NATIONAL OPEN UNIVERSITY OF NIGERIA

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GENETICS I

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NATIONAL OPEN UNIVERSITY OF NIGERIA

Module 1

UNIT 1 INTRODUCTION TO GENETICS

1.0 INTRODUCTION

A feature of students' attitude to Genetics is that it is a very difficult course, which one takes only because it is compulsory. Some students reinforce this negative attitude by the rationalization that they do not intend to do post-graduate work in Genetics. These attitudes are not deceptively correct because they make you neglect some of the more important aims of education. If you avoided the challenge posed by some courses, you would be denying your intellect the stimulation it needs to spur it to greater heights.

Besides, for a long time, Nigerian secondary school students have been denied adequate exposure to Genetics because some people avoided the challenge. Genetics is a vital aspect of everyday life and of Biology, and no biologist, regardless of his level or interest, should avoid a meaningful exposure to it.

Dobzhansky, aptly summarizes the need for a broad exposure as follows:

> "The advancement of science is, in the main, the business of specialists. And as science expands, the specialists tend to become narrow specialists. Some specialists have become disgustingly narrow. Narrow specialists are ENDANGERED and DANGEROUS (emphais mine) – endangered because

> their own inner lives are impoverished; dangerous because they are liable to be easy prey for exploitation by those with power or with money, for purposes inimical to both science and to the interests of mankind as a whole … There should exist, however, scientists able and willing now and then to abandon the protective shells of their specialties, and to engage in surveying broad vistas … people at large will have their inner life enriched if they gain an appreciation of what science and scientific attitude really are. Some aspects and achievements of science are everyone's business" (Dobzhansky, 1964).

It is hoped that at the end of the course, you would have gained an understanding of the principles governing the transmission of hereditary traits. All societies are interested in understanding how certain traits are inherited in living things, including man.

The puzzle about genetic inheritance in man is perhaps most succinctly expressed in this portion of a poem by Aldous Huxley's "Fifth philosopher":

A million million spermatozoa
All of them alive;
Out of their cataclysm but one poor Noah
Dare hope to survive

And among that billion minus one
Might have chanced to be
Shakespeare, another Newton, a new Donne
But the One was Me

Why was that one me? Why do normal parents produce an albino and short parents a tall child, or tall parents a short child? It is important for our well-being that we should be able to answer simple questions about heredity without resorting to "old wives tales". But Genetics is not solely concerned with man, it is of great importance in agriculture.

It is further hoped that at the end of this course, you will be able to appreciate the fact that:

> "Increased knowledge of heredity means increased power of control over the living things, and as we come to understand more and more the architecture of the plant or animal we realize what can and what cannot be done towards modification or improvement …

It is not, however, in the economic field, important as this may be, that Mendel's discovery is likely to have most meaning for us: rather it is in the new light in which man will come to view himself and his fellow creatures, if it is shown that the qualities of man, his body and his intellect, his immunities and his disease, even his very virtues and vices, are dependent upon the ascertainable presence or absence of definite unit-characters (genes) whose mode of transmission follows fixed laws, and if also man decides that his life shall be ordered in the light of this knowledge, it is obvious that the social system will have to undergo considerable changes" (Punnett, 1910).

This course deals with the basic principles governing heredity. Examples are chosen merely to illustrate these principles. To that extent therefore, you will not be expected to memorize examples, which may be new to you. This approach is dictated not only by the fact that the basic laws of heredity are applicable to most organizations, but also by the belief that with a good understanding of the principles one can make extrapolations to explain particular situations.

Much of the difficulty, which students have with Genetics stems from the fact that they had been used to purely descriptive aspects of biology. Genetics on the other hand largely entails logical reasoning based on a number of interdependent principles often involving some calculations. These calculations are within the scope of anyone who has studied elementary mathematics.

Genetics is a course which demands alertness and consistent work in the forms of reading and practice.

A note of warning should be sounded here: You would be deceiving yourself and also doing yourself a disservice, if you merely read genetics as literature. It indeed entails practicing on questions that boarder on the principles and laws of genetics. You will have to work examples typifying these principles and laws to have the concepts of genetics running in your blood.

2.0 OBJECTIVES

At the end of this unit, you would be expected to:

1. Develop an appreciation of the growth of Genetics
2. Know some of the important names in the development of Genetics
3. Know some of the theories in the evolution of Genetics, as well as the merits and demerits of such theories.

3.0 MAIN CONTENT

3.1 History of Genetics

Genetics is primarily and originally a science dealing with heredity i.e. the transmission of characteristics from parents to offspring. From such considerations, laws are derived concerning the relationships. In addition, genetics also involves a study of the factors, which show the relationship between parents and offspring and which also account for the many characteristics which organisms possess. You are familiar with the observations that "Like begets like", that children tend to resemble their parents as well as their siblings (or sibs i.e. their brothers and sisters), but they also tend to vary or look different from one another in many ways.

Genetics is the science, which tries to account for similarities and variations between related individuals. The science studies the transmission of hereditary factors from parents to offspring. Put differently, it is a study of biological "communication" between generations using the hereditary factors. Another facet of the science is the study of the expression or effect of the factors during development.

If one were to put the above "descriptive definition" of Genetics in a capsule form, Bateson, who coined the term Genetics in 1906 aptly defines it as follows:

Genetics is the science dealing with heredity and variation, seeking to discover laws governing similarities and differences in individuals related to descent. The factors which are transmitted were called "Genes" by Johannsen in 1909.

