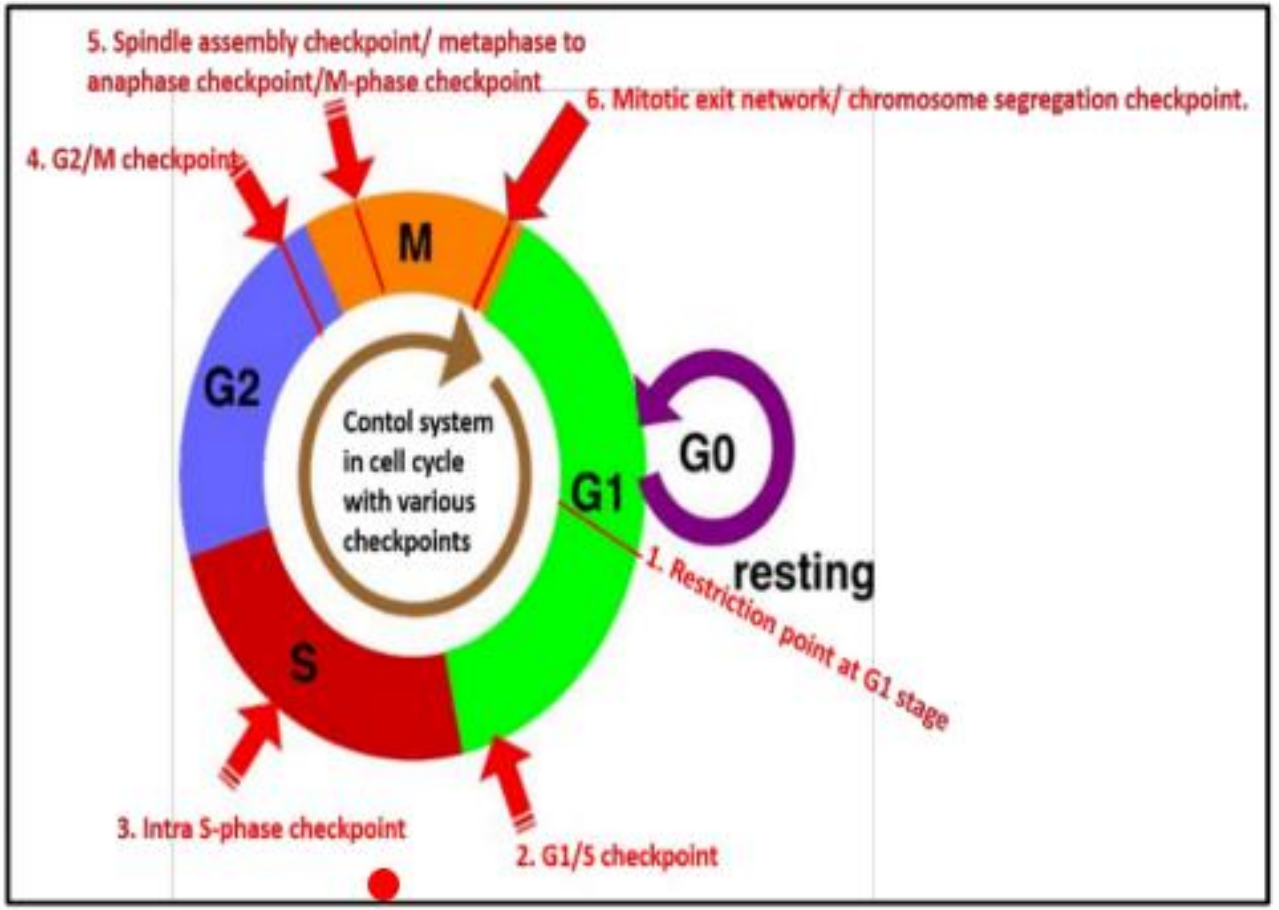
Cell division and function



Part 2

Cell cycle control and various checkpoints

1. Cell cycle checkpoints are the various control points or surveillance mechanism sets at different stages of cell cycle events to keep in check - **the distribution of complete and accurate replicas of the genome to daughter cells** . 2. For example, when cells have DNA damages that have to be repaired, cells activate DNA damage checkpoint that arrests cell cycle. After repairing of DNA damage, only then cell will enter the next stage of cell cycle.



