Welcome to

Aakash + BYJU'S NOTES

Principles of Inheritance and Variations

Key Takeaways

Introduction to Genetics

- Mendel's Hybridisation Experiments
- Significance and Unappreciation
- Important Terminology
- Pea Plant - Merits and Characters
- Resurface of Mendel's work

Monohybrid Cross

- Punnett square
- Reciprocal Cross
- Back Cross
- Mendel's Observation
- Test Cross
- Concept of Dominance

Exceptions to Mendelian Inheritance

- Incomplete dominance
- Co-dominance
- Multiple alleles

Dihybrid Cross

- Law of Independent Assortment
- Two Genes Interactions
- Shortcut Formulas

Chromosomal Theory of Inheritance

- Sutton and Boveri experiments

Linkage and Recombination

Polygenic Inheritance and Pleiotropism

Sex determination

Based on sex chromosomes

Based on haplodiploid system

Mutation

Chromosomal Aberrations

Gene Mutations

Genetic disorders

Mendelian Disorders

Chromosomal Disorders

Cytoplasmic Inheritance

Summary

Introduction to Genetics

Genetics

Branch of biology dealing with the study of genes and its inheritance.

Gene : Distinct sequence of nucleotides of DNA that codes for a specific protein. It is the physical and functional unit of heredity. Wilhelm Johannsen coined the term gene.

Inheritance :

- Process by which characters are passed on from parents to progeny
- Basis of heredity (transmission of genes from one generation to another)

Variations : Difference in progeny as compared to the parents

Mendel's Hybridisation Experiments

- **Gregor Mendel** is considered the **father of genetics.**
- Conducted hybridisation experiments on **garden peas** (*Pisum sativum*) for seven years (1856-1863)
- Laid the foundation of modern genetics
- Applied **mathematical logic and statistical analysis** to problems in biology
- Explained the **phenomenon of inheritance**
- Large sampling size gave greater credibility to his data
- Initial no. of pea plant varieties was 34, then 22 but ultimately worked with only **7 pairs** of varieties.

Mendel's Experiments in Pea Plant

Merits

As an experimental model

Experimental organism: *Pisum sativum*

- Short life span of **one year**
- Requires **less maintenance** and **labour**
- **Multiple plants** can be grown in **small area**
- Availability of pure varieties
- Exhibits a variety of visible characters with **contrasting traits**
- **Self-fertilising**, mating can be controlled easily
- Produces a large number of seeds

Contrasting traits		Character
Tall plant	Short plant	Plant height
Violet flower	White flower	Flower colour
Axial flower	Terminal flower	Position of flower
Green pod	Yellow pod	Pod colour
Inflated pod	Constricted pod	Pod shape
Yellow seed	Green seed	Seed colour
Round seed	Wrinkled seed	Seed shape

Mendel's Experiments

Significance

- Duration of experiments - **8 consecutive years**
- Number of plants experimented – approx. **28,000 plants**
- Data set – Minimum **three generations** for each of the **7 characters**
- Obtained interesting results which were **explained mathematically** and **statistically**
- Published his work in the **"Journal of the Royal Horticultural Society"** in **1865**
- **Factors** are discrete units which are passed on from one generation to another

Unappreciation

- Not widely publicized because of **poor communication**
- Contemporaries believed in **blending theory** and **did not accept his results**
- Asked to show the **physical existence of "Factors"**
- Usage of **mathematics** to explain biological phenomena **unaccepted** and **misunderstood**
- Mendel's conclusion about heredity were **ahead of his time**
- **Failed to reproduce the results on Hakweed** (*Hieracium*). It was due to non-availability of pure lines. **'Pure line'** was coined by **Johannsen** in 1900.

Resurface of Mendel's work

Hugo de Vries

Carl Correns

Erich Von Tschermak

- These three scientists **independently rediscovered** the same concepts as that of **Mendel** in 1900s.
- They were unaware of Mendel's work initially, but later acknowledged Mendel as the pioneer.
- Mendel's work resurfaced and got the appropriate recognition.

Important Terminology

Character - Heritable feature that varies among individuals

Trait - Each variant of a character

Allele - Slightly modified forms of the same gene. The term allele was given by Bateson

Factors - Something stably passed down, unchanged, from parent to offspring through the gametes, over successive generations

Phenotype - Visible physical trait of an organism

Genotype - Actual genetic make-up of an organism

Homozygous- Identical alleles on the homologous chromosomes (Example: TT, tt)

Heterozygous- Dissimilar alleles on the homologous chromosomes (Example: Tt, Rr)

Dominant - Trait which can express itself over contrasting trait

Recessive - Trait which cannot express itself over contrasting trait/ is suppressed by dominant or contrasting trait

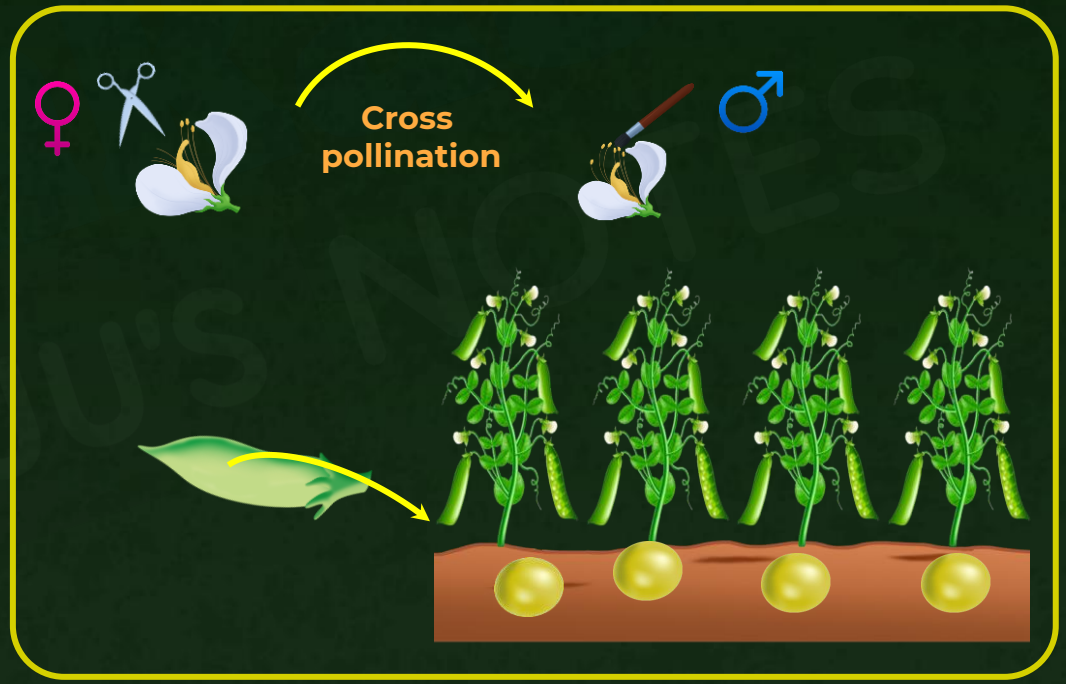
Monohybrid Cross

It is a cross between plants differing in **only one character.** Mendel selected plants which undergo self-fertilisation for several generations, such that their traits remain unchanged. They are known as **pure lines/true breeds.**

Monohybrid experiment technique

1. Stamen are removed
2. Pollens are transferred
3. Seeds are sown
4. Plants obtained in this generation are called Filial 1 progeny or the F_1

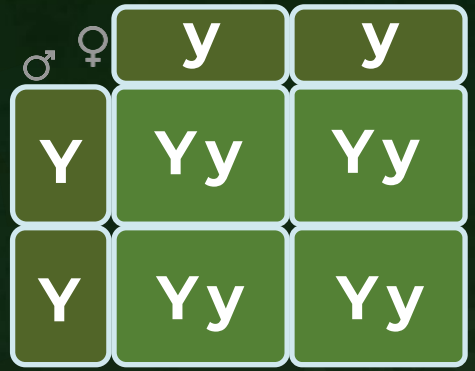
Observation : All the plants of F_1 generation develop yellow coloured seeds



Monohybrid Cross

When yellow seeded pea plant (YY) was crossed with a green seeded pea plant (yy), all the offspring were yellow.

Monohybrid Cross F_1



Genotype of F_1 generation

100% of F_1 generation has Yy genotype

Phenotype of F_1 generation

100% of F_1 generation has phenotype yellow

- **Law of Dominance** - When two alleles are different or in **heterozygous condition**, then one **dominates** the expression of the other.
- **Law of Segregation** - During gamete formation, **pair of alleles segregate** such that **each gamete receives only one allele** from the pair.
- Mendel arrived at these two laws based on the **monohybrid cross.**

Punnett Square

Reginald C. Punnett gave the simplest way of representing a cross.

Monohybrid Cross F_1

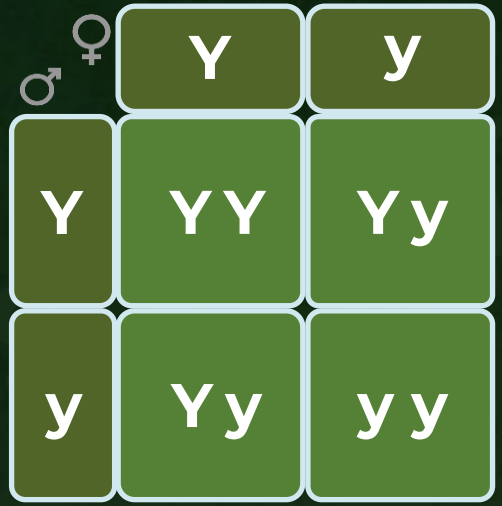
Genotype of F_1 generation

100% of F_1 generation has genotype Yy

Phenotype of F_1 generation

100% of F_1 generation has phenotype yellow

Monohybrid Cross F_2



Genotype of F_2 generation

25% of F_2 generation has genotype YY

50% of F_2 generation has genotype Yy

25% of F_2 generation has genotype yy

Phenotype of F_1 generation

75% of F_2 generation has phenotype yellow
25% of F_2 generation has phenotype green

Mendel's Observations

The **F_1 dominating trait** also appeared **in F_2 generation,** whereas the **recessive trait which disappeared in F_1, reappeared in F_2** in 1 of the 4 plants.
Traits were not blended in progeny

Trait

- Traits expressed in both F_1 and F_2 generation
  - Dominant trait
- Traits that are not expressed in F_1 but are expressed in F_2
  - Recessive trait

Trait

- Homozygous
  - YY (Dominant trait is expressed) Or yy (Recessive trait is expressed)
- Heterozygous
  - Yy (Always dominant trait is expressed)

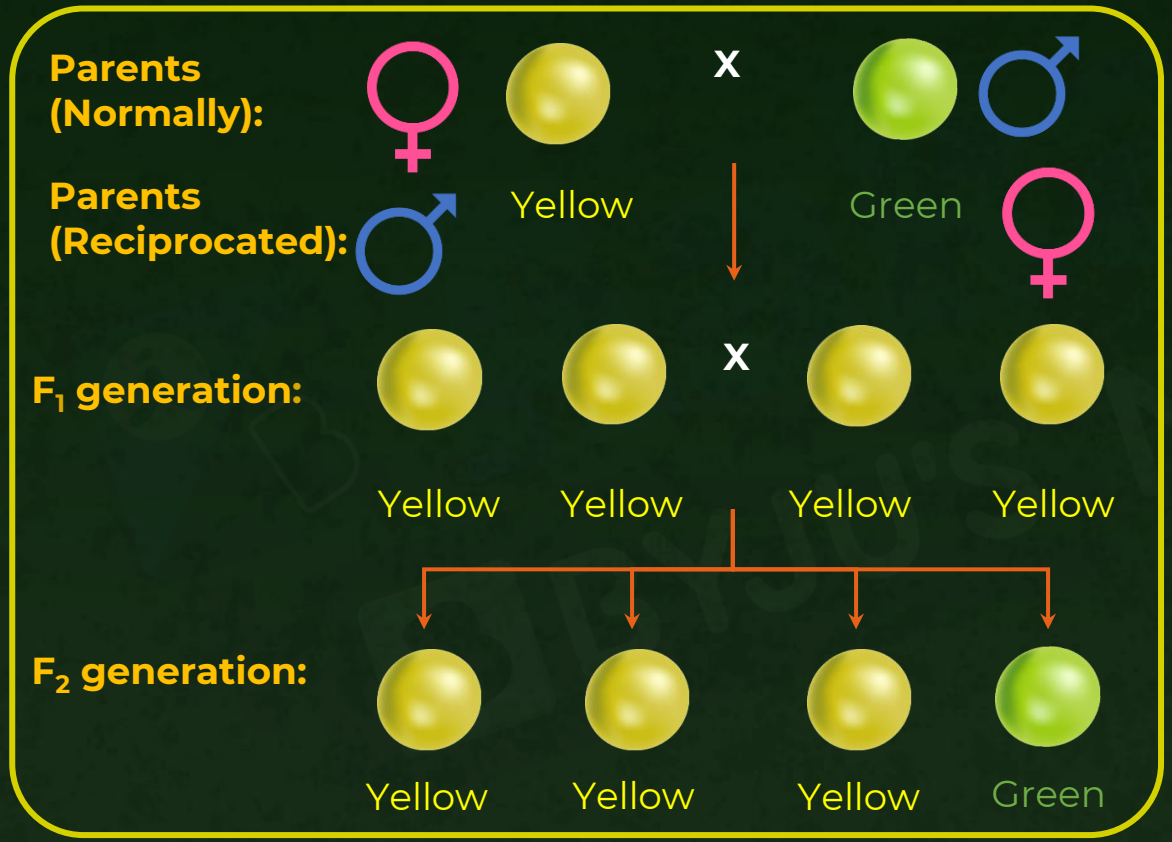
Mendel's Observations

Dominant trait

Recessive trait

Pod	Stem	Seed	Flower
Inflated (Full)	Axial flowers	Yellow	Violet
Green	Tall (6 - 7 ft)	Round	
Constricted	Terminal flowers	Green	White
Yellow	Dwarf (3/4 - 1 ft)	Wrinkled	

Reciprocal Cross



Reciprocal Cross

A paired cross in which traits of male and female parents are switched.

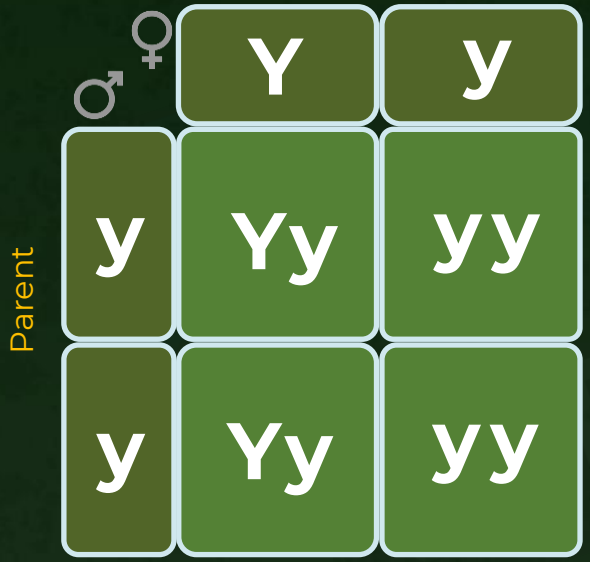
Reciprocal cross yielded same ratio of progeny
F_1 = all yellow
F_2 = yellow : green = 3 : 1

Test Cross

It is a cross performed to determine whether offspring is **homozygous or heterozygous** dominant by crossing with the recessive parent.