As mentioned above, Genetics provide explanations to the phenomenon of heredity and variation. It is therefore, not surprising that the beginning of genetics dated back to the centuries before Christ. Around 400 BC Hippocrates theorized that small representative elements of all parts of the parental body are concentrated in the semen. It is these elements, which provide the building blocks for the corresponding parts of the embryo. According to this theory characteristics acquired by parents can be transmitted to offspring.

Aristotle (384-322 BCE), one century later disproved the theory postulated by Hippocrates (about 470 BC-about 410 BC), pointing out the facts that crippled and mutilated parents do not always produce abnormal offspring.

Aristotle, in turn advanced the theory that the father's semen provides the plans according to which the amorphous blood of the mother is to be shaped into the offspring. Put differently the semen supplied the FORM while the mother's blood supplied the SUBSTANCES. It is important at this point to note that Aristotle recognized that biological inheritance consists of a transmission of information for embryonic development, and not simply a transmission of samples of body parts. The fact that the information in the seminal fluid could not be seen, it was regarded as a mystical influence. Early in the 17th century, Harvey called this influence the AURA SEMINALIS.

In the 17th and 18th centuries, new theories of inheritance were propounded, following the discoveries of the egg and the sperm. One theory was the PREFORMATION THEORY, which depending on the school of thought, stated that either the egg or the sperm contains the entire organism in a miniaturized but perfect form. In the case of men, the theory postulated a miniature human being, called a homunculus, present in the sperm. This theory was postulated by Jan Swammerdam (1637-1680). Not too surprisingly there were scientists who claimed that they saw homunculi in spermatozoa. They even drew diagrams to illustrate what they saw. One person who made an elaborate drawing of homunculus was Nicolass Hartsoeker (1656-1725). The major drawback with the pre-formation theory is the fact that is implies that one homunculus contained another, which in turn contained yet another ad infinitum.

Another theory of development was the THEORY OF EPIGENESIS. In the 18th century, Christian Wolff (1679-1754) discovers that adult structures in plants and animals arise from embryonic tissues, which do not resemble the corresponding adult structures. In other words, there is no pre-formation. But Wolff thought that mysterious vital forces were responsible for what he thought was a *de novo* origin of adult parts. Wolff's view modified in the 19th century by Karl Ernst Von Baer (1792-1876) who stated that adult parts arise as a result of a gradual transformation or differentiation of embryonic tissues into increasingly specialized tissues. Although the modified epigenetic theory is correct. It did not account for the form in which the materials to be transformed existed in the original embryonic cell, zygote.

Early in the 19th century, Pierre-Louis Maupertuis (1698-1759) postulated that minute particles from each part of the body of the parents are united in sexual reproduction such that during development particles from the male dominate in some cases; in other cases those form the female parent dominate. In one important aspect, this theory recognized the fact that an offspring receives two of each type of particle, one from each parent, but exhibits only one. However, by suggesting that the body parts contribute

particles, this theory leads to the theory of evolution advanced by Jean-Baptiste Lamarck (1744–1829). According to Lamarck's interpretation characteristics such as well-developed muscles acquired by parents in the course of their life can be transmitted to their offspring. This idea was formalized by Charles Darwin (1809-1822) as the "Provisional Hypothesis of Pangenesis." According to Darwin, exact miniature replicas, called *gemmules*, of the body parts and organs are carried in the blood stream, to be assembled in the gametes. In the zygote, the gemmules from both sexes come together and are parceled out to form the appropriate structures during development. Since a gemmule is an exact replica of a parental part it means that acquired characteristics should be inherited by the offspring. If that were so it would be easy to understand evolution. Recall that the theory of pangenesis is essentially the same theory advanced by Hippocrates in the 5th century B. C. and disproved by Aristotle.

The theory of pangenesis lends itself readily to testing, and it was tested by August Weismann (1834–1914), toward the end of the 19th century. He cut off the tails of mice for 22 generations, yet the offspring of such mince continued to show tails of normal length in every generation. The experiment can be represented schematically as follows:

Generation I: Cut off tails of the mice and mate them.

Generation II: Offspring with tails; repeat operation

Generation III:Offspring with tails; repeat operation

Generation IV: Offspring with tails; repeat operation
: :

: :

Generation XXI: Offspring with tails; repeat operation

Generation XXII: Offspring with tails.

The result therefore showed that it cannot be true that acquired characteristics can be inherited.

In spite of this proof there are people who still accept the inheritance of acquired characteristics. Perhaps the most prominent adherent in recent times was the Russian, Trofim Lysenko (1898–1976). He coerced many Russian geneticists to accept the theory, because he wielded political power.

To replace the theory of pangenesis August Weismann (1834-1914) proposed the GERMPLASM THEORY in 1885. According to this theory, multicellular organisms are made up of two types of tissues, viz the somatoplasm and the germplasm. The somatoplasm is made up of tissues which are essential for the functioning of the organism, but they do not determine what is transmitted to the offspring. In other words, changes in the somatic tissues are not transmitted. The tail of a mouse is a type of somatic tissue. On the other hand the germplasm is a tissue whose sole function is the formation of gametes. Since the gametes give rise to the offspring, changes in the germplasm may lead to changes in the offspring. Notice, however, that the theory does not indicate what the germplasm transmits.

Many biologists including Josef Gottlieb Kolreuter (1733-1806) compared the similarities and differences between plant hybrids and their parents. A hybrid is an offspring from two different parental types. Kolreuter found that although hybrids from two parental stocks are usually similar, such hybrids if fertile usually produce offspring which show considerable diversity. The results of such hybridization studies were recorded simply as qualitative observations.