Cell cycle checkpoints/control points	What surveillance /roles these checkpoints do?
1) Restriction point at G1 stage.	a) This is a point of no return at which cell is committed to divide or die by becoming unresponsive to any more external signals. If the cell has improper size or other defects it **enters the temporary stage of resting called G_0 phase**.
2) **G1/S checkpoint**	a) Keeps an eye over DNA damages and ensures that the everything is ready for DNA synthesis. b) Ensures the **proper cell size and availability of nutrients required** for **further stage of the cell cycle**. If any of these are not adequate, there will be **cell arrest and cell go for apoptosis** (cell death).
3) **Intra S-phase checkpoint**	a) This occurs at the middle of the S-phase which is the phase of synthesis of DNA. **b) keeps an eye over proper DNA replication**, any damages or lesions in DNA will stall replication forks during replication process and so on

4) G2/M checkpoint	a) **If DNA synthesis is not completed, cells do not enter** into mitotic phase and goes for apoptosis. b) checks for the mitotic machineries that are required for the next stages. Cell ensures that all the materials are available for carry out division through next stage as well as genome integrity is also maintained
5) Spindle assembly checkpoint or metaphase to anaphase checkpoint	a) This checkpoint **works between metaphase to anaphase stage of M-phase. .** **b) Improper assembly of mitotic spindle fibres prevents the initiation of anaphase.** When spindle fails to attach to the kinetochore of one sister chromatid, the checkpoint do not allow it to enter the anaphase.
6) Mitotic exit network or chromosome segregation checkpoint.	a) **Proper segregation of daughter chromosomes during telophase** and **cytokinesis** is monitored by this checkpoint.

What happens if you lose one of checkpoints?

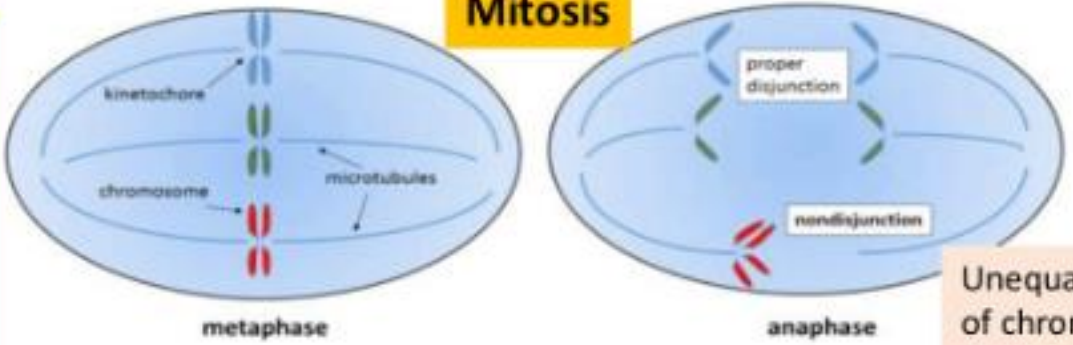
1. **Checkpoint failure often causes mutations and genomic arrangements resulting in genetic instability**. Genetic instability is a major factor of birth defects and in the development of many diseases, most notably cancer. Therefore, checkpoint studies are very important for understanding mechanisms of genome maintenance as they have direct impact on the ontogeny of birth defects and the cancer biology.

2. **Non-disjunction as a result of failure of spindle assemble checkpoint**. For example, if the spindle assemble checkpoint do not work properly and missed it out, the abnormality arises in the cell, as a result of which, one daughter cell contains two copies of chromosome while the other daughter cells lacks that chromosome. This abnormality in the cell is called **Non disjunction.**

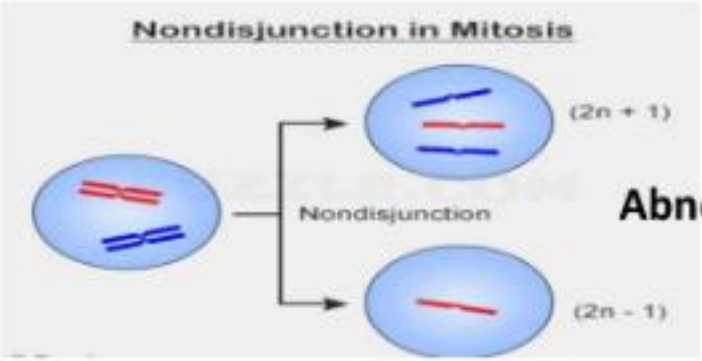
Non disjunction:

Failure of Spindle-assembly checkpoint or metaphase to anaphase transition causing unequal distribution of chromosomes in daughter cells.