Heterozygous

Offspring



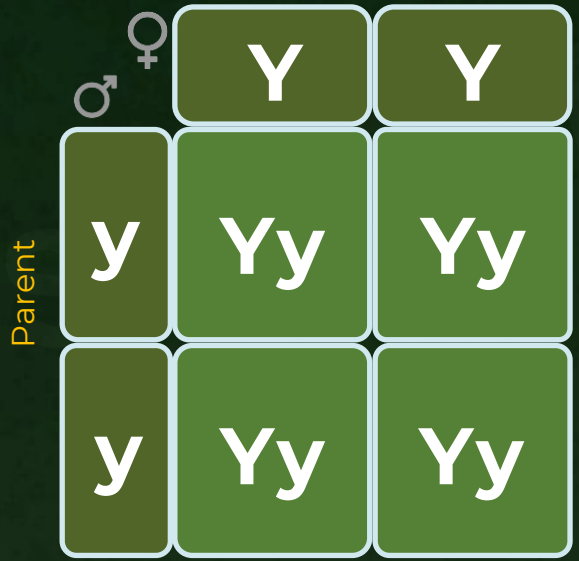
50% offspring are yellow

50% offspring are green

Plant was heterozygous dominant

Homozygous

Offspring

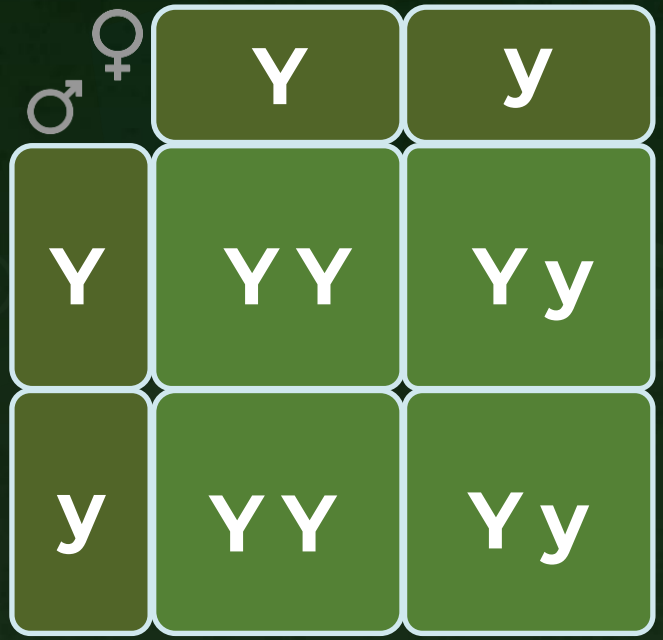


100% offspring are yellow

Plant was homozygous dominant

Back Cross

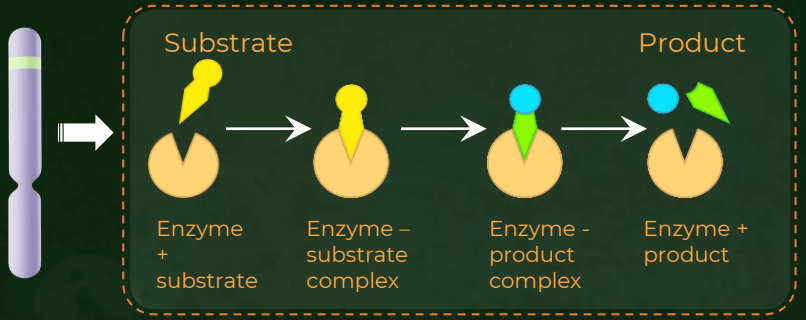
Back cross is a cross of an offspring with one of its parent plant
Test cross is a type of back cross



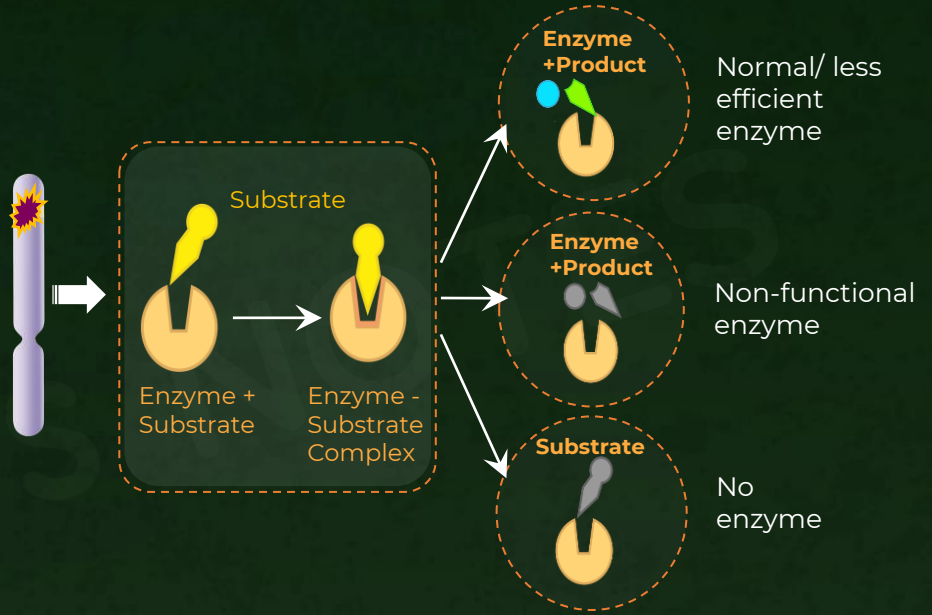
100% offspring are yellow

The Concept of Dominance

Mendel's law failed to explain the concepts of **incomplete dominance** and **co-dominance.**



- For example, a gene contains the **information** for producing an enzyme. Now there are two copies of a gene i.e., **two allelic forms**.
- The **normal allele** produces the **normal enzyme** which is needed for the **transformation** of a substrate S.



- This allele can change due to **some modifications.**
- They are **mutated allele / modified enzyme / faulty / no transformation.**

The Concept of Dominance

- When the modified allele produces a **non-functional enzyme** or **no enzyme**, the **phenotype** may be affected.
- The phenotype/trait will only be **dependent** on the **functioning** of the **normal allele**.
- The unmodified, fully functional allele, which represents the **original phenotype** is the **dominant allele** and the **modified allele** is generally the **recessive allele**.
- So, the **recessive trait** is seen only when both the alleles present produce **non-functional** enzyme or **no enzyme** at all.

Dominant allele

- Normal
- Unmodified
- Fully functional
- Original phenotype

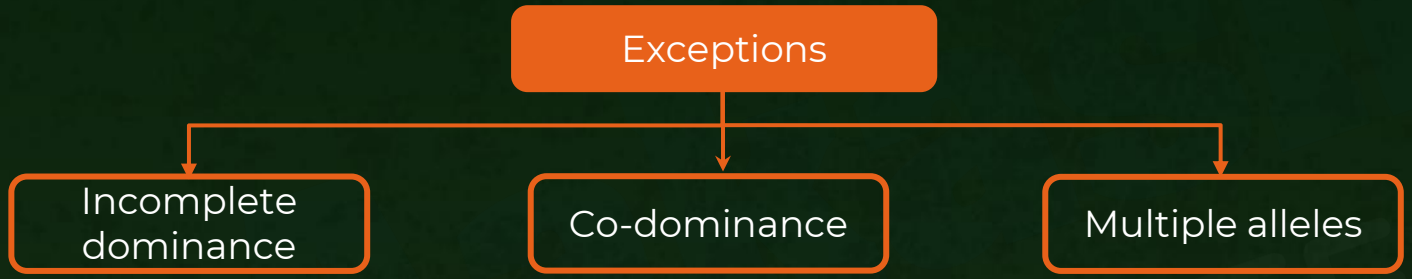
Recessive allele

- Modified
- Non-functional

The Concept of Dominance

- Now, in cases of **co-dominance** or **incomplete dominance**, the **new alleles do not produce useless or non-functional enzymes.**
- Instead, they produce an **enzyme** that actually has the ability to **give rise to a new or different trait**.
- Hence, when the two different alleles are present together in an individual, one of the two things happens:
    - The physiological process initiated by the **different alleles result in a new trait**, which can be seen as a **blend** of the homozygous traits (Incomplete dominance).
    - The **two alleles are expressed independent of each other** and hence both the alleles are expressed together in the phenotype (co-dominance).

Exceptions to Mendelian Inheritance



Examples:

- *Mirabilis jalapa* (Four o'clock)
- Snapdragon / *Antirrhinum majus* (Dog flower)

Examples:

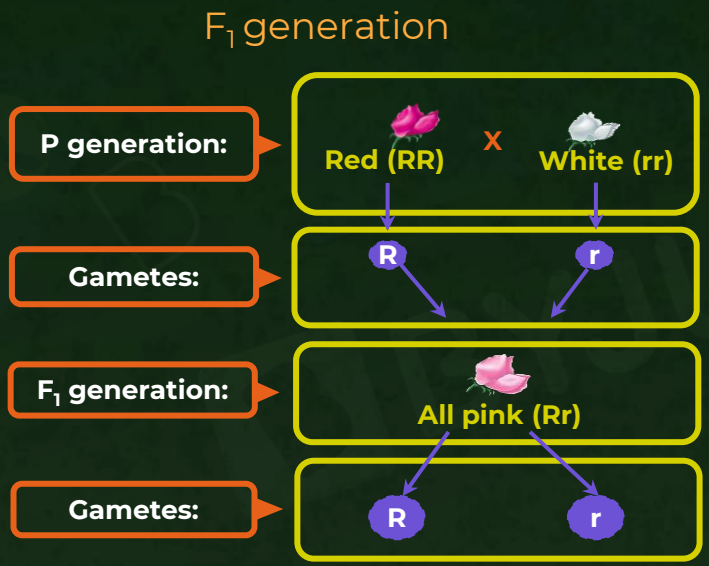
- Shorthorn cattle
- Human ABO blood groups

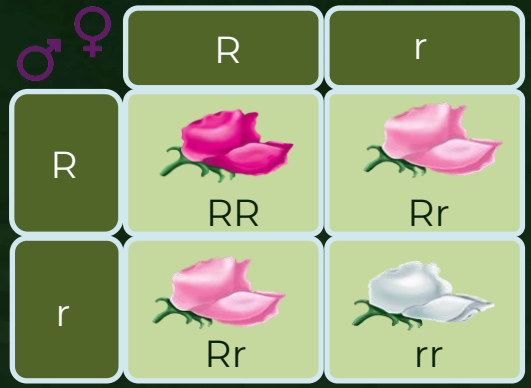
Example:

- ABO blood groups

Incomplete Dominance

- Incomplete dominance is a form of **intermediate inheritance** in which one allele for a particular trait is not expressed completely over its paired allele.
- A **new phenotype** is formed.
- Hence, the **law of segregation** is not followed.





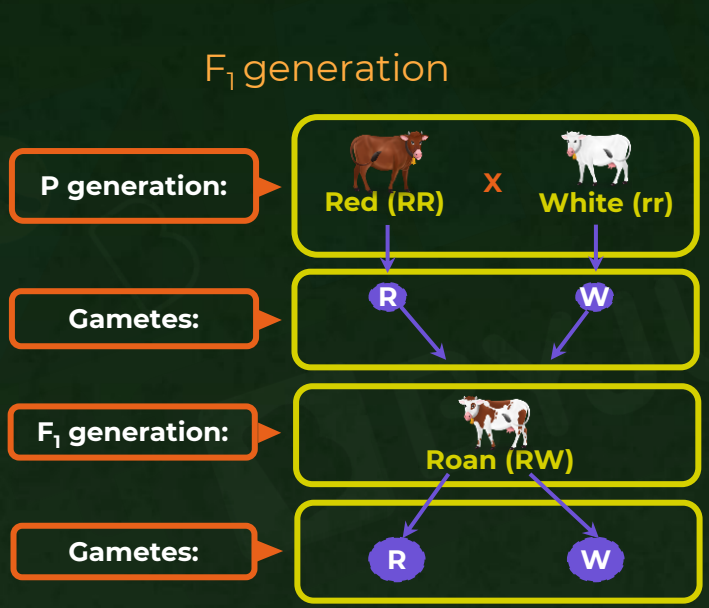
F_2 generation

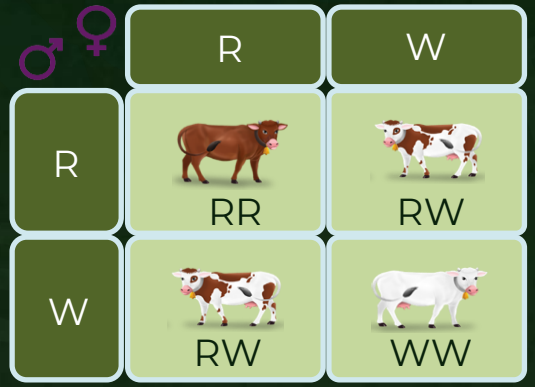
Phenotypic ratio - Red : Pink : White
1 : 2 : 1

Genotypic ratio - RR : Rr : rr
1 : 2 : 1

Co-dominance

- In F_2 generation, both the alleles are heterozygous individual but **do not show dominant – recessive relationship** or **intermediate condition.** Rather, they **express their traits independently** and are known as **codominant alleles**.
- **Law of dominance** is not followed.



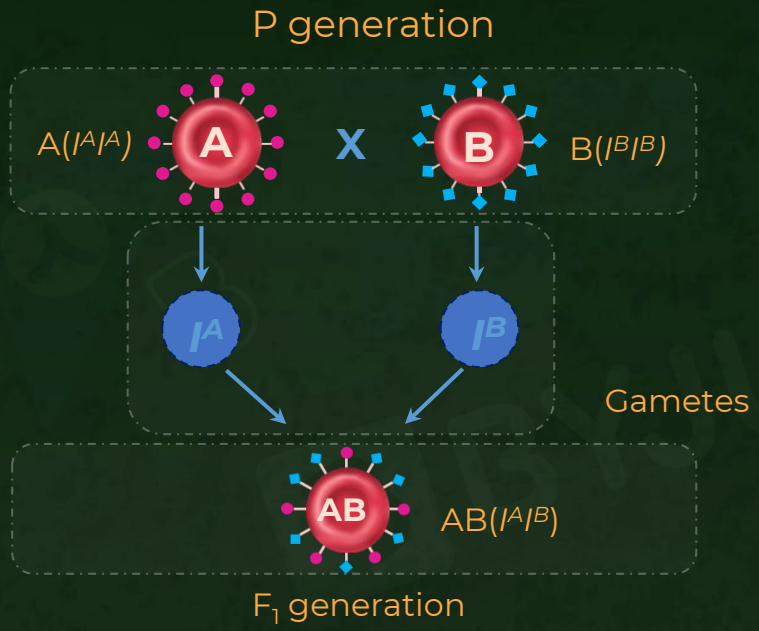


F_2 generation

Phenotypic ratio -	Red : Roan : White 1 : 2 : 1
Genotypic ratio -	RR : RW : WW 1 : 2 : 1

Co-dominance in Blood Groups

Based on presence or absence of antigens A and B on RBCs, there are four different blood groups I^A and I^B are **co-dominant**, and hence they create a **new blood group AB** which has both the **antigen A** and **antigen B.**



F_2 generation

♂ \ ♀	I^A	I^B
I^A	A (I^AI^A)	AB (I^AI^B)
I^B	AB (I^AI^B)	B (I^BI^B)

Phenotypic ratio(F_2) - A : AB : B = 1 : 2 : 1

Genotypic ratio(F_2) - I^AI^A : I^AI^B : I^BI^B = 1 : 2 : 1

Multiple Alleles

- **More than two alleles** of the same gene in a population
- **ABO blood group is controlled by *I* gene and has three alleles - I^A, I^B, *i***
- **ABO blood group** shows co-dominance and dominant recessive relationship also

Allele from parent 1	Allele from parent 2	Genotype of offspring	Blood types of offspring	Type of dominance
I^A	I^A	I^AI^A	*A*	-
I^A	I^B	I^AI^B	*AB*	Co-dominance
I^A	*i*	I^Ai	*A*	Dominant - recessive
I^B	I^A	I^AI^B	*AB*	Co-dominance
I^B	I^B	I^BI^B	*B*	-
I^B	*i*	I^Bi	*B*	Dominant - recessive
i	*i*	*ii*	*O*	-

