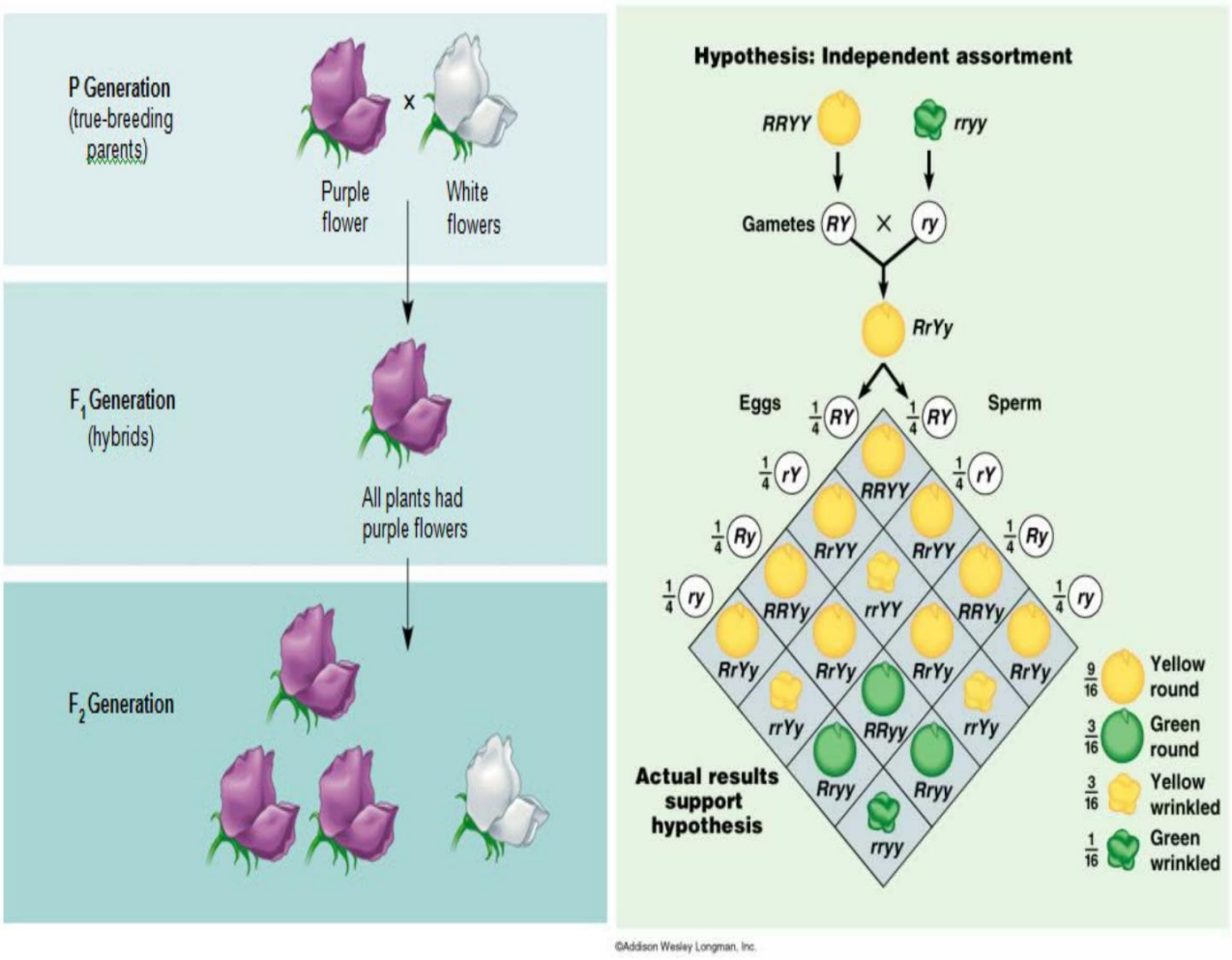
EXTENSION OF MENDELIAN INHERITANCE: BEYOND MENDELIAN GENETICS (part 1)

Mendelian genetics was about: (revise)

Nuclear monogenic genes, each consists of only 2 alleles present on different chromosomes following the rule of complete dominance (simple dominance): **One copy** of the dominant allele is sufficient to produce the dominant phenotype. Recessive allele **does not affect** the phenotype of heterozygotes. The phenotype of the homozygous dominant (AA) organism is similar to that of the heterozygous one (Aa).

The gene obeys both Mendel laws: Monohybrid cross produces 3:1 phenotypic ratio of F_2 and Dihybrid cross produces 9:3:3:1 phenotypic ratio of F_2.



Non-Mendelian inheritance is a general term that refers to any pattern of inheritance in which traits do not segregate in accordance with Mendel's laws and do not express a typical dominance/recessive relationship. That is, the F_1 and F_2 values do not match the predicted values of the proportions of progenys' phenotypes observed by Mendel.