Kolreuter and many others after him did not record the ratios in which the original parental characters occurred among the progeny. As we shall see later, it is therefore not surprising that the early hybridizers did not discover any underlying principles of inheritance. Thus, even though they made many important observations, the hybridizers pre-date the origin of genetics.

In many ways Genetics is a precise and somewhat mathematical science dealing with specific offspring ratios which are predictable on the basis of the known genetic constitutions of the parents. In the reverse process, the genetic constitution of the different types of offspring they produced.

Gregor Johann Mendel (1822-1884), an Austrian monk, is regarded as the father of Genetics. It is generally agreed that Mendel's success can be attributed to the fact that he was lucky in choosing the garden pea, *Pisum sativum,* for his studies. This plant, although, normally self-pollinating can be easily cross-pollinated. Mendel was also successful because he studied the inheritance of single contrasting characters (i.e. smooth versus wrinked), unlike his predecessors who studied several characters simultaneously. Equally important was the fact that Mendel counted and carefully recorded the numbers of each type of offspring from each of his crosses.

Mendel published his results in 1866 after he had reported them at a Natural Science meeting in 1865. He clearly stated the laws of inheritance which can be derived from his results. The law constitute the foundation stones of

Genetics. In spite of the fundamental nature of Mendel's discoveries and the clarity with which he stated his results and conclusions, his papers had no immediate impact on the scientific world. However, one Russian botanist, Ivan Ivanovich Schmalhausen (1884-1963) stressed the importance of Mendel's findings soon after they were published. Mendel's discovery did not have an immediate effect because the related information required for understanding his deductions were not available at the time. Thus it may be said that Mendel was "ahead of his time".

After publication of Mendel's results other relevant information about development were provided by various workers. In 1875, Oscar Hertwig (1849-1922) and later, Hermann Fol, and Eduard Strasburger described the process of fertiliztion including the fusion of the egg and the sperm nuclei. Between 1880 and 1885, Fleming, van Beneden and Strasburger described chromosomes and their division in mitosis as well as their constancy in number. Later Hertwig and Strasburger developed the theory that the nucleus contains hereditary materials. These discoveries were reflected in Weismann's theory of the Germplasm. Weismann postulated that in the process of gametogenesis, i.e. the formation of gametes there must be a reduction in half of the number of chromosomes. If that were not so, there would be a doubling of the chromosome number at each fertilization. However, as mentioned earlier the chromosome number is constant from generation to generation. The postulate by Weismann of reduction in chromosome number was later observed by Boveri and other investigators. The process involved is *meiosis.*

Three investigators unaware of Mendel's work and results independently carried out similar plant breeding experiments. During the process of writing their findings for publication, they each came across Mendel's paper and they referred to it in their rediscovery of the Mendelian laws of inheritance. Although the three people, Correns, Hugo de Vries and Tschermak are generally regarded as the rediscoverers, some scientists (Stern & Sherwood, 1966) do not think that Tschermak's work on its own could have yielded the laws of inheritance. Hence, there should be only two rediscoverers.

Although the laws of inheritance were first demonstrated with plants, Bateson in 1902 showed that the laws apply equally to animals.

From this brief history of Genetics one would hope that you would derive and appreciate the tortuous steps leading to the establishment of various laws in science.

4.0 CONCLUSION

The history of genetics has been discussed in the Unit so as to let you appreciate the toils and labour of those who had worked in the field before. You could also develop your own ideas in Genetics and be reckoned with as one of the greats.

5.0 SUMMARY

Genetics is a vital aspect of everyday life and of biology and biologists, and even non-biologists, should be fully exposed to it. Every father wants to be sure that the baby brought from the hospital is his own, and farmers want improved farm products – both animals and plants.

These aspects are being further improved by genetic engineering which results in better agricultural products. Increased knowledge of heredity through genetics means increased power of control over living things.

Genetics is the science dealing with heredity and variation and is governed by laws. The history of genetics dated even before Christ. Hippocrates, Aristotle Maupertuis, Lamark, Mendel and Charles Darwin are some of the eminent scientists who have contributed to the knowledge of Genetics.

Genetics is a precise and somewhat mathematical science dealing with specific offspring ratios which are predictable on the basis of the known genetic constitutions of the parents. It should not be studied like literature but examples should be worked out so as to be acquainted with the mathematical rules guiding heredity.

Self Assessment Questions

1) Discuss the beliefs of Hippocrates with regards to inheritance
2) What was Aristotle's theory that shattered Hippocrate's theory on heredity

Answers to Self Assessment Questions

1) Refer to Section 3.1

2) Refer to Section 3.1

6.0 TUTOR MARKED ASSIGNMENT

1) Discuss the current theories regarding heredity.

7.0 REFERENCES

Williams, G. O. (2001). BIY 302 – Genetics – I. Distance Learning Institute, University of Lagos.

Stern, C., and E. R. Sherwood. 1966. *The Origin of Genetics*. W. H. Freeman and Company.

UNIT 2 CHROMOSOME THEORY OF INHERITANCE

1.0 INTRODUCTION

Some of the materials covered under this topic is repetition of what we covered as part of the "History of Genetics." However, this is necessary in order to reduce the problem of recall at such an early stage.

The chromosomal theory of inheritance is the idea that genes, the units of heredity, are physical in nature and are found in the chromosomes. The theory arose at the turn of the twentieth century, and became one of the cornerstones of the modern understanding of genetics.

2.0 OBJECTIVES

The nucleus controls the activity of the cell. It is therefore, reasonable to assume that the genes which constitute the ultimate basis of what a cell is must also be in the nucleus, specifically, on the chromosomes. You should be able to explain:

1) The parallels between the behaviour of genes and chromosomes, which led to the formation of the chromosome theory of inheritance;
2) The essential features of the chromosome theory;
3) The evidence in support of the theory.