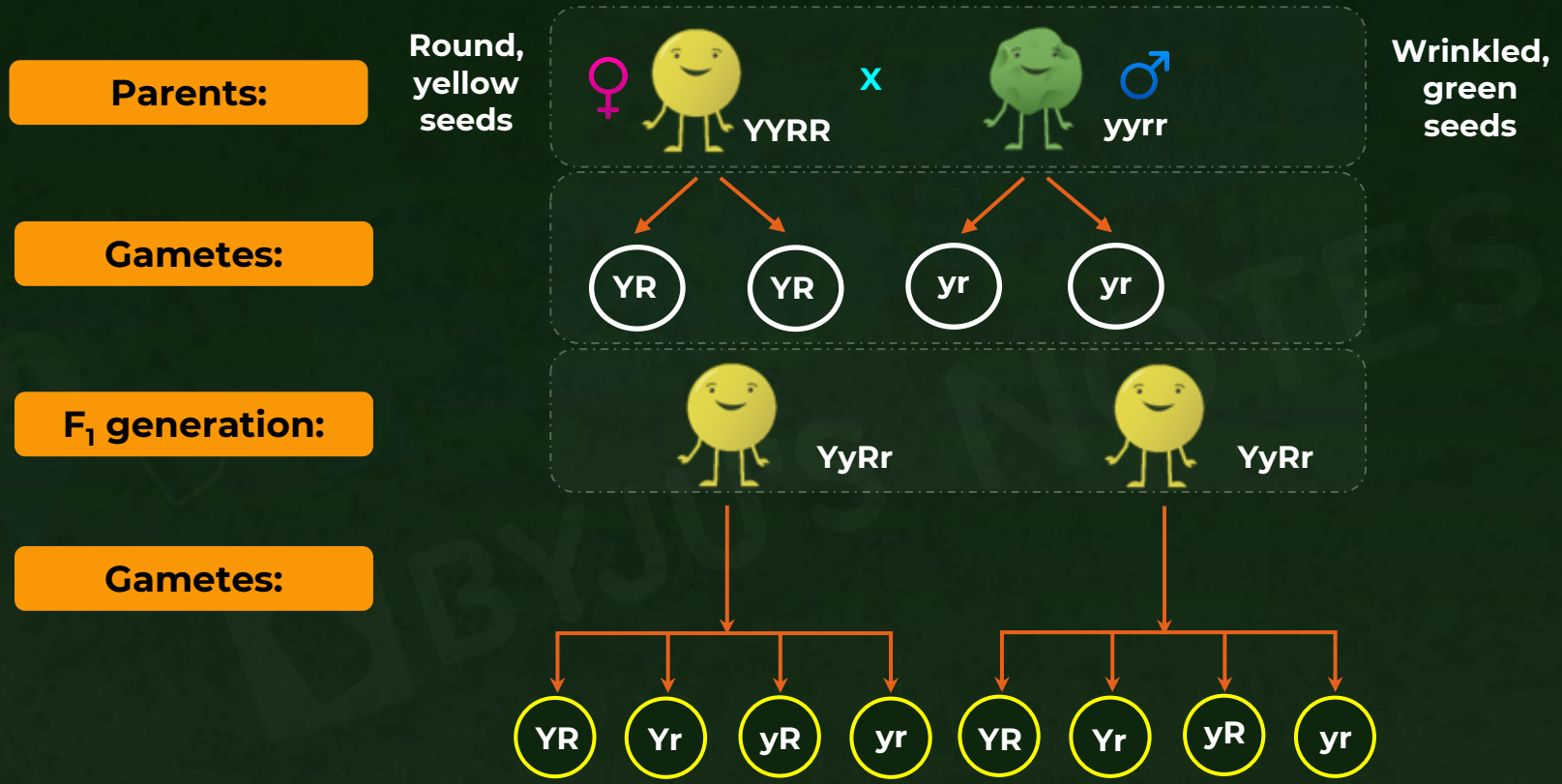
Human blood groups (ABO)

Phenotype	Genotype
O	*ii*
A	I^AI^A, I^Ai
B	I^BI^B, I^Bi
AB	I^AI^B

Dihybrid Cross

- It is a **cross between two individuals with two different observable characters.** E.g., Having two different alleles for each of the two character.
- The parents are round and yellow (**homozygous dominant for both traits**) and wrinkled green (**homozygous recessive for both traits**).
- In that case, the F_1 generation will produce yellow and round seeds (heterozygous dominant for both genes). F_1 generation is then self-pollinated.

Dihybrid Cross - F_1 Generation



Dihybrid cross - F_2 generation

♂ \ ♀	YR	Yr	yR	yr
YR	YYRR	YYRr	YyRR	YyRr
Yr	YYRr	YYrr	YyRr	Yyrr
yR	YyRR	YyRr	yyRR	yyRr
yr	YyRr	Yyrr	yyRr	yyrr

Phenotypic ratio- 9:3:3:1

Yellow, round - 9

Yellow, wrinkled - 3

Green, round - 3

Green, wrinkled - 1

Law of Independent Assortment

- The **phenotypic ratio** for the **F_2 generation in a dihybrid cross** is **9:3:3:1**; while the **genotypic ratio is 1:2:1:2:4:2:1:2:1**.
- The **dihybrid cross** helped **Mendel to deduce the law of independent assortment**.
- **Law of independent assortment** - When two pairs of traits are combined in a hybrid, the segregation of one pair of characters is independent of the other pair of characters.
- It implies that **there is no connection** or linkage between the segregation events of the two genes.

Two Genes Interactions

- When two genes of the same allelic pair or genes of two or more different allelic pairs influence one another. Then it is called **two gene interaction**.
- **Non-allelic genetic interactions** : Interactions between genes located at different loci on the same chromosome or on different but non-homologous chromosomes controlling a single phenotype to produce a different expression
- Some of these interaction are as follows:
    - Complimentary genes
    - Duplicate genes
    - Epistasis

Two Genes Interactions

- **Complimentary genes:** Two genes present on separate loci that interact together to produce dominant phenotypic character
- **Duplicate genes:** When dominant alleles of two gene loci produce the same phenotype, they provide a 15: 1 ratio, irrespective of whether they are inherited together or separately.
- **Epistasis:** Gene which masks (hides) the action of another gene (non-allelic) is termed as **epistatic gene.**

  The gene whose effects are masked is called **hypostatic gene**.

  - **Dominant epistasis** - one allele of the gene that shows epistasis can mask alleles of the other gene
  - **Recessive epistasis** - two alleles have to be inherited in order for the phenotype of the second gene to be masked

Shortcut to find number of phenotype, genotype and gametes

- **Types of gametes = 2^n** — **for all gametes**
- **Types of phenotypes = 2^n**
- **Types of genotypes = 3^n**

only in case of self fertilisation

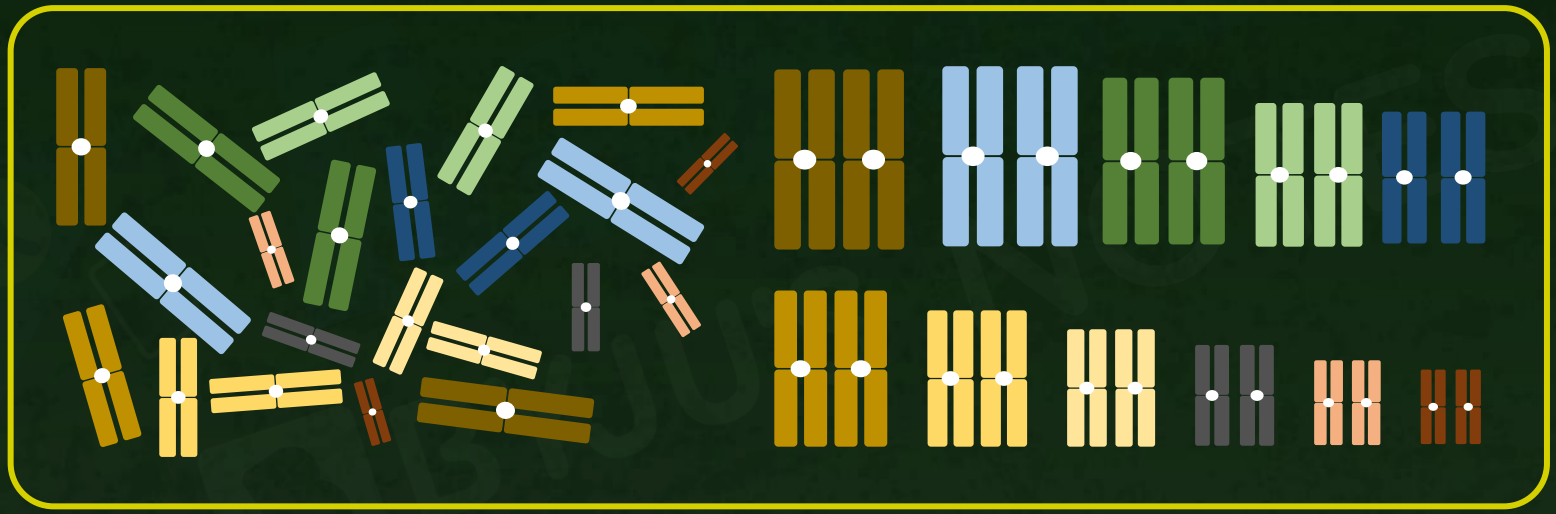
where n is the number of heterozygous gene pair

Chromosomal Theory of Inheritance

- Scientists **Walter Sutton** and **Theodore Boveri** independently performed some experiments
- Observed cell division and discovered that chromosomes are present in pairs, and separate during cell division specifically in meiosis
- Conclusions reinforced Mendel's work which is now known as the **chromosomal theory of inheritance**
- Genes are found on specific locations of the chromosomes and the behavior of these chromosomes during meiosis can explain Mendel’s laws of inheritance
- **Factors = Genes**

Sutton and Boveri's Experiment-1

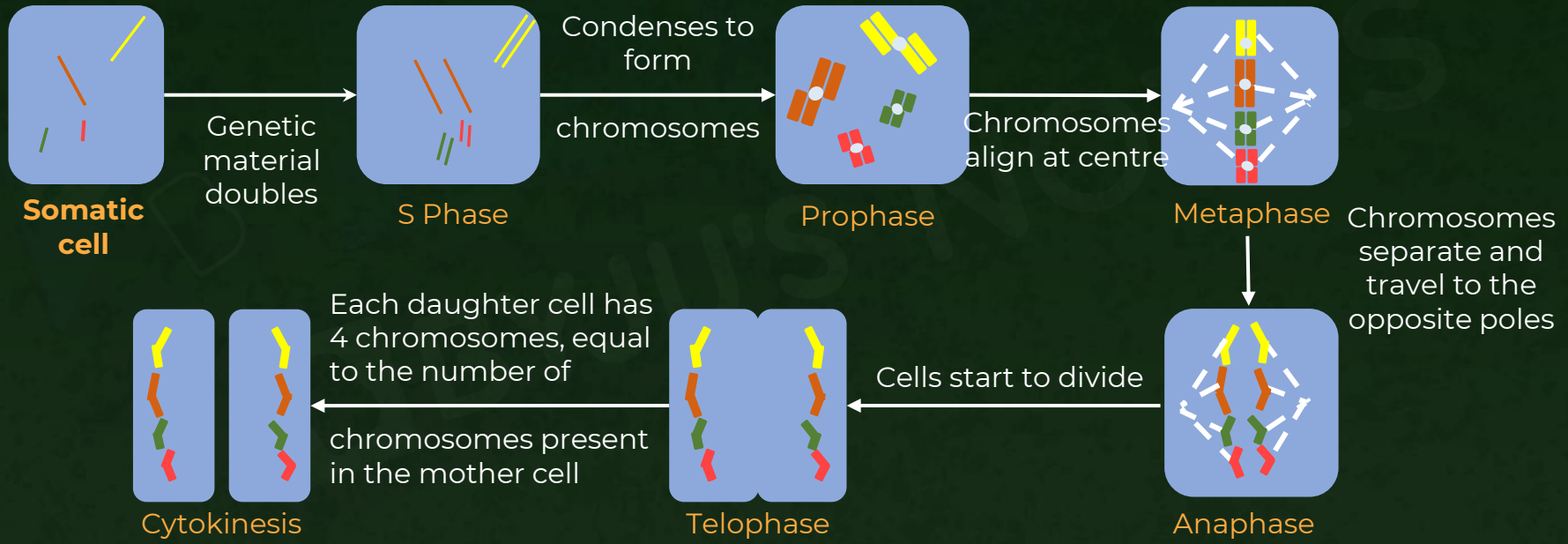
- **Sutton** conducted the experiment on **lubber grasshopper,** observed that it had **22 chromosomes** in each cell
- Every chromosome had an identical pair which are now known as **homologous pairs**



- **Conclusion: Every chromosome had an almost identical partner. So, chromosomes occur in pairs**

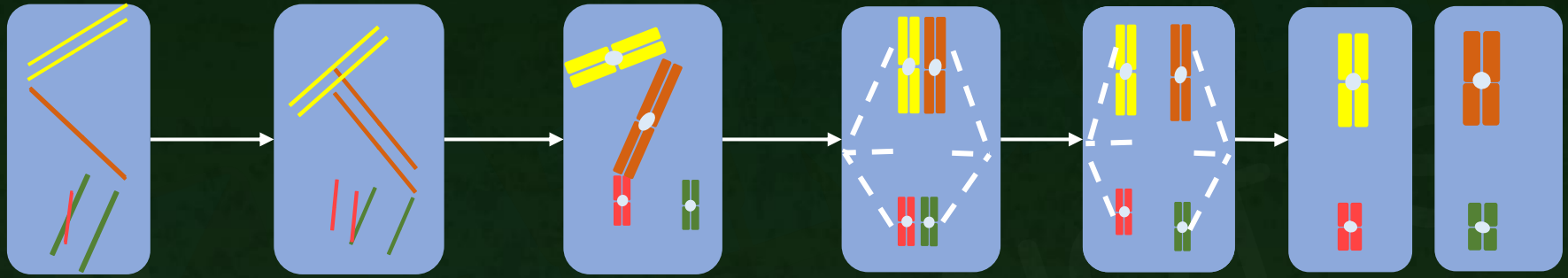
Sutton and Boveri's Experiment-2

- **Boveri** worked on **Ascaris** and found that the organism has **4 chromosomes**
- **Observation:** Two types of cells in ascaris; In the present era we call them as **somatic cells** and the **Germ cells**, each divides differently



Sutton and Boveri's Experiment-2

Germ cell



S phase

Genetic material doubled

Prophase I

Chromosomes are formed

Metaphase I

Homologous pairs of chromosomes align on either side of equatorial plate

Anaphase I

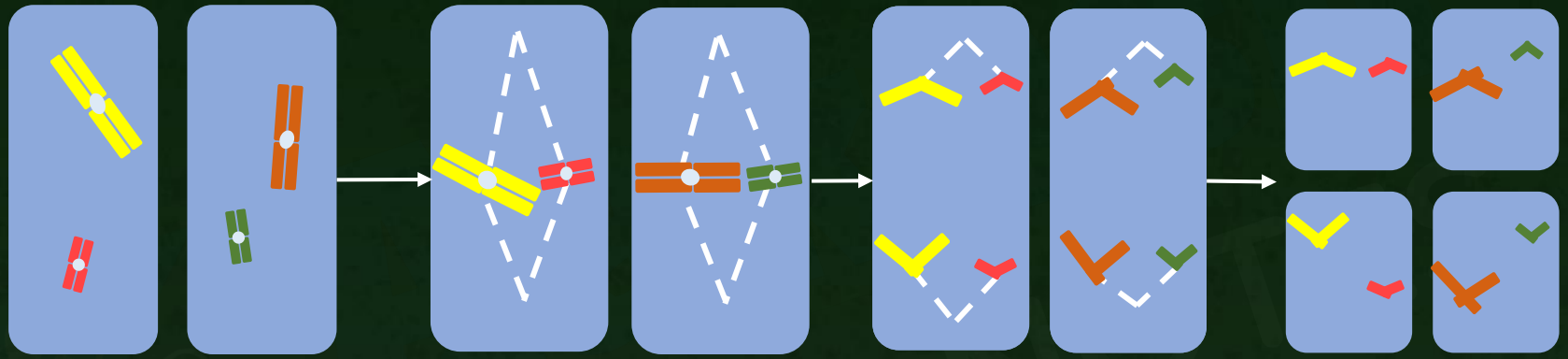
Identical pairs separate and move to opposite poles

Telophase I

Karyokinesis completed which will be followed by cytokinesis

Sutton and Boveri's Experiment-2

Germ cells



Prophase II

As the cells start to divide chromatin condenses to form chromosomes.

Metaphase II

The chromosomes arrange themselves at the centre.

Anaphase II

Chromosomes separate and travel to opposite poles.

