Genetics

Subject : Genetic diseases part 1

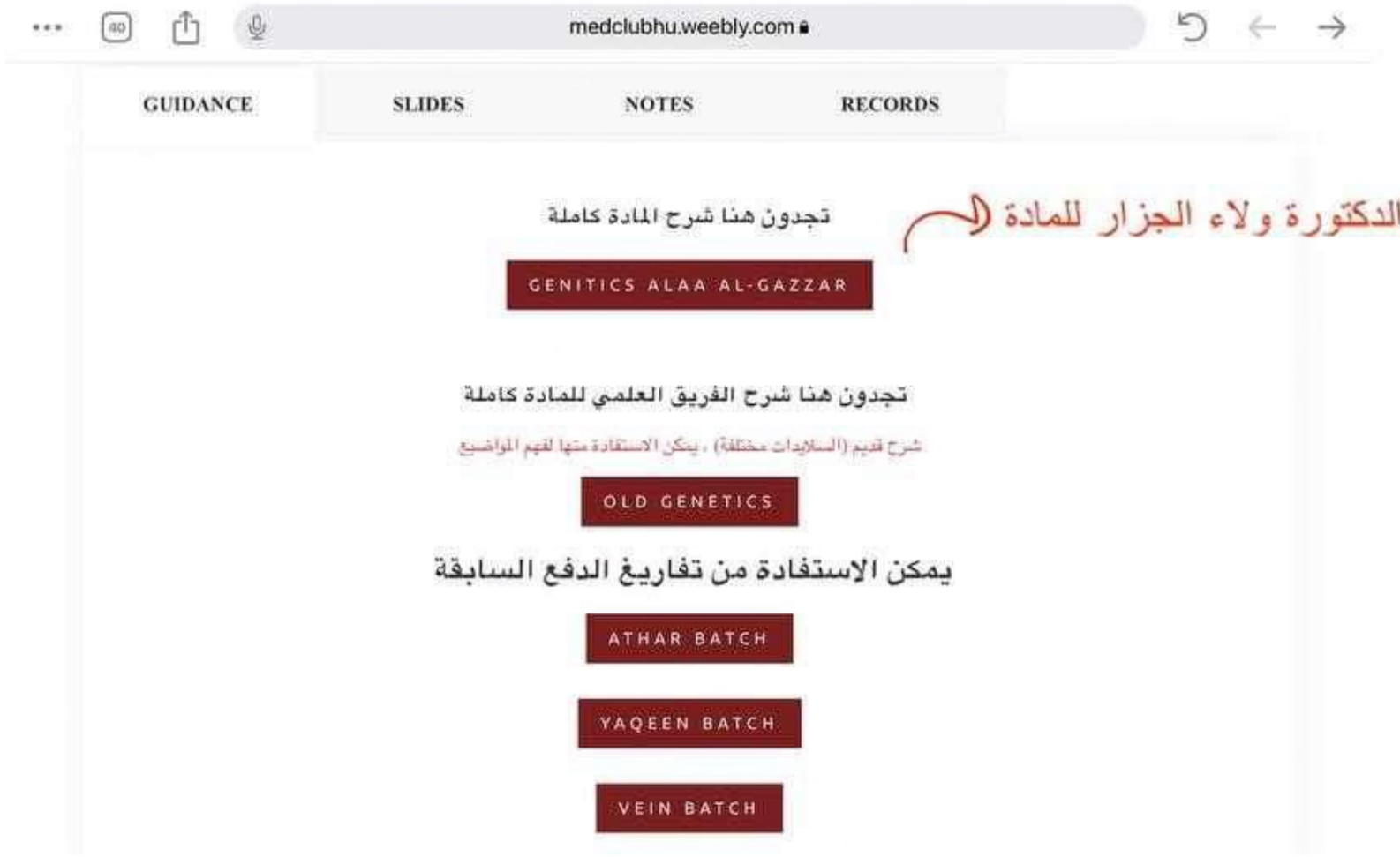
Lec no : 25

Done By : Noor Zamel

وَقُل رَّبِّ زِدْنِي عِلْمًا

تجدون في guidance مادة الجينتكس على موقع النادي :

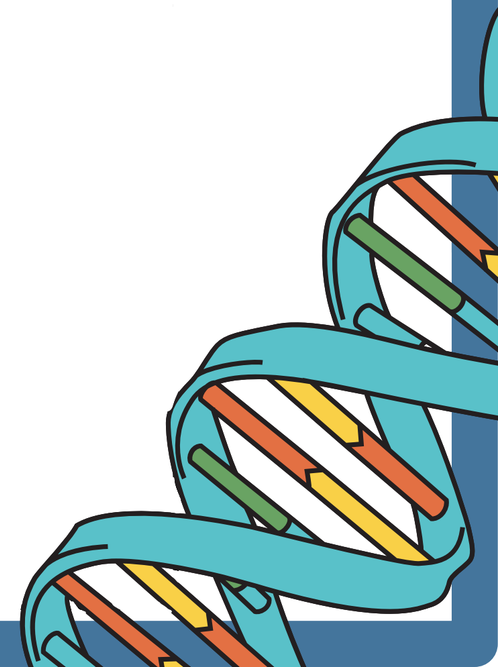
للوصول الى guidance الجينيتكسو تفاريغ المادة كاملة :



شرح الدكتورة ولاء الجزار للمادة

كل اعمال الفريق العلمي تنشر على قناة التيليغرام

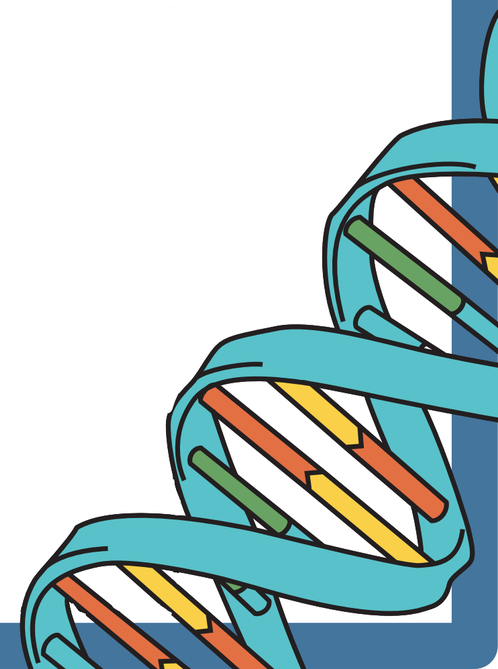
Lec 25



GENETIC DISEASES

By

Dr. Walaa Bayoumie El Gazzar



- Genetic diseases are classified into four types:

Chromosomal disorders

Mitochondrial disorders

Monogenic disorders

Multigenic (multifactorial) disorders

Chromosomal disorders

- Results from alterations in chromosomal **numbers** or **structure**, which is also called **chromosome aberrations**.

بعض الإنحرافات في الكروموسومات سواءً عددهم او التركيب تاعهم

Numerical changes

اول اشي رح نحكي عن التغير في العدد

- **Polyploidy**: when the changes involves a set number of chromosomes(numerical change in the whole set of chromosomes)

لو لقينا أنه الـ cell فيه site كامل صار فيه مشكلة مثلاً بدل 2 sites صارو ٣ او ٤

- **Aneuploidy**: in which the changes is limited to the number of individual chromosomes (numerical change in part of the chromosome set) .