There are several situations in which the proportions of phenotypes observed in the progeny do not match the predicted values.

Exceptions to, or **violations of, Mendel's laws**: What can cause there to be exceptions to Mendel's laws?

1. **non-disjunction**: The segregation of alleles is prevented if homologous chromosome pairs fail to separate during meiosis 1.
2. **gene linkage**: This can prevent independent assortment. Linked genes are on the same chromosome. Genes that are on the same chromosome can be inherited together, but crossing over during meiosis may separate them.
3. **mutation** is a permanent change of the nucleotide sequence of the genome of an organism, virus, or extrachromosomal genetic element. Mutations result from unrepaired damage to DNA or to RNA genomes (typically caused by radiation or chemicalmutagens).

4. Chromosomal Aberrations (abnormalities or anomaly)

They include the variation at the Chromosomal level. These changes may be as missing, extra, or irregular segment of chromosome. It can also be from an atypical number of chromosomes or a structural abnormality in one (within the chromosome) or more chromosomes (between chromosomes). Chromosome anomalies usually occur when there is an error in cell division following meiosis or mitosis. It is the most dramatic examples of genomic instability.

There are several situations in which reject Mendel rules and laws:

I. Monogenic inheritance: allelic relationships

II. Monogenic inheritance: gene action

III. Polygenic inheritance: gene interaction.

IV. Sex related gene: Sex-linked, sex influenced and sex limited

V. Cytoplasmic inheritance

VI. Environmental effects on gene expression

I. For single-gene inheritance: Allelic relationships in genes

Allelic relationships of genes may be:

A. No dominance relations

B. Lethal genes

C. Multiple alleles

A. No dominance relations in Eukaryotic organisms

Mendel's followers have revealed the appearance of phenotypes in new ratios that **do not express** a typical dominance/recessive (complete dominance) and **do not obey** Mendel's first law. That is, the F_1 and F_2 do not match the predicted values of the proportions of progenies' phenotypes observed by Mendel. Those different phenotypic dominances were incomplete, partial, co- and over-dominance and can be explained as followings:

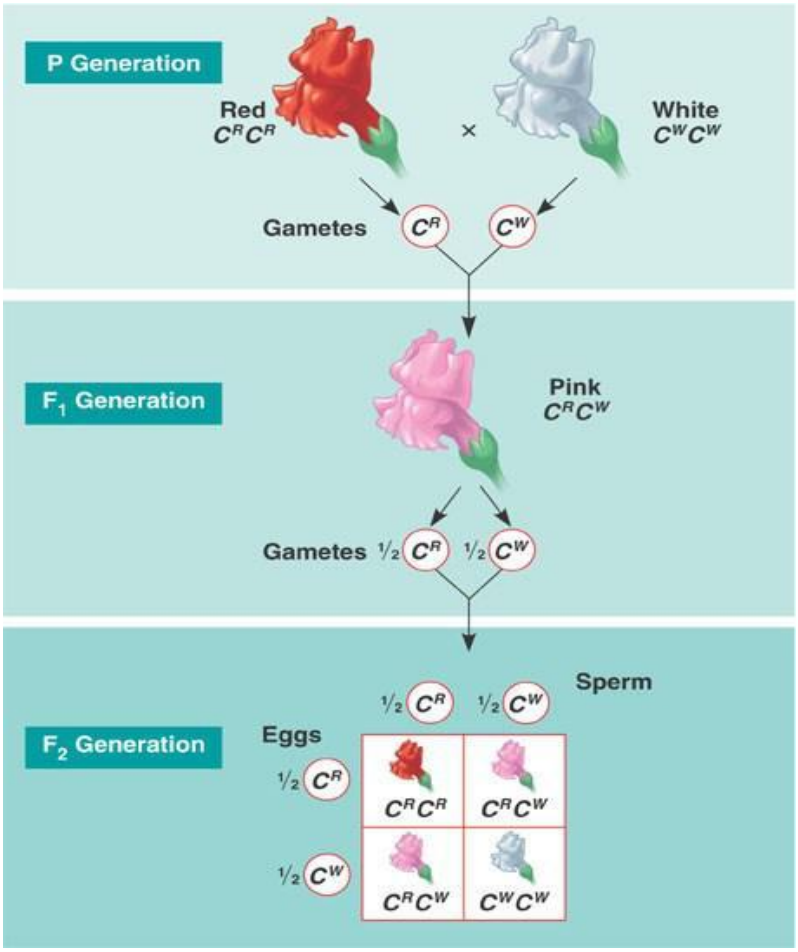
1. Incomplete (Intermediate) Dominance

A dominant phenotype is not expressed even though an individual carries a dominant allele i.e. **not fully dominant**. So, the phenotype of the heterozygous organism (Aa) is in **intermediate state** between the phenotype of both homozygous dominant and recessive (AA and aa) organisms i.e. AA phenotype

≠ Aa phenotype.