3.0 MAIN CONTENT

3.1 Deduction of Chromosome Theory of Inheritance

Hertwiig working with sea urchins and some other investigators working with other organisms, discovered that two equal-sized nuclei, one from the sperm and the other from the egg fuse at fertilization. This is in spite of the fact that the egg is much larger than the sperm. In other, words the difference is in the amount of cytoplasm not the nuclear content. Based partly on this fact and the results of crossing (mating) different types, Hertvig, and Strasburger also in 1885 advanced the theory that the cell nucleus must contain the hereditary materials.

Earlier in 1883, Eduoard van Beneden (1846-1910) had discovered in Parascaris equorum (formerly Ascaris megalocephala – these names seems to be still preferred) that the fertilized egg of this nematode contains only four chromosomes. Furthermore, at the time of fertilization, the sperm and the egg nuclei contain two chromosomes each. In the light of this fact one could be more specific about the equal nuclear contribution by both the male and female parent to the zygote. The components of the nucleus that are visibly distributed during cell division are the chromosomes. It is therefore, quite logical to conclude that because the parents contribute equal numbers of chromosomes, the chromosomes must be the carriers of hereditary material.

Reasoning without the benefit of knowledge of van Beneden's discovery, Wilhelm Roux (1850-1924), also in 1883, in a purely hypothetical discussion of the significance of the mitotic process strongly implied (did not say so categorically) that the chromosomes are the bearers of hereditary materials. Roux's approach was teleological i.e. he started from the standpoint that there must be a reason for the elaborate mitotic process. (For example, it is teleological to say that we developed eyes because we needed to see). The question in essence was "why should the division of a simple structure like nucleus be so complicated?'

According to Roux, if one assumed that there are in the nucleus, very many submicroscopic units which control the life processes of cell, then it would be understandable that great care should be taken in dividing the nuclear content.

On the other hand, mere constriction of the cell would be sufficient for dividing the cytoplasm. Roux reasoned that a suitable method for ensuring an identical distribution of the very many submicroscopic units into each daughter cell would be for each unit to be divided first, and then the sister units would be separated. The tasks of division and separation would however be greatly facilitated if the units were arranged like beads on a string. There would be several such assemblies, carrying different units, in the cell. During cell division each "string of beads" would then split longitudinally, and the halves would move into separate daughter cells. Roux

then went on to say that because the mitotic process is so elaborate it must serve a purpose in the organism. The purpose is the equal distribution of the nuclear material important for the physiological and developmental processes of the cell. We know today that Roux's "units" are the *genes,* the hereditary material, and they are carried on the chromosomes.

In formulating his theory of the Germplasm in 1885, Weismann specifically said that the chromosomes function as the carriers of hereditary units, but the chromosome theory was still to be clearly stated.

After the rediscovery of the Mendelian Laws in 1900, it did not take long before the genes and the chromosomes were identified. The fact that the observable type of transmission of chromosomes (i.e. the cytological evidence) corresponds to the deduced type of transmission of genes (the Mendelian Laws of inheritance) was pointed out independently by Sutton and by Boveri in 1903. Their conclusions constitute the Chromosomes Theory of Inheritance. The main points of the theory are:

1. That genes are located on chromosomes such that one member of a pair of genes is on one chromosome and the other member is on a partner chromosome, i.e. the homologous chromosome with which it synapses in meiosis.

2. Different pairs of genes are located on different chromosomes. This is not to say that there is only one gene on each chromosomes. Rather, the point is that non-homologous chromosomes carry different genes. There is more than one gene on each chromosome.

The parallels between the genetic and cytological facts which form the basis for the theory are:

i) In diploid organisms, genes occur in pairs and so do chromosomes.

ii) Members of a gene pair separate at the time of gamete formation so that each gamete receives only one member of the pair. The same is true for chromosomes (cf. Anaphase-I).

iii) The members of different gene pairs recombine at random at the time of segregation during gamete formation.

Sutton and Boveri did not have corresponding evidence for chromosomes but they also did not have evidence to the contrary. Recall the fact that the metaphase-I orientation of one bivalent did not influence the orientation of

another vivalent. This piece of evidence was provided later and it confirmed the assumption that No. (iii) was also applicable to chromosomes.

The most convincing proof of the theory that genes are on chromosomes was provided by Theodor Boveri in his experiments with the sea urchin. Boveri worked with a species in which 2n = 36. In other words at fertilization each gamete contributes a haploid number of chromosomes of n = 18. Normally, only one sperm fertilizes an egg but there are rare exceptions in which more than one sperm fertilizes the egg. This condition is called polyspermy. It is called dispermy when only two sperm are involved. Polyspermic embryos die early in development. We shall consider the simplest case, i.e. the dispermic embryos. Boveri found that there was great viariability in the time of death and also in the type of organ whose abnormal development led to death.

The sea urchin embryo can be divided into four quadrants, each of which arose from one of the first four cleavage blastomeres cells. Boveri observed that the four quadrants often develop differently, thus one quadrant may be normal and the other three abnormal but in different ways and to different degrees. This variability in development of different parts of the same embryo was a very important observation by Boveri. How does one acccount for it?

At fertilization in the sea urchin the sperm contributes a centriole which divides to form the two poles i.e. the asters of the mitotic spindle which is formed as the asters move apart. Each of the 18 chromosomes contributed by each gamete in normal fertilization becomes duplicated and comes to lie at the metaphase plate (equatorial plate). This is normal mitosis. The zygote contains 36 chromosomes and two blastomeres are formed as a result of the first cleavage. Following the second cleavage a total of four blastomeres gives rise to cells which will form one quadrant of the embryo.