Telophase II and Cytokinesis

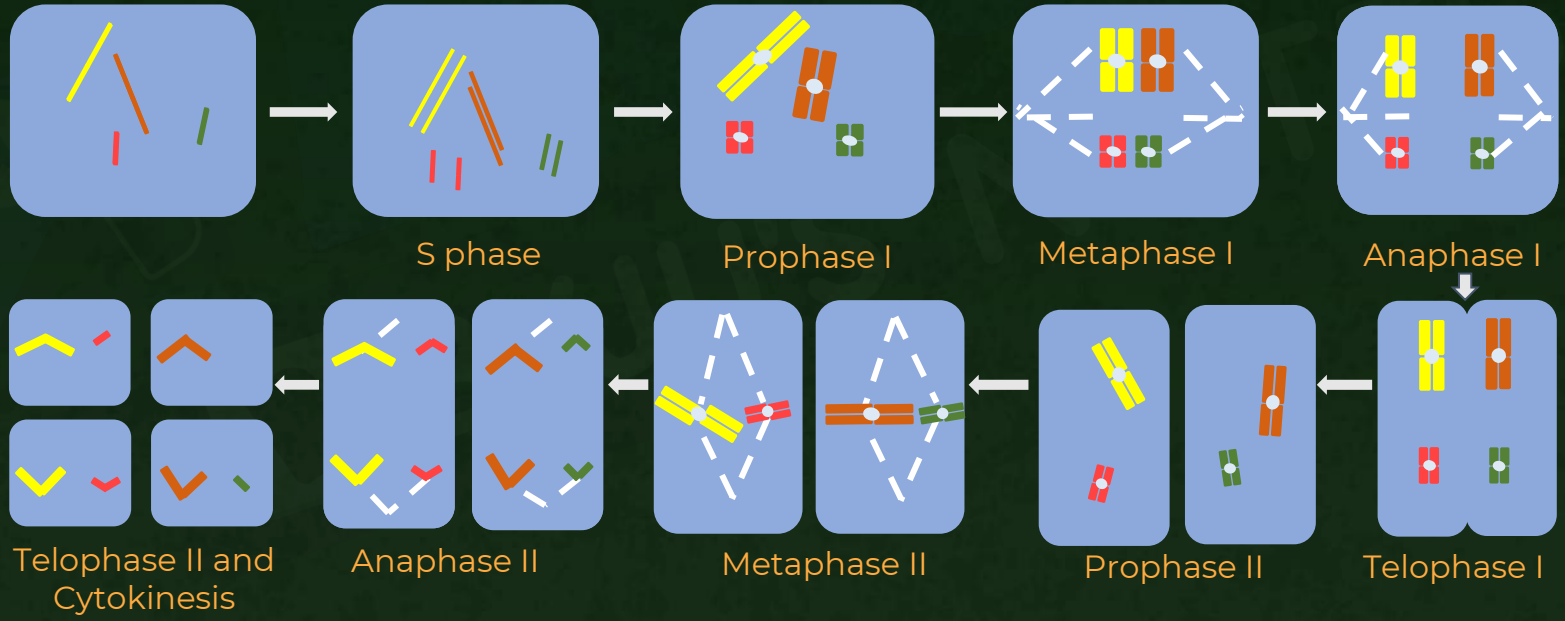
By the end of the division he observed 2 chromosomes and 4 cells were formed.

- **Conclusion:** **Meiosis reduces number of chromosomes in germ cells by half**
- **Chromosomes segregate during gamete formation**

Sutton and Boveri's Experiment-3

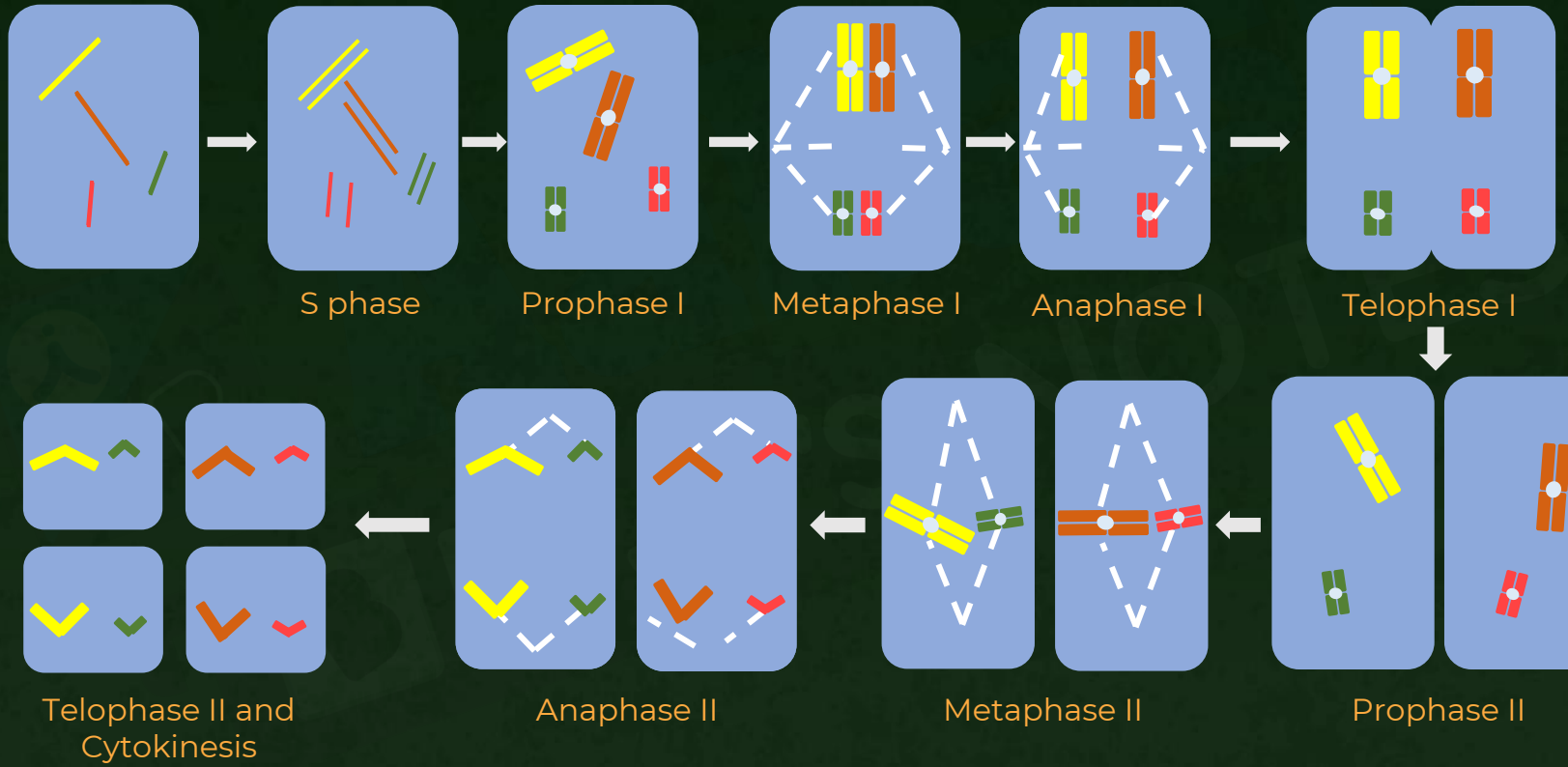
- **Sutton** conducted another experiment on the **same lubber grasshopper.** observed that it had **22 chromosomes** in each cell
- For simplicity, consider **only 4 chromosomes**
- With these **2 sets of homologous chromosomes**, there are **two possibilities** for meiosis

Possibility I

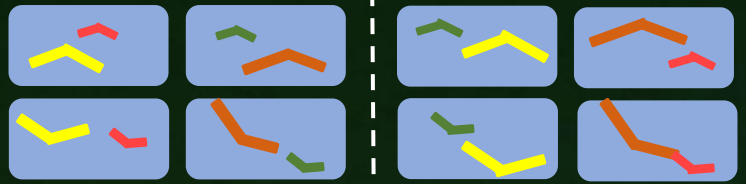


Sutton and Boveri's Experiment-3

Possibility II



Sutton and Boveri's Experiment-3



Possibility I **Possibility II**

- On comparing both possibilities, we find:

  In **case I, yellow and red** are together

  In **case II, yellow and green** are together
- **Each chromosome** separated independent of each other
- When they were separated into gametes, the set of chromosomes in each daughter cell ended up having a mixture of the parental and non- parental traits, but not necessarily the same mixture as that of other daughter cells.
- Hence, it can be concluded that **during gamete formation, chromosomes** in a homologous pair **separate independently** of other homologous pairs of chromosomes.

Chromo-somes somatic cell (2n)	Chromo-somes germ cells (n)	Number of possible combinati-ons in germ cell (2^n)
4	2	$2^2 = 4$
6	3	8
10	5	32

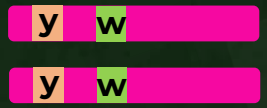
Linkage and Recombination

Morgan's Experiments: Morgan hybridised yellow-bodied, white-eyed females to brown-bodied, red-eyed males

Parental generation

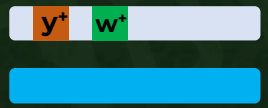
Homozygous recessive parent

Yellow bodied, white eyed

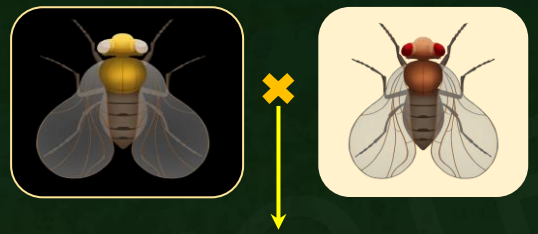


Homozygous dominant parent

Brown bodied, red eyed



F_1 generation



F_2 generation

Yellow bodied, white eyed

Brown bodied, red eyed

Brown bodied, white eyed

Yellow bodied, red eyed

Parental gene combinations

Non-parental gene combinations

Observation: Two genes did not segregate independently of each other. F_2 ratio deviated from the 9:3:3:1 ratio.

Linkage and Recombination

- Physical association of genes on the chromosome is called **linkage.**
- Frequency of recombination between gene pairs on the same chromosome is a measure of the distance between genes
- When genes are grouped on the same chromosome
  - Some genes are very **tightly linked** (showed very low recombination)
  - Some are **loosely linked** (showed higher recombination)

Genes tightly linked

F_2 generation	Body colour and eye colour (cross A)
Parental type	98.7%
Recombinant type	1.30%

Genes loosely linked

F_2 generation	Wing size and eye colour (cross B)
Parental type	62.8%
Recombinant type	37.2%

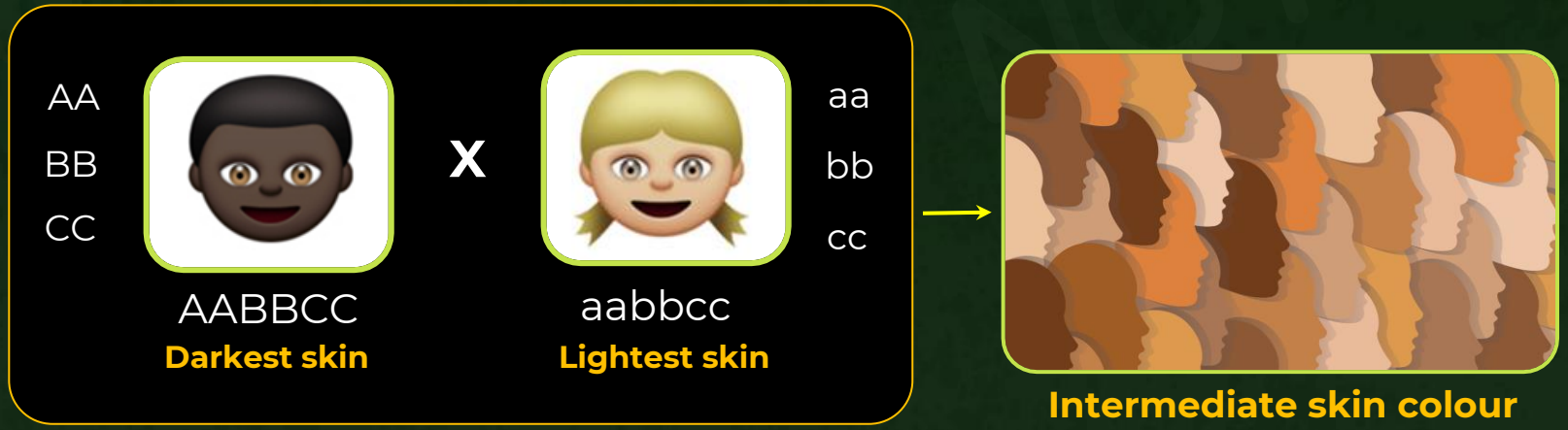
Recombination $\propto \frac{1}{\text{Linkage}}$

Chromosomal Mapping

- It is the process of **determining the position of specific genes on specific chromosomes and constructing a diagram of each chromosome showing the relative positions of the genes.**
- Sequence and the relative distances between various genes is graphically represented in terms of recombination frequencies or cross over values (COV). This is known as **linkage map of chromosome.**
- Distance or cross over units are called **centimorgan** (cM) or **map unit.**
- The recombination frequency depends upon the distance between the genes.
- **Distance between the genes** and the **crossing over** is **directly proportional** to each other.
- The **first chromosomal map** or genetic map was made for *Drosophila*.

Polygenic Inheritance

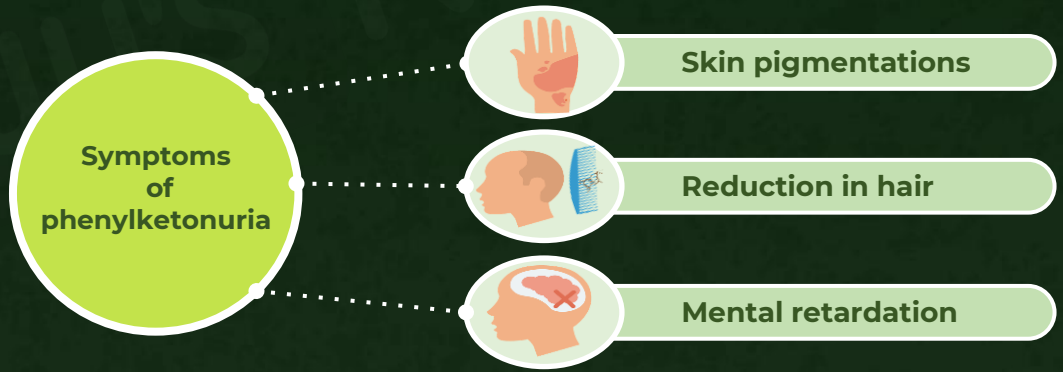
- Characters like **height and skin colour** are controlled by three or more genes and are called polygenic traits.
- Inheritance of such types of traits is called **polygenic inheritance.**
  - Phenotype reflects the **contribution** of each **allele,** i.e., the effect of each allele is **additive**
  - **Polygenic inheritance** also takes into account the **influence of environment**



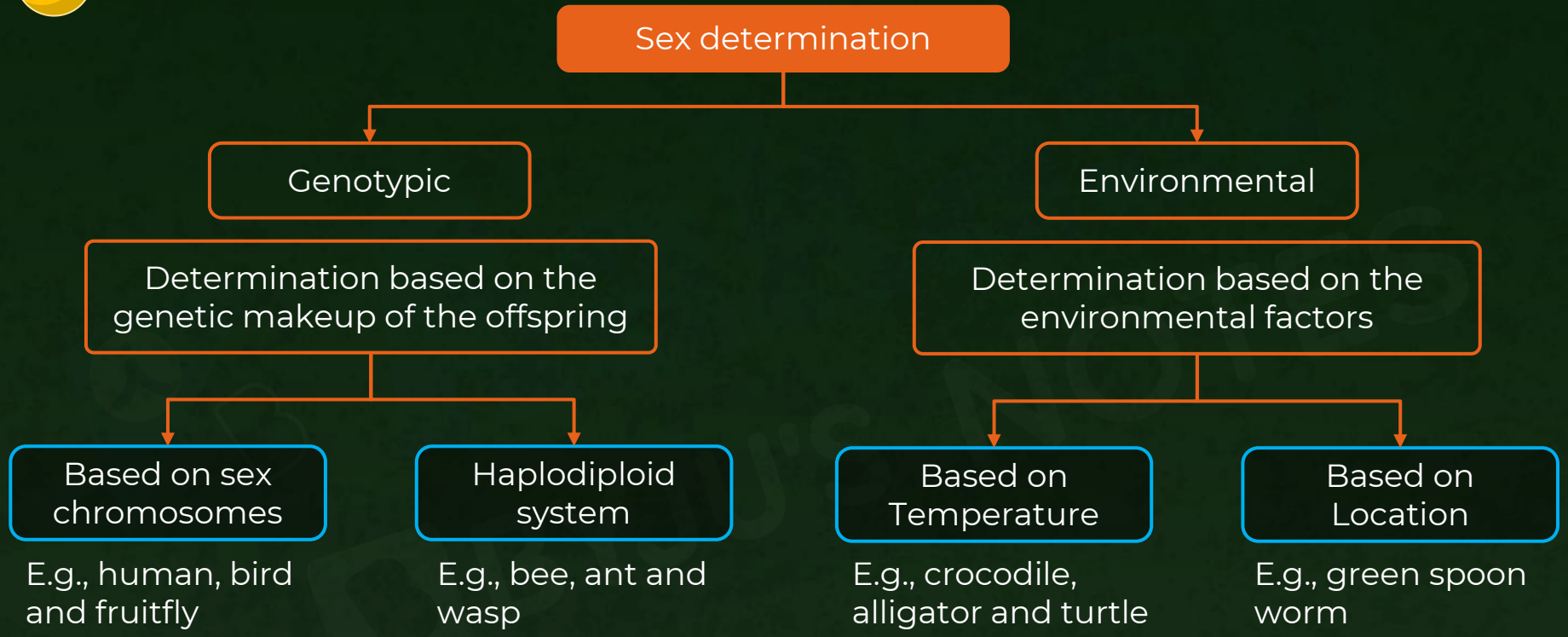
Pleiotropism

- Single gene exhibits **multiple phenotypic expression**
- Example: Effect of a gene on metabolic pathway which contributes to different phenotype in **Phenylketonuria**
- Effected enzyme **: Phenylalanine hydroxylase** (Enzyme is either missing or severely reduced.)
- Caused due to **single gene mutation**
- So, the metabolic pathway associated with the enzyme is disrupted and leads to multiple phenotypes