اما لو المشكلة بكروموسوم واحد مثلاً مش بال site كامله فيه part-ب

(more common in human)

* الـ normal Somatic Cells فيهم ٤٦ كروموسوم = ٢٣ زوج

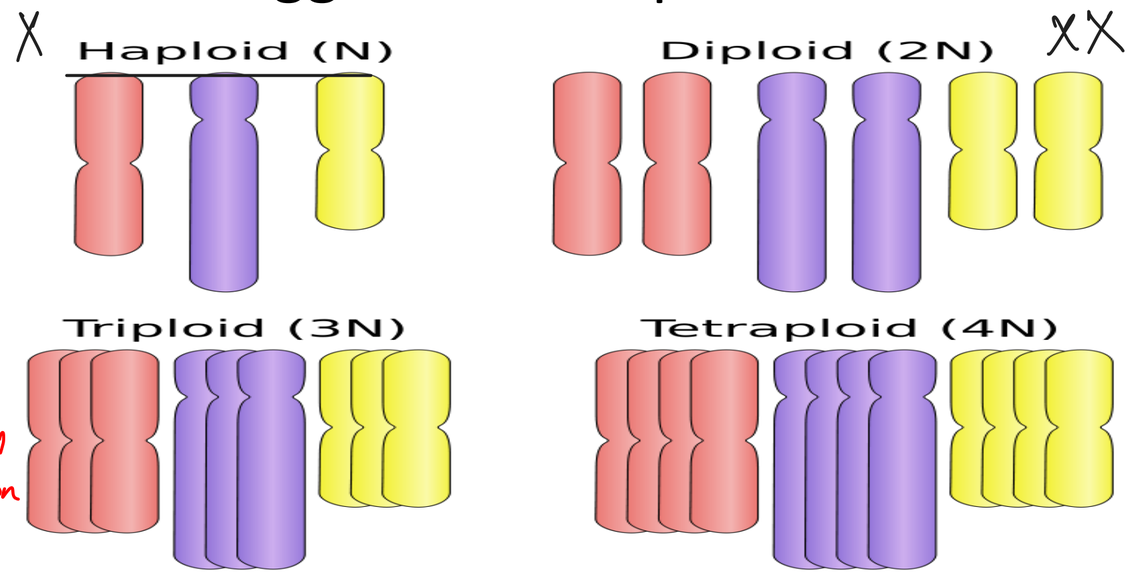
2 sites =

1 site = 23 Chromosome

- True polyploidy rarely occurs in humans, but it may occur in some tissues (especially in the liver) while aneuploidy is more common.

- Human polyploidy appears in the form of triploidy, with 69 chromosomes (also called 69, XXX), and tetraploidy with 92 chromosomes (also called 92, XXXX).
- *The letter x is used to represent the number of chromosomes in a single set.*

- Triploidy, is usually responsible for 17 % of spontaneous abortions. The main causes of this mutation is due to fertilization with a diploid spermatocyte or egg or the fertilization of normal egg with two sperms.



Diploid egg + normal Sperm
XX + X
⇓
XXX Triploid

normal egg
X

2 normal Sperms
X
X

لو السبرمز عملوا penetration

⇓
XXX Triploid

١٧ ٪ من النساء الحوامل اللي بصيرلهم إجهاض في اول ٣ شهور يكون السبب انه الجنين Triploid يعني عنده 3 sites من الكروموسومات

طيب ليه بصير Triploid ؟
بكون ال Sperm او ال egg اللي صارلهم Fertilization الـ Ubnormal عدد الكروموسومي عندهم قبل مايكونوا بالوضع الطبيعي 23 (haploid)
↓
Diploid بكون

مشكلة بـ part من الكروموسوم
إما اكتسبنا جزء او خسرنا

- **Human aneuploidy** is the result of adding an extra chromosome or losing a single chromosome which happens during cell division when chromosomes do not separate properly between the two new cells.

- The defect may take place in germ cells at birth leading to birth defects or may occur in somatic cells and associated with some cancer cells development.

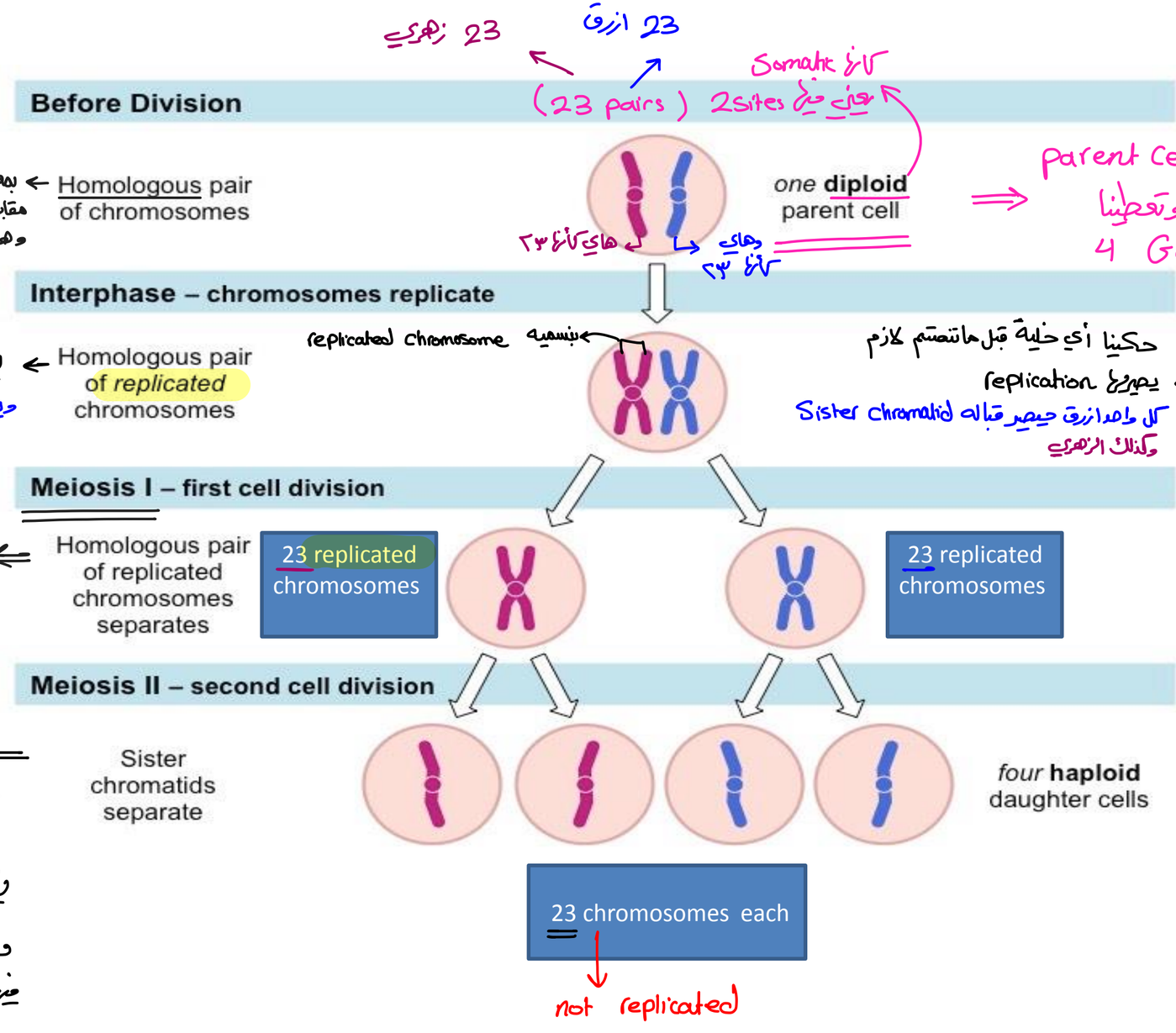
بروح اذا صار خطأ اثناء انقسام الخلية وهلاح نعرف كيف بتنقسم ↓ سلايد ١١

في حالة صار مزبطة اثناء الـ cell devision رح تأثر الـ Somatic cells وممكن تقلب Cancer cells

- **Nondisjunction** of chromosomes occurs when either homologues pairs fail to separate during anaphase I or sister chromatids fail to separate during anaphase II of meiosis.
- **Nondisjunction is the failure of homologous chromosomes (in meiosis I) or sister chromatids to separate properly (meiosis II and mitosis) during cell division.**
- The result is that single gamete has 2 copies of one chromosome and the other has no copy of that chromosome.