<u>Eg:</u> In *Antirrhinum* flowers (حنك السبع) and Carnation flowers (قرنفل)

In the cross between its red and white flowers, all the F_1 generations have **pink flowers** (instead of red in complete dominance). When self-fertilization of F_1, the F_2 ratio was **1 red: 2 Pink: 1 white** (instead of 3 red: 1 white).



Antirrhinum flowers

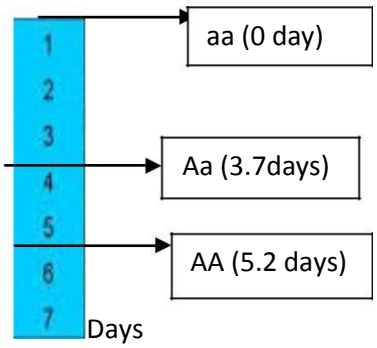
Carnation flowers

2. Partial-Dominance

When the heterozygous (Aa) is **near one** of the homozygous, the dominance is called Partial Dominance.

Eg: Flowering time of peas (blooming time)

The flowering time of homozygous recessive is considered as 0 days (closed flowers) and the flowering time of homozygous dominant (AA) is 5.2 days to open. The heterozygous (Aa) is near one of the homozygous; in this case it is near AA as its flowering time is 3.7 days to open.



Closed flowers

Open flowers

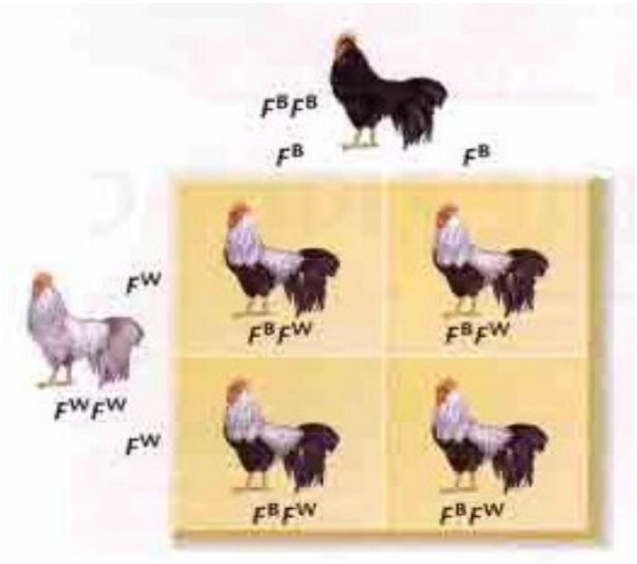
3. Co-dominance (Mosaic Dominance)

Where the alleles forming the genotype of the heterozygous organism is **fully and equally expressed** in phenotype i.e. both the dominant and recessive characters are present. AA phenotype ≠ Aa phenotype.

Eg: a. mosaic of red and white hairs in roan heterozygous shorthorn cattle.

Brown (C^BC^B) Patched (C^BC^W) Brown (C^WC^W)

b. mosaic black and white areas in the Andalusian fowl.



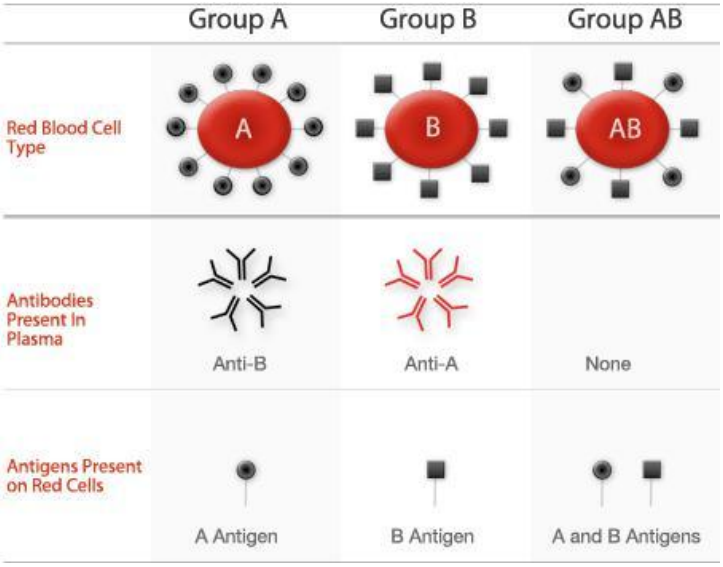
Mixed feather (F^BF^W)

c. mosaic of red and white color of Camellia flowers.