When there is dispermy, two centrioles are introduced into the egg. Each divides giving rise to two asters. The effect of dispermy is the production of four asters in the zygote. The four asters are arranged like the corners of a square. When such a zygote divides, four blastomeres are formed at once in the first division. As mentioned earlier, each blastomere gives rise to a quadrant in the embryo.

In order to answer the question we posed earlier, we have to try to answer another question, namely, “How do the chromosomes behave in a quadripolar division?’ The zygote in question is made up of contributions from two sperm and the egg. The nucleus of each of these gametes contains 18 chromosomes, therefore, there will be 54 chromosomes. This is a 3n number of chromosomes and it is said to be a triploid number. The chromosomes are

duplicated as in normal mitosis. However, when they move on to the equatorial plates of the spindle, they are distributed at random on the spindles. The consequence of this random distribution is that each of the four resulting blastomeres may contain different types of numbers of chromosomes.

Boveri was able to show that the abnormal development of a dispermic embryo was the result of the erratic chromosome distribution rather than dispermy per se. In other words, dispermy does not invariably lead to abnormal development. Bovery analyzed his results as follows: He found that the size of a nucleus is dependent on the number of chromosomes present in it. Therefore, he compared the sizes of the nuclei with the degree of developmental success (i.e. the degree of normal development) in each quadrant of an embryo as well as with degree of developmental success in quadrants having similar-sized nuclei in other embryo.

Table 2.1 Comparison of Development in Two Dispermic Embryos

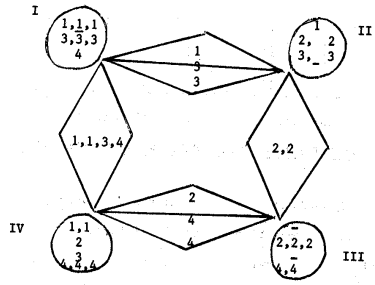
	EMBRYO A				**EMBRYO B**			
Nuclear Size	**QUADRANTS**				**QUADRANTS**			
	I	II	III	IV	I	II	III	IV
1		+					111	
2	1111		+			11		
3								+
4				11	+			

1111 = Highest degree of developmental success.

From Table 2.1, one can see that similar-sized nuclei may result in different abnormalities, hence the different degrees of developmental success. Boveri therefore concluded that the variability in development is a reflection of qualitative rather than quantitative differences between nuclei in different quadrants. For instance if development were dependent on nuclear size only, quadrants I and III having similar-sized nuclei should have had similar degrees of developmental success.

Let us now look at a hypothetical example using only four instead 18 types of chromosomes. In this example we shall also assume that in order to have normal development, each type of chromosome must be represented at least once. Since n = 4, the dispermic zygote would contain 12 chromosomes.

Recall that the distribution of the chromosomes on the spindles is a random process. The diagram below is therefore only one of many possible ways in which the 12 chromosomes might be distributed on the four spindles. In this arrangement, only one quadrant develops normally.



Note: 1 - 4 = Chromosome types

1 - IV = Blastomeres that will form quadrants

I & IV = Have equal-sized nuclei. Some for II and III.

Only IV is normal since all 4 types of chromosomes are present.

Since Boveri was aware that the chromosomes vary in shape and size he concluded that there are qualitative differences between chromosomes. Specific abnormalities would therefore, arise when particular chromosomes were missing. This would be the case only if different chromosomes carried different genes.

As a further test of his hypothesis about qualitative differences between chromosomes, Boveri found the expected frequency with which any quadrant might lack all three of any one of the 18 types of chromosomes. He found that the expected frequency compared favourably with the observed frequency of abnormally developing quadrants.

One of the main points of the chromosome theory is that different chromosomes carry different genes. It is pertinent under the circumstances to ask whether the chromosomes are stable structures or whether they disintegrate during interphase and are reassembled during prophase. If that were so it would also be probable that genes would "move" from one chromosome to possibly a non-homologous chromosome. There would also be the possibility that the genes are not normally carried on chromosomes. The fact that chromosomes are stable structures which maintain their integrity even during interphase, was established by Boveri using the

fertilized eggs of *Parascaris equorum.* In this nematode the arms of the chromosomes are not completely retracted at the end of telophase to give a spherical nucleus. Boveri found that at the end of telophase, the two daughter nuclei are mirror images of each other as shown in Fig. 2.2.

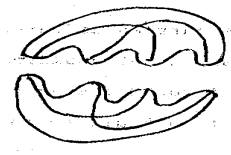


Fig. 2.1: Mitotic Daughter Nuclei of *P. Equorum* (2n = 2)

These nuclei retain their shape until the next prophase when the chromosomes reappear. The chromosomes reappear with their tips still in the projectins from the nucleus. It is therefore, reasonable to conclude that the chromosomes did not lose their identity from generation to generation.

3.2 Other Evidence in Support of the chromosome Theory

In our consideration of cell division, we found that the chromosomes in a cell could be considered as sets, such that a diploid cell would have two sets of chromosomes. The general terms used to describe the number of whole sets of chromosomes is ""ploidy". Continuing on the same theme, there are *euploid aneuploidy* conditions. The term euploidy is used to describe variations in the numbers of whole sets of chromosomes haploid = n; diploid = 2n; traploid = 3n. These variations which involve whole sets of chromosomes generally result in normal development. Aneuploidy on the other hand refers to variations in the numbers of individual chromosomes. Such variations give unbalanced sets of chromosomes.