- If either of these gametes unites with another during fertilization, the result is aneuploidy , so that one trisomic cell will have one extra chromosome (2n +1). Another cell will be monosomic has one missing chromosome (2n -1) = mostly lethal

Homologous pairs of chromosomes are pairs of chromosomes that have the same genes at the same (locations) but may have different variants of those genes



بعض كل كروموسوم من الاب مقابله الكروموسوم اللي من الام وهاد توضيح خارجي

23 زهري 23 ازرق (23 pairs) 2sites Somatic كل خلية عدا الجنسية

هاي كل ٢٣ وهاي كل ٢٣

parent cell هاي الـ اللي المفروض تنقسم وتعطينا 4 Gametes

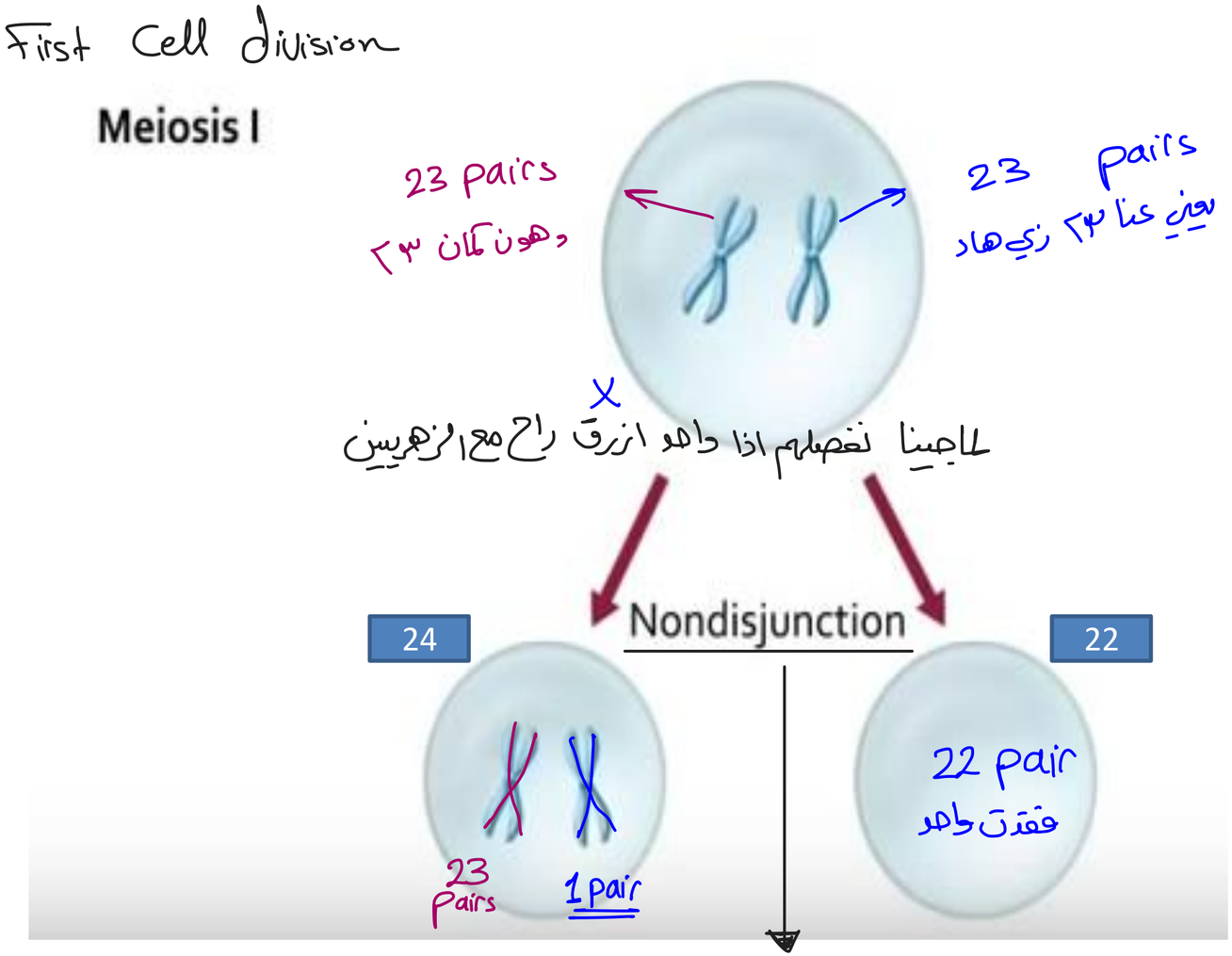
حكينا أي خلية قبل ما تنقسم لازم يصير replication كل واحد ازرق حيصير قباله Sister Chromatid وكذلك الزهري

رح يصير تضاعف لمكونات الخلية حيصير 23 replicated Chromosome من الاب و 23 replicated Chromosome من الام

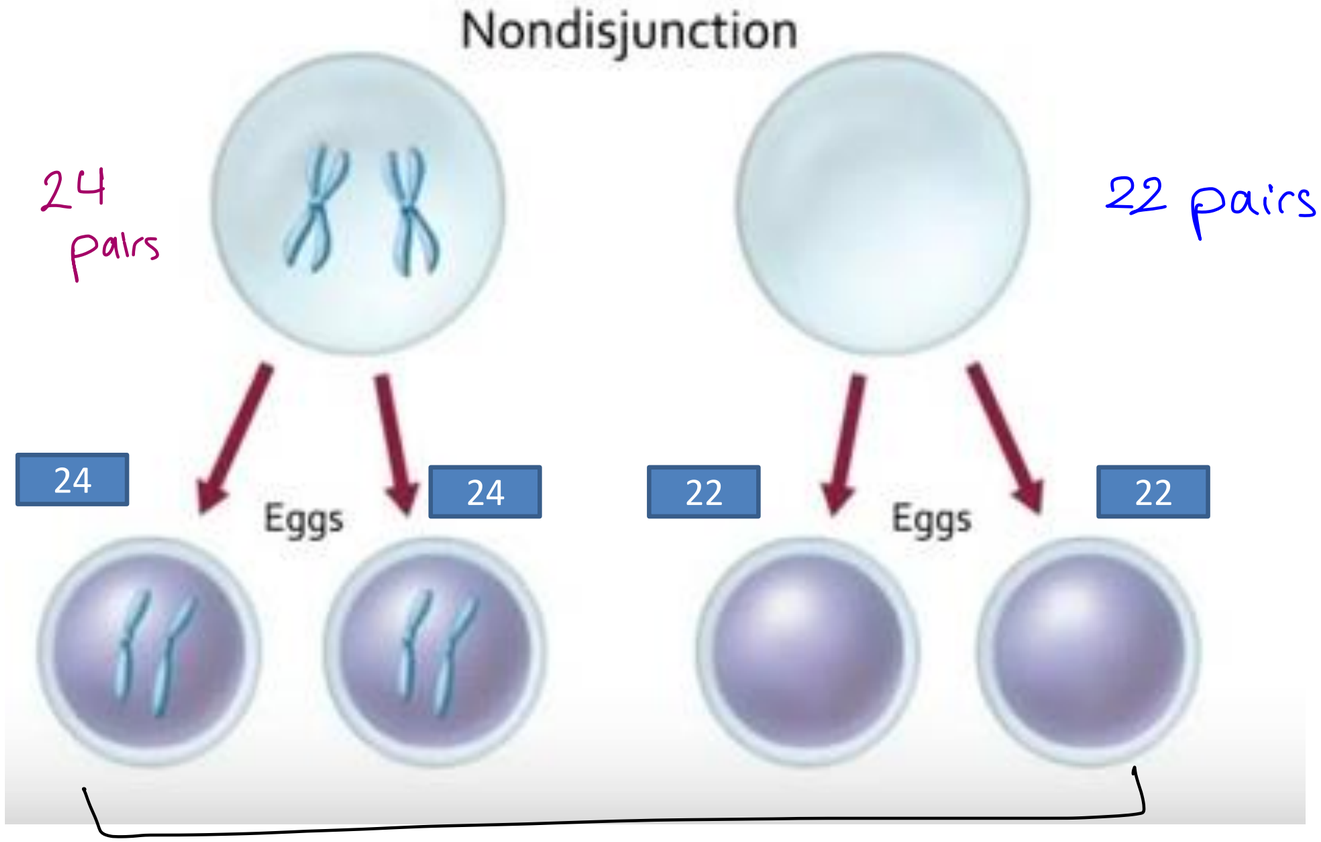
هلا حتنقسم الخلية لخليتين الزهري بخلية والازرق بخلية