Camellia flower (C^RC^W)

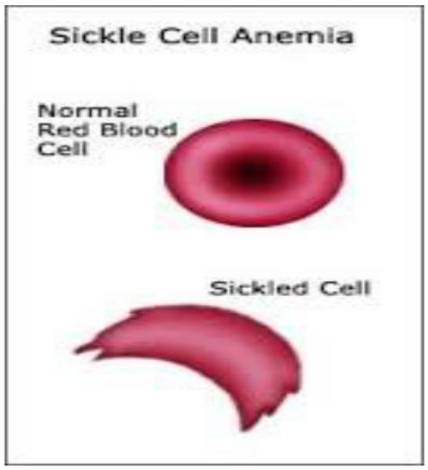
d. AB blood groups

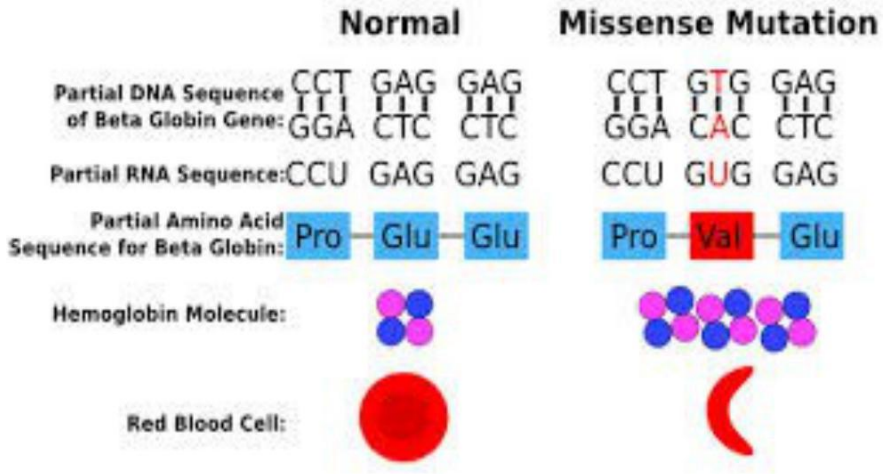
Persons with A blood-type is controlled by I^A allele which synthesis Antigen A, Persons with B blood-type is controlled by I^B allele which synthesis Antigen B, but some persons may have AB blood-type is controlled by both I^A and I^B forming Antigens A and B.



c. Sickle-cell anemia

Persons with *normal discoid biconvex erythrocytes* have the hemoglobin genotype (Hb^A Hb^A); whereas Hb is for haemoglobin and A is for normal erythrocyte, which constitute of normal hemoglobin with glutamic acid (amino acid) group. Person with *sickle-cell anemia* have the heamoglobin genotype (Hb^S Hb^S); whereas Hb is for haemoglobin and S is for Sickle-shaped erythrocyte, which constitute of abnormal hemoglobin with valine amino acid group. In *heterozygous* persons (Hb^A Hb^S); both types of erythrocytes are present in the same time.





Symbolism of No-dominance alleles:

Dominant alleles are usually indicated either by an italic uppercase letter (*D*)

Recessive alleles are usually indicated either by an italic lowercase letter (*d*)

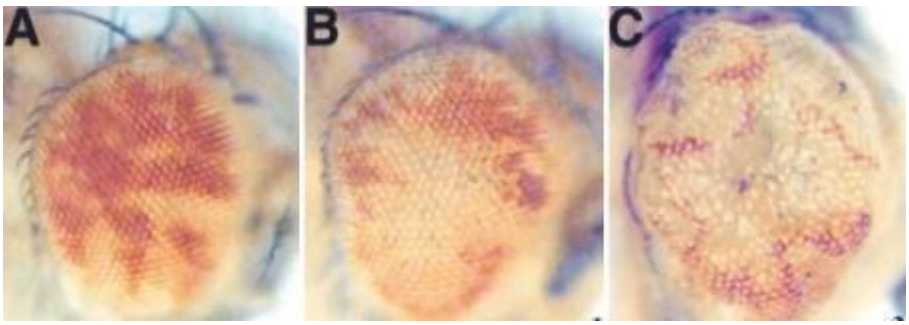
If **no dominance** exists, Capital letters with different superscripts were used to denote alternative alleles i.e. reveal that each allele can express itself in the presence of its alternative in heterozygous.

Eg: Normal haemoglobin allele is $\mathbf{Hb^A}$ and Sickle cell allele is $\mathbf{Hb^S}$

4. Over-Dominance

Where heterozygous organism **may exceeds** the phenotype expression of the homozygous dominant and recessive parents.

Eg: In *Drosophila*; marked increase in the amount of certain fluorescent pigment in heterozygous red-eyed (ww^+, A) comparing with those of the homozygous red-eyed parents ($w^+ w^+$, B) and white-eyed parents (ww,C).



Drosophila eyes

B. Lethal genes

They are caused drastic effect on both structure and function of the organism **causing its death**. Lethal alleles may be **dominant** or **recessive** according to the expression of one or both alleles

1. Dominant lethal genes

They are lethal in heterozygous (Aa) organisms by the effect of a **single dominant allele (A)** i.e. A in Aa genotype. It is rarely considered in genetics, as they are produced by spontaneous mutation and cannot be inherited!? Which makes sense: how can you give an allele to your offspring if you don't survive the prenatal phase.