Mitosis



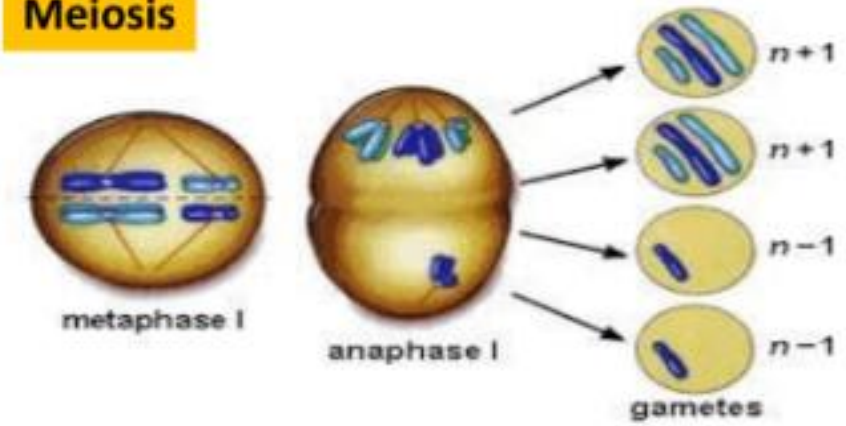
Unequal distribution of chromosome during metaphase to anaphase transition: failure of spindle – assembly checkpoint



Abnormal daughter cells

Meiosis

Why "abnormal" because normal chromosome number is not maintained?

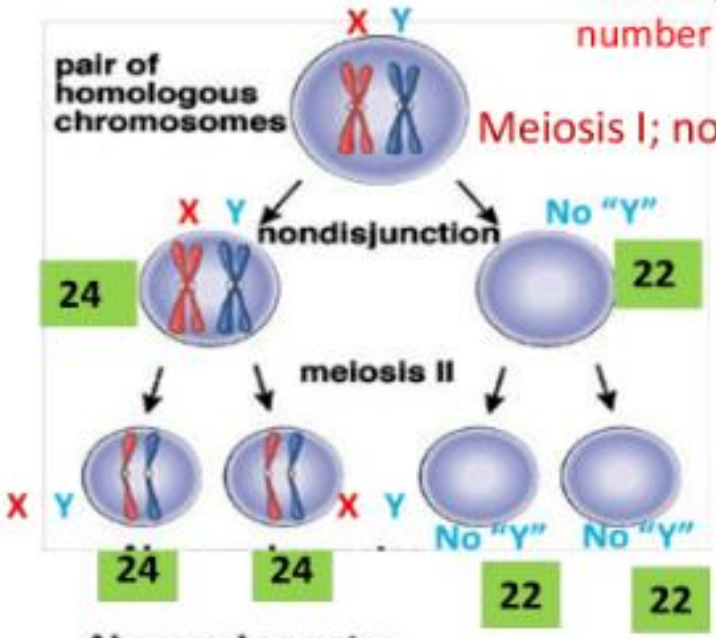


Abnormal gametes

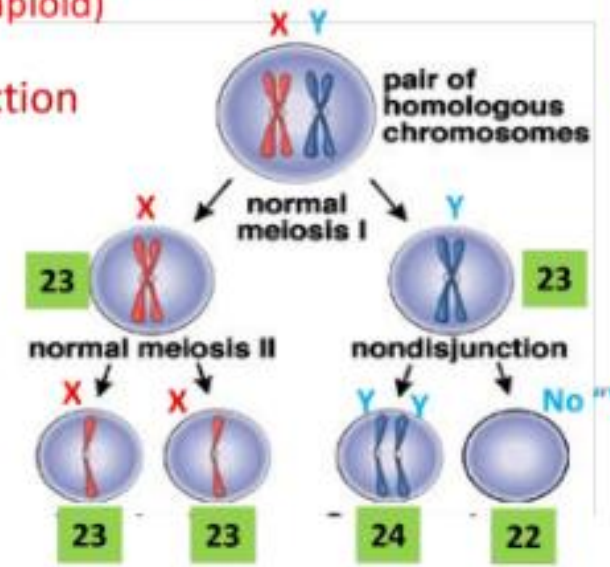
Non-disjunction can happen either in meiosis I … metaphase to anaphase transition or meiosis II during metaphase to anaphase transition

Taking example here the separation of X and Y homologous pair.

