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 **Genetic Interaction and Lethal Genes**

 **(for M.Sc. II Semester, Paper III)**

 Mendel’s monohybrid and dihybrid crosses gave a clear conception that for the determination of single phenotypic trait of an organism, two alleles or allelomorphs of a single gene inter- acted in various ways. Such as out of two allelomorphs of a single gene, one allelomorph might show simple (complete) dominance over the action of other which was recessive; or both allelomorphs might have partial or incomplete dominant relationship or both allelomorphs might have equal expres- sion or codominant relationship. These kinds of genic or genetic interactions occur in between the two allelomorphs of a single type of gene and are usually referred to as **intra- allelic** or **allelic genetic interactions**. These kinds of genetic interactions give the classical ratios of 3 : 1 and 9 : 3 : 3 : 1. But, in addition to intra-allelic genetic interactions, **non-allelic** or **inter-allelic genetic (genic) interactions** also occur. In inter- allelic genetic interactions, the independent (non-homolo- gous) genes located on the same or on different chromosomes interact with one another for the expression of single pheno- typic trait of an organism. The discovery of the inter-allelic genetic interactions has been made after Mendel and they can be best understood by considering the way by which a pheno- typic trait is goverened by a gene.

**TIME OF GENETIC INTERACTION**

The gene is a chemical determiner. Whereas a phenotypic trait results from the combined action of many genes and their products constantly interacting with the environment. The environment includes not only ecological factors such as temperature and the amount or quality of light, but also internal factors such as hormones and enzymes. The enzymes are proteins and the specific molecular organization of protein is determined by genes. The enzymatic proteins perform catalytic function in various cellular chemical (metabolic) reactions and causing the splitting or union of various molecules. Each cellular chemical reaction involves stepwise conversion of one substance called **precursor** into another, called **end product**. Each step being mediated by a specific enzyme. All the subsequent steps of a chemical reaction constitute the **biosynthetic pathway**.

Thus, a simplest biosynthetic pathway includes various steps, each step is catalyzed by a specific enzymatic protein and each enzymatic protein in its turn depends on a specific gene for its production. For example, we may consider a simple biosynthetic pathway which transforms a precursor substance ‘P’ into the end product ‘C’ in following three subsequent steps :

g + g + g +

1 2 3

  

**P** (precursor) e1 ~~ ~~**A** — e2 ~~ ~~ **B** — e3 ~~ ~~**C** (end product)

In this biosynthetic pathway each metabolite (A, B, C) is produced by the catalytic action of

different enzymes (e , e ,e .....e , specified by different wild type genes (g +, g +, g + g +). When more

1 2 3 x 1 2 3 x

than two or more genes become involved in the specification of enzymes for different steps of a common biosynthetic pathway, the phenomenon of genetic interaction occurs. If substance C is

essential for the production of a normal phenotype and the recessive mutant alleles g1, g2, g3 produce defective enzymes, then a mutant or abnormal phenotype would result from a genotype homozygous recessive at any of the three loci. If wild gene g + becomes mutant, the conversion of metabolite B to

3

C does not occur and substance B tends to accumulate in excessive quantity; if g + becomes mutant, substance A will accumulate. Thus, the mutant genes caused “**metabolic blocks**” in synthetic pathway.

2

An organism with a mutation only in gene g + could produce a normal phenotype, if it was given either substance B or C, but an organism with a mutation in gene g + has a specific requirement for substance C for the production of normal phenotype. Thus, gene g + becomes dependent upon g + for

2

3

3 2

its expression as a normal phenotype. If the genotype is homozygous for the recessive g2 allele, then

the biosynthetic pathway ends with substance A. Neither g + nor its recessive allele g has any effect

3 3

on the phenotype. Thus, genotype (g2g2) can hide or mask the phenotypic expression of alleles at the g + locus. Originally a gene or locus which suppressed or masked the action of a gene at another locus was termed **epistatic gene**. The gene or locus which was suppressed by a epistatic gene was called

3

**hypostatic gene**. Later studies revealed the fact that both loci or genes (*i.e.,* epistatic and hypostatic) could be epistatic to one another. Presently, the term epistasis (Greek, standing upon) is used for almost any type of allelic genetic interaction.

**Difference Between Dominance and Epistasis**

The phenomenon of dominance involves intra-allelic gene suppression, or the masking effect which one allele has upon the expression of another allele at the same locus, while the phenomenon of epistasis involves inter-allelic gene suppression or the masking effect which one gene locus has upon the expression of another. The classical phenotypic ratio of 9 : 3 : 3 : 1 observed in the progeny of dihybrid parents becomes modified by epistasis into ratios which are various combinations of the 9 : 3 : 3 : 1 groupings.

**NON-EPISTATIC INTER-ALLELIC GENETIC INTERACTIONS**

In certain cases, two pairs of genes determine a same phenotype but assorted independently, produce new phenotypes by mutual non-epistatic interactions and the F2 phenotypic ratio 9 : 3 : 3 : 1

**GENETIC INTERACTION AND LETHAL GENES**

**47**

remains unaltered. Two pairs of genes which interact to affect size and shape of comb but are independently transmitted exist in chicken.

