Chapter 4--Modifications of Mendelian Ratios

Alleles--Modified genetic information for the gene product (Alternative forms).

Wild-type--Usually most frequent, usually dominant.

Mutation--Only source of new alleles

Symbols for ebony a recessive body color mutation.

e^+ / e^+	**Homozygous gray (wild-type)**
e^+ / e	**Heterozygous gray (wild-type)**
e / e	**Homozygous ebony**

Incomplete or Partial Dominance

- **Heterozygotes have phenotype Intermediate to both homozygous parents**

Example 1 -- Snapdragons

P_1	R^1R^1 (red)	X	R^2R^2 (white)
F_1	R^1R^2 (pink)	X	R^1R^2
F_2	$1R^1R^1$: (red)	$2R^1R^2$: (pink)	$1\ R^2R^2$ (white)

Example 2 -- Chickens

F^1 = Normal Feathers
F^2 = Frizzled Feathers
F^1F^2 = Mildly Frizzled Feathers

Other Problems Associated with Frizzled Feathers:

✓ **Functional and developmental abnormalities of other organs**

✓ **Difficulty with thermalregulation**

<u>PLEIOTROPY</u>: Multiple phenotypic effects of a single allele.

Codominance: Heterozygotes exhibit the phenotype of both homozygous parents.

Examples: ABO and MN Blood groups.

ABO System is characterized by the presence of antigens on the surface of RBCs

Genotype	Antigen	Phenotype
I^AI^A	A	A
I^AI^O	A	A
I^BI^B	B	B
I^BI^O	B	B
I^AI^B	A,B	AB
I^OI^O	NEITHER	O

***Question*: Could a child with blood type O be produced from parents with blood types A and B**

***Answer*: Only if: I^AI^O X I^BI^O**

***Question*: A mother and her child have blood type O. Which blood group can the father *NOT* belong to?**

***Answer*: Father cannot be blood type AB**

M and N blood groups: MM, MN, NN

Lethal Alleles

1. Recessive lethal mutations tolerated as heterozygotes, fatal as homozygotes.

✓Examples of traits in *Drosophila* with recessive lethal alleles.

Curly wings, Plum eyes, Stubble bristle

All behave as homozygous recessive lethal alleles BUT are dominant in heterozygous state.

✓ Many examples in humans--

--i.e., Tay Sachs disease

-- homozygous recessive--lethal

--heterozygous produces 1/2 of enzyme, but individuals are phenotypically normal

Lethal alleles (continued)--

2. Dominant Lethal mutations
Rarely observed
Example--Huntington's Disease

Problem involving lethal allele:

Coat Color in mice:

A -- Wild-type = Agouti

A^Y -- Dominant mutation that is also a recessive lethal.

A^YA	**--**	**produces yellow fur**
A^YA^Y	**--**	**lethal**

***Question*: What is the F1 genotypic and phenotypic ratio from crossing two yellow individuals?**

P_1 Yellow X Yellow

(A^YA) (A^YA)