كل خلية من الخليتين فيها 23 replicated Chromosome كل Sister Chromatid رح يروح لجهة وينفصلوا وهيك بتكون ٤ خلايا كل وحدة منهم فيها ٢٣ كروموسوم

★ First Cell division



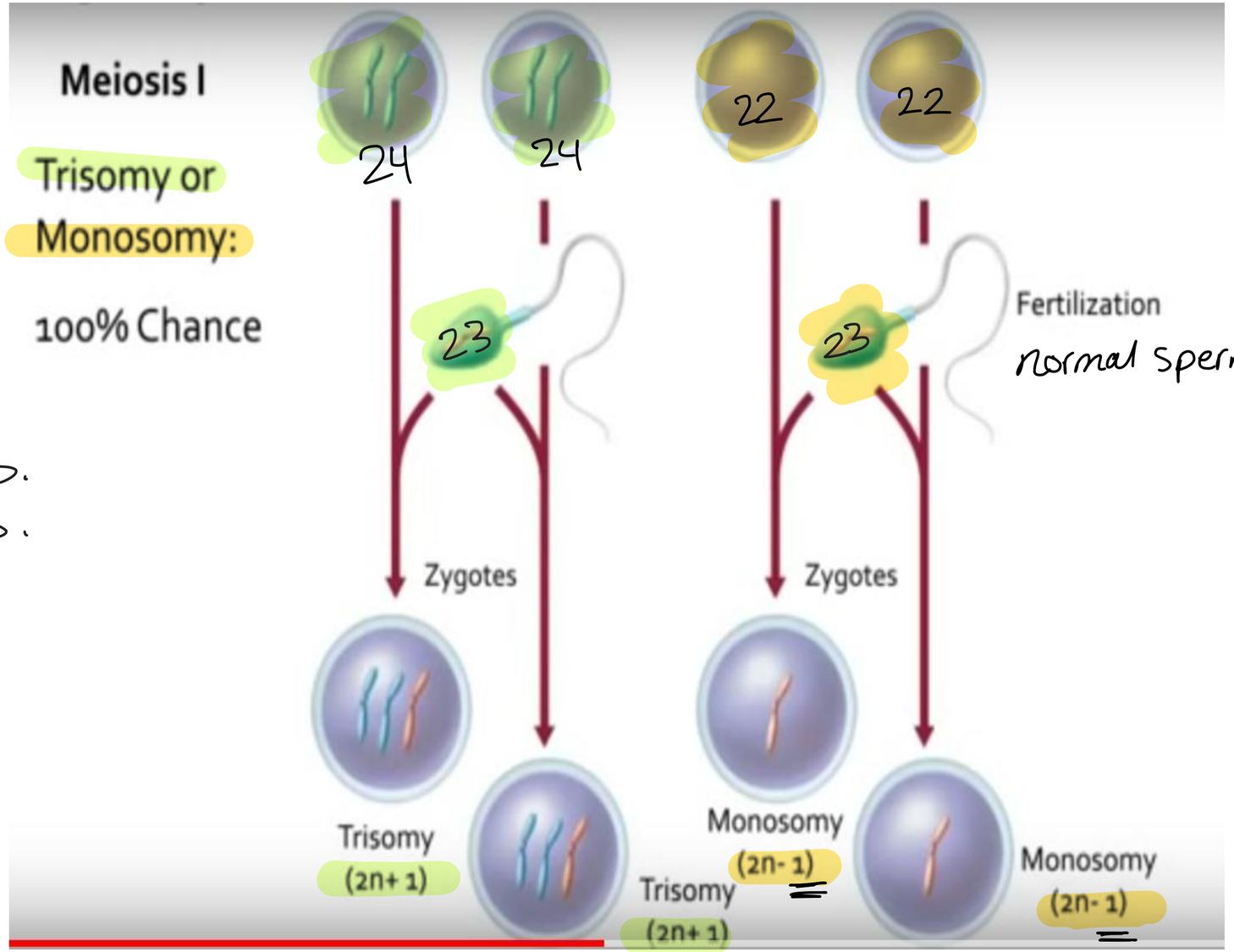
☆ Second cell division



(23 + 1) 24 pairs

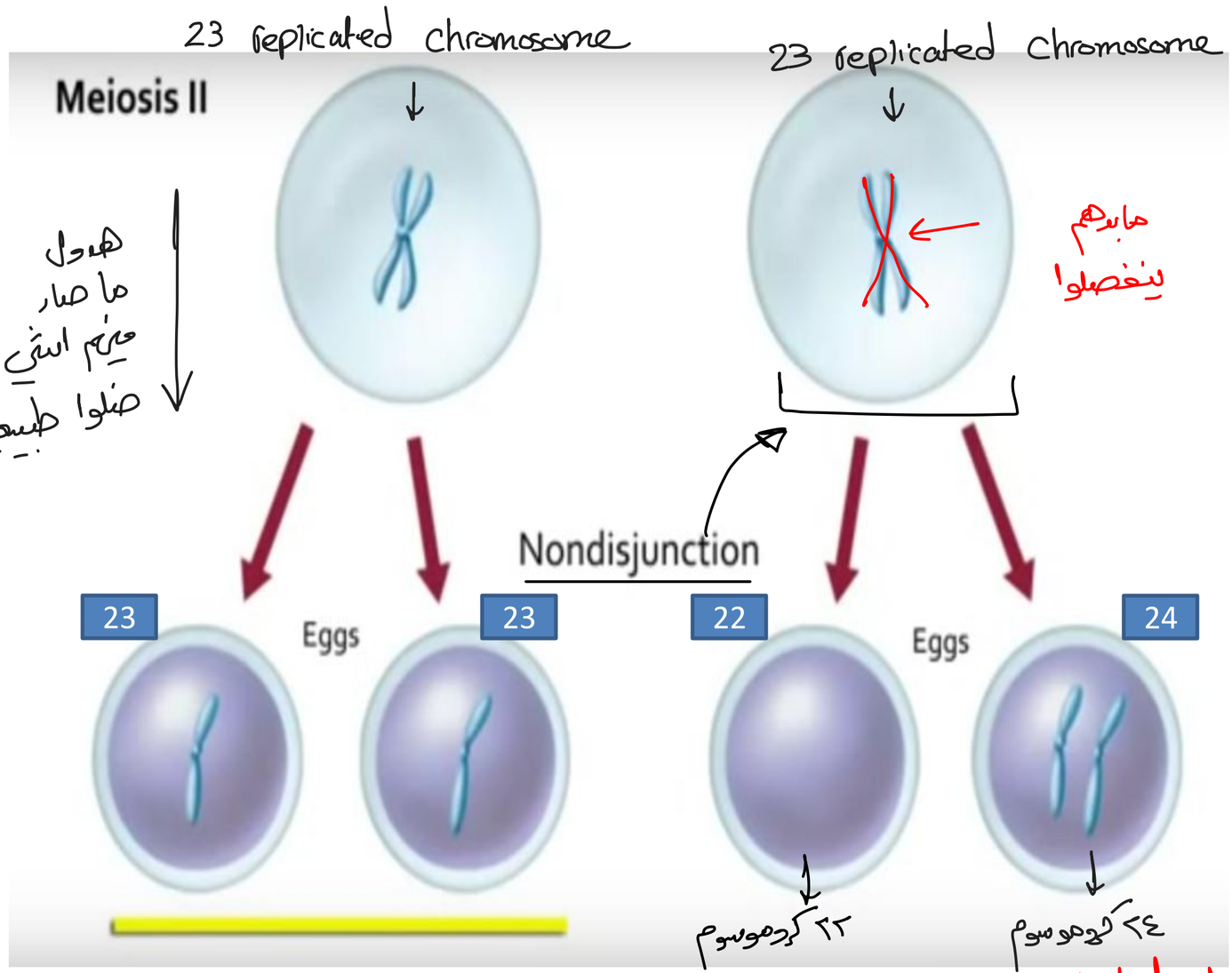
22 pairs

كل الإنتاج خطأ