Diseased state - Phenylketonuria



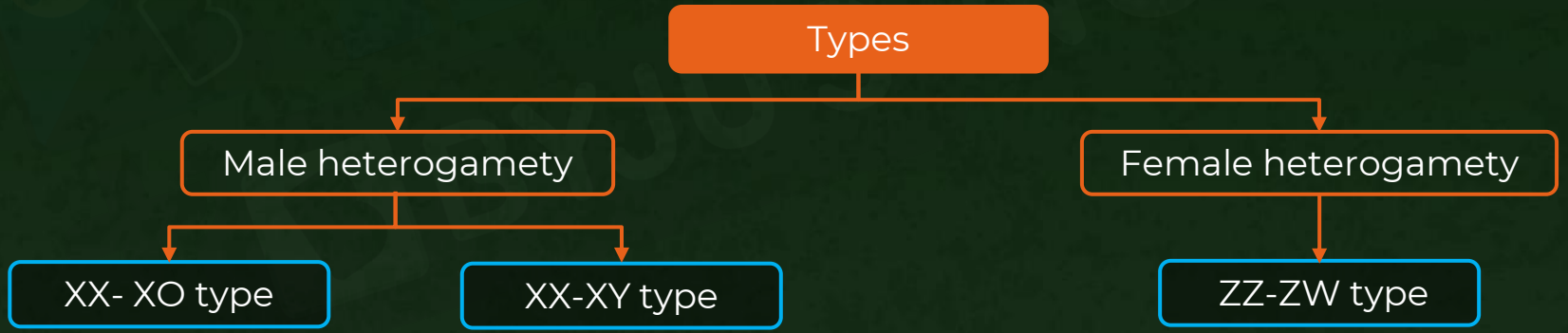
Sex Determination



Sex Determination

Based on sex chromosomes

- Sex determination is a biological mechanism which determines the development of sexual characteristics in an organism
- First studied by **Henking (1891)** in insects
  - Discovered **X chromosome** and named it '**X-body**'
  - Unable to explain its significance
  - Lead to the development of the **chromosomal mechanism** of **sex determination**



Sex Determination

Based on sex chromosomes

XX - XO type

♂ \ ♀	X	X
X	X X	X X
O	X O	X O

50% males 50% females

Eg: Grasshopper

Female → XX Male → XO

- Male has only **one X** chromosome, whereas female has **two X** chromosomes.
- Males produce two different types of gametes.
- Eggs fertilized by sperm having **X chromosome** develop into females and those fertilized by sperm, without **X chromosome** develop into males.
- Fertilising sperm determines whether the offspring will be male or female.

Sex Determination

Based on sex chromosomes

XX - XY type

♂ \ ♀	X	X
X	X X	X X
Y	X Y	X Y

50% Males 50% Females

Eg: Humans and *Drosophila*


Female → XX


Male → XY


Female → XX


Male → XY

- Males have **one X** and **one Y** sex chromosomes, whereas females have **two X** chromosomes.
- Males produce two different types of gametes.
- Eggs fertilized by sperm having **X chromosome** develop into females and those fertilized by sperm, with **Y chromosome** develop into males.
- Fertilising sperm determines whether offspring will be a male or female.

Sex Determination

Based on sex chromosomes

ZZ - ZW type

♂ \ ♀	Z	W
Z	Z Z	Z W
Z	Z Z	Z W

50% males 50% females

Eg: Birds

Sex chromosomes → Z | W

Female → ZW

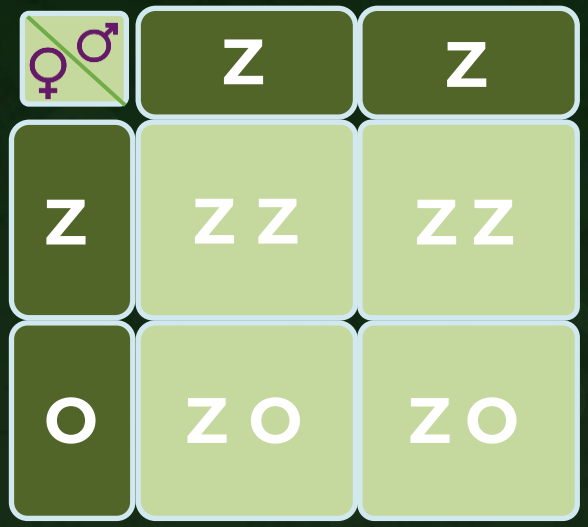
Male → ZZ

- Females have **one Z and one W** chromosome, whereas males have **two Z** chromosomes.
- Females produce two different types of gametes.
- Sperm fertilising egg having Z **chromosome** develop into males.
- Sperm fertilising egg having W **chromosome** develop into females.

Sex Determination

Based on sex chromosomes

Sex determination - Butterflies and Moths : ZZ-ZO Type



Female → ZO Male → ZZ

- In butterflies, the **females** have only **one sex chromosome**, besides the autosomes whereas **male** has **two sex chromosomes**.

Sex Determination

Based on the Haplodiploid system

- Based on the **number of sets of chromosomes**
- Seen in **honeybees**
- Individuals in a colony of honeybees:
    - Females (Queen and Worker) are diploid → Develop from fertilised eggs.
    - Males (Drone) are haploid→ Develop from unfertilised eggs parthenogenetically.

Worker ♀

Drone ♂

Queen ♀

Sex Determination

Based on Haplodiploid system

Female
(Queen)

2n = 32
(Diploid)

Meiosis

Eggs

n = 16

Parthenogenesis

Haploid male (n= 16)

Male
(Drone)

n = 16
(Haploid)

Mitosis

Sperm
n = 16

n = 16

Fertilization

Diploid female (n= 32)

Queen (Fertile female)

Worker (Sterile female)

Sex linked inheritance

- X-chromosome **does not pass directly from one parent to the offspring** of the same sex but follows a **criss-cross inheritance.**
- A **male transmits** his traits to his **grandson through daughter** (Diagynic), while a **female transmits** the traits to her **granddaughter through her son** (Diandric).

Sex limited traits

- Autosomal genes found in both sexes but express in one sex only
- **E.g.,** : Milk glands in female, beard in man, deep male voice, antlers in male deer, brilliant plumage in pea-cock, female or male musculature

Sex influenced traits

- Autosomal genes which are influenced by the sex of the bearer
- These traits appear more frequently in one sex than in the other.
- **E.g.,** : Pattern baldness (affected by male sex hormone/testosterone)
- Short index finger in male

Holandric traits

- Y-linked traits, transferred from male to male only
- **E.g.,** : Porcupine skin
- TDF (Testes determining factor)
- Hypertrichosis

Mutation

Mutation is a phenomenon that results in **alteration of DNA sequences** and consequently results in changes in the **genotype** and **phenotype.**

Chromosomal level

DNA level

Types

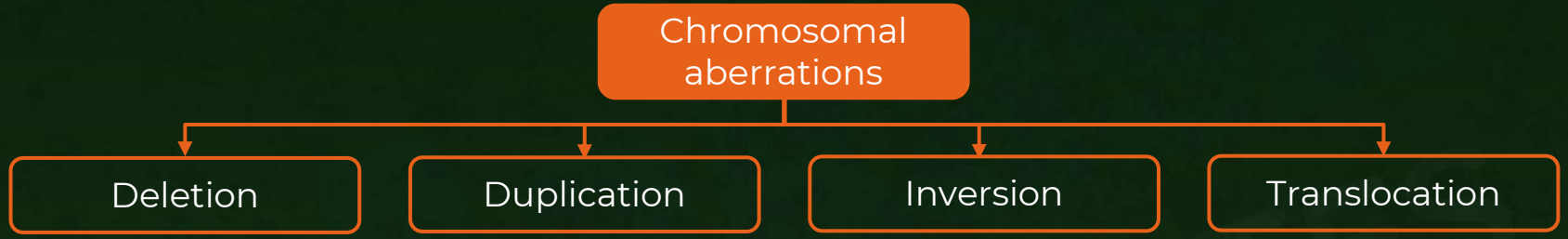
Chromosomal aberrations

- Deletion
- Duplication
- Inversion
- Translocation

Gene mutations

- Point mutation
- Frameshift mutation

Chromosomal aberrations



- Portion of chromosome deleted.
- Cri du chat syndrome arises due to deletion.

- Part of chromosome duplicated.

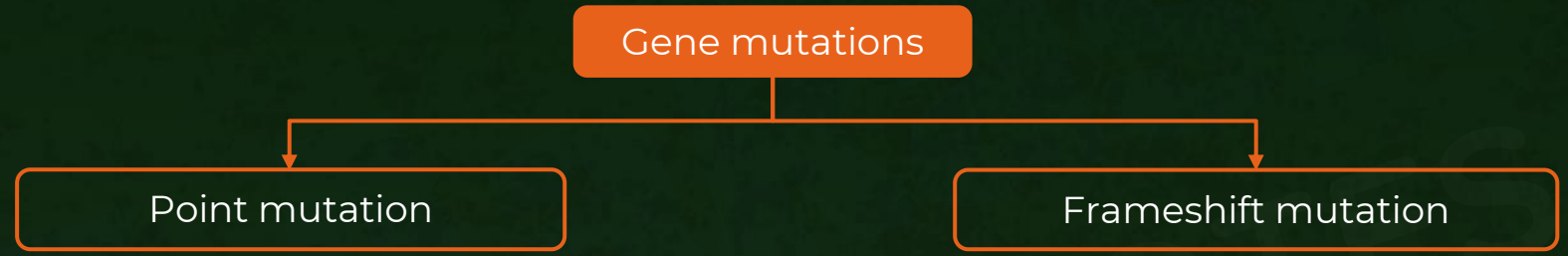
- Segment of chromosome breaks off and reattaches in the reverse order.

- Exchange of chromosomal segments between non-homologous chromosomes.

Reasons for chromosomal aberration

- Chromosomal aberrations occur due to **non-disjunction** of chromosome.
- This error occurs during the **anaphase** of the **cell division**.
- Sometimes, the **chromosomes fail to split** leading to one gamete having more chromosomes and the other gamete having less chromosomes.

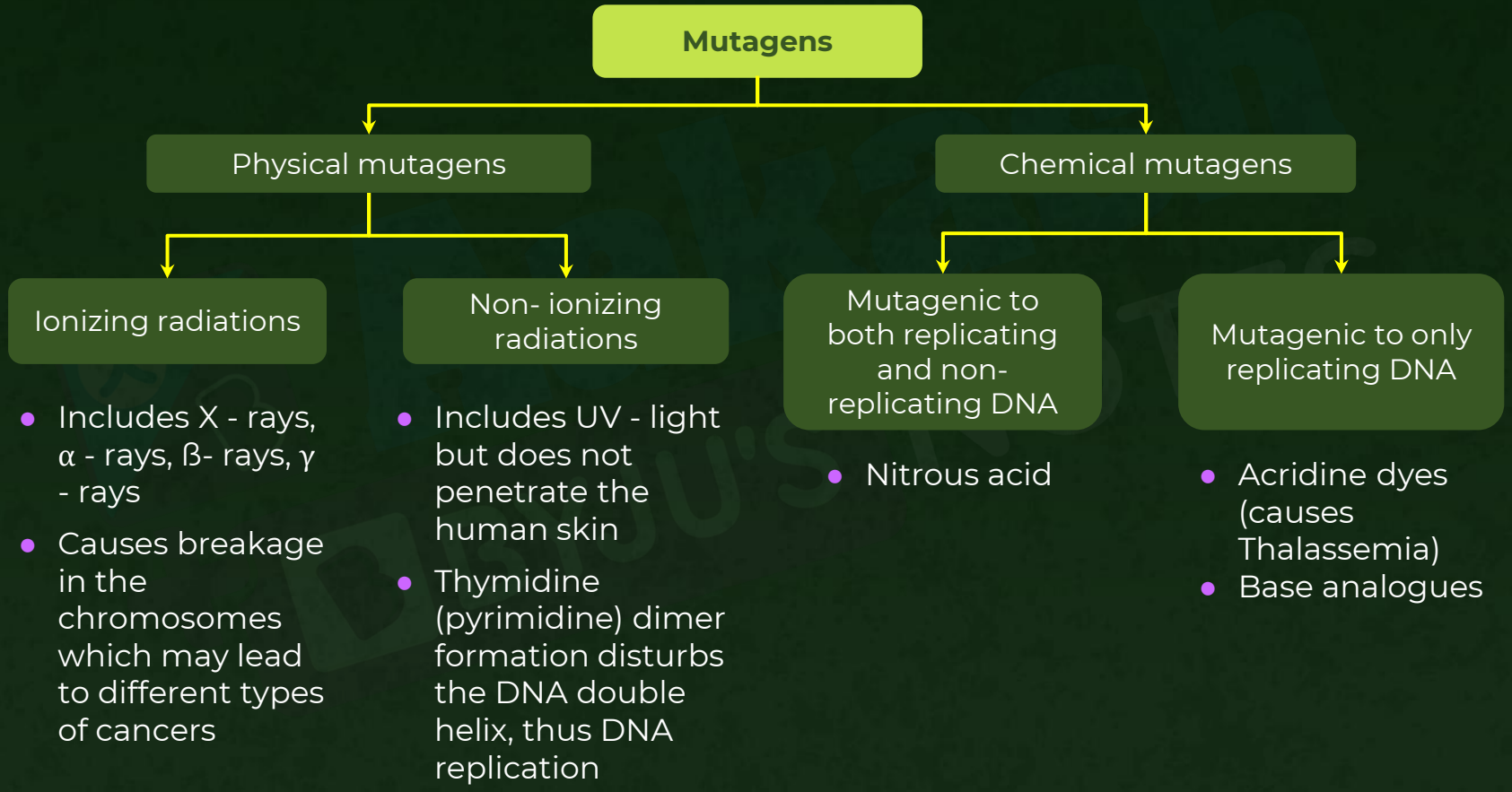
Gene Mutation



- Change in a **single base pair** of DNA
  - **Sickle cell anaemia** is caused due to **point mutation.**

- **Deletions** and **insertions** of base pairs of DNA.

Mutagens



Genetic Disorders

Mendelian disorders

- **Alteration** or **mutation** in a single gene
- Follows **Mendelian pattern of inheritance**
- Pattern of **inheritance** can be **traced** in a family by the **pedigree analysis**
- May be **dominant** or **recessive**
- Examples - Haemophilia, Cystic fibrosis, Sickle cell anaemia, Colour blindness, Phenylketonuria, Thalassemia, etc.