**Example**

**Combs in fowl** (**9 : 3 : 3 : 1**)**.** The classical case of genetic interaction of two genes is discovered by **Bateson** and **Punnett** (1905–1908) in fowls. There are many different breeds of domestic chicken. Each breed possesses a characteristic type of comb. The Wyandotte breed has a comb called “rose”, the Brahmas breed has a comb called “pea”, and the Leghorns have a comb called ‘single’. Each of these types can be bred true.

A cross of chicken with a rose comb to one with a single comb produces ¾ rose and ¼ single, showing dominance of rose over single. Another cross between pea combed and single combed chickens produces pea and single combed chickens in the ratio of 3 : 1, showing dominance of pea over

**P1**

Rose RRpp

Pea rrPP

**F1**

Walnut RrPp

Walnut RrPp

**F2 analysis**

Phenotypes

Walnut

RRPP RRPp RrPP

RrPp

Rose

Pea

Single

Genotypes

RRpp

rrPP

rrpp

Ratio

9

Supplemental

Explanation interaction of R and P

**Fig. 4.1.** Supplementary inheritance. Inheritance of the shape of the comb in chickens.

|  |  |  |
| --- | --- | --- |
| Rrpp | rrPp |  |
| 3 | 3 | 1 |
| Dominance | Dominance | Recessiveness |
| of R over r | of P over p | of rr and pp |

**GENETICS, HUMAN GENETICS AND EUGENICS**

**48**

single. But, when a rose combed chicken crossed with that of pea combed, the F1 progeny was found with a different type of comb known as ‘walnut’ (Malay breed). When the F1 walnut combed chickens were bred together, in F2 all four types of combs, *i.e.,* 9/16 walnut, 3/16 rose, 3/16 pea and 1/16 single appeared (Fig. 4.1).

These peculiar results were interpreted by **Bateson** and **Punnett** as follows : The rose comb is caused by the combination of homozygous recessive genes “pp” and homozygous or heterozygous dominant genes ‘RR’ or ‘Rr’. The pea comb is supposed to be produced by combination of a homozygous recessive condition (rr) and homozygous or heterozygous dominant condition (PP or Pp). While, the single type comb is produced by the double recessive, rrpp, genes. Thus, R gene determines the shape of rose comb and P gene determines the shape of pea comb, but when both genes happen to come together in single individual due to cross between rose and pea combed chickens, they interact to produce a walnut comb in F1. In the cross of two walnut chickens, two genes interact variously and

produces four types of offsprings in F2.

Thus, here two pairs of genes interact to produce comb size and shape in fowl. During the inheritance of combs in fowls, the genes themselves do not determine the development of a character (presence or absense of comb) and simply modify a character determined by a basic gene and, therefore, known as **supplementary** or **modifying genes**.

**KINDS OF EPISTATIC INTERACTION**

When in dihybrid crosses, the epistatic interactions occur between two genes, less than

four phenotypes appear in F2. Such bigenic (two gene) epistatic interactions may be of following six types:

1. **Dominant Epistasis (12 : 3 : 1)**

When out of two genes, the dominant allele (*e.g.,* A) of one gene masked the activity of alleles of another gene (*e.g.,* B) and expressed itself phenotypically, then A gene locus is said to be epistatic to the B gene locus (Table 4-1). Because, the dominant allele A can express itself only in the presence of either B or b allele, therefore, such type of epistasis is termed as **dominant epistasis**. The alleles of hypostatic locus or gene B will be able to express themselves phenotypically only when gene locus A may contain two recessive alleles (aa). Thus, the genotype AA BB or Aa Bb and AA bb or Aa bb produce the same phenotype whereas the genotype aa BB or aa Bb and aa bb produce two additional phenotypes. The dominant epistasis modify the classical ratio of 9 : 3 : 3 : 1 into 12 : 3 : 1 ratio.

**Table 4-1.**

**Mode of dominant epistasis.**

|  |  |
| --- | --- |
|  |  |
| **Epistatic alleles** | **Hypostatic alleles** | **Phenotypic expression of allele** |
| 1. AA, Aa
2. aa
3. aa
 | BB, Bb, bb BB, Bbbb | A BB |

**Example**

**Dominant epistatis in dogs.** Among dogs, the colours of coats depend upon the action of two genes. One gene locus has a dominant epistatic inhibitor allele (I) of coat colour pigment (see Table 4-2). The allele I prevents the expression of colour allele at another independently assorting, hypostatic gene locus (B or b) and produces white coat colour. The alleles of hypostatic gene locus (BB, Bb, or bb) express only when two recessive alleles (ii) occur on the epistatic locus, *i.e.,* ii BB or ii Bb produces black and ii bb produces brown individuals. When two such white coat colour

**GENETIC INTERACTION AND LETHAL GENES**

**Table 4-2.**

**Mechanism of dominant epistasis in dogs.**

**49**

dogs are crossed, in F1 the white, black and brown coat colours appear in 12 : 3 : 1 ratio as shown in (Fig. 4.2).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Epistatic alleles** | **Hypostatic alleles** | **Phenotypic expression of allele** | **F2 Phenotypic ratio** |
| 1. II, Ii
2. ii
3. ii
 | BB, Bb, bb BB, Bbbb | I (no pigment) B (Black)b (Brown) | White=12 Black=3 Brown=1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **P:** | White (Male)Ii Bb | X | White (Female)Ii Bb |
| **P Male gametes**  | IB | Ib | iB ib |
|  |  |  |  |  |
| **P Female gametes** IB | II BBWhite | II BbWhite | Ii BBWhite | Ii BbWhite |
| Ib | II BbWhite | II bbWhite | Ii BbWhite | Ii bbWhite |
| **F1 :**iB | Ii BBWhite | Ii BbWhite | ii BBBlack | ii BbBlack |
| ib | Ii BbWhite | Ii bbWhite | ii BbBlack | ii bbBrown |