From the discussion of Boveri's sea urchin experiments above, it is obvious that aneuploidy provides a lot of information in support of the theory that genes are located on chromosomes. The same is true for the assertion that different chromosomes carry different genes. In this section then we shall be considering mainly evidence from aneuploid conditions.

In discussions of chromosomes one often talks of karyotype and idiogram. A karyotype is an individual's chromosomes complement in terms of number and size of chromosomes as well as the location of the centromere in the different chromosomes. The idiogram on the other hand is a diagrammatic representation of an individual's karyotype with the different chromosomes arranged in order of decreasing size.

In the plant, *Datura,* the haploid number is 12. Occasionally unusual plants may arise. These unusual plants contain 25 instead of the normal 24 chromosomes. These plants look different from the normal diploid plant.

Twelve different types each having 25 chromosomes can be identified in terms of the seed capsule. It was found that each of the twelve variants possessed a different one of the twelve types of chromosomes. In other words, in each variant, a given chromosome was present in triplicate. This aneuploid condition in which three instead of two of a given chromosome are present is described as a trisomy. Thus, if the different chromosomes are numbered 1 – 12, an individual with Trisomy – 1 (or Triplo – 1) has three of chromosomes – 1 present. Note that as we said earlier, these trisomic plants have only one chromosomes extra, hence the total number is 25 or 24 + 1 which can be stated as 2n + 1; with the exception of the particular chromosome under consideration all the other chrommosomes are in pairs. With respect to the example of Datura under consideration, the aneuplooid effect due to Trisomy – 2 and so on. Because the effect of each trisomy is distinguishable from all the others, it is logical to conclude that different chromosomes carry different genes.

Normally in mitosis, the two daughter chromosomes move to opposite poles during anaphase. Very rarely, however, mistakes do occur and both daughter chromosomes migrate to the same pole. This situation is described as non-disjunction. Non-disjunction can also occur in both meiosis –I and meiosis-II. In the former case, homologous chromosomes would be involved while the latter would be similar to mitotic non-disjunction. Non-disjunction will give rise to aneuploid conditions.

Trisomic conditions also occur in man. One example is Trisomy – 21. This chromosome imbalance produces a condition known as Down's syndrome. The term syndrome is used when a number of symptoms characterise an ailment. This particular case was first described by Down. In man, the diploid number is 46 but those affected with Down's syndrome have 47 chromosomes, the extra being chromosome – 21. Amongst other symptoms, affected individuals are mentally retarded.

Where it has been studied (e.g. U.S.A.) the occurrence of Trisomy – 21 (production of an egg with 24 chromosomes) has been found to be associated with the age of the mother. The proof of the effect of maternal age is that in general population, the occurrence of Trisomy – 21 is one in 600 live births.

However, when different age groups are considered separately, the frequency for mothers about 20 years old is one in 3,000, but for mothers around 45 years, the frequency of occurrence rises to one in 40 live births. The rise in

frequency starts when the woman is about 35 years. A corresponding study keeping the female age fairly constant but varying the father's age does not show any difference between age groups. The reason for the association with the age of the mother is not known.

Non-disjunction is not the only cause of Trisomy – 21. Although it was said earlier that every chromosome maintain its integrity (with the exception of reciprocal exchange between homologues during crossing-over) it sometimes happens that a portion of one chromosome is transferred to another chromosome, usually or non-homologue. This phenomenon is known as trans-location. Chromosome – 21 is a very small chromosome while 14 is fairly large. In some very rare individuals the bulk of 21 has been translocated to 14 to give a chromosome designated 14.21.

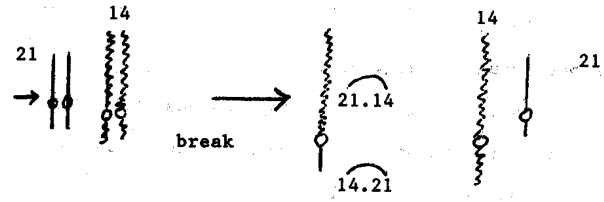


Figure 2.2: Translocations Involving Human Chromosomes 14 and 21

The translocation occurs as shown above in a diploid individual. The small chromosome 21.14 is lost without any adverse effect and so the person has 45 chromosomes, but is normal because virtually all of 14 and 21 are combined in the 14.21 chromosome. If the egg produced carries both the 14.21 and the free 21, it would have two doses instead of one of 21. Fertilisation by a normal sperm would therefore, produce an individual with 46 chromosomes but with three effective doses of chromosome – 21. Notice that the fact that particular effects are associated with specific trisomic conditions and also, the fact that the translocated 14.21 can be transmitted unchanged are proof that chromosomes retain their integrity.

If non-disjunction can produce a gamete containing two of one type of chromosome, the reverse situation is also possible. There are cases known in which as organism carries only one instead of two of a given chromosome; such individuals are said to be monosomic for that chromosome. Monosomy – 21 is not known in man, so the condition is assumed to be non-viable. The same is true for monosomy – 14. These cases illustrate the point that in some organisms, unlike the sea urchin studied by Boveri, the mere presence of some genes is not a sufficient condition for normal development, rather the genes must be present in a balanced dose. In *Drosophila melanogaster*, a fruit fly, the haplo – IV (monosomy – IV) condition survives although the fines have reduced viability and fertility. Some other aneuploid conditions are:

Tetrasomy = 2n + 2 i..e. two extra of a given chromosome.
Double Trisomy = 2n + 1 + 1 i.e. one extra of each of two different chromosomes.