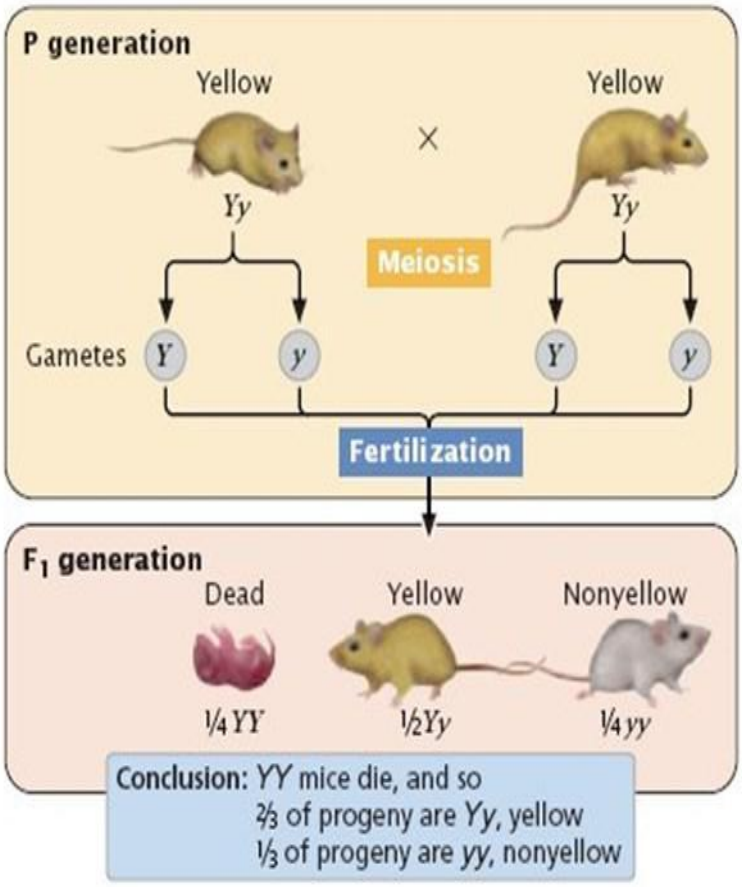
Eg: In *Drosophila*; mutant (irradiated) male may produce sperms carrying dominant lethal allele sperms which will prevent the fertilization of female egg and so, the development of the offspring.

2. Recessive lethal genes

They are **lethal in homozygous individuals** by the effect of both dominant (AA) alleles or recessive alleles (aa).

Eg: (1) In coat color of rats

Yellow color (Yy) is dominant to black coat (yy). The cross of yellow and yellow produce the phenotypic and genotypic ratios 2 yellow (Yy) :1 black (yy) instead of the genotypic ratio 1yellow (YY) :2 yellow (Yy) :1 (yy), fig below. Dissection of pregnant females demonstrated that the YY embryos (1/4 of the offspring) died soon after conception i.e. the allele of yellow color had a dominant phenotype on coat color but at the same time, it had a recessive lethal effects (effect when 2 dominant alleles are present) so, the homozygous yellow YY were invalid.



Coat color of rats

Eg: (2) <u>Sickle cell anemia</u>

They are lethal in homozygous individuals by the effect of both recessive alleles (Hb^SHb^S).

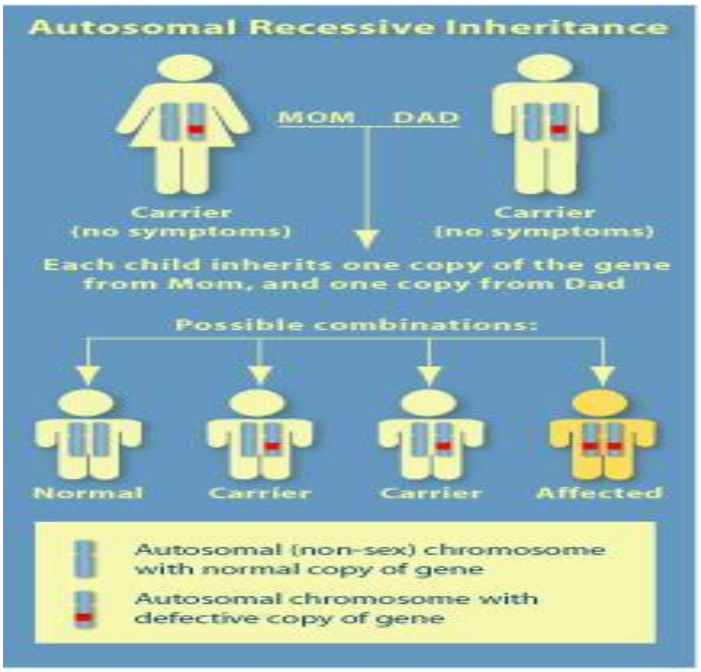
Where, Persons with *normal discoid biconvex erythrocytes* have the hemoglobin genotype (Hb^A Hb^A); Person with *sickle-cell anemia* have the heamoglobin genotype (Hb^S Hb^S) and *heterozygous* persons (Hb^A Hb^S) is a holder for *sickle-cell anemia* disease (Sickle trait).