**F1 Phenotypic ratio :** 12/16 White : 3/16 Black : 1/16 Brown or 12 : 3 : 1.

**Fig. 4.2.** Checkerboard derived from a cross between two heterozygous white coated dogs showing 12 : 3 : 1 ratio due to dominant epistatic inhibitor genes.

1. **Recessive Epistasis (9 : 3 : 4)**

Sometimes the recessive alleles of one gene locus (aa) mask the action (phenotypic expression) of alleles of another gene locus (BB, Bb or bb alleles) (see Table 4-3). This type of epistasis is called **recessive epistasis**. The alleles of B locus express themselves only when epistatic locus has dominant alleles (*e.g.,* AA or Aa). Due to recessive epistasis the phenotypic ratio 9 : 3 : 3 : 1 becomes modified into 9 : 3 : 4 ratio.

**Table 4-3. Mode of action of recessive epistasis.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Epistatic alleles** | **Hypostatic alleles** | **Phenotypic expression of allele** |
| 1. a a
2. AA, Aa
3. AA, Aa
 | BB, Bb, bb BB, Bbbb | a Bb |

**Example**

**Recessive epistasis in mice.** In mice various types of epistatic genetic interactions have been

**GENETICS, HUMAN GENETICS AND EUGENICS**

reported. The most interesting case is of recessive epistasis in coat colours. The common house mouse occurs in a number of coat colours, *i.e.,* agouti, black and albino. The agouti colour pat- tern is commonly occurred one (wild type) and is characterized by colour banded hairs in which the part nearest the skin is gray, then a yellow band and finally the distal part is either black or brown. The albino mouse lacks totally in pigments and has white hairs and pink eyes.

**Table 4-4.**

**Mode of action of recessive epistasis in alleles for coat colour in mice.**

Different coat colours in mice.

**50**

|  |  |
| --- | --- |
|  |  |
| **Epistatic alleles** | **Hypostastic alleles** | **Phenotypic exp- ression of allele** | **F2 Phenotypic ratio** |
| 1. cc | AA, Aa, aa | c | Albino=4 |
| 2. CC, Cc | AA, Aa | A | Agouti=9 (due to supplementary genes) |
| 3. CC, Cc | aa | a | Black=3 |

When a homozygous black (CC aa) is crossed with a homozygous albino (cc AA) in F1 all agouti (Cc Aa) offsprings appear. When, the F1 agouti are crossed among themselves in F2 agouti, black and albino offsprings appear in the ratio of 9 : 3 : 4 as shown in the Fig. 4.3.

**P1 :** Black X Albino CCaa ccAA

**P1 gametes :** (Ca)  (cA)

**F1 :** Agouti

CcAa

**F1 Male gametes**  CA Ca cA ca

|  |  |  |  |
| --- | --- | --- | --- |
| CC AAAgouti | CC AaAgouti | Cc AAAgouti | Cc AaAgouti |
| CC AaAgouti | CC aaBlack | Cc AaAgouti | Cc aaBlack |
| Cc AAAgouti | Cc AaAgouti | cc AAAlbino | cc AaAlbino |
| Cc AaAgouti | Cc aaBlack | cc AaAlbino | cc aaAlbino |

**F1 Female gametes**

 CA

Ca

**F2 :** cA

ca

**F2 Phenotypic ratio :** 9/16 Agouti : 3/16 Black : 4/16 Albino.

**Fig. 4.3.** Checkerboard derived from a cross between coloured (black) and albino mice showing 9 : 3 : 4 ratio due to recessive epistatic genes.

**Supplementary genes.** In the cross between black (CCaa) and albino (ccAA) mice, one thing becomes apparent that two independent pairs of genes (*i.e.,* C–c and A–a) have interacted in the production of the phenotypic trait (*i.e.,* coat colour) in such a way that one dominant (C) produces its effect whether or not the second (A) is present, but the second (A) gene can produce its effect only in the presence of the first. These genes (*i.e.,* C and A) have been termed as **supplementary genes** (see **Villee** *et al.,* 1973).

**GENETIC INTERACTION AND LETHAL GENES**

**51**

1. **Duplicate Genes with Cumulative Effect (9 : 6 : 1)**

Certain phenotypic traits (*e.g.,* coat colouration) depend on the dominant alleles of two gene loci. When the dominant condition (homozygous or heterozygous) at either locus (but not both) produces the same phenotype, the F2 ratio becomes 9 : 6 : 1.