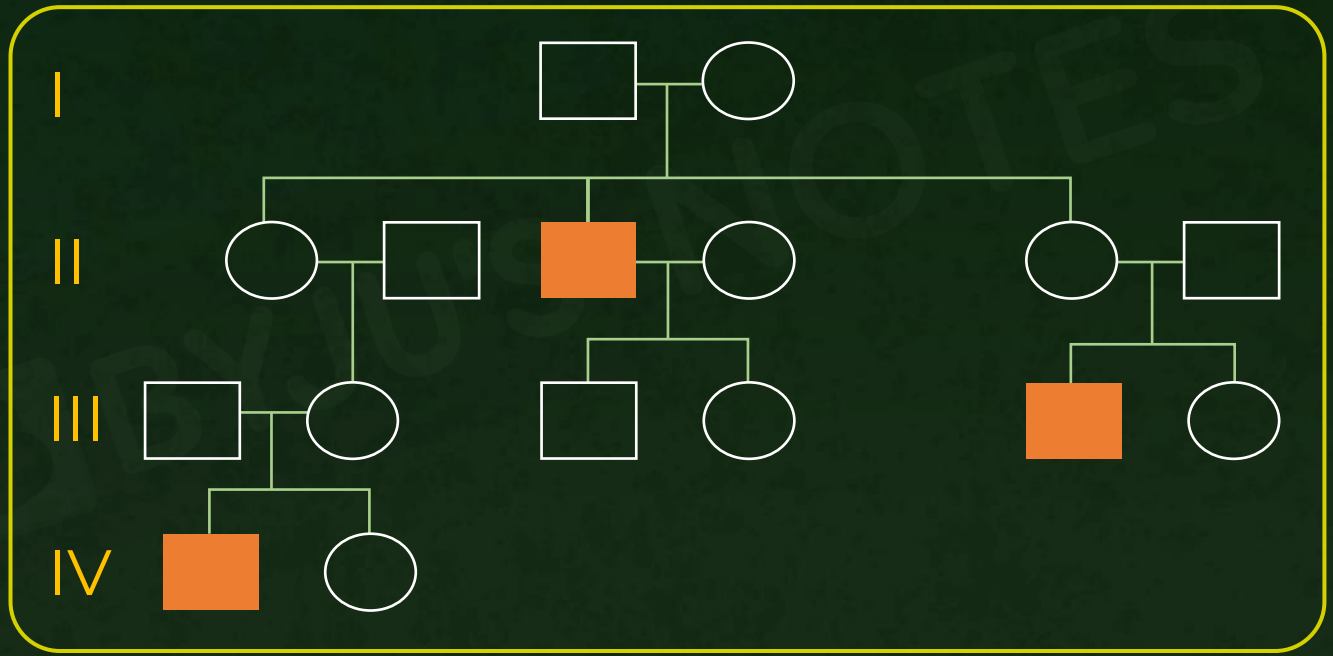
Chromosomal disorders

- Caused due to **absence** or **excess** or **abnormal** arrangement of one or more chromosomes
- **Aneuploidy** - **gain** or **loss** of one or few chromosomes
- **Polyploidy** - **increase** in a **whole set of chromosomes**
- **Failure of cytokinesis** after telophase results in polyploidy

Pedigree Analysis

- Analysis of traits in several **generations** of a family is called the **pedigree analysis.**
- Inheritance of a particular trait is represented in the family tree over generations.
- In human genetics, it provides a strong tool, helps in tracing the **inheritance** of a **specific trait**, **abnormality** or **disease.**

Pedigree chart



Pedigree Analysis

- Symbols used in pedigree analysis

Unaffected/ Normal male

Unaffected/ Normal female

Sex unspecified

Affected female

Affected male

Carrier female

Carrier male

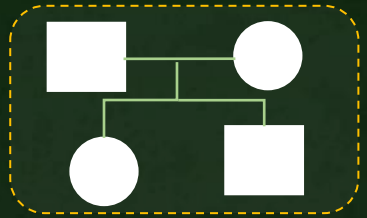
Carrier female

Carrier male

Mating

Mating between relatives (consanguineous mating)

5 unaffected offspring



Parents above and children below (in the order of birth- left to right)

Mendelian Disorder

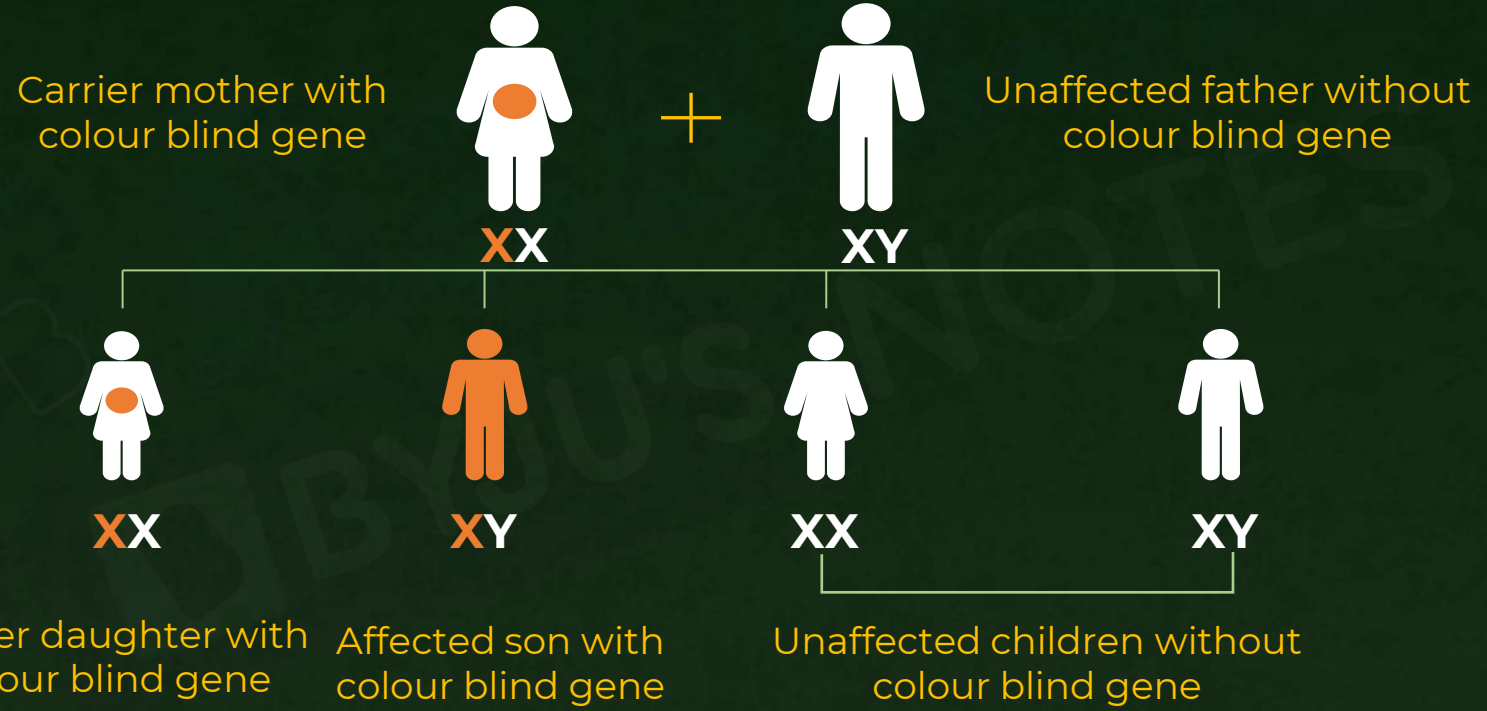
- A **sex-linked recessive** genetic disorder in which:
  - there is a defect in either red or green cone of eye
  - person is unable to discriminate between red and green colour.
- Defect is due to mutation in **genes** present in the X chromosome.
- **Males suffer more** when compared **to females; females** are usually **carriers.**

Colour blindness

- Son of a woman who carries the colour blind gene has a **50 percent** chance of being colour blind.
- A daughter will not normally be **colour blind**, unless her mother is a **carrier** and her **father** is **colour blind.**
- Occurs in 8% of males and 0.4% of females.

Mendelian Disorder

Colour blindness

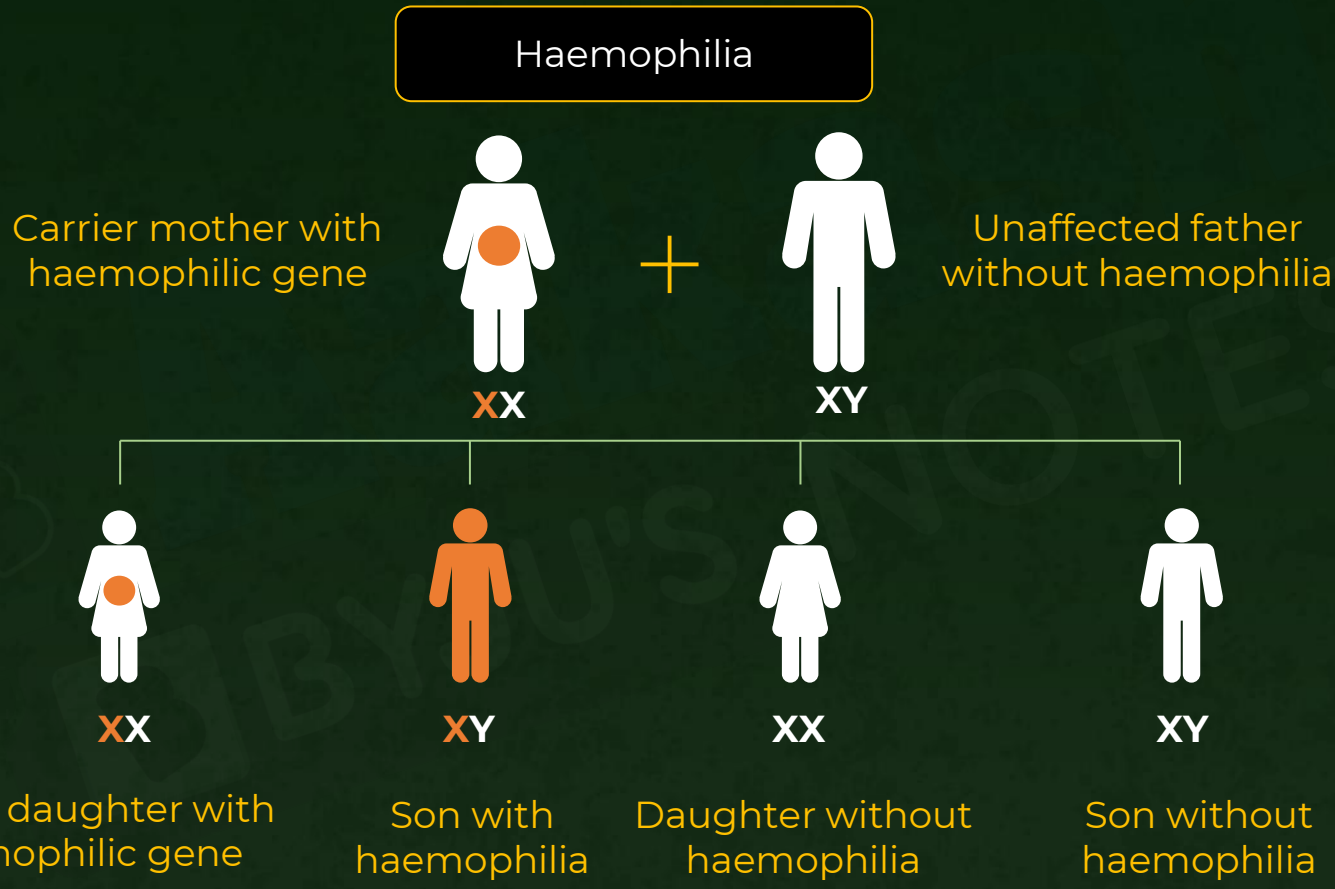


Mendelian Disorder

Haemophilia

- It is **a sex-linked** recessive disease.
- A single protein that is a part of the **cascade** of **proteins** involved in the **blood clotting** is affected, this is **Haemophilia A** (more severe)
  - A simple cut results in non-stop bleeding in affected individuals.
- Heterozygous female (carrier) for **haemophilia** may **transmit** the disease to sons.
- The family pedigree of Queen Victoria shows a number of haemophilic descendants as she was a carrier of the disease.
- **Haemophilia B** (Christmas disease) - plasma thromboplastin is absent. Inheritance is just like Haemophilia A
- Possibility of a female becoming a **haemophilic** is **extremely** rare.
  - Mother of such a female has to be carrier and the father should be haemophilic.

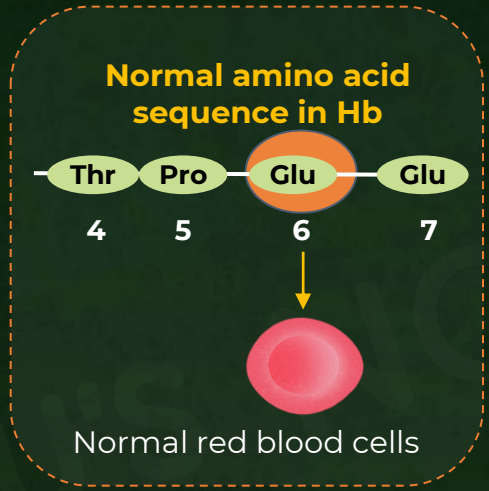
Mendelian Disorder

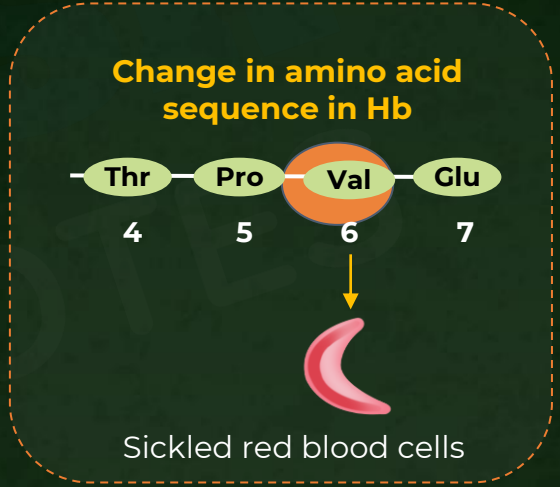


Mendelian Disorder

Sickle-cell anaemia

- **Inherited red blood cell disorder**
- **Autosome linked recessive** trait
- Transmitted from parents to the **offspring** when both the **parents** are carrier (**heterozygous**) for the gene
- Not enough healthy red blood cells to carry oxygen throughout the body
- Person has **abnormal haemoglobin**





- **Mutation** in the **Hb gene** causes abnormal Hb synthesis resulting in the formation of sickle shaped cells
- Change in amino acid sequence is caused due to point mutation
- **Glutamic acid** in the **6th position** of the **beta globin** chain is **replaced** by **Valine**
- Causes change in Hb and thereby in RBCs, from biconcave to sickle shaped

Mendelian Disorder

Sickle-cell anaemia

- Heterozygous (Hb^AHb^S) individuals
  - Appear apparently unaffected, but they are carriers of the disease
  - **50 percent probability** of transmission of the mutant gene to the progeny
  - Exhibits **sickle-cell trait**

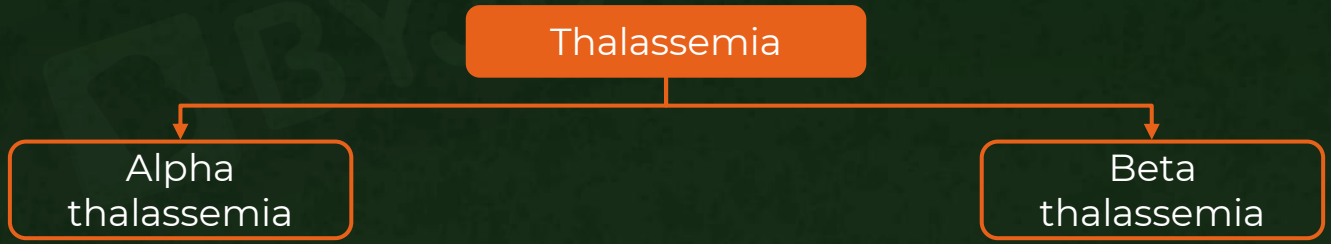
Inheritance (Carrier x Carrier)

♂ \ ♀	Hb^A	Hb^S
Hb^A	Hb^AHb^A Normal	Hb^AHb^S Carrier
Hb^S	Hb^AHb^S Carrier	Hb^SHb^S SCA