Trisomy ← ٪٥٠
monosomy ← ٪٥٠

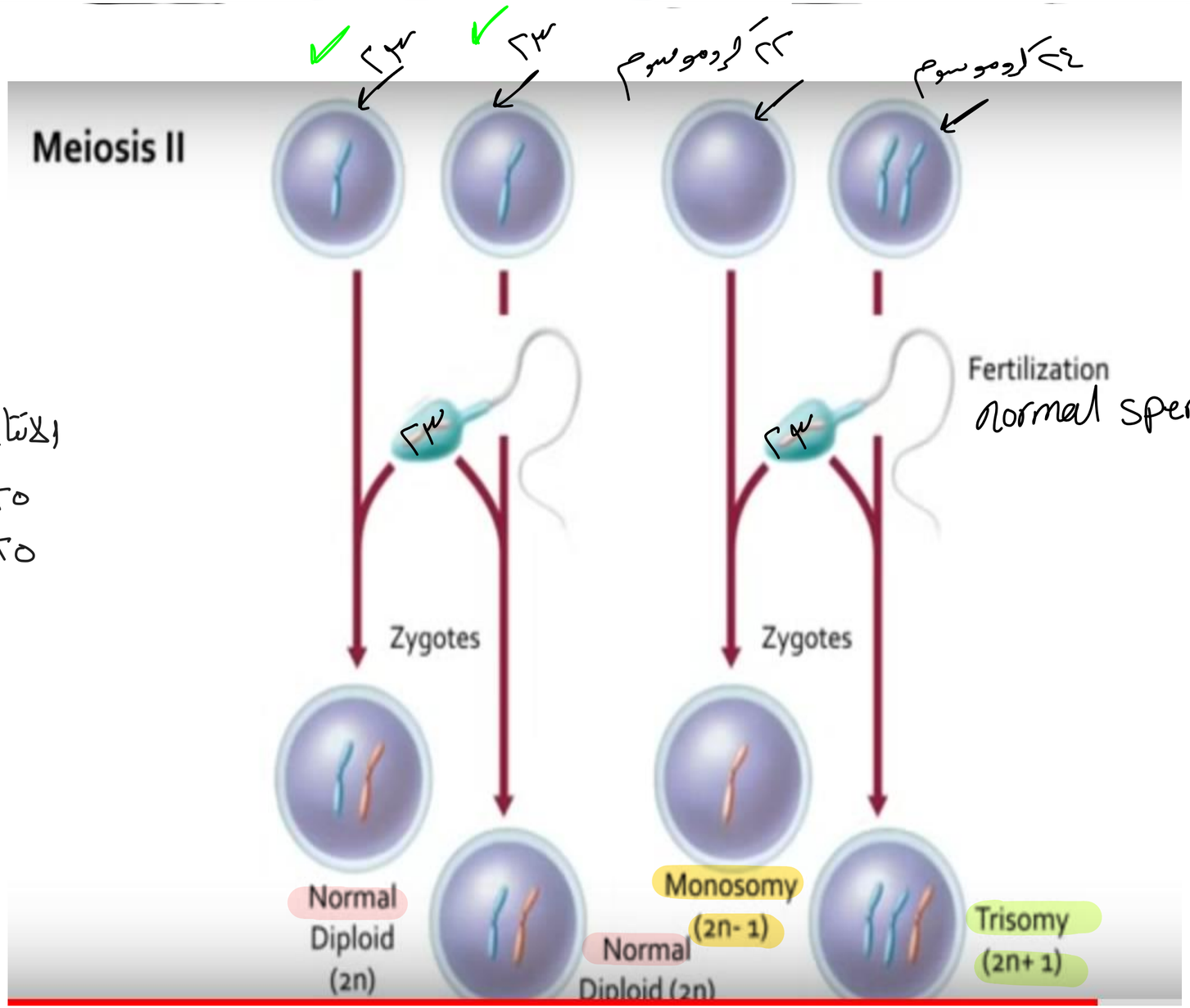
*
بعض المشاكل لو كانت
بالـ First cell division
كل الانتاج رح يكون
حيوان اما ٢٣ او ٢٤



طيب لو المشكلة كانت بالـ 2nd cell division يعني الـ Sister Chromatid ما انفصلوا

⇐ المشكلة بتصير لو واحد من الكروموسومات ما انفصلوا الكروماتيدات بتكون دضلو ماسكين ببعض