$Hb^A Hb^S$ X $Hb^A Hb^S$

$Hb^A Hb^A : Hb^A Hb^S : Hb^S Hb^S$

1(survive): 2 (survive): 1(died)

So, Survival Rate = 1: 2



Eg: (3) <u>Albinism of</u> *Zea* <u>leaf</u>

They are **lethal in homozygous individuals** by the effect of both recessive alleles (cc).

Albinism means the absence of chlorophyll, which lead to the death of seedlings within 2 weeks. Where, (C) represents the dominant allele that control the production of chlorophyll (green seedlings) and (c) represents the recessive allele that causing the absence of chlorophyll (albino seedlings)

So, the cross between heterozygous green *Zea* plants (Cc) will produce offspring with survival ratio of 3 (green) : 0 (albino).

Cc X Cc

CC : Cc : cc Green: Green:

Albino 1(survive): 2 (survive):

1(died)

So, S.R. = 3: 0

C. Multiple Alleles

— In Mendel's experiments, there are one or two kinds of alleles in a gene pair but in some cases the genetic traits are controlled by more than 2 alleles and so called **multiple alleles**. These alleles are the alternative forms for the same gene (performed by mutation) and are distributed among the different individuals, where each individual has only 2 alleles maximum.

— Symbol: A^1, A^2, A^3 or A_1, A_2, A_3 or $A^{\text{the name of character}}$

Eg: (1) In coat color of rabbit

The allele of agouti coat color (C) is completely dominant and albino (c) is completely recessive to agouti (C), chinchilla (c^{ch}) and Himalayan (c^h) alleles.

The relative dominance relationships are $C > c^{ch} > c^h > c$, where:

Agouti (C): banded hairs with gray base, yellow band and black tip,

Chinchilla (c^{ch}): banded hairs with gray base and black tip with no yellow band,
Himalayan (c^{h}): banded hairs with white base and black tip
and Albino (c): totally white.


Rabbit coat

Rabbit coat color

Allele	Phenotype
C	Rabbit with fully colored coat
c^{ch}	Rabbit with light gray coat
c^{h}	Himalayan rabbit: white with dark ear tips, nose, paws, and tail
c	Albino rabbit

Order of dominance C → c^{ch} → c^{h} → c

<u>All the possible genotypes</u>:

CC, Cc^{ch}, Cc^{h}, Cc

$c^{ch}c^{ch}$, $c^{ch}c^{h}$, $c^{ch}c$

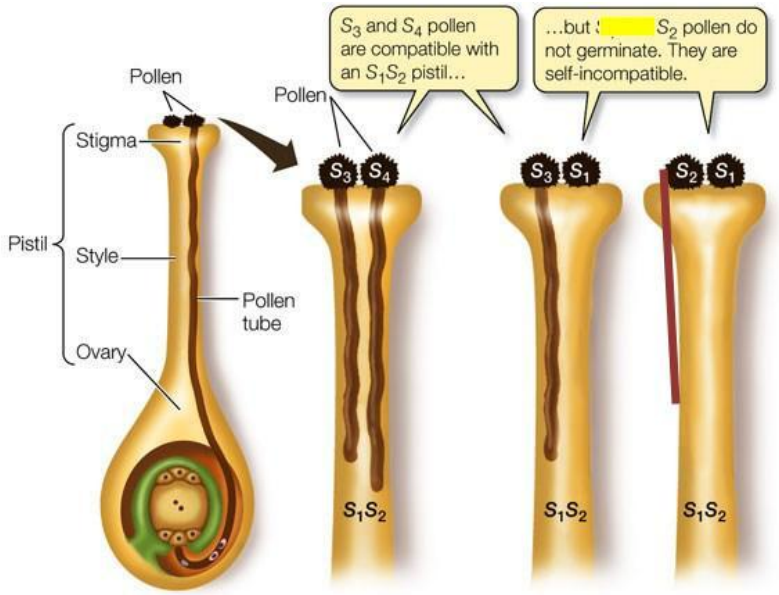
$c^{h}c^{h}$, $c^{h}c$

cc

Eg (2). Self-sterility in *Nicotiana tabacum* (tobacco)

In this plant, self-sterility was controlled by a series of multiple alleles called S^1, S^2, S^3,….