**Table 4-5.**

**Mode of action of mutually supplementary genes.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Epistatic alleles** | **Hypostatic alleles** | **Phenotypic expression of alleles** |
| 1. a a | bb | Neither a nor b |
| 1. a a
2. AA, Aa
 | BB, Bbbb | B only }single gene effect A only |
| 4. AA, Aa | Bb, Bb | A+B A and B alleles |
|  |  | mutually supplement each other |

**Example**

**Cumulative effect in coat colour of pigs.** In the Duroc-jersey breed of pigs, coat colour is influenced by two pairs of genes that interact in peculiar manner (Table 4-6). Sandy coat colour results from a dominant gene S, and the homozygous recessive (ss) is white in colour. Sandy coat colour may also result from a non-allelic dominant gene R; its homozygous recessive (rr) is also white. When a sandy pig (SS rr) is crossed with a second sandy pig (ss RR), the F1 offsprings were found with red coloured coats. Such interactions are said to be the result of **mutually**

Duroc-jersey pig.

**supplementary genes**. When F1 red coated pigs cross bred among them- selves they produce red, sandy and white coats in the ratio of 9 : 6 : 1 as shown in the Figure 4.4.

|  |  |  |  |
| --- | --- | --- | --- |
| **P :** | Sandy | X | Sandy |
|  | SS rr |  | ss RR |
| **P gametes :** | (Sr) |  | (sR) |
| **F**1**:** |  | Red |  |
|  |  | Ss Rr |  |
| **F1 cross :** | Male | X | Female |
|  | Ss Rr |  | Ss Rr |

**F1 Male gametes**  SR Sr s R sr

|  |  |  |  |
| --- | --- | --- | --- |
| SS RRRed | SS RrRed | Ss RRRed | Ss RrRed |
| SS RrRed | SS rrSandy | Ss RrRed | Ss rrSandy |
| Ss RRRed | SsRrRed | ss RRSandy | ss RrSandy |
| Ss RrRed | Ss rrSandy | ss RrSandy | ss rrWhite |

**F2 Female gametes**

 SR

Sr

**F2 :** sR

sr

**F2 Phenotypic ratio :** 9/16 Red : 6/16 Sandy : 1/16 White or 9 : 6 : 1.

**Fig. 4.4.** A cross between two strains of pig having sandy coats producing 9 : 6 : 1 ratio due to mutually supplementary genes.

**GENETICS, HUMAN GENETICS AND EUGENICS**

**Table 4-6.**

**Mode of action of mutually supplementary genes for coat colour in pig.**

**52**

|  |  |
| --- | --- |
|  |  |
| **Epistatic alleles** | **Hypostatic alleles** | **Phenotypic****Expression of alleles** | **F2 Phenotypic****ratio** |
| 1. rr | ss | Neither r nor s (No pigment)S} RR+S (Mutually suppl- ementary genes)\* | White=1 |
| 2. rr | SS,Ss |  |
| 3. RR, Rr | ss |  |
| 4. RR, Rr | SS, Ss | Red=9 |

\* Presence of dominant alleles on both epistatic and hypostatic loci produce cumulative phenotypic expression.

1. **Duplicate Recessive Genes (or Complimentary genes) (9 : 7)**

If both gene loci have homozygous recessive alleles and both of them produce identical phenotypes, the F2 ratio 9 : 3 : 3 : 1 would become 9 : 7. In such case, the genotypes aa BB, aa Bb, AA bb, Aa bb, and aa bb produce one phenotype (Table 4-7). Both dominant alleles when present together, complement each other and are called **complementary genes** and produce a different phenotype. A case of such complemental inheritance, resulting from the combined action of complemental genes is known in sweet peas.

**Table 4-7.**

**Mode of action of complementary genes.**

|  |  |
| --- | --- |
|  |  |
| **Epistatic allele** | **Hypostatic allele** | **Phenotypic expression of alleles** |
| 1. a a
2. AA, Aa, aa
3. AA, Aa
 | BB, Bb, bb bbBB, Bb | } No Phenotype productionPhenotype expression dueto dominant alleles on both loci (complementation of gene action) |

**Example**

When a pure line variety of white flowered sweet pea (*Lathyrus odoratus*) was crossed with another pure line variety of white flowered sweet pea, in F1 purple or red flowered plants were produced

(Table 4-8). The F1 plants when self-pollinated or crossed among themselves, produced the F2 generation with the phenotypic ratio of 9 coloured and 7 white flowered plants.



|  |
| --- |
| Purple, red and white flowers of pea. |

**GENETIC INTERACTION AND LETHAL GENES**

**53**

**Table 4-8. Mode of action of complementary alleles in the production of coloured flowers in sweet pea.**

**Epistatic alleles**

}write = 7

Coloured=9

Neither c nor E or e Neither C or c nor e

Both C+E (complementation)\*

EE, Ee, ee e e

EE, Ee

1. c c
2. CC, Cc
3. CC, Cc

**F2 Phenotypic ratio**

**Phenotypic expression of allele**

**Hypostatic alleles**

\* Chromogen production due to complementation of C and E (*i.e.,* dominant epistatic and hypostatic alleles).

These surprising results could be understood by analysing the mechanism of colour production

in flowers. A given enzyme (genetically controlled as to absence or presence in a given individual) acts upon chromogen (a colourless colour base whose absence or presence is also genetically controlled) to produce the purple or red colour of flowers. The dominant allele or alleles (CC or Cc) of gene C are responsible for the presence of chromogen, while the homozygous recessive alleles (cc) of this gene are responsible for the absence of chromogen. Likewise, the dominant alleles of gene E in homozygous (EE) or heterozygous (Ee) conditions caused the production of an enzyme which is necessary for colour production from chromogen, while homozygous recessive (ee) condition does not produce any such enzyme.