Normal gamete chromosome number is : 23 (haploid)



Abnormal gametes: two gametes have one extra and two gametes have one less chromosome than normal.



Meiosis II; nondisjunction in **one of the daughter cells.**

Gametes have usual number of chromosomes.

One gamete has one extra and the other has one less chromosome.

"Abnormal Sperms"..... **22 + XY** (24 chromosome) X Normal ovum..... **22 + X**

Fertilization ↓

44 + XXY **Klinefelter's syndrome**

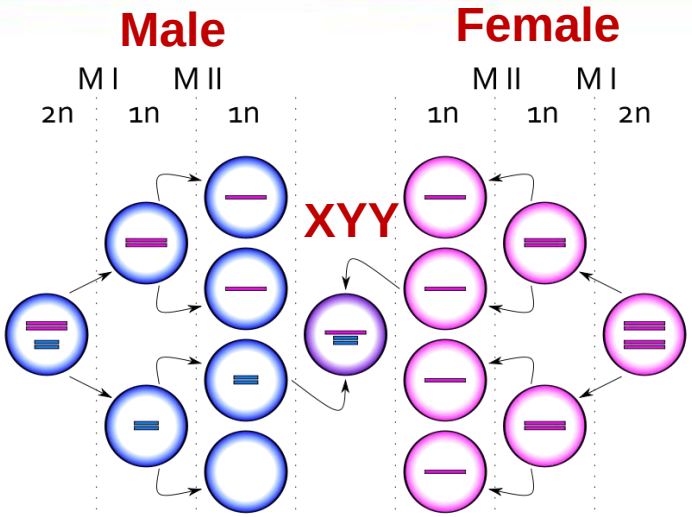
"Abnormal Sperms"..... **22 + O** (22 chromosome) X Normal ovum..... **22 + X**