A pollen grain carrying a self-sterility allele (S^1) cannot grow (no pollen tube) on its-or any-female style carrying one or both of the same allele (S^1) in its ovules, but successfully fertilize female style of the other types of alleles as S^2, S^3,…



The possible crosses are:

S^1S^1 ♂ and S^1S^1 ♀ produce 100% sterile offspring

S^1S^1 ♂ and S^1S^2 ♀ produce 100% sterile offspring

S^1S^2 ♂ and S^1S^1 ♀ produce 50% sterile : 50% fertile offspring

S^2S^2 ♂ and S^1S^1 ♀ produce 100% fertile offspring

Eg (3) ABO blood groups

Human blood type is an example of both co-dominance and a trait with multiple alleles. ABO blood group is of immense importance. For it is extensively used in blood transfusion in the case of accidents, severe anemia, or surgery etc. Landsteiner was the first to identify such blood groups. The variation in the blood groups is because of the membrane proteins of red blood cells (erythrocytes).

Some of the membrane proteins get glycosylated (addition of sugars) differently thus they produce various types of blood groups. Persons belonging to A blood group contain A type of glycosylated protein in the membrane of erythrocytes. (Similarly "B" and the "O" type). These physiological phenotypes are due to the presence of A, B and O genes controlled by **3 alleles**: $\mathbf{I^A}$ allele which determine the synthesis of antigen A, $\mathbf{I^B}$ allele which determine the synthesis of antigen B, $\mathbf{I^o}$ **or i** doesn't synthesis either A or B antigens.

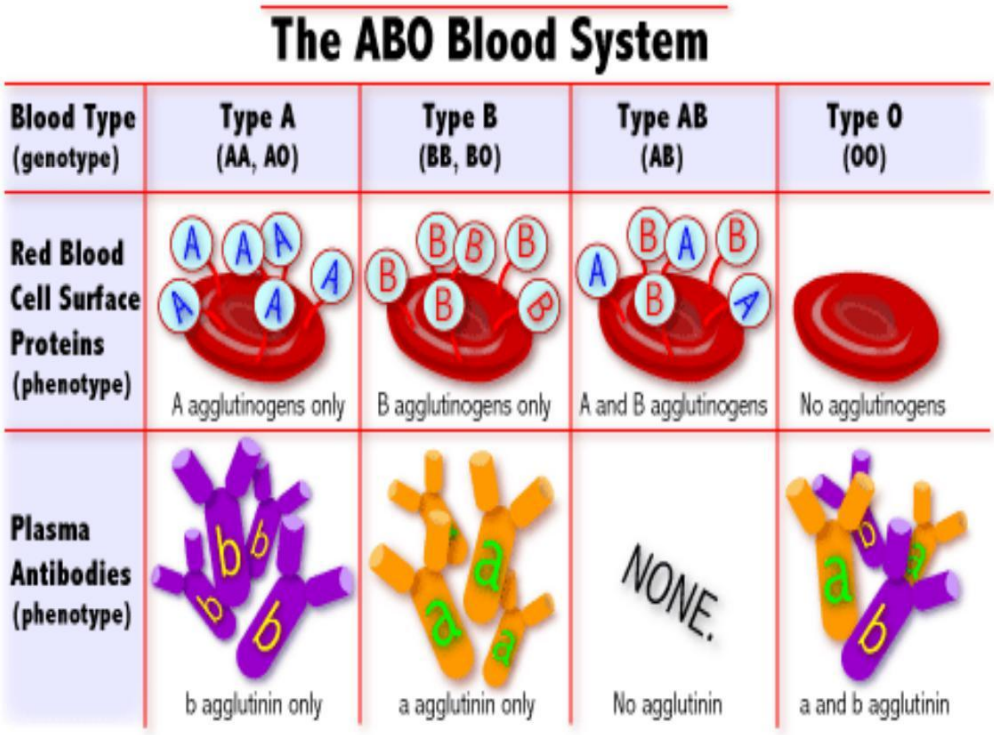
Each person will have **TWO** of those alleles (table below). Both A and B alleles dominate the O allele: ($\mathbf{I^A = I^B > i}$)

ABO blood group has **6 genotypes** and **4 phenotypes**: the genotypes of human blood may fall into any of the following 6 types: AA, BB, OO, AB, AO or BO, while the phenotypes of human blood are A, B, AB and O.

Identification of the blood types is very essential for blood transfusion, because, if by chance or mistake, blood of A type is given to B type person or vice-versa, the man who gets such blood type dies because of agglutination or aggregation of blood cells. This aggregation is due to antigen-antibody reaction.

AB blood type is considered as universal acceptor and O blood type is a universal donor.