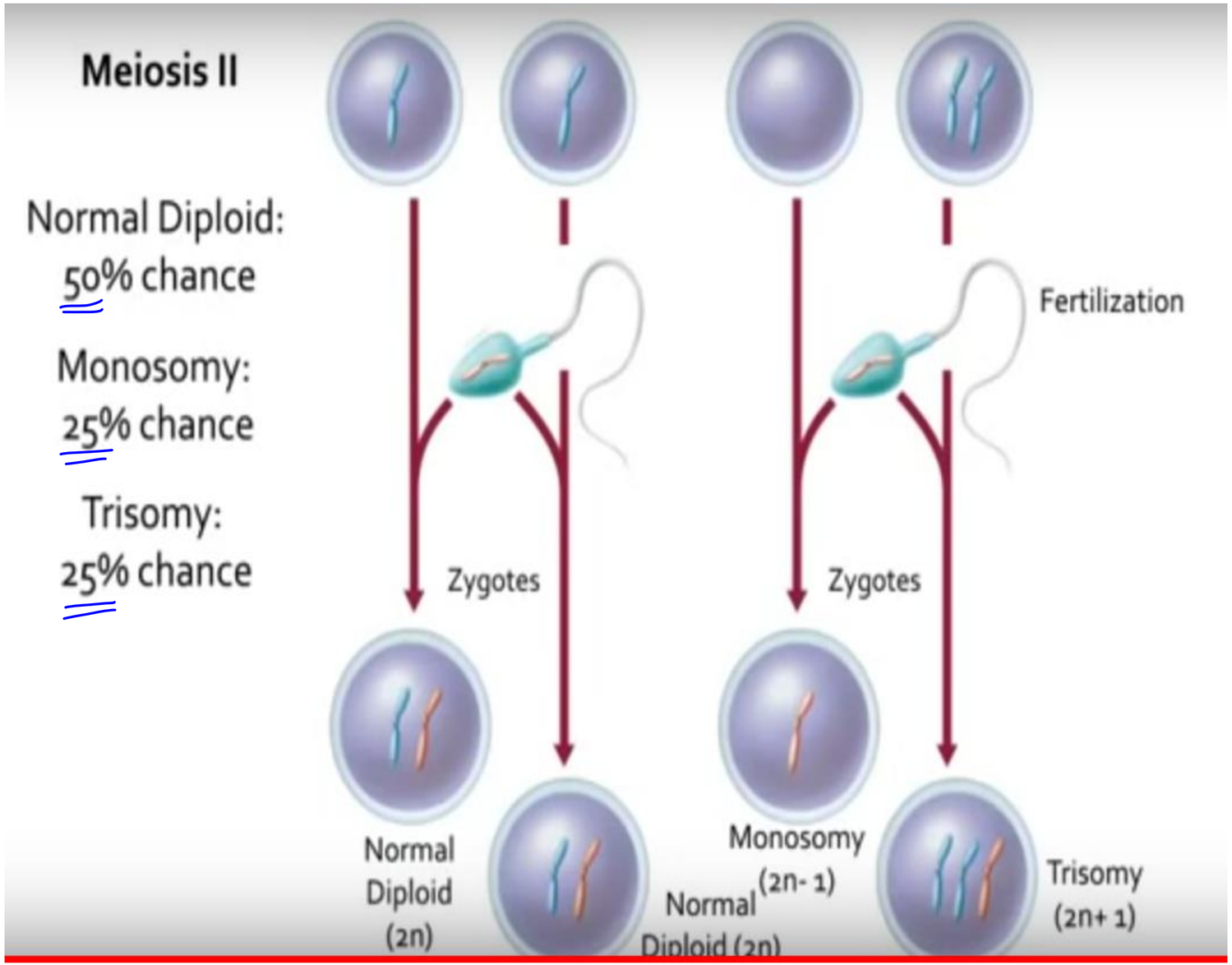
⇐ بالتالي هون فرضنا إنه يكون نص الانتاج صحيح أعلى



الإنتاج حوالي ٥٠٪ سليم

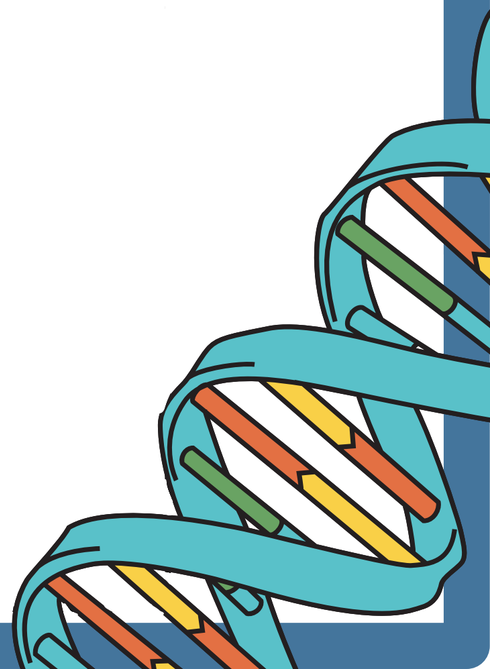
Trisomy ← ٢٥٪

Monosomy ← ٢٥٪


Meiosis II
Normal Diploid:
50% chance
Monosomy:
25% chance
Trisomy:
25% chance
Fertilization
Zygotes
Zygotes
Normal
Diploid
(2n)
Normal
Diploid (2n)
Monosomy
(2n- 1)
Trisomy
(2n+ 1)

- The frequency of nondisjunction is quite high in humans, but the results are usually so damaging to the growing zygote that miscarriage occurs very early in the pregnancy.

- The abnormality in chromosomes number may occur in **somatic** or **sex** chromosomes.



Human disorders due to chromosome alterations in autosomes (Chromosomes 1-22)

← الكروموسومات الجسمية من ١ - ٢٢

حكينا انه اغلب حالات nondisjunction الـ abortion بصير لهم خلال فترة الحمل الأولى لكن في حالات بيولدوا وبنشوفهم بالطبيعية وهي ٣

- There are only 3 examples of trisomies that result in a baby that can survive for a time after birth; while other trisomies can be very severe and the baby usually dies in utero.
- **A. Down syndrome (trisomy 21):** ← يعني ٣ نسخ من الكروموسوم رقم 21
- The result of an extra copy of chromosome 21.
- People with Down syndrome are 47, 21+.

← العدد الكلي يكون ٤٧ بدل ٤٦

← يعني الكروموسوم الزيادة عنده الزوج ٢١

الكلام المكتوب هون لا يهمم
في exeptions

و في احصائيات بتحكي طفل كل ... ١ ← طفل من كل ... ٧ طفل بينولد Down Syndrome

- Down syndrome affects 1:700 children and alters the child's phenotype either moderately or severely: characteristic facial features, short stature; heart defects susceptibility to respiratory disease, shorter lifespan prone to developing early leukemia. → عرضة إلها أكثر من الأطفال الطبيعيين

صفاتهم — من الوجه

و في اشخاص مابيين عليهم بنعرف من ال genetic test وكمان يكبروا بيبين أكثر

- Often the patients are sexually underdeveloped and sterile, with some degree of mental retardation.

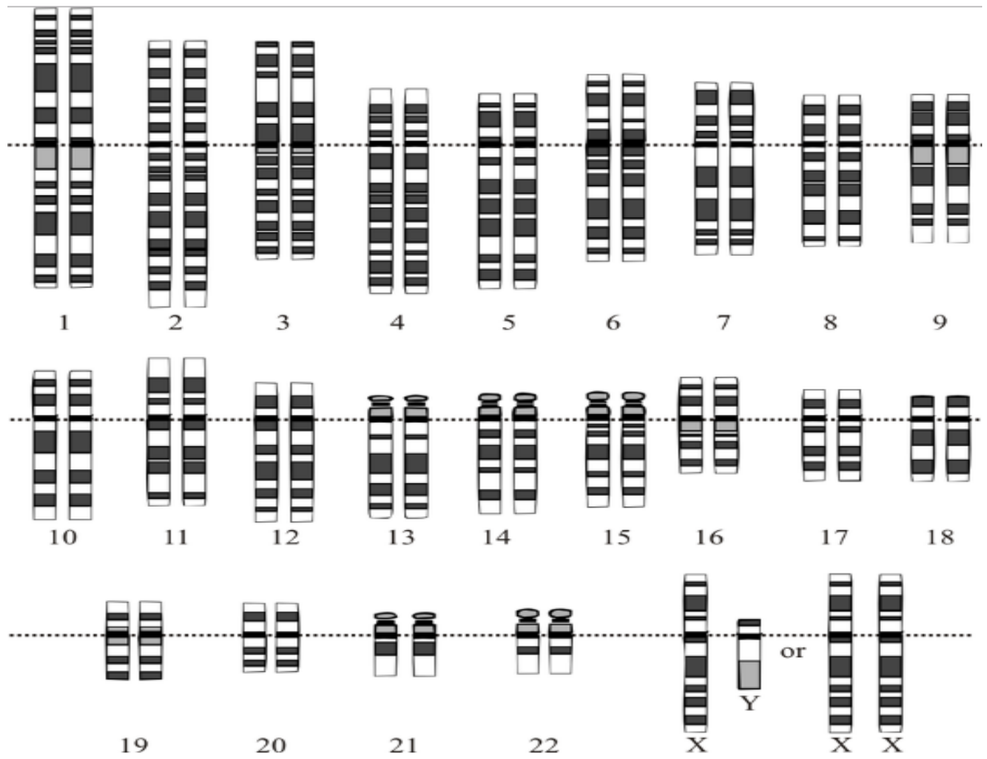
بس الكلام هاد هو صح كتير لانه ال females منهم بكونو Subfertile او fertile يعني بقدروا ينجبوا اما ال males ← Sterile