	A^Y	A
A^Y	A^YA^Y	A^YA
A	A^YA	AA

Genotypic Ratio: $1A^YA^Y$: $2A^YA$: $1AA$

Phenotypic Ratio: 2/3 Yellow : 1/3 Agouti

***Gene Interactions*-- Several genes influence a particular characteristic.**

***EPISTASIS*--When the expression of one gene masks or modifies the expression of another gene.**

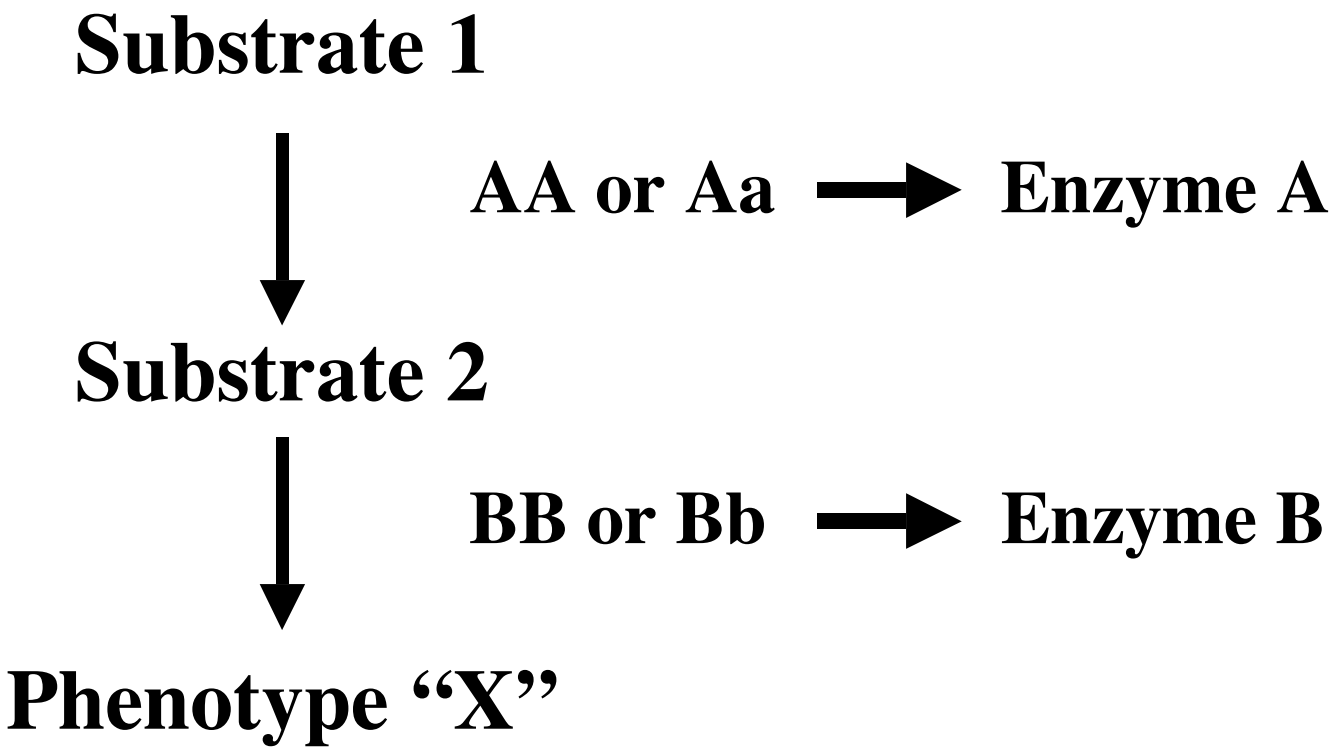
The gene that is doing the masking is called the EPISTATIC GENE.

Epistasis results in modifications of typical Mendelian ratios.

General model of Epistasis:

A -- produces Enzyme product A
a -- nonfunctional variant of enzyme product A

B -- produces enzyme product B
b -- nonfunctional variant of enzyme product B



Any combination of the above will produce phenotype "X"

Homozygous recessive for one or both Loci will result in non-X phenotype

AaBb X AaBb

9	**A-B-**	**9 "X" Phenotype**
3	**A-bb**	
3	**aaB-**	**7 non- "X" Phenotypes**
1	**aabb**	

aa is epistatic to B

bb is epistatic to A

Labrador retrievers -- coat color is controlled by 2 non-linked autosomal genes

A- = Black **aa = Chocolate**
bb = Yellow, regardless of the genotype at the "A" - locus

***Question*: What will be the F_1 genotypic and Phenotypic ratios from mating 2 black labrador Retrievers that are both double heterozygotes?**

Black X Black

AaBb AaBb

Genotypic Ratio:

1 AABB
2 AABb
1 Aabb

2 AaBB
4 AaBb
2 Aabb

1 aaBB
2 aaBb
1 aabb

Phenotypic Ratio

9 Black (A-B-)
3 Chocolate (aaB-)
4 Yellow (--bb)

Complementation Analysis -- Used to determine when 2 mutations, both of which produce a similar phenotype, are in the same, or different, genes.

To answer this, you cross the two mutant strains and examine the F_1 generation.

If the F_1 generation is all wild-type, then the Mutations affect 2 different genes.

If the F_1 generation all have the mutation, then These are alleles of the same gene.

***Example*: You have a pure breeding line of white poodles. You cross a dog from your line with an dog from a separate line of pure breeding white poodles.**

P_1: White X White

F_1: All Black

What are the genotypes of the two white poodles as well as the black F_1 poodles and what genetic phenomenon does this example illustrate?

P_1: aaBB (white) X AAbb (white)

F_1: AaBb (Black)

Epistasis

Sex-Linkage

Mammals and *Drosophila*

XX = Females

XY = Males

1. **Genes on Y-chromosome = Holandric or Y-linked**

2. **Genes on X-chromosome = X-linked or sex-linked.**

Males are hemizygous for traits on the X-chromosome.

Sex-Limited & Sex-Influenced Traits

Inheritance is affected by the sex of the individual but not necessarily by genes on the X-chromosome.

Sex-Limited **-- Expression of a specific phenotype Is limited to one sex.**

Sex-Influenced **-- Sex of the individual influences The expression of a phenotype that IS NOT LIMITED TO A SEX.**

Sex-Limited Trait -- Hen Feathering vs. Cock Feathering in domestic fowl.

	FEMALES	MALES
HH	Hen-feathers	Hen-feathers
Hh	Hen-feathers	Hen-feathers
hh	Hen-feathers	COCK-FEATHERS

Trait is controlled by a single autosomal locus whose expression is modified by hormones.

Remove ovaries from hh and become cock-feathered at next molt.

Leghorn Chhickens → **ALL hh**

Seabright Bantams → **ALL HH**

Hamburgs → **H- or hh**

Sex-Influenced traits appear in both sexes BUT, the relationship between genotype and phenotype is different between the sexes.

Example: Pattern baldness in humans

Female (Bb) **Male (Bb)**

	B	b
B	**BB**	**Bb**
b	**Bb**	**bb**

Results:

1/4 BB **Bald whether male or female**
1/2 Bb **Bald males, non-bald females**
1/4 bb **non-bald males and females**

Therefore, B is dominant in males and recessive in females!

Phenotypic Expression
Internal vs. External Environment

Penetrance **-- % of individuals with a mutant genotype that show at least some degree of expression of the mutant phenotype.**

ey^+ = wild-type **ey = eyeless**

P_1 : ey^+/ey X ey^+/ey

F_1: 250 ey^+/ey^+ 500 ey^+/ey 250 ey/ey

Expect: 750 wild-type 250 eyeless

Observe: 900 wild-type 100 eyeless

Penetrance: **100/250 = 40%**

Expressivity **-- Range of expression of a mutant genotype.**

Eyeless (ey/ey) -- complete loss of both eyes to 2 completely normal eyes.

Genetic Background: Suppression and Position

GENETIC SUPPRESSION**: Examples of genetic background modifying primary gene products.**

Vermilion (v/v); wild-type (v^+/-)

v/v su-v/su-v = wild-type
v/v su-v^+/ su-v = vermilion

✓ corrects error in translation
OR
✓ provides an alternative pathway

***Position Effect*:**

White Locus -- Sex-linked recessive
w^+/w = wild-type

Translocation to heterochromatin--
w^+/w = mottled red & white.

Environmental Effects:

1. Nutritional Effects:

- ✓ **Phenylketonuria -- cannot metabolize phenylalinine**
- ✓ **Galactosemia**
- ✓ **Lactose Intolerance**

2. Temperature:

- ✓ **Siamese cats & Himalayan rabbits**
- ✓ **Darker fur at extremities is due to loss of function of gene for coat color at warmer body temperature.**

ONSET OF GENETIC EXPRESSION:

TAY-SACHS DISEASE--

- ✓ **Autosomal recessive**
- ✓ **Lethal lipid metabolism disease**
- ✓ **New born appears normal for 5 - 6 months**
- ✓ **Death before 4 years of age**

HUNTINTON DISEASE--

- ✓ **Autosomal Dominant**
- ✓ **Affects frontal lobe of cerebral cortex**
- ✓ **Progressive cell death over more than a decade**
- ✓ **30 - 50 years of age.**

***GENETIC ANTICIPATION*-- Occurrence of A genetic disorder progressively earlier and with Increased severity in successive generations.**

Examples in humans:

- ✓ **Myotonic Dystrophy**
- ✓ **Fragile-X Mental Retardation**
- ✓ **Kennedy Disease**

Myotonic Dystrophy -- Autosomal Dominant

Mild = Cataracts as adult, little or no muscular weakness

Severe = Severe myopathy, may be mentally retarded

Extreme = Fatal just after birth.

***Genomic Imprinting*: Genetic expression varies based on the parental origin of the chromosome carrying a particular allele.**

Imprinting or "marking" is thought to occur before or during gamete formation.

Hunting disease **-- early onset most often if of paternal origin.**

Myotonic dystrophy **-- early onset most often if of maternal origin.**

Two different disorders in humans due to a deletion of a specific region of chromosome 15.

1. Prader-Willi Syndrome (PWS):

- ✓ **Deletion ON paternal 15**
- ✓ **Maternal 15 is normal**
- ✓ **Symptons**
  - **mental retardation**
  - **obesity**
  - **diabetes**

2. Angelman Syndrome (AS):

- ✓ **Deletion ON maternal 15**
- ✓ **Paternal 15 is normal**
- ✓ **Symptons**
  Behavioral & Mental retardation.

Only 60% of individuals with Prader-Willi syndrome exhibit the deletion of paternal 15.

What about the other 40%?

- ✓ **Inherited both copies of the normal 15 from mother**
- ✓ **Uniparental disomy**
- ✓ **Why would such an individual have PWS?**