Nullisomy = 2n – 2 i.e. a given chromosome has both members absent.

The significance of chromosomes as well as dosage of chromosomes with respect to characteristics exhibited by organisms extends to sex determination as we shall see later. It is sufficient to mention one extreme example here, namely, the honey –bee in which male are haploid while females are diploid.

When an organism has more than two whole sets of chromosomes i.e. 3n or more such as individual is described as being polyploid. The 3n individual is a triploid individual; tetraploid = 4n and pentaploid = 5n. Polyploidy is rather common in plants but it is rare and often easily recognizable because with certain limits they are larger than their diploid counterparts.

4.0 CONCLUSION

Rather than try to summarize the examples considered, it is sufficient to say that the chromosome theory of inheritance states that the genes are an integral part of the chromosomes. The basis for this generalization is the fact that particular deviations from say the normal diploid chromosome number, whether euploid or aneuploid have specific detectable effects. These specific effects are an indication that chromosomes carry genes and more specifically that different chromosomes carry different groups of genes.

5.0 SUMMARY

We have learnt that genes are borne on chromosomes, and occur in pairs in diploid organisms. The gene pairs separate at the time of gamete formation so that each gamete receives only one member of the pair. Pairing is restored when members of different gene pairs recombine at random. The randomness of recombination is the basis of genetics.

Self Assessment Questions

1) Explain the following terms:
   a) Haploid b) Diploid c) Polyploidy
2) Describe what is meant by non-disjunctions
3) Explain trisomy in man

Answers to self Assessment Questions

1. a) Haploid: Set of chromosomes (impaired) that occurs in sex cells; denoted by (n)
   b) Diploid: Set of Chromosomes (paired) that are found in somatic
   cells; denoted by (2n)
   c) Polyploidy: Set of chromosomes more than 2n i.e. 3n or more; more common in plants than in animals. Polyploid individuals are often easily recognizable because with certain limits they are larger than their diploid counterparts.
2. Non-disjunction is when in mitosis the two daughter chromosomes move to some poles during anaphase.
3. Trisomy in man usually involves chromosome 21, which instead of being in pairs occurs in triplet. This chromosome imbalance produces a condition known as Down's Syndrome.

6.0 TUTOR MARKED ASSIGNMENT

1) Explain the conditions that give out the chromosomes (DNA) as the genetic materials

7.0 REFERENCES

Williams, G. o. 2001: biy 302 – Gnetics – 1 Module. Distance Learning Institute, University of Lagos.

UNIT 3 PRINCIPLES OF SEGREGATION (MENDEL'S FIRST LAW OF INHERITANCE)

1.0. INTRODUCTION

You will recall that Mendel succeeded where many before and after him had failed. Mendel succeeded for two major reasons.

1. He analyzed his results both in a qualitative as well as in a quantitative way.

2. In making his initial crosses, he chose pairs of clearly contrasting characters for which each of the plants he started with words true/pure breeding. The term true breeding is used to describe cases in which a cross between two individuals possessing the same character yields only progeny which are identical with one another and with the parents with respect to that character. It is also applicable to cases of self-fertilization yielding the same results.

2.0 Objectives

In this and subsequent units you are not expected to memorise specific examples, instead, you should understand how the principles involved can be derived from the examples used. This unit is supposed to inculcate an understanding of:

1. Some of the terms used in Genetics. In this and other units new terms are used. They are an essential part of the vocabulary of Genetics. You have to learn them whenever they occur.

2. What is involved when a cross is written.

3. The steps, types of evidence and types of deductions which led to Mendel's formulation of the first law of inheritance.

4. To recognize the evidence which indicates monohybrid inheritance.

5. To explain the bases for the various phenotypic and genotypic ratios.

6. To make the necessary deductions of phenotype from genotype and vice-versa, as well as derive offspring from parents and vice-versa.

7. To state and explain the first law in your own words.

3.0 MAIN CONTENT

3.1 Mendel's first Law of Inheritance

Mendel made many crosses, and for each cross he used a pair of characters which were such that a plant can only exhibit one but not both characters. A cross was made by transferring pollen grains from the anthers of one plant to the stigma of another plant or of the same plant for cross-pollination and self-pollination respectively.

The plants used for the initial cross constitute the parental or P-generation. Their progeny constitute the First Filial generation, abbreviated as F_1 – generation. The progeny of the F_1 as a result of either crossing two F_1 or of self pollinating an F_1 constitute the F_2 or, second filial generation.

In one experiment, Mendel crossed parents which were true breeding for yellow seeds with parents which were true breeding for green seeds. This cross was done in two ways:

1. Yellow (ovum) x green (pollen) $\longrightarrow$ Yellow F_1

2. Green (ovum) x yellow (pollen) $\longrightarrow$ Yellow F_1

In cross-1, the yellow parent was the female parent and in cross-2 the role were reversed. Cross-2 is referred to as a reciprocal cross of cross-1 or vice-versa. In other words the characters used in a reciprocal cross are exactly the same at the initial

cross; the difference is merely a reversal of male and female roles. The F_1 progeny of the two crosses are indistinguishable from each other and from the yellow parent. In both crosses also all the F_1 were yellow.

The reciprocal cross provides a very important piece of information. The fact that the progeny of the two crosses are identical indicates that the male and female contributions to the progeny are equal. This is in spite of the fact that the pollen grain contributes virtually no cytoplasm to the offspring. Mendel deduced that fact of equal hereditary contribution from his results and as we saw earlier, it was only much later that Hertwig and others provided cytological evidence that the nuclear contributions are indeed equal. Mendel's conclusions for reciprocal crosses are also applicable to animals. The result obtained from the reciprocal cross is therefore, evidence in support of the chromosomes theory of inheritance.