The appearance of 9 : 7 ratio instead of 9 : 3 : 3 : 1 ratio from the cross of two white flowered sweet pea plants (CC ee X cc EE) can be illustrated as follows :

**P :** White flowers X White flower CC ee cc EE

  

**P gametes :** (Ce) (cE)

**F1 :** Purple flower X Purple flower Cc Ee CcEe

**F1 Male gametes**  CE Ce cE ce

|  |  |  |  |
| --- | --- | --- | --- |
| CC EEPurple | CC EePurple | Cc EEPurple | Cc EePurple |
| CC EePurple | CCeeWhite | Cc EePurple | Cc eeWhite |
| Cc EEPurple | Cc EePurple | cc EEWhite | cc EeWhite |
| Cc EePurple | Cc eeWhite | cc EeWhite | cc eeWhite |

**F1 Female gametes**

 CE

Ce

**F2 :**

cE

ce

**F2 phenotypic ratio :** 9/16 purple : 7/16 white or 9 : 7.

**Fig. 4.5.** Complementary genes : production of 9 : 7 phenotypic ratio in sweet peas due to complementary genes.

**Table 4-10. Mode of action of duplicate genes in producing triangular seed capsules in *Capsella*.**

**GENETICS, HUMAN GENETICS AND EUGENICS**

**54**

1. **Duplicate Dominant Genes (15 : 1)**

If the dominant alleles of both gene loci produce the same phenotype without cumulative effect, the 9 : 3 : 3 : 1 ratio is modified into a 15 : 1 ratio (Table 4-9).

**Table 4-9.**

**Mode of action of duplicate dominant genes.**

**Example**

The seed capsules of shepherd’s purse (genus *Capsella)* occur in two different shapes, *i.e.,* triangular and top-shaped. When a plant with triangular seed capsule is crossed with one having top-shaped capsule, in F1 only triangular, character

appears. The F1 offsprings by self crossing produce the F2

generation with the triangular and top-shaped seed capsules in the ratio of 15 : 1. Two independently segregating dominant genes (A and B) have been found to influence the shape of the capsule in the same way (Table 4-10). All genotypes having dominant alleles of both of these genes (A and B) would produce plants with triangular-shaped capsules. Only those with the genotype aa bb would produce plants with top-shaped capsules. The results of this example has been shown in Figure 4.6.

*Capsella*, flattened, triangular seedpods.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Epistatic alleles** | **Hypostatic alleles** | **Phenotypic expression of alleles** |
| 1. AA, Aa
2. AA, Aa
3. a a
4. a a
 | bbBB, Bb BB, Bbbb | } Same phenotype (A,B, A+B) (Presence of one dominant allele on both or either loci result insame phenotype)Another phenotype (a or b) (Absence of dominant allele on both or either loci results in different phenotype). |

|  |  |
| --- | --- |
|  |  |
| **Epistatic alleles** | **Hypostatic alleles** | **Phenotypic expression of alleles Phenotypic ratio** |
| 1. AA, Aa | bb | } Phenotype of either or both Triangular=15 dominant alleles, *i.e.,* A or B or bothRecessive phenotype of a and b alleles Top-shaped=1 |
| 2. AA, Aa | BB, Bb |
| 3. a a | BB, Bb |
| 4. a a | bb |

|  |  |  |  |
| --- | --- | --- | --- |
| **P :** | Triangular | X | Top-shaped |
|  | AA BB |  | aa bb |
| **P gamete :** | (AB) |  | (ab) |
| **F1 :** | TriangularAa Bb | X | TriangularAa Bb |

**GENETIC INTERACTION AND LETHAL GENES**

**55**

**F1 Male gametes**  AB Ab aB ab

**F2 Female gametes**

|  |  |  |  |
| --- | --- | --- | --- |
| AA BBTriangular | AA BbTriangular | Aa BBTriangular | Aa BbTriangular |
| AA BbTriangular | AA bbTriangular | Aa BbTriangular | Aa bbTriangular |
| Aa BBTriangular | Aa BbTriangular | aa BBTriangular | aa BbTriangular |
| Aa BbTriangular | Aa bbTriangular | aa BbTriangular | aa bbTop-shaped |

 AB

Ab

**F2 :** aB

ab

**F2 Phenotypic ratio :** 15/6 Triangular : 1/16 Top-shaped or 15:1.

**Fig. 4.6.** Duplicate dominant genes : a cross between two strains of *Capsella* having triangular and top-shaped seed capsules to get 15 : 1 F2 dihybrid ratio.

1. **Dominant and Recessive Interactions (13 : 3)**

Sometimes, the dominant alleles of one gene locus (A) in homozygous (AA) and heterozygous (Aa) condition and the homozygous recessive alleles (bb) of another gene locus (B) produce the same

phenotype, the F2 phenotypic ratio becomes 13 : 3 instead of 9 : 3 : 3 : 1. In such case, the genotype AA BB, AABb, Aa BB, Aa Bb, AA bb and Aa bb produce same phenotype and the genotype aa BB, aa Bb and aa bb produce another but same phenotype (Table 4-11).