Mendelian Disorder

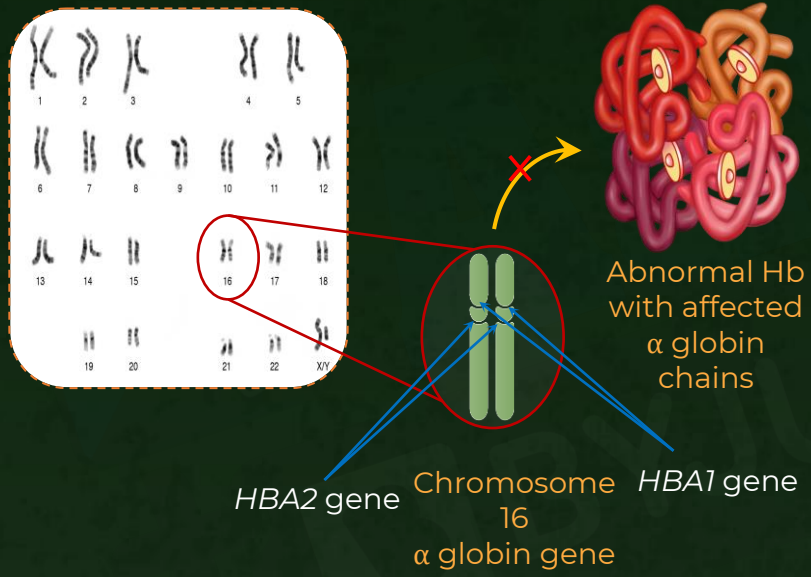
Thalassemia

- **Autosome-linked recessive** blood disease
- Blood disorder resulting from **inadequate Hb** synthesis
- Transmitted when both the partners are **unaffected carriers** (heterozygous) for the gene defect
- It could be due to either **mutation** or **deletion**
  - Results in reduced rate of synthesis of one of the globin chains (**α or β chains**) that make up **haemoglobin**

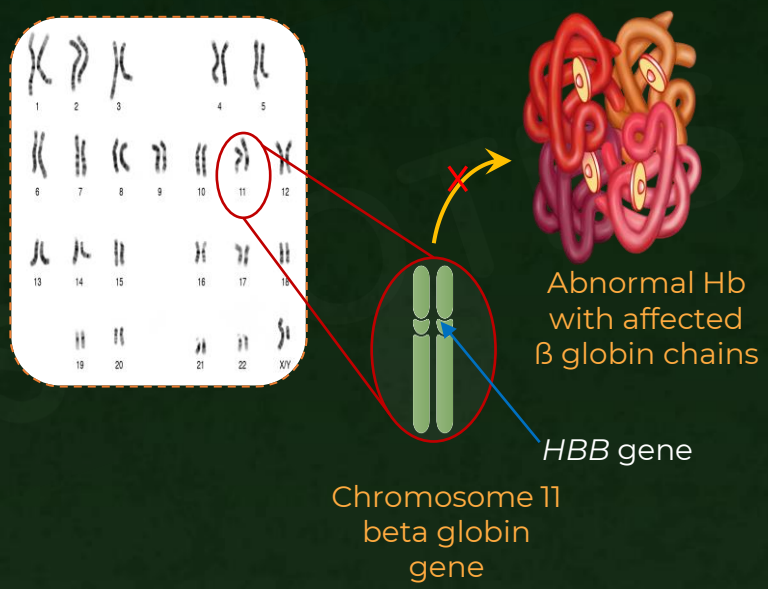


Mendelian Disorder

Alpha thalassemia



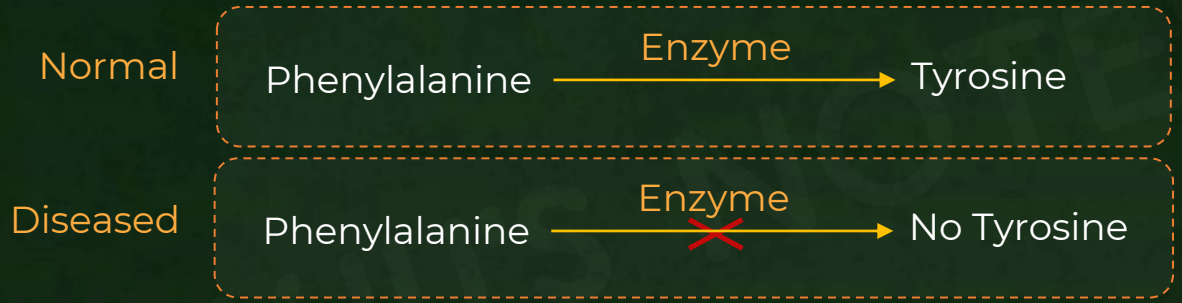
Beta thalassemia



Mendelian Disorder

Phenylketonuria

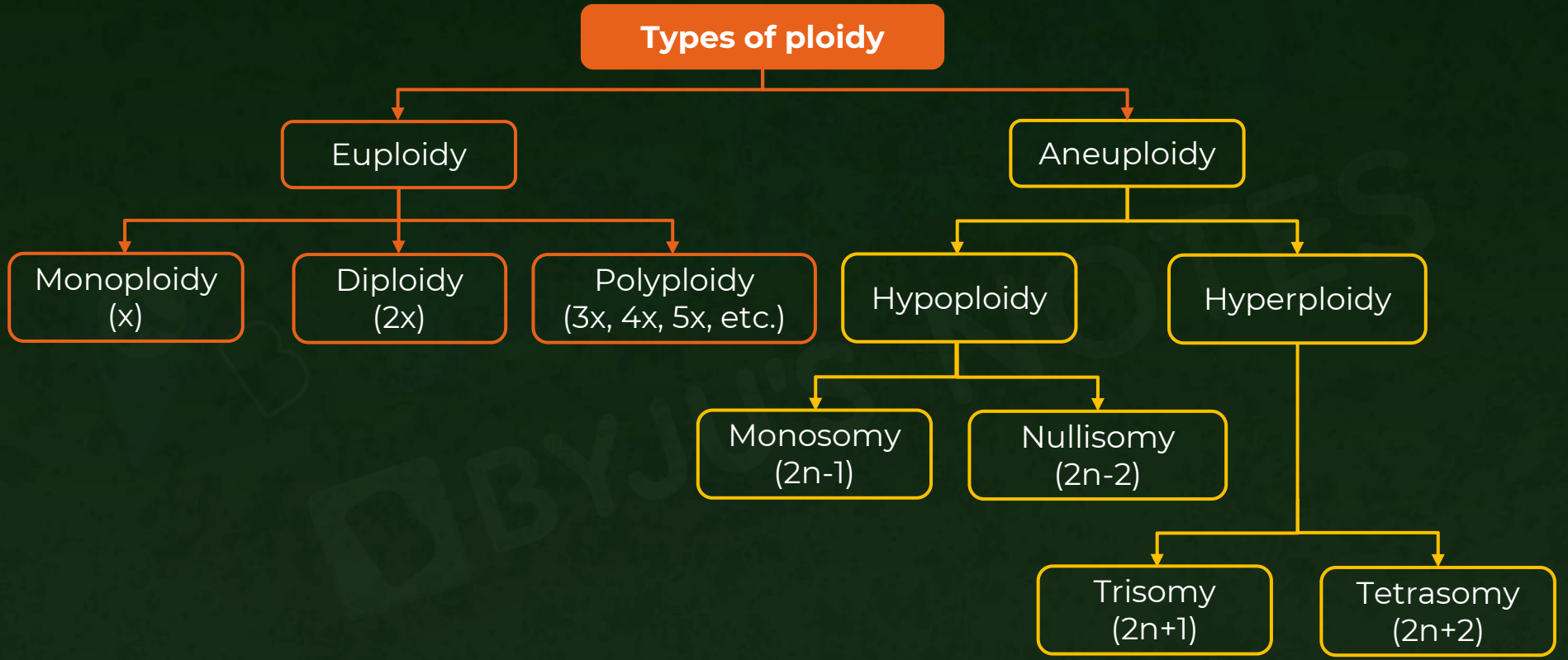
- **Autosomal recessive** trait
  - Affected individual **lacks** an enzyme that converts the amino acid **phenylalanine** into **tyrosine**



- **Phenylalanine** is accumulated and converted into **phenylpyruvic acid** and other derivatives.
- Accumulation of these in brain results in **mental retardation.**
- Excreted through **urine** because of its **poor absorption** by kidney

Chromosomal Disorder

Disorders created by imbalance in chromosome number and chromosomal rearrangement.



Types of chromosomal disorders

Types of chromosomal disorders - I

Types of ploidy

- Nullisomy (2n-2)
  - Non-survivable
- Monosomy (2n-1)
  - Turner's syndrome
    - Absence of one X chromosome
    - Occurs in female
    - Males die before birth
    - Chromosome composition: 45+X
  - Cri-du-chat syndrome

Types of chromosomal disorders - II

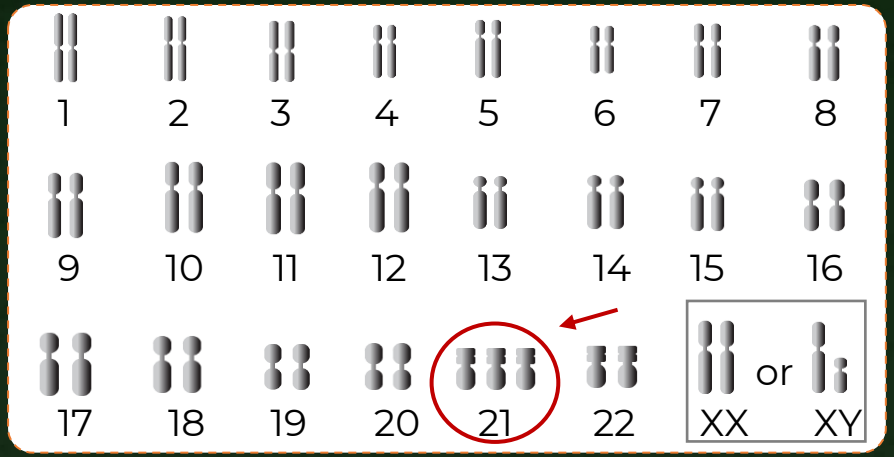
Types of ploidy

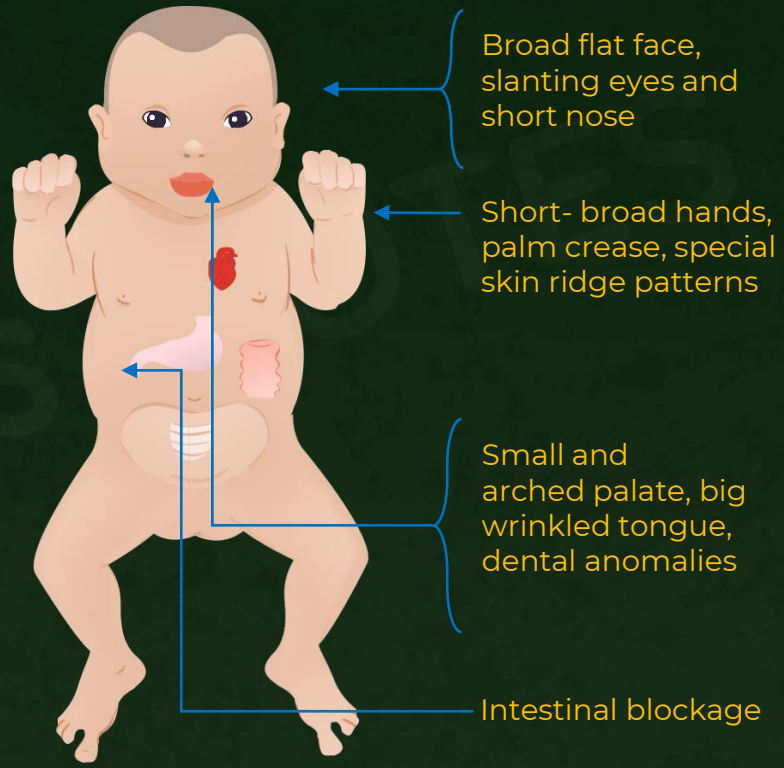
- Trisomy (2n+1)
  - Down's syndrome
    - Trisomy of 21st chromosome
    - Occurs in both males and females
    - Symptoms: Broad palm, physical, psychomotor mental growth retarded, furrowed tongue, partially open mouth
  - Triple X syndrome
  - Edwards syndrome
  - Klinefelter syndrome
    - 47 + XXY
    - Occurs only in male
    - Symptoms: Gynaecomastia and sterility

Chromosomal Disorder

Down's syndrome

- Trisomy of **21st** chromosome
- Occurs both in **females** and **males**
- First described by **Langdon Down**
- Karyotype**: 47, XX, + 21 for females and 47, XY, + 21 for males**