"الإعاقة العقلية" بتختلف من أشخاص للتانيين

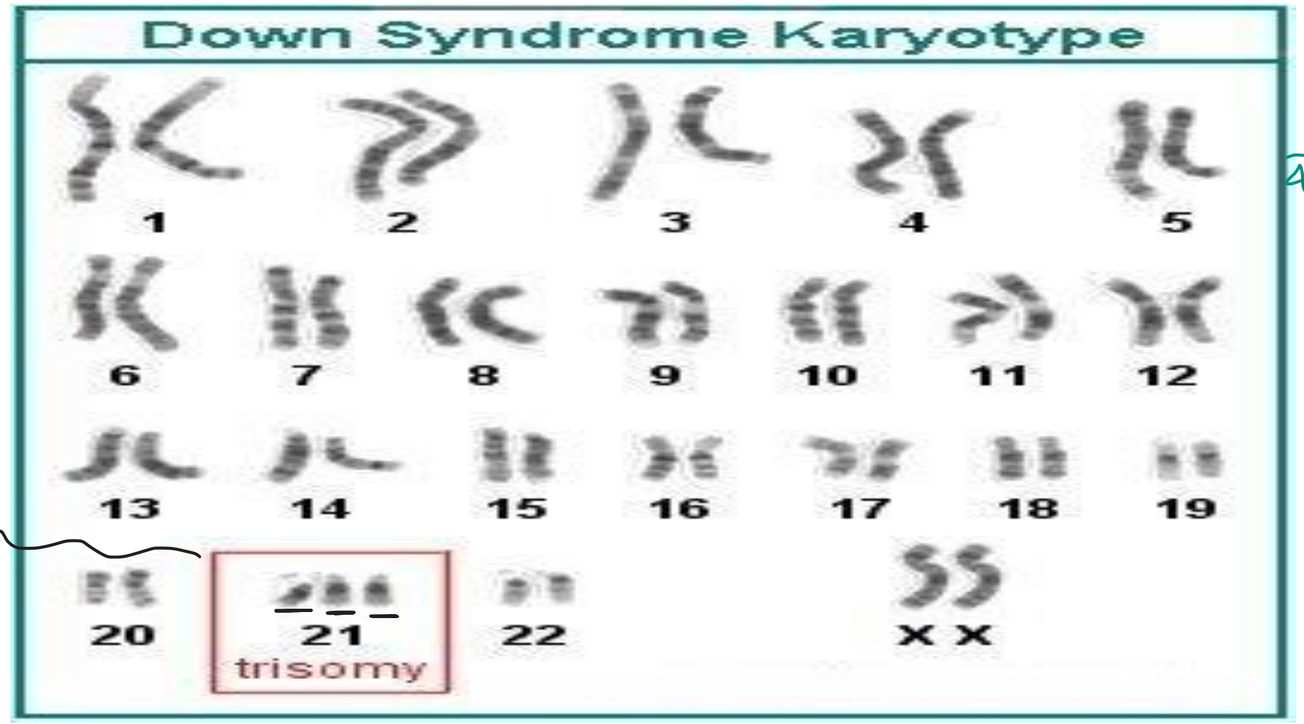
- Down Syndrome is correlated with age of mother but can also be the result of nondisjunction of the father's chromosome 21.

كلما عمر الأم زاد كلما زادت إحتمالية ولادة طفل Down syndrome

* وبدنا نعرف انه ال nondisjunction ممكن يصير عند ال males كمان في ال Sperm كلش بس ال males ما بأثر



Normal human Karyotype.



life expectancy الـ

زمان كانت ٢٥ سنه

اما هلا ممكن توصل لـ ٦٠ سنة

Down Syndrom

Genetic test

A karyotype is the number and appearance of chromosomes in the nucleus of an eukaryotic cell. Karyotypes describe the chromosome count of an organism and what these chromosomes look like under a light microscope. Attention is paid to their length, the position of the centromeres, banding pattern, any differences between the sex chromosomes, and any other physical characteristics.

فيه أجزاء هذا الكروموسوم بتكون غامقه وأجزاء فاتحة وهدول محسوبين لكل كروموسوم

شو بنشوف فيه ؟

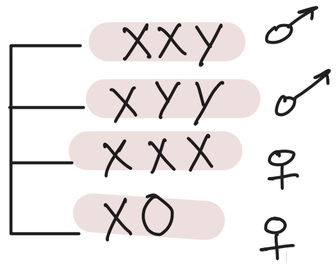
- **B. Patau syndrome (trisomy 13):** serious eye, brain, circulatory defects as well as cleft palate. 1:5000 live births. Children rarely live more than a few months.

- **C. Edward's syndrome (trisomy 18):** almost every organ system affected 1:10,000 live births. Affected children generally do not live more than a few months.

أصعب من ال Down Syndrom وبكونوا كل ال organs effected تقريباً

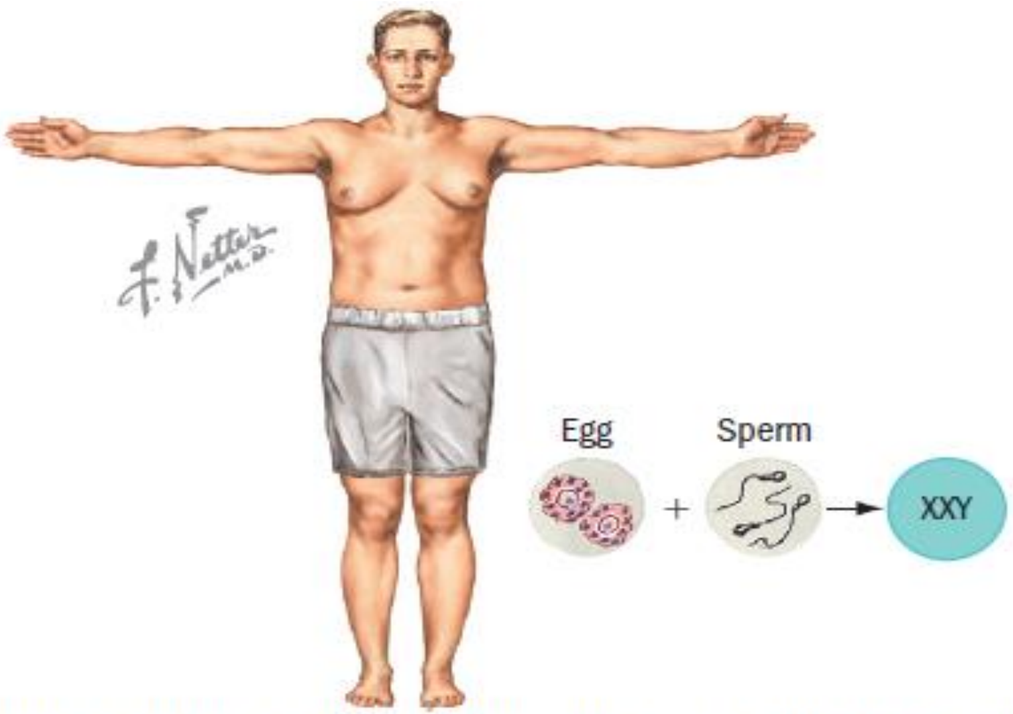
خلصنا الnondisjunction الي محكن تصير بال autosomes هلاح نحكي عن اللي بصيروا بال Sex chromosomes