**Table 4-11.**

**Mode of action of interaction between dominant and recessive alleles.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Epistatic alleles** | **Hypostatic alleles** | **Phenotypic expression of allele** |
| 1. AA, Aa
2. a a
 | BB, Bb, bbBB, Bb, bb | A inhibits B or b (No phenotype of B or b)a does not inhibit B or b (Phenotype of B or b) |

**Example**

White Leghorn and white Plymouth Rock.

In Leghorn type of fowl the white colour of feather is caused by the domi- nant genotype CC II, similarly the white colour of feathers of Plymouth Rock breed is caused by the recessive genotype cc ii (Table 4-12). When both white va-

rieties of fowl are crossed, in F1 white coloured hybrids appear. The F1 hybrids in F2 produce the white and coloured offsprings in the ratio of 13 : 3, as have been illustrated in Fig. 4.7.

**GENETICS, HUMAN GENETICS AND EUGENICS**

**Table 4-12. Method of interaction between dominant and recessive genes.**

**56**

|  |  |
| --- | --- |
|  |  |
| **Epistatic alleles** | **Hypostatic allele** | **Phenotypic expression of allele** | **F2 Phenotypic ratio** |
| 1. II, Ii
2. ii
3. ii
 | CC, Cc, cc CC, Cccc | I (dominant inhibitor)C (due to recessive inhibitor i) c (due to c and i) | White = 12Coloured = 3White = 1 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **P :** | White LeghornCC II |  | X | White Plymouth Rockcc ii |
|  |  |  |  |  |
| **P gametes :** | (C I) |  |  | (c i) |
| **F1 :** | WhiteCc Ii |  | X | WhiteCc Ii |
| **F1 male gametes**  | CI | C i |  | cI ci |
| **F1 female gametes** |  |  |  |  |
|  CICi **F2 :**cIci |  |  |  |

**F2 phenotypic ratio :** 13/16 white : 3/16 coloured breeds or 13 : 3.

|  |  |  |  |
| --- | --- | --- | --- |
| CC IIWhite | CCIiWhite | Cc IIWhite | Cc IiWhite |
| CC IiWhite | CCiiColoured | Cc IiWhite | Cc iiColoured |
| Cc IIWhite | Cc IiWhite | cc IIWhite | cc IiWhite |
| Cc IiWhite | Cc iiColoured | cc IiWhite | cc iiWhite |

**Fig. 4.7.** A cross between two white coloured breeds of fowls to get 13 : 3 F2 dihybrid ratio.

The various epistatic ratios can be summarized in the following table :

**Table 4-13. Summary of various epistatic ratios.**

|  |  |
| --- | --- |
|  |  |
| **Genotype** | **A–B–****(AA BB, Aa BB, AA Bb, Aa Bb)** | **A–bb (AA bb, Aa bb)** | **aa B– (aa BB, aa Bb)** | **aa bb** |
| Classical ratio | 9 | 3 | 3 | 1 |
| Dominant epistasis | 12 | 3 | 1 |
| Recessive epistasis | 9 | 3 | 4 |
| Duplicate gene with cumulative effect | 9 | 6 | 1 |
| Duplicate dominant genes | 15 | 1 |
| Duplicate recessive genes | 9 | 7 |
| Dominant and recessive interaction | 13 | 3 |
|  |  |  |

**GENETIC INTERACTION AND LETHAL GENES**

**57**

**ATAVISM OR REVERSION**

While we were discussing the cross between two white flowered sweet pea plants we observed that F1 hybrid had purple colour unlike their immediate parents but like their remote ancestors. The appearance of such offsprings which resemble with their remote ancestors are called **throwbacks**, **atavisms** or **reversions**.

**LETHAL GENES**

**Lethal genes** are mutant genes and result in the death of the individual which carries them. Death of the individual occurs either in the prenatal or postnatal period prior to sexual maturity. A **fully** (completely) **dominant lethal allele** kills both in homozygous and heterozygous states. Individuals with a dominant lethal allele die before they can leave progeny. Therefore, the mutant dominant lethal is removed from the population in the same generation in which it arose. **Recessive lethal genes** kill only when they are in a homozygous state and they may be of two kinds : 1. one which has no obvious phenotypic effect in heterozygotes and 2. one which exhibits a distinctive phenotype when heterozygous.

The **completely lethal genes** usually cause death of the zygote, later in the embryonic development or even after birth or hatching. Complete lethality, thus, is the case where no individuals of a certain genotype attain the age of reproduction. However in many cases lethal genes become operative at the time the individuals become sexually mature. Such lethal genes which handicap but do not destroy their possessor are called **subvital**, **sublethal**

Snapdragons.

or **semilethal** genes. The lethal alleles modify the 3:1 phenotypic ratio into 2 : 1.