In the next step of the experiment, Mendel planted the yellow F_1 seeds and self-pollinated (selfed) them when they flowered. This step of the experiment is the same as crossing two F_1 yellow. The yellow F_1 seeds gave different results from crosses between two parental yellow types. While the parental yellows were pure breeding the F_1 yellow were not. Yellow F_1 progeny from reciprocal crosses gave identical F_2, confirming the initial conclusion. The F_2 progeny consisted of yellow and green seeds. When Mendel pooled the results of the F_1 crosses he got 6,022 yellow and 2,001 green F2. Further analysis gave a ratio of 3.01 yellow: 1 green among the F_2.

Using the same scheme Mendel tested a number of characters. His results for some crosses are shown below:

Note that it is no longer necessary to specify the sex of each parental type. You are not expected to memorize this table. It is simply to give credence to the conclusions drawn.

Table 3.1: Some results of Mendel's experiments on Sweet Pea

S/No	Parental Characters	F_1	F_2	Ratios
1	Yellow x Green Seed	All yellow	6022 yellow; 2001 green	3.01;1
2	Round x wrinkled	All round	5474 round; 1850 wrinkled	2.96:1
3.	Green x yellow Pods	All green	428, green; 152 yellow	2.82:1
4.	Axial x terminal flowers	All axial	651 axial: 207 terminal	3.14:1

Although only four crosses are shown in the table, it is obvious that even though a particular character is not visible in the F_1 it is not lost nor is it modified i.e. it does not blend with the other character. The fact that it remains unchanged can be shown by comparing the F_2 green with the parental green; they are indistinguishable in other words the hereditary unit responsible for the green colour was merely latent in the F_1. Mendel called the hereditary units "factors". Wilhelm Ludvig Johannsen (1857-1927) called them "genes" later.

Also in the table we find that in each cross all the F_1 resemble one parent and there is a constant ratio of approximately 3:1 of the two parental characters. In order to account for these results Mendel made assumptions and explained his results along the following lines.

He assumed that each of the true breeding parents carries two identical hereditary factors which are responsible for their particular character. For instance, in the first cross the yellow parent would carry two identical factors making for yellowness, and the same would be true for the green parent. These factors can be represented with symbols. We can, therefore, represent the two factors in the yellow parent as YY. The two factors in the green parent can be represented as YY. When each parent produces gametes, the pairs of factors separate so that only one factor enters a gamete (compare Mendel's assumption which the separation of homologous chromosomes in anaphase-I and also with August Weismann's theory of reduction). As a result of the separation, the gametes from the yellow parent contain only Y factor and those from the green parent contains only one y factor also. Each parent produces only one type of gamete but there is no way to distinguish between the two Ys or the two ys in the green parent.

When the gametes from the two parents fuse at fertilization, a zygote i.e. the F_1 is formed containing two factors, one Y and one y. Hence the F_1 may be designated Yy. From the table, the observed character exhibited by the F_1 is yellow, which corresponds to the Y-factor inherited from the yellow parent. Since a y-factor was also inherited from the green parent but not exhibited, the y-factor is latent in the F_1.

The yellow character is said to be *dominant* over the green character because when the two types of factors responsible for both characters are present in the same individual only the yellow character is exhibited. In the same way the Y-factor is said to be dominant over the y-factor. The green character is said to be ***recessive*** to the yellow character. The same terminology is used to describe the relationship of the y-factor to the Y-factor.

The factor for the yellow trait is designated Y because yellow is dominant and the factor for green is designated y because green is recessive. The same letters used as the symbol for both the yellow and green characters because they are alternate forms of the same character. In other words a seed is either yellow or green but not both. Although we have been using gene (hereditary factor) and character interchangeably, the character is the effect produced by the gene. The symbols Y and y are therefore alternate forms of the same gene. They are called *alleles*. Alleles are modifications of the same gene, hence variations of the same symbol are used to designate them.

We assumed earlier that each parent carried a pair of alleles for the characters in question, hence we would use symbols to represent the genetic constitution of each parent and also of the offspring. The term for the genetic constitution is *genotype*. For example the genotype of the yellow parent is YY. The effect produced by the genotype (which we had called character) is called the *phenotype*. Before continuing with our discussion of Mendel's experiment, it is important to draw your attention to the fact that identical phenotypes do not necessarily indicate identical genotypes. In the example under consideration the phenotype of the F_1 are indistinguishable from that of the yellow parent yet according to our explanation so far the yellow parent is YY while the yellow F_1 are Yy.

According to Mendel's assumption, given the parental genotype and the types of gametes produced, the F_1 are Yy. What type of gametes would the F1 produce? We had concluded that because the F2 green was not different from the green in the P-generation, the contribution of the green parent to the F1 must have retained its integrity and merely remained latent. In effect therefore, we also have to assume that the y allele remained unchanged in the F1. In spite of the difference in genotype there is no reason to assume that the processes leading to gamete formation in the F1 would be different. Again the two alleles must separate so that only one, Y or y, enters each gamete. It is most important that you recognize the fact that only one allele would be in any given gamete. When both alleles were identical as in the parental generation, each parent produced only one type of gamete. But you will

recall that at the end of meiosis-I each daughter cell contains one member of a homologous pair of chromosomes. Genes are on chromosomes so the same situation applies. More specifically then, 50% of the gamete formed by each F1 would contain the Y-allele and the other 50% would contain the y-allele.

Fertilization i.e. gametic fusion according to Mendel