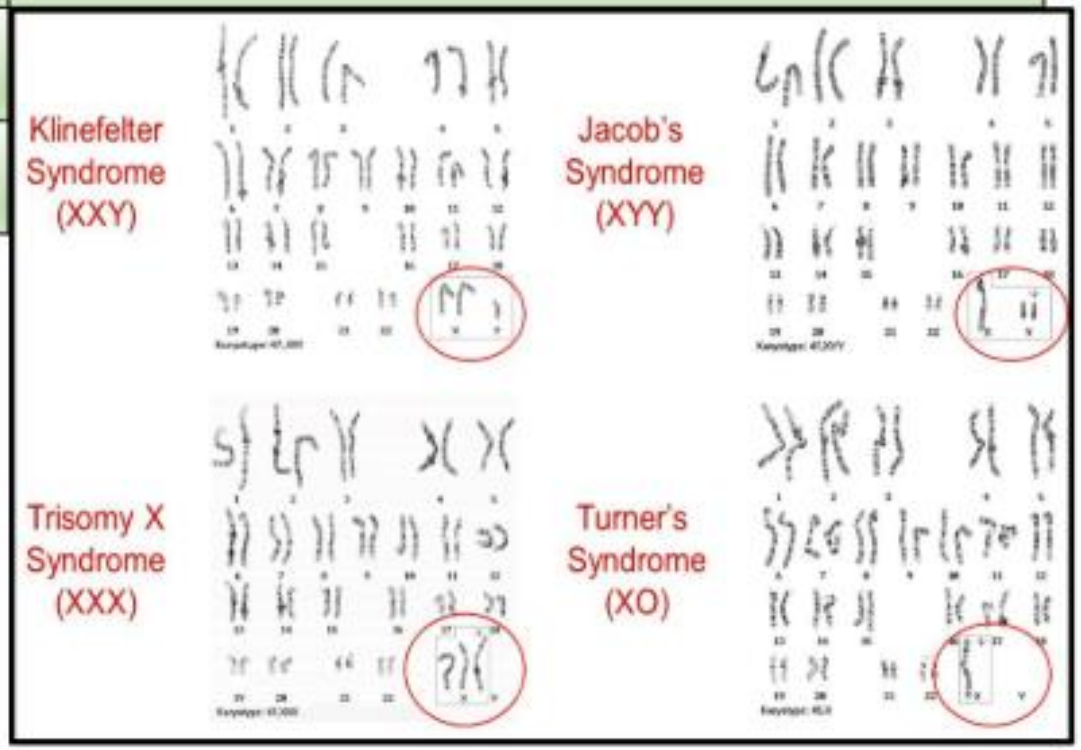
Fertilization ↓

44 + XO **Turner's syndrome**

Disorders due to Non Disjunction of Sex chromosomes

Non-disjunction in Sex chromosomes	Individual's chromosome notation	Physical appearance and symptoms
1) Turner's syndrome	44 + XO	Women with one X-chromosome, short height, webbed neck, lack of underarm and pubic hair, underdeveloped ovaries
2) Klinefelter's syndrome	44 + XXY	Symptoms in males include like tall height, low IQ scores, speech and language difficulty, sterility
3) Jacob's Syndrome	44 + XYY	
4) Trisomy X syndrome	44 + XXX	





Non-disjunction in "Autosomes"	notation	Symptoms
1) Trisomy 18 (Edward's Syndrome)	45 + XX or 45 + XY (extra copy of chromosome 18	Slow growth before birth, low birth weight, abnormal organ growth, heart defects, small head, 90-95% mortality rate during the first year.
2) Trisomy 13 (Patau syndrome)	45 + XX or 45 + XY (extra copy of chromosome 13	Heart defects, abnormalities of the eyes, ears, brain and spinal cord, cleft palate and or lip, small head, low IQ scores, speech and language difficulty, sterility
3) Trisomy 21 (Down Syndrome)	45 + XX or 45 + XY (extra copy of chromosome 21	

Sample questions

1) If cell has 46 chromosomes at the beginning of mitosis, then at anaphase there would be a total of

a) 46 chromosomes

b) 92 chromosomes

c) 23 chromatids

d) 46 chromatids

2) If a cell has 46 chromosomes at the beginning of meiosis, then at anaphase I there would be a total of

a) 23 chromatids

b) 46 chromatids

c) 46 chromosomes

d) 92 chromosomes

3) During cell cycle sister chromatids are pulled apart during

a) Metaphase

b) Anaphase

c) Prophase

d) Interphase

4) The minimum number of meiotic division to obtain 100 sperms

a) 25
b) 50
c) 75
d) 100

5) **How many mitotic division must occur in a cell of the root tip to form 128 cells**

a) 7
b) 8
c) 64
d) 128

6). **Homologous chromosome include**

a) one smaller and one bigger chromosome
b) one chromosome from each parent
c) one complete and one incomplete chromosome
d) none of the above

7) T/F: Interphase is usually divided into 3 phases: G1, S, G2.

8) The _____ is the regular sequence of growth and division that cells undergo.

9) _____ is the stage of the cell cycle where the cell grows to its mature size, copies it DNA, and prepare to divide.

10) Cells can not get too big because:

A. there is not enough DNA to support large cells

B. diffusion is too slow to provide for large cells

C. the surface area of a cell increases too fast for the cell membrane to meet its needs.

D. all of the above

11) DNA is replicated during:

A. interphase

B. prophase

C. metaphase

D. cytokinesis

Score yourself, how many of the following you can answer

Few additional questions to remember:

1) What do you understand by homologous chromosomes or homologous pair?
2) What is spindle fibres made of?
3) What is the component name that gives rise to spindle fibres?
4) What is centromere?
5) Which notation of chromosome number of Telophase II 22+X or 22+XX is correct?
6) Which notation of chromosome number of Anaphase I 44 + XX or 22 + X is correct?
7) Do polar bodies are haploid or diploid?
8) Do spermatids are haploid or diploid?
9) How many mitotic divisions **a cell** has to undergo to give rise to 64 cells?
10) At which stage of Prophase I, crossing over takes place?
11) What actually happens in crossing over?
12) What is the name of point of crossing over?
13) Which is the longest phase of cell cycle? Why it is the longest phase?
14) Spindle proteins are synthesized in which phase of Interphase?
15) Do you find nuclear membrane in **metaphase** of cell division? When again it reappears in cell division?