**Examples of Lethal Alleles**

* 1. **Lethal alleles in plants.** In plants, recessive lethal alleles are known which produce **albinism**, where absence of chlorophyll is lethal (fatal) to them. Following two examples illustrate this fact :
		1. In snapdragons (*Antirrhinum majus*) three types of plants occur : 1. green plants with chlorophyll ; 2. yellowish green plants with carotenoids, usually are re- ferred as pale green, **golden** or **auria** plants and 3. white plants without any chlorophyll. The homozygous green plants have the genotype CC and the homozygous white plant has the genotype cc. The auria plants have the genotype Cc because they are heterozygotes of green and white plants. When two such auria plants are crossed, the F1 progeny has identical phenotypic and genotypic ratio of 1 : 2 : 1 (*viz.,* 1 green (CC) : 2 auria (Cc) : 1white (cc). But

the white plants because lack chlorophyll pigment, therefore, die to modify the ratio of 1 : 2 : 1 into 1 : 2 or 2 : 1. In this case the homozygous recessive genotype (cc) is lethal.

|  |  |  |  |
| --- | --- | --- | --- |
| **F1 heterozygote :** | AuriaCc | X | AuriaCc |
| **F2 :** | 1 Cc Green | : 2 Cc :Auria | 1ccWhite (lethal) |
|  | or lCC | : 2 Cc or | 1 : 2. |

Thus, c allele exhibits a lethal effect when homozygous and a distinctive phenotypic effect (*e.g.,* auria) when heterozygous.

**GENETICS, HUMAN GENETICS AND EUGENICS**

**58**

* + 1. In maize (*Zea mays*) the amount of chlorophyll is controlled by a recessive allele (g) which exhibits a lethal effect in homozygous (gg) and in heterozygous condition (Gg) has phenotype similar to homozygous condition for dominant gene GG. It modifies 3 : 1 phenotypic ratio into 2 : 1.

**F1 heterozygote :** Green X Green

Gg Gg

**F2 :** 1 GG : 2 Gg : 1 gg

Green Green White (lethal) or 1 GG : 2 Gg or 1 : 2 or 2 : 1.

* 1. **Lethal alleles in animals.** Among animals, the following three examples exhibit the role of recessive lethal alleles :

Coat colour in mice is gov- erned by multiple alleles.

* + 1. The inheritance of mouse body colour was studied by the French geneticist, **L. Cuenot** in 1905. The coat colour of mice is governed by a multiple allelic series (see Chapter 10) in which A allele determines **agouti** or mousy-coloured coat, AY allele determines **yellow** coat and a allele forms **black** coat. The dominance hierarchy is as follows : AY >A>a. The AY allele also acts as a **recessive lethal**, since in the homozygous state (AYAY), it kills the individual in early embryonic stage (*i.e.,* during gastrulation). Thus, when two yellow coated heterozygotes (AYA) are crossed, they produce a progeny showing a ratio of 2:1 since homozygous yellow (AYAY) individuals are never borned due to lethal effect of AY gene :

**Parents :** Yellow X Yellow AYA AYa

(Hybrid of yellow and agouti)  (Hybrid of yellow and black)

|  |  |  |  |
| --- | --- | --- | --- |
| **Progeny :** | 1AYAY : | 2 AYA : | 1 Aa |
|  | Homozygous Yellow (die in uterus) | Heterozygous Yellow | Agouti |

or 2 Yellow : 1 Agouti or 2:1.

* + 1. In the chicken an incompletely dominant gene (cp) in heterozygous condition (cp/+) cause “creeper” condition. The creeper birds have much shortened and deformed legs and wings, giving them a squatty appearance and creeping gait. A cross of two creeper birds yields viable offsprings in the ratio of 2 creepers : 1 normal. The homozygous creepers having such a gross deformities that they die during incubation.

|  |  |  |  |
| --- | --- | --- | --- |
| **F1 :** | cp/+Creeper (Heterozygous) | X | cp/+ Creeper |
| **F2 :** | 1 cp/cp :Creeper | 2cp/+ :Creeper | 1+/+Normal |
|  | (Homozygous; dies) | (Heterozygous) | (Homozygous) |

* + 1. In cattle, a recessive lethal gene in homozygous condition (aa) causes calves to born “amputated” which die soon after birth. The cross between two carriers (a+) produces the following result :

**Parents :** Normal X Normal a+ a+

**P gametes :** a + a +

**Progeny :** 1aa : 2a+ : 1 ++

{

{

Amputated Normal

(die)

**GENETIC INTERACTION AND LETHAL GENES**

**59**

* + 1. In *Drosophila* various sublethal and sex-linked lethal genes have been reported. The genes for vestigial wings and genes for white eyes are best examples of sublethal genes of *Drosophila.* Both of these genes reduce the viability of flies up to greatest extent. In *Drosophila,* certain recessive lethal genes like curly wings (Cy), plum eyes (Pm) and stubbles (Sb) influence the viability of the flies when present in homozygous condition.
	1. **Lethal alleles in human beings.** In humans several hereditary diseases have lethal effects. Few important lethal genes of man are following :
		1. **Congenital ichthyosis.** One of the most typical cases of a recessive lethal gene in man is expressed in congenital ichtyosis. At birth children afflicted with this disease have a crusted leathery skin with deep fissures down to the subcutaneous tissue; the fissures lead to bleeding, infection and death. Congenital ichthyosis occurs only when there occurs homozygous condition for its recessive lethal genes.

Small pale abnormally - shaped RBC are associated with thalassemia major. The darker cells likely represent normal RBCs, from a blood transfusion

* + 1. **Infantile amaurotic idiocy.** A recessive allele in homozygous condition causes a fatal disease called **infantile amaurotic idiocy** in juvenile stage. Bearers of this genotype begin to lose their eye sight between the age of four to seven years. The complete blindness is followed by mental degen-

eration and finally death before adolescence.