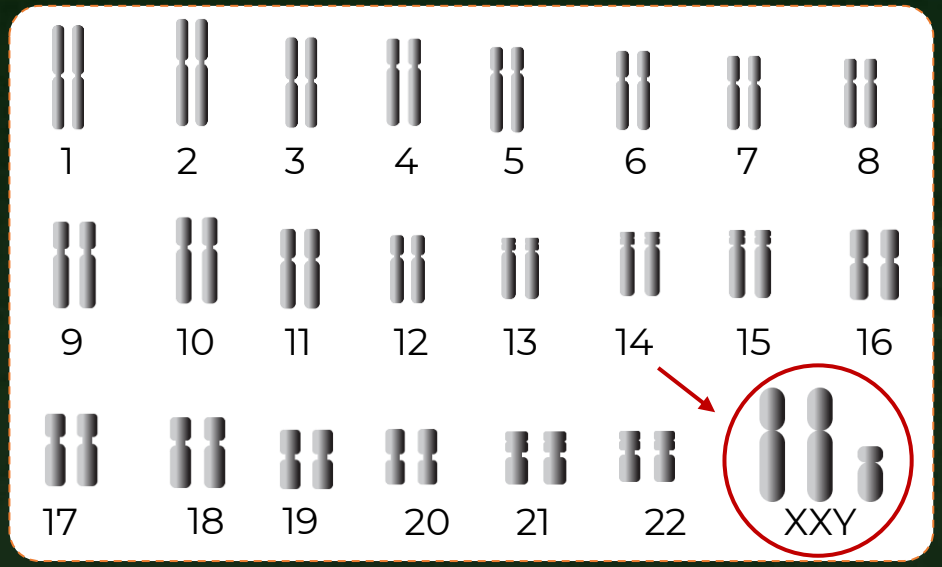


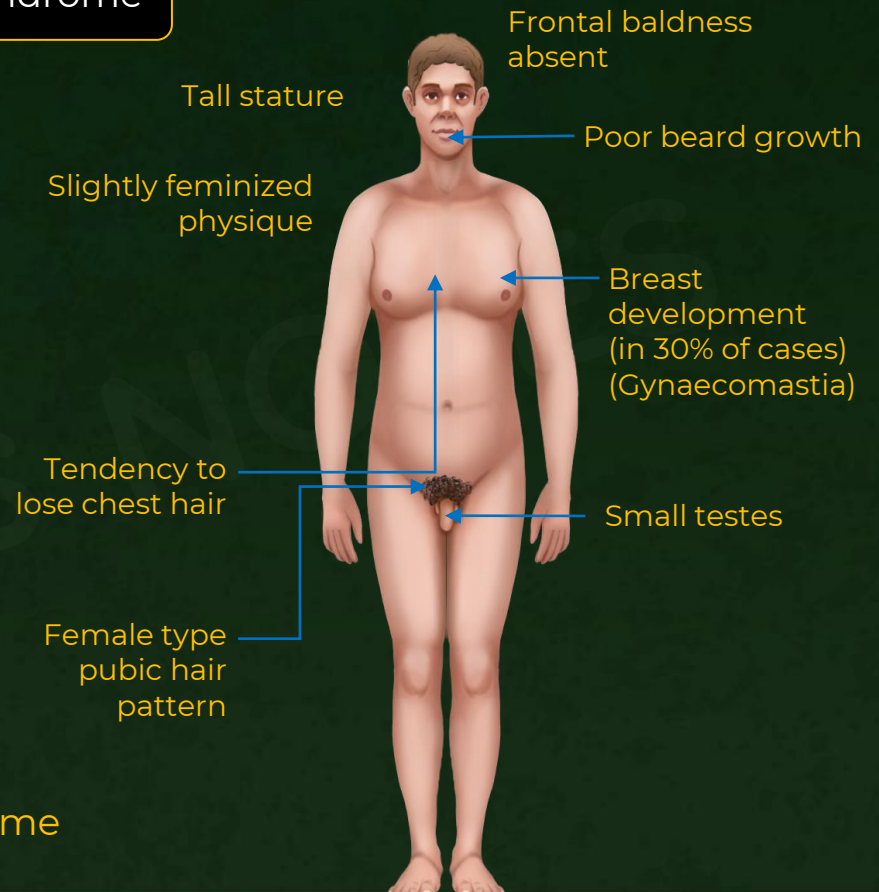


Chromosomal Disorder

Klinefelter's syndrome

- Occurs only in **males**
- Extra X chromosome
- Karyotype: **47+XXY**



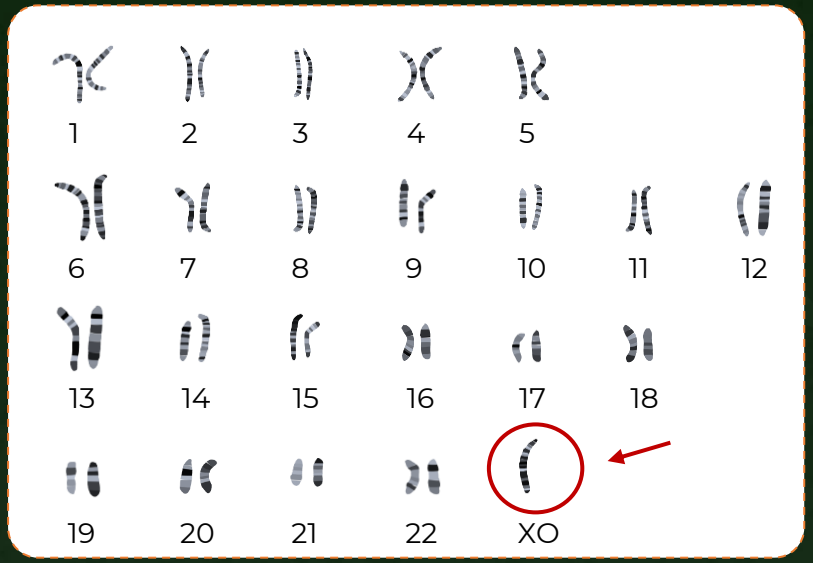


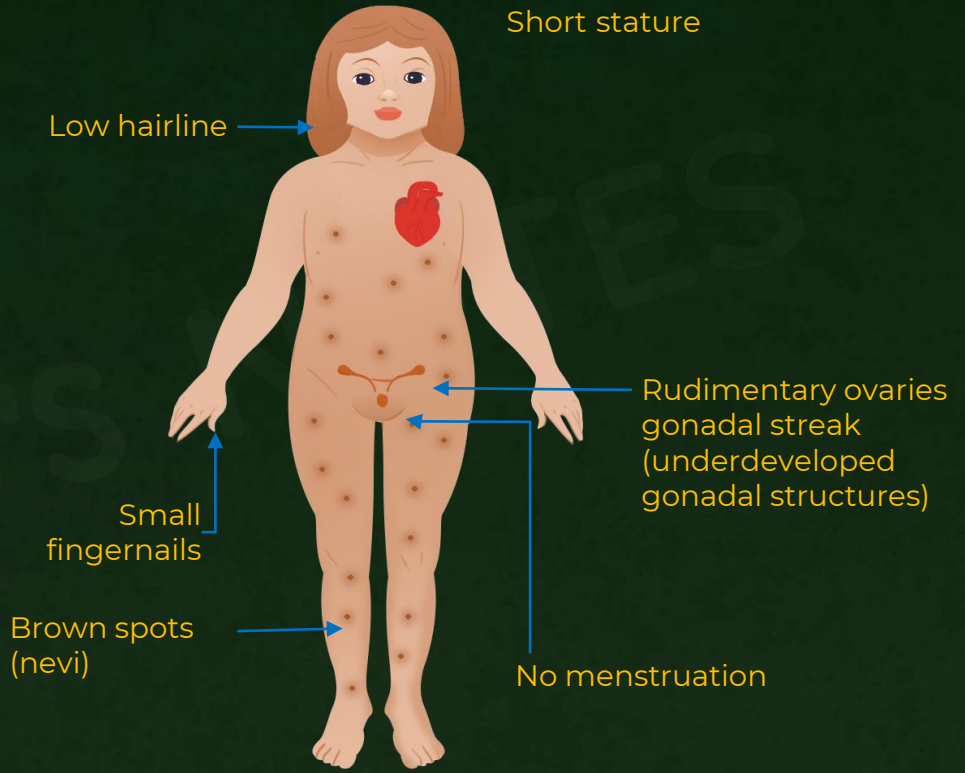
An extra X chromosome results in Klinefelter's syndrome

Chromosomal Disorder

Turner's syndrome

- Occurs in **females**
- Loss of **one X** chromosome
- Karyotype: **45+X**





Cytoplasmic Inheritance

- **Self-replicating genes** (DNA) are **present in the cytoplasm** (mitochondrial DNA and chloroplast DNA) also, called **plasmagenes**, together constitute **plasmon** (like genome).
- **Inheritance of characters** by plasmagenes is called extranuclear or **extrachromosomal inheritance**
- Examples:
  - **Maternal inheritance** : Contribution of female parent is more, as cytoplasm in egg is always much more than the sperm. E.g., coiling of shells in snails
  - **Organelle inheritance** : DNA is present in mitochondria and chloroplast which controls the inheritance of some characters. E.g., plastid inheritance in *Mirabilis jalapa* (4 O'clock plant)

Summary

Character - Heritable feature that varies among individuals

Trait - Each variant of a character

Allele - Slightly modified forms of the same gene. The term allele was given by Bateson

Factors - Something stably passed down, unchanged, from parent to offspring through the gametes, over successive generations.

Phenotype - Visible physical trait of an organism

Genotype - Actual genetic make-up of an organism

Homozygous- Identical alleles on the homologous chromosomes. (Example: TT, tt)

Heterozygous- Dissimilar alleles on the homologous chromosomes. (Example: Tt, Rr)

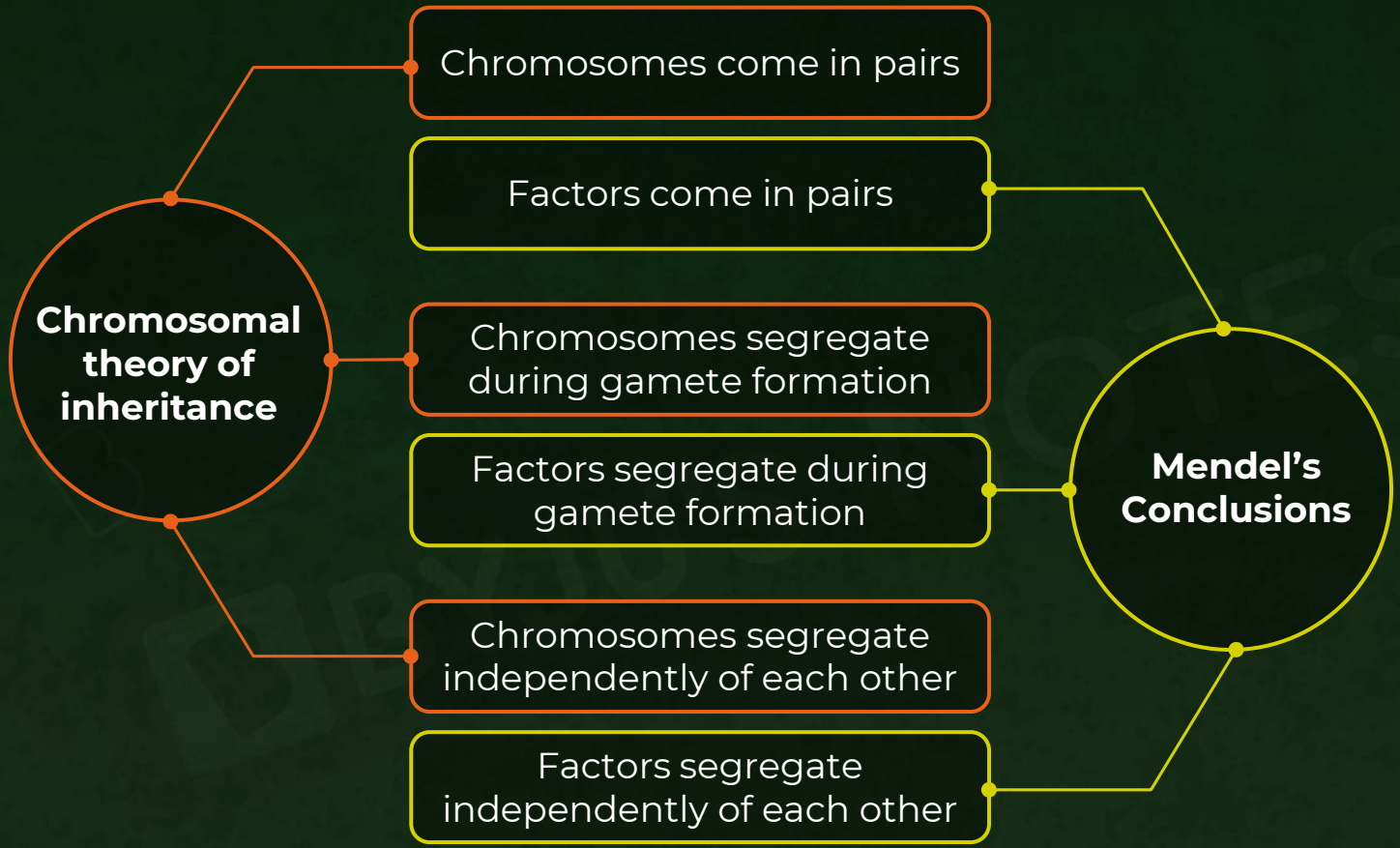
Dominant - Trait which can express itself over contrasting trait.

Recessive - Trait which cannot express itself over contrasting trait or suppressed by dominant or contrasting trait.

Summary

- **Law of Dominance** - When two alleles are different or in **heterozygous condition**, then one **dominates** the expression of the other
- **Law of Segregation** - During gamete formation, **pair of alleles segregate** such that **each gamete receives only one allele** from the pair
- Mendel arrived at these two laws based on his **Monohybrid cross**
- **Law of independent assortment** - When two pairs of traits are combined in a hybrid, the segregation of one pair of characters is independent of the other pair of characters
- Hence, there is **no connection** or linkage between the segregation events of the two genes

Summary



Summary

Complete dominance

Phenotypic ratio

Red : White

3 : 1

Genotypic ratio

RR : RW : WW

1 : 2 : 1

Co-dominance

Phenotypic ratio

Red : Roan : White

1 : 2 : 1

Genotypic ratio

RR : RW : WW

1 : 2 : 1

Incomplete dominance

Phenotypic ratio

Red : Pink : White

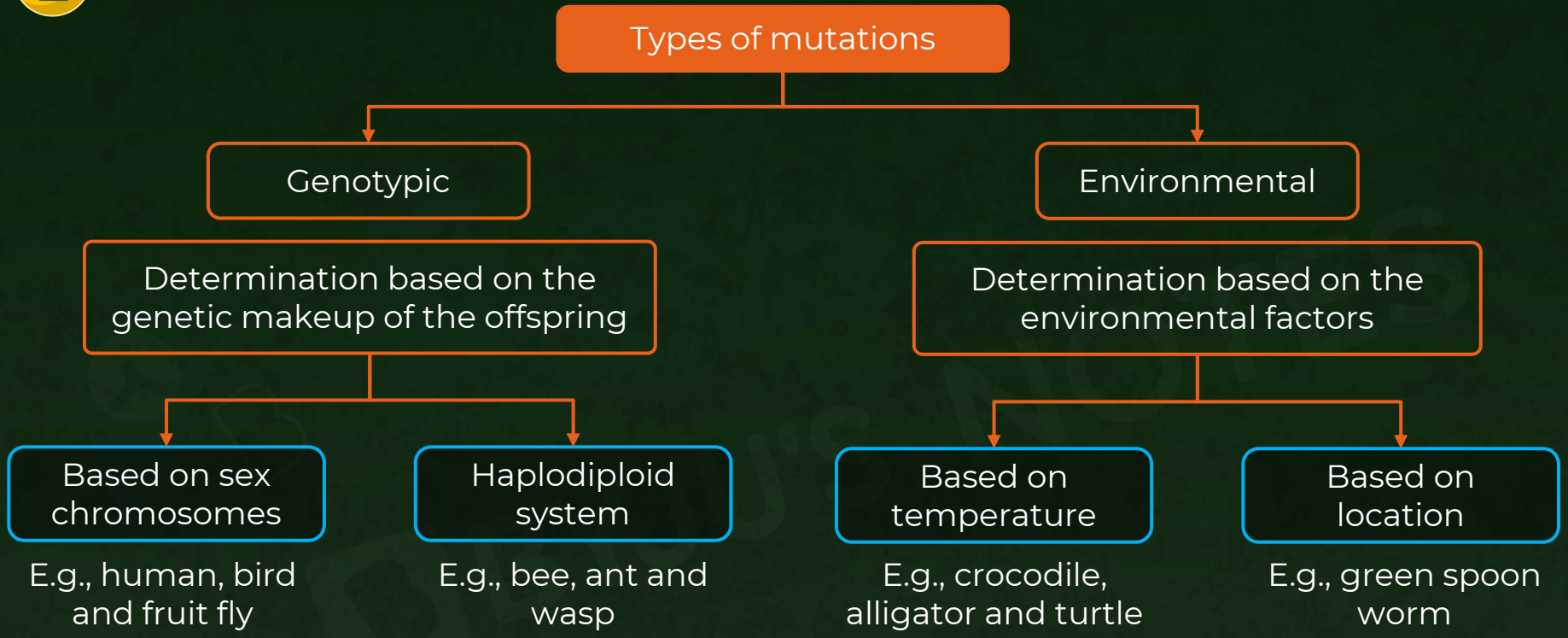
1 : 2 : 1

Genotypic ratio

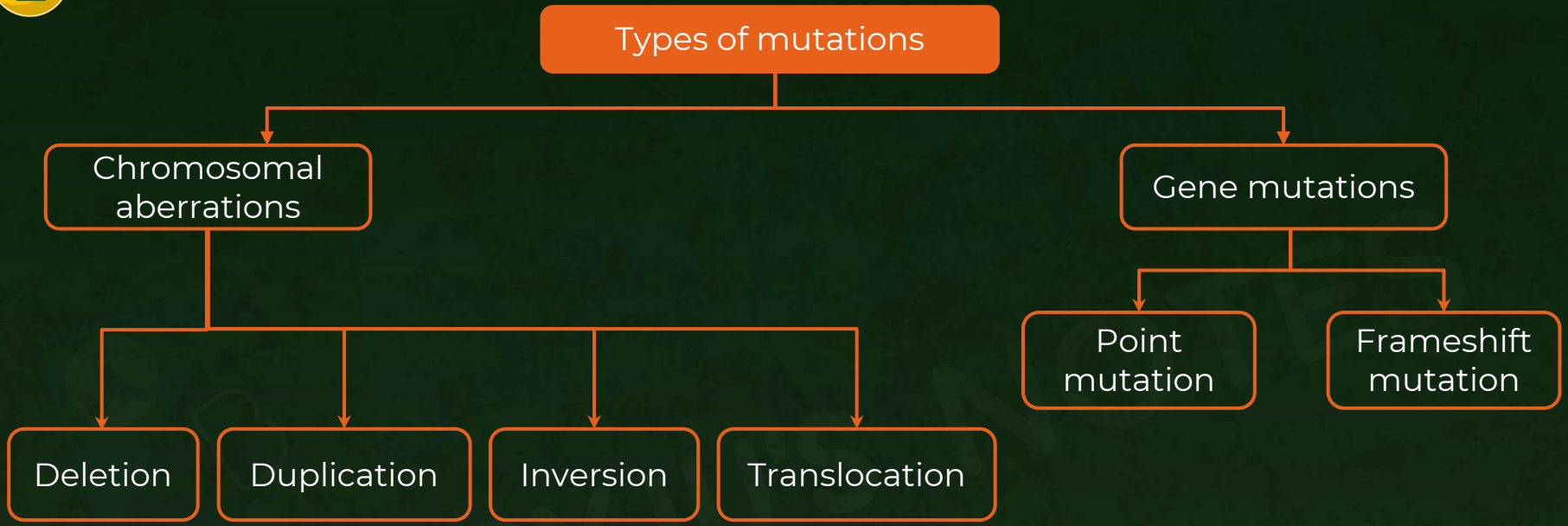
RR : RW : WW

1 : 2 : 1

Summary



Summary



Summary

Mendelian disorders

- Colour blindness
- Haemophilia
- Sickle-cell anaemia
- Phenylketonuria
- Thalassemia

Chromosomal disorders

- Down's Syndrome
- Klinefelter's Syndrome
- Turner's Syndrome