❖**Nondisjunction of the sex chromosomes** (X or Y chromosome) is potentially fatal, but many affected people can survive. There are 4 examples:



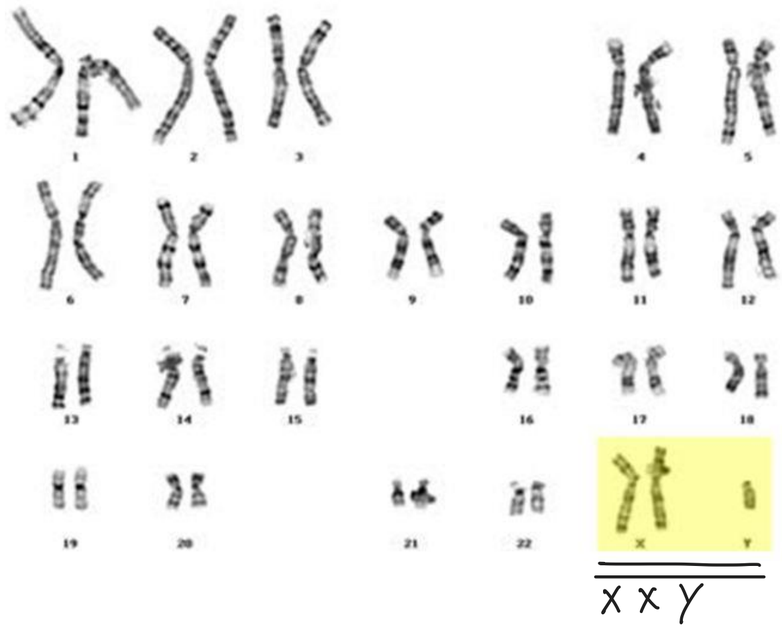
* من أشهرهم ⟸ • **A. 47, XXY males(Klinefelter syndrome):** Male sex organs; unusually small testes, sterile. Breast enlargement and other feminine body characteristics. Normal intelligence.

يغلب عليه شكل الFeminine



Klinefelter's syndrome is an inherited disorder of males. Males have an extra X chromosome and don't develop normal male sexual characteristics of puberty; however, most men with Klinefelter's syndrome can live normal lives.

Klinefelter syndrome: Karyotype



- **B. 47, XYY males:** Individuals are somewhat taller than average and often have below normal intelligence

ماتكون واع فكرة normal or below inteligence

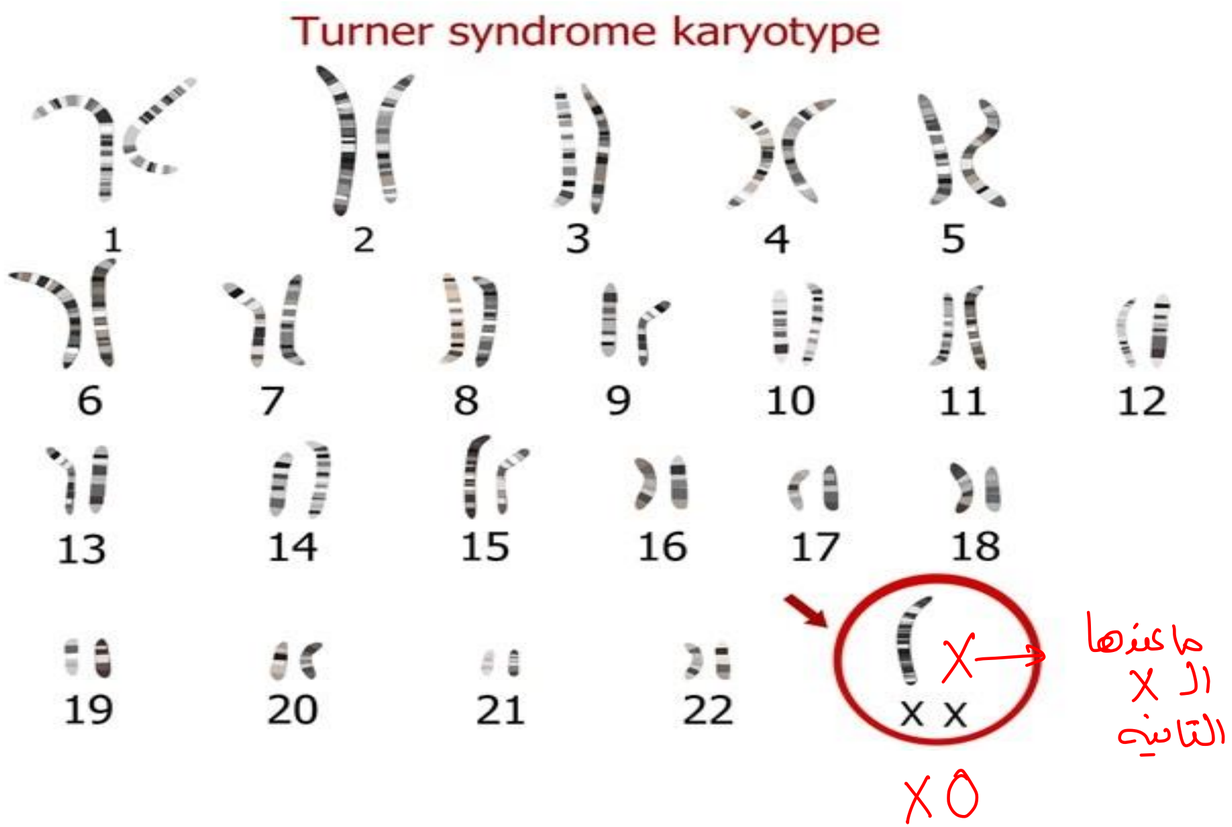
- **C. 47, XXX females (Trisomy X).** 1:1000 live births - healthy and fertile usually cannot be distinguished from normal female except by karyotype

in females

- **D. XO (Monosomy X)** also called **Turner's syndrome**: 1:5000 live births; **the only viable monosomy in humans** -women with Turner's have only 45 chromosomes!!! XO individuals are genetically female, however, they do not mature sexually during puberty and are sterile. Short stature and normal intelligence.

  Approximately 99% of pregnancies affected with Turner syndrome are miscarried.

٩٩٪ من الحوامل أصلاً حيصير معهم abortion حالات قليله اللي رح تشوفهم عايشين


Turner syndrome karyotype
1
2
3
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9
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17
18
19
20
21
22
X X
X
ماعندها ال X التانيه
XO