* + 1. **Thalassemia. Thalassemia** or **Cooley’s anaemia** is a haemoglobin disease somewhat similar to sickle cell anaemia. It occurs mostly in children (in India and other countries such as Italy, Greece and Syria) and is nearly 100 per cent fatal (lethal). Thalassemia is controlled by a single gene c which in homozygous condition (cc), produces the severe Cooley’s anaemia or **thalassemia major** and causes death of the patient. The heterozygous condition of this lethal gene (Cc) results in a mild form of the disease called **thalasemia minor** or **microcythemia** (see **Gurdon**, 1968).

**PENETRANCE**

The ability of a given gene or gene combination to be expressed phenotypically to any degree is called **penetrance**. It is of following two kinds :

1. **Complete Penetrance**

Most dominant and recessive genes in homozygous conditions and many completely dominant genes even in heterozygous conditions give their complete phenotypic expressions. Such genes are called to have **complete penetrance**.

**Examples of Complete Penetrance**

* 1. In pea the alleles (RR) for red flowers and the alleles (rr) for white flowers have complete penetrance in homozygous conditions.
	2. In *Drosophila* the recessive alleles for vestigial wings in homozygous conditions have complete penetrance.
	3. In guinea pigs the dominant allele ‘B’ for black coat has complete penetrance both in homozygous and heterozygous conditions.
1. **Incomplete Penetrance**

Some genes in homozygous as well as in heterozygous conditions fail to provide complete (cent per cent) phenotypic expression of them. Such genes are called to have **incomplete penetrance**.

**GENETICS, HUMAN GENETICS AND EUGENICS**

**60**

**Examples of Incomplete Penetrance**

1. Polydactyly in man is thought to be produced by a dominant gene P. The normal condition with five digits on each limb is produced by the recessive genotype (pp). Some heterozygous individuals (Pp) are not polydactylus and, therefore, has a penetrance of less than 70%.
2. In man, the tendancy to develop diabetes mellitus (a condition in which there is an excess of sugar in the blood) is controlled by certain genes. However, not everyone carrying the genes for diabetes actually develops the condition, for these genes have incomplete penetrance.

**Effects of environment on penetrance.** The environmental factors and genetical background have some definite effect on the degree of penetrance of a gene. For example, when various twins which carry genes for diabetes mellitus are studied, it is found that the disease appears only in those cases which ate more carbohydrate foods (starch and sugars).

**EXPRESSIVITY**

A trait though penetrant, may be quite variable in its phenotypic expressions. The degree of effect produced by a penetrant genotype is called **expressivity**.

**Example of expressivity.** In man the polydactylous condition may be penetrant in the left hand (6 fingers) and not in the right (5 fingers); or it may be penetrant in the feet and not in the hands.

**Effects of environment on expressivity.** The expressivity of a given gene is often influenced by environmental conditions. For instance, the expressivity of completely penetrant gene for vestigial wings in *Drosophila* is influenced by the temperature at which the fly develops, with the effect being most obvious at lower temperature.

Other examples of environmental effects on the expressivity of a gene includes such cases as the differences in the severity of symptoms of an inheritable allergy, or the differences in height of identical twins who have been raised in different home (with different diets), or who have had different medical histories (one with a serious childhood disease, the other escaping this disease).

**PLEIOTROPISM**

Uptill now we have observed that a specific gene has a specific effect upon a specific phenotypic trait or in other words, each gene (allele) has its relation with a single phenotypic trait, but, this is not the case. A single gene often influences more than one phenotypic trait. However, it may be that one gene may cause evidently well marked expression of

A young cystic fibrosis patient. This disease is a case of pleiotropy. These patients have prob- lems with breathing & digestion. They produce rather viscous mucus, particularly in the gut, pancreas and lungs. Male patients are infertile.

some phenotypic trait (**major effect**) then the others with less evident phenotype (**secondary effect**). Most genes have their multiple effects and are called **pleio- tropic genes**. The phenomenon of multiple effect (mul- tiple phenotypic expressions) of a single gene is called **pleiotropism**.

**Examples of Pleiotropism**

1. In *Drosophila* the recessive gene for vestigial wings cause vestigial wings in homozygous condition. However, careful observations show that other traits as well are affected—(i) the tiny wing- like balancer behind the wings; (ii) certain bristles; (iii) the structure of the reproductive organs; (iv) egg production is lowered, and, (v) longevity is reduced.
2. In human, the gene for disease **phenylketo- nuria** has pleiotropic effect and produces various abnormal phenotypic traits, collectively called **syn-**

**GENETIC INTERACTION AND LETHAL GENES**

**61**

**drome**. For example, the affected individuals secrete excessive quantity of amino acid phenylalanine in their urine, cerebrospinal fluid and blood. They become short stature, mentally deficient, with widely spaced incisors, with pigmented patches on skin, with excessive sweating, and with non-pigmented hairs and eyes.

1. The AY allele for yellow coat in mice is also a good example of pleiotropic gene. It affects two characters : coat colour and survival. It is most probable that both effects of the AY allele are the result of same basic cause which promotes the yellowness of coat in a single dose and death in double dose. Genetic analysis has revealed that lethal pleiotropic AY allele basically affects the cartilage of mice and cause death.

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