BLOOD TYPE	GENOTYPE	CAN RECIVE BLOOD FROM
A	I^AI^A (AA) I^Ai (AO)	A, O
B	I^BI^B (BB) I^Bi (BO)	B, O
AB	I^AI^B (AB)	A, B, AB, O
O	ii (OO)	O



Blood type of cells	Genotype	Antibodies made by body	Reaction to added antibodies	
			Anti-A	Anti-B
A	I^AI^A or I^Ai^O	Anti-B		
B	I^BI^B or I^Bi^O	Anti-A		
AB	I^AI^B	Neither anti-A nor anti-B		
O	i^Oi^O	Both anti-A and anti-B		

LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 10.14 ABO Blood Reactions Are Important in Transfusions

Eg (4) Human Skin Color

There isn't a single gene with two alleles for darker brown or lighter white rather, there are multiple alleles skin; for that gene with additive effect, and the combination you inherit determines your skin color. Suppose one person has black skin and his mate has white, many different combinations are possible, so humans exhibit black skin, white skin, or some shade in between.

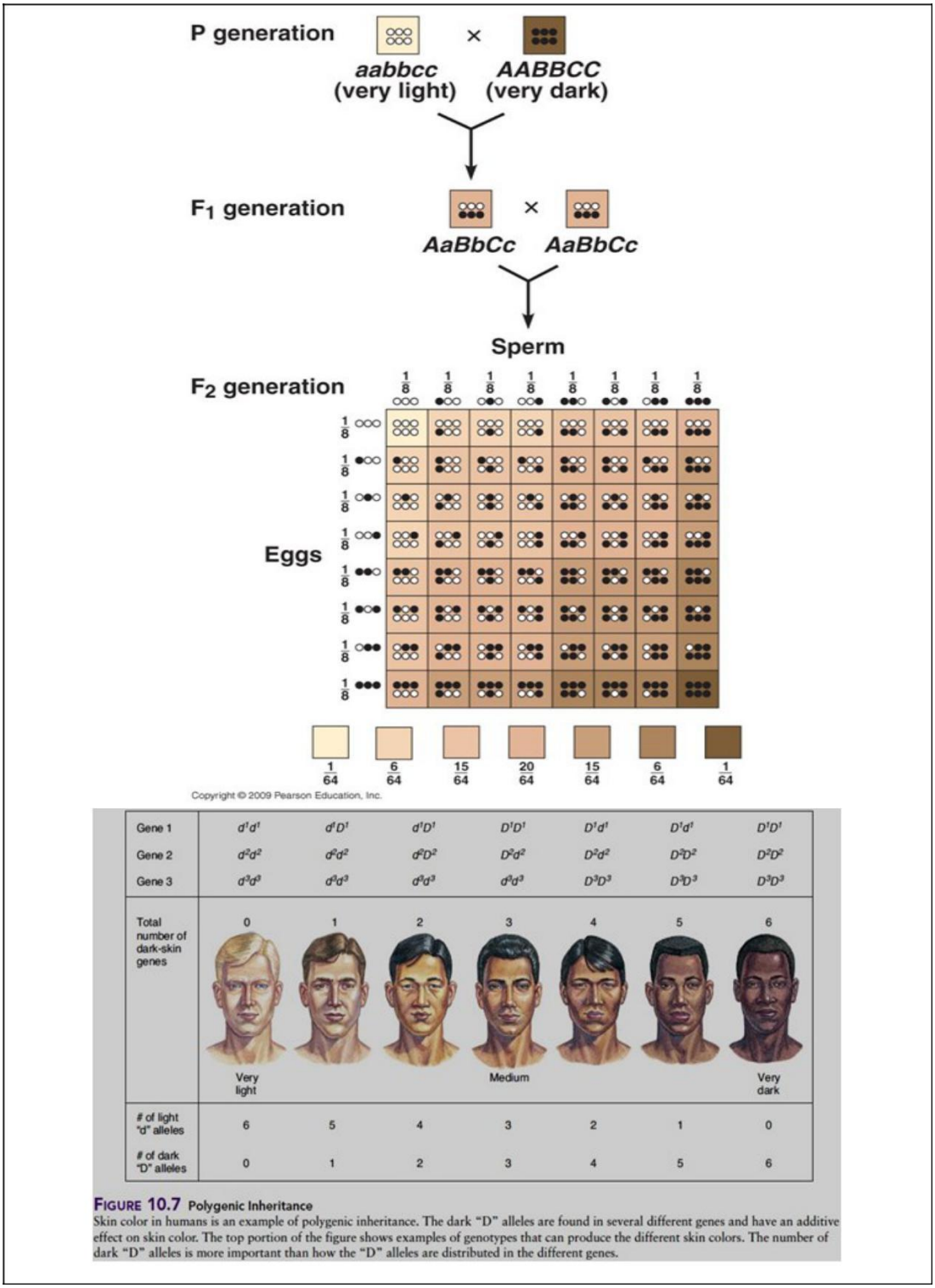


FIGURE 10.7 Polygenic Inheritance
Skin color in humans is an example of polygenic inheritance. The dark "D" alleles are found in several different genes and have an additive effect on skin color. The top portion of the figure shows examples of genotypes that can produce the different skin colors. The number of dark "D" alleles is more important than how the "D" alleles are distributed in the different genes.

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