GENETICS OF SEX

In majority of animals as well as dioecious plants (i.e. plants in which a given individual produces only sperm or egg) one pair of chromosomes can be distinguished morphologically from the rest. This pair of chromosomes has a role in sex determination. The chromosomes are called **sex chromosome**. All other chromosomes which are the same in both sexes are called the **autosomes.**

The number of sex chromosome may vary in certain species. Up to 8 – 12 sex chromosomes may occur in some lower animals, multiple sex chromosomes can also be found in some dioecious species of plants. Unlike the other chromosome pairs of a species (i.e. the autosome), the sex chromosome i.e. the X and Y chromosome differ from another in size i.e. they are of unequal size, shape and or straining qualities. Though, during meiosis they pair and act as a homologous segment.

In most animals and dioecious plants, the males contain one X and one Y chromosome (i.e. XY) and females have XX.

Birds, butterflies, some fishes and some species of strawberry plants have the reverse type of chromosomal sex determinations i.e. the females are equipped with an X and Y chromosome. In birds and butterflies, the sex chromosomal constitution is frequently denoted as ZW for female and ZZ for male.

The sex that can produce either X or Y chromosome containing gametes is called **heterogametic**. In the majority of species, with the exception of butterflies, some fishes, most silkworms, the females have two X chromosomes and are therefore called **homogametic.**

CLASSIFICATION OF SEX CHROMOSOMES IN DIPLOID ORGANISMS

Sex chromosomes in diploid organisms can be classified into four different methods:

i. XX – XY method or ***Lygaeus*** **mode of sex determination**

ii. XX – XO method or ***Protenor*** **mode of sex determination**

iii. ZZ – ZW method

iv. ZZ – ZO method

In the first two methods, the males are **heterogametic** i.e. produces two kinds of gametes as far as sex chromosomes are concerned, but the female produced only one kind of gamete and is called **homogametic sex.**

In methods (iii) and (iv) above, the male is homogametic sex and produces only one gamete whereas the female is the heterogametic sex as it produces two types of gametes.

XX – XY METHOD

In this case, the females were XX, but males were XY. Half the sperm carry an X and half a Y. The so-called XY type occurs in a wide variety of animals including *Drosophila melanogaster* (Fruit flies) and mammals and as well as in at least some plants e.g. angiosperm genus Lychnis.

XX-XO METHOD

In many insects e.g. bugs, grasshoppers and cockroaches there is a chromosomal difference between the sexes i.e. females are referred to as XX (i.e. having two X chromosome and male as XO) i.e. (having one X chromosome). In this case, all the eggs of such species carry an X chromosome. Only half the sperms have one X and the other half has none.

In both XX-XY and XX-XO methods described above, all the eggs have one X chromosome, whereas two kinds X and Y or X and O in the male and in each case the male is **heterogametic** (producing two kinds of gametes) whereas the female is **homogametic** sex (producing but one kind of gamete).

ZZ – ZW METHOD

In this case the male is **homogametic** while the female is **heterogametic**. Therefore, the females are thus ZW and males are ZZ. Birds, including the domestic fowl/chicken, butterflies and some fish,

reptiles, amphibians belong to this group. In fowl for example, the female is indeed heterogametic and is therefore characterized by the ***Lygaeus*** type of sex determination.

ZZ-ZO METHOD

In this case, the males (ZZ) are homogametic which the females (ZO) are heterogametic, but female only have one Z chromosome. Therefore, in both ZZ – ZW and ZZ – ZO, the females are heterogametic whereas the males are homogametic.

SUMMARY OF SEX CHROMOSOME TYPES

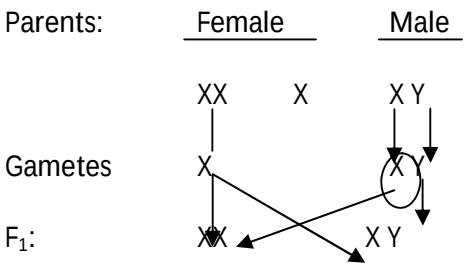
The various types of chromosomal differences between the sexes may be summarized as follow:

Females	Males	Examples
XX	XY	Drosophila, humans and other mammals
XX	XO	Bugs, grasshopper and cockroaches
ZW, ZO	ZZ, ZZ	Birds, butterflies, moths, some fish, amphibians, reptiles, etc.

N.B: Note that the W chromosome of the chicken is not a *strong female determining element.* Recent investigations shows that sex determination in chickens and other birds is dependent upon the ratio between the Z chromosomes and the number of autosomal sets of chromosomes

<u>The four sex chromosome methods of sex determination</u>

XY method of sex determination



Female Male

This crossing will produce a 1: 1 sex ratio in each generation.

XO method of sex determination

Parents: Female Male

XX X XO

Gametes: (X) (X O)

F_1: XX X O

Female Male

In this case too, a 1:1 sex ratio is produced in the progeny.

In both examples above, the male XY or XO are the **heterogametic sexes** while the XX female is homogametic.

ZW method of sex determination

Male Female

Parents: ZZ x ZW

Gametes Z Z W

F_1: ZZ ZW

Male Female

Note: also that 1:1 sex ratio also occur here.

ZO method of sex determination

Male female

Parents:	ZZ	X	ZO
Gametes	Z		Z O
F_1:	ZZ		ZO
	Male		Female

In both ZZ – ZW and ZZ – ZO, the heterogametic females are ZW and ZO, but ZZ is the homogametic males.

INTERSEXES

In some organisms e.g. *Drosophilia melanogaster* (Fruit fly), some individuals are very large, exhibited a variety of morphological abnormalities, usually very sterile and expressed both male and female morphology. Individuals exhibiting these are called **intersexes. Intersexes** are sterile individuals that display secondary sex characters between those of male and female. In such individuals, the ratio of number of X chromosomes to the number of sets of autosomes (A) when calculated is greater than 0.5 but less than 1.0 (i.e X/A is > 0.5 but < 1.0). This method was developed by Calvin Bridges in 1916 and is still been used till date.

Bridges realized that the critical factor determining sex is the ratio of X chromosomes to the number of sets of autosomes (A) that is present. Normal (2X:2A) and triploid (3X:3A) females each have a ratio equal to1.0, and both are fertile. As the ratio exceeds unity (3A:2A or 1.5, for example), we have what is called **superfemale** or what is now called **metafemales.**

Normal (XY:2A) and sterile (XO:2A) males each have a ratio of 1:2, or 0.5. When the ratio decreases to 1:3, or .33, as in the case of an XY:3A male, infertile metamales result. Other flies recovered by Bridges had X:A intermediate between 0.5 and 1.0. These flies are generally larger, sterile and display secondary sex characters between males and females and are appropriately called intersexes.

The mechanism of sex differentiation in ***Drosophila*** may be summarized as follows:

- Sex is governed by the ratio of number of X chromosomes to the sets of autosomes. Thus, females have X/A ratio =1.0; males = 0.5
- Gene for maleness per se are apparently carried on the autosome, those for femaleness on the X chromosome.
- The Y chromosome governs male fertility rather the sex itself.
- An X/A ratio greater than 1.0 or less than 0.5 (> 1.0 or < 0.5) results in certain characteristic malformations (i.e. ***metafemales and metamales***).
- An X/A ratio (< 1.0 but > 0.5) produces individuals intermediate between males and females (intersexes). The degree of femaleness is greater where X/A ratio is closer to 1.0, and the degree of maleness is greater where that ratio is closer to 0.5.

The table below explains the formation of intersexes and other sexual morphology seen in *Drosophila melanogaster*.

Chromossome formulation (Note: The numerators are the assumed X chromosome numbers and the denominators are the number of sets of autosomes	Ratio of X chromosomes to autosome sets	Resultant sexual morphology or sex designation
3X/2A	1.5	Metafemale
3X/3X	1.0	Female
2X/2A	1.0	Female
3X/4A	0.75	Intersex
2X/3X	0.67	Intersex
X/2A	0.50	Male
XY/2A	0.50	Male
XY/3A	0.33	Metamale

SEX DIFFERENTIATION

1. **Genetic Sex**: Normal females have two X chromosomes, normal male have one X and one Y. Genes on these chromosomes determines femaleness or maleness. Therefore, one can say that females have genetic sex designation XX and males having the XY although exceptional cases do occur.
2. **Gonadal sex:** Chemical substances called **inductors** produced by embryonic XX cells act on the cortical region of undifferentiated gonads to bring about development of ovarian tissue. In XY embryos, however, inductor stimulates production of testes from medulla of the undifferentiated gonads. Hence, the XX genetic sex is associated with ovarian gonadal sex and XY with testicular gonadal sex.
3. **Genital sex**: XX embryos normally developed ovaries, female external genitalia and Mullerian ducts. XY embryos develop testes, male external genitalia and Mullerian ducts. XY embryos develop testes, male external genitalia and Wolffian ducts. In XX embryos, Wolffian ducts are suppressed, in XY embryos, the Mullerian ducts remain undeveloped. Thus, there is a distinction between male and female genital sex.
4. **Somatic sex:** production of gonadal hormones continues to increase until at puberty when secondary sex characteristics appear. These include amount and distribution of hair (e.g. facial, body, pubic etc), general body proportions, fats over hips and things and breast development in the females as well as increased larynx size and deepening of the voice in the male.
5. **Sociopsychological sex:** In most individuals, genetic, gonadal, genital and somatic sexes are consistent. XX persons for example develop ovaries, female genitalia, female secondary sex characters. These persons are raised as females and adopt the feminine

gender role under whatever cultural pattern has been established in the society of which they are members. A similar consistency from genetic sex to sociopsychological sex is seen for XY individuals. On the other hand, some individuals display an inconsistency of some kind or degree among these levels of sexuality. Discordance involving the genetic and anatomical result in inter-sexuality

TWO COMMON SEX CHROMOSOME ANOMALIES IN HUMANS

These are the **Klinefelter syndrome** (47,XXY) and the **Turner syndrome** (45,X).

CHARACTERISTICS OF INDIVIDUALS WITH KLINEFELTER SYNDROME

(i) This syndrome is commonly seen in males and affected individuals are tall, having long arms and legs and large hands and feet

(ii) They usually have genitalia and internal ducts that are male, testes are rudimentary and fail to produce sperm.

(iii) There is slight enlargement of the breast, a condition known as **gynecomastia.** This ambiguous sexual development is often referred to as **intersexuality** and can lead to abnormal social development.

(iv) Hips are often rounded

(v) Intelligence of affected individual is often below normal

CHARACTERISTICS OF INDIVIDUALS WITH TURNER SYNDROME

i. In turner syndrome, affected individual has female external genitalia and internal ducts, but the ovaries are rudimentary

ii. Affected individuals always have short stature (usually below 5 ft)

iii. There is underdeveloped breasts and at times, a broad chest may be noted.

iv. Intelligence of individuals with Turner syndrome is usually normal.

General forms/designations of these two syndromes in humans are shown in the table below.

However, a **47,XYY or for short XYY condition** is a form of Klinefelter syndrome that need special consideration (***See table below***).

Sex chromosome anomalies in human and their frequencies

Designation	Chromosome constitution	Kartyotype designation	Somatic chromosome number	General sex phenotype or seen in	Signs / characteristic	Usual fertility	Estimated frequency per 1000 births	Estimated number
Klinefelter syndrome	AAXXY	47XXY	47	Males	Affected males have undeveloped testis that cannot produce sperm. Testes are very small. Affected men are mentally retarded, arms are longer, unusual breast development	sterile	2.0	Very high
Klinefelter syndrome XXYY	AAXXYY	48XXYY	48	Males	Manifestations are more severe than 47 XXY type	Not reported	Very low	Very low
Klinefelter XXXYY	AAXXXYY	49XXXYY	49	Males	Manifestations are severe than 47XXY type	Not yet report	Very low	Very low
XYY	AAXYY	47XYY	47	Males	Affected individuals have low or subnormal intelligence, there is low sperm count, Affected males with XYY are more aggressive and commit crimes of violence than normal males. However, in some countries individuals with this karyotype are critically been examined before	Generally highly infertile	0.7 – 2.0	Very high

					judgement is passed and at times, judges are been lenient in their judgement for individual with XYY karyotype. *It must be noted that the general sex phenotype of individual with XYY is male.*			
Triplo, X, Y Tetra-X, Y	AAXXXY AAXXXXY	48XXXY 49XXXXY	48 49	Males Males	Manifestations are severe than 47XXY type Very severe manifestations and sperm count is also very low.	Cannot produce Cannot produce at all	Very low	Very low
Turner syndrome	AAXO	45, X	45	Females	Affected individuals has female external genitalia and internal ducts, but ovaries are rudimentary, individual appear very short in stature, breed chest and webbed neck	Cannot produce, but if not severe, very few cases of motherhood have been	1 in 3000 births of females, a frequency lower than Klinefelter syndrome	Very high

						reported		
Triplo – X	AAXXX	47XXX	47	Female	Results in female differentiation, sterility or mental retardation, undeveloped secondary sexual characteristics.	Affected women in this case are perfectly normal	1 in 1200 female birth	Very high
Tetra – X	AAXXXX	48XXXX	48	Females	Syndromes associated with this karyotype are similar, but more pronounced than 47XXX. Disruption of delicate balance of genetic information for female development. Affected females have low intelligence	Unknown	Very low	Very low
Penta – X	AAXXXXX	49XXXXX	49	Female	Syndrome more severe than 47 XXX and the extra X chromosome disrupt the delicate balance of genetic information necessary for normal female development. Affected female have progressively reduced intelligence.	Affected women cannot produce	Very low	Very low

Karyotypes, other than 45, X also lead to Turner syndrome. These include individuals called **mosaics** with two apparent cell lines, each exhibiting a different karyotype. Such cell lines result from a mitotic error during early development. The most common chromosome combinations being **45, X/46, XY and 45, X/46,XX.**

The occurrence of the Turner syndrome is not as high as that of Klinefelter syndrome. One possible explanation for this is that most of the 45, X fetuses die in utero and are aborted spontaneously.

CAUSES OF KLINEFELTER AND TURNER SYNDROME

Both syndromes results from non-disjunction of the X chromosomes during meiosis. These karyotypes and their corresponding sexual phenotypes allow us to conclude that the Y – chromosome determines maleness in humans. In its absence, the sex of the individual is female, even if only a single X – chromosome is present.

Non-disjunction is the failure of paired chromosomes to segregate or separate during the anaphase stage of the first or second meiotic division. The result is the production of two abnormal gametes, one of which contains an extra chromosome (n+1) and the other lacks a chromosome (n-1). Fertilization of such gametes produces 2n+1 or 2n – 1 aneuploid zygote.

MECHANISM OF SEX DETERMINATION IN HUMAN BEINGS

Individuals that have at least one Y chromosome are, with exception of unusual cases are ordinarily male with regard to external genitalia and general phenotype, though they may be sterile. In contrast, persons with one or more X chromosomes are ordinarily phenotypically female as long as no Y is present, though again, infertility sometimes occurs.

The usual situation in human beings may be summarized as follows:

1. Autosomes do not play any part in determining sex.
2. Genes on the Y chromosome determine maleness (provided a controlling – X linked gene permits testicular differentiation).
3. Genes on the X chromosome determine femaleness in the absence of any Ys.

SEX RATIO

The actual proportion of male to female offspring is called sex ratio.

In humans, one of the sexes is heterogametic (i.e. XY) and the other is homogametic (i.e. XX), the ratio of males to female is expected to follow the rule of Mendelian test cross (1:1 ratio).

In humans, there is a slight deviation from the expected 1:1 sex ratio. In many countries including those that have census exercise, the ratio of males to females in humans is still not 1:1. In some countries, number of males outnumber that of the females and in some, it is vice versa.

This deviation from the expected 1:1 is believed to be caused by:

1. Selective fertilization of the X or Y – chromosome bearing gametes, or
2. By differential survival of the two sexes previous to birth.

Sex ratio can be assessed in two ways:

a. Primary sex ratio which reflects the proportion of males to females conceived in a population.

b. Secondary sex ratio reflects the proportion of each sex that is born. The secondary sex ratio is much easier to determine than the primary; but has the disadvantage of not accounting for disproportionate embryonic or fetal mortality should it occur. In most countries of the world, secondary sex ratio in human population that had been determined using census data, does not equal to 1.0

COMPOSITION OF X AND Y CHROMOSOME

The sex chromosomes are quite dissimilar in size (i.e the X and Y are of different size). The sex chromosomes (X and Y) often are of unequal size, shape and or staining qualities. The Y chromosome in normal male is considerably smaller and lacks most of the gene sites contained on the X. However, during meiosis, they often pair which indicates that they contain at least some homologous segments or portions or regions of the X that is homologous with a similar small bit of the Y.

Note the following very well:

Genes on the homologous regions of X and Y chromosomes are said to be **incompletely sex-linked or partially sex- linked** and may recombined by crossing over in both sexes just as do the genes loci on homologous autosomes.

Genes on the non-homologous or differential region of the X chromosome are said to be **completely sex-linked.**

Few genes are also known to settle in the **non-homologous or differential portion of the Y chromosome**. Such genes are completely Y-linked genes and are called **holandric genes.**

The non-homologous portions of X and Y chromosomes are also known as the **differential regions of X and Y chromosomes.**

In X chromosome, the differential region or the non-homologous portions are completely sex-linked, whereas the differential region or the non-homologous portions of Y contain holandric genes. The differential region of Y chromosome is subdivided into three other regions called **suppressor, promoter and fertility regions**. These three sub-regions contains essentially holandric genes. These various sections in the X and Y chromosomes are shown in the diagram below.

Note

X = X chromosome

Y = Y chromosome

The parts labeled "a" on both the X and Y chromosomes are the homologous portions or segments of the X and Y chromosomes and contain incompletely sex-linked genes.

The part labeled "b" on the Y chromosome is the non-homologous or the differential region of the Y chromosome which contain mainly holandric genes, or the Y-linked genes. The upper part of this region is called **suppressor region, the middle is the promoter and this is followed by the fertility region.** In short, these three sub-regions are properly called differential or non-homologous region of Y chromosome.

The part labeled 'c' on the X chromosome is called non- homologous or differential region of X chromosome and this region **contains completely sex-linked genes.**

HOLANDRIC GENES

These are genes that occur normally on the Y chromosome only and therefore are not expressed in females. In human, these genes are found in the differential or non- homologous portion of Y chromosome. In such cases, the trait would be expressed only in males and would always be transmitted from father to son. These genes are completely Y-linked or properly called the holandric genes.

SEX-LINKED OR X-LINKED GENES

Genes located exclusively on the X chromosome are called sex-linked or X-linked genes. These are genes located only on the X chromosome in XY species or the Z chromosomes in ZW species. These genes control sex-linked traits. Examples of such sex-linked traits in humans include:

1. Colour blindness and there are two types

a. *Deutan* colour blindness

b. *Protan* colour blindness

In deutan, the green sensitive cones are defective and this is due to an X-linked recessive gene. It affects human males more than females. It affects about 8% males and 0.75 of females. Deutan colour blindness appears to be the most commonly encountered sex-linked trait in human beings.

When there is defect on the red-sensitive cones, we have what is called protan. This is much less common than deutan type, occurring in only 2% of males and in 4 women out of about 10,000.

2. Other common human sex-linked trait is the Haemophilia: Haemphilia is a well known disorder in which blood clotting is deficient because of a lack of the necessary substrate thromboplastin. Haemophilia is a sex-linked recessive condition. There are two common types of haemophilia and these are

- Haemophilia A
- Haemophilia B

Haemophilia A is characterized by lack of antihemophilic globulin (or Factor VIII). This is the most common of the haemophilic conditions.

Haemophilia B is popularly known as the ***Christmas disease*** and this occur as a result of deficiency of clotting Factor IX or plasma thromboplastic component (PTC). This is a milder form of the condition.

SEX-LINKED LETHAL

These are genes whose effect causes death. The gene for haemophilia is a recessive sex-linked lethal for it often cause death. Sex-linked lethal by bring about death will alter the sex ratio in a progeny.

A good example is the **Duchene or muscular dystrophy**. This is a life shortening disorder in which the affected individual, though apparently normal in early childhood, exhibits progressive wasting

away of the muscles, resulting in confinement to a wheelchair by about age 12 and death in the teen years. Both haemophilia and Duchene are due to recessive sex-linked genes. At present, there are no known means of arresting this condition. The gene responsible is a lethal and will certainly change the sex ratio in a given group of offspring over time.

SEX-LIMITED GENES

Are those whose phenotypic expression is determined by the presence or absence of one of the sex hormones. Their phenotypic effect is limited to one sex or the other.

Sex-limited inheritance patterns are quite different from those of sex-linked genes. The latter may be expressed in either sex, though with differential frequency. Sex-limited genes express their effects in only one sex or the other, and their action is related to sex hormones. They are principally responsible for secondary sex characters.

Familiar examples of sex-limited traits are:

1. **Hen-feathering and cock-feathering in the domestic fowl.** For example, in some species of fowl, males and female may exhibit pronounced differences in plumage. In some species, males have long pointed and curved feathers on tail and neck, but feathers of the female are shorter and les curved. Males are cock-feathered and the females are hen-feathered.

For example in breeds called Sebright, birds of both sexes are hen-feathered. In other breed such as Hamburgs and Wyandottes, both males and females are hen-feathered. In the case of Leghorns, all the females are hen-feathered and males are cock-feathered (i.e they have long, pointed, curving neck and tail feathers)

Breeds	Genotype	Female	Male
Sebright bantams	HH	Hen-feathered	Hen-feathered

Hamburg and Wyandotte	Hh	Hen-feathered	Hen-feathered
Leghorns	hh	Hen-feathered	Cock-feathered

In this case, Sebright bantams are all *HH*, Hamburg and Wyandotte may be *H-* or *hh*; but Leghorns are all *hh.* Cockfeathering, where it occurs is limited to the male sex.

2. **Beard development in human beings is a sex-limited character** as men normally have beards whereas women normally do not, however when the sex hormone production is high, changes may result in a genuine bearded lady.

SEX-INFLUENCED GENES

Sex influenced genes are those whose dominance is influenced by the sex of the bearer. In other words, if the expression of a phenotype is not limited to one sex. In sex-influenced inheritance, individual's sex influences the phenotype.

In contrast to X-linked inheritance, patterns of gene expression may be affected by the sex of an individual even when the genes are not on the X chromosome. In numerous examples in different organisms, the sex of the individual plays a determining role in the expression of a phenotype. In some cases, the expression of a specific phenotype is absolutely limited to one sex; in others, the sex of an individual influences the expression of a phenotype that is not limited to one sex or the other. This distinction differentiates **sex-limited inheritance** from **sex-influenced inheritance.**

In both types of inheritance, autosomal genes are responsible for the existence of contrasting phenotypes, but the expression of these genes is dependent on the hormone constitution of the individual.

Common examples of sex-influenced inheritance/trait include:

i. Pattern baldness in humans. This is more prevalent in males than in female, where it is rare and usually involves marked thinning rather than total loss of hair on the top of the head.

ii. Horn formation in sheep which is dominant in males

Coat pattern or spotting in cattle (Mahogany and white, which are dominant in males, recessive in females; Red and white are dominant in females, but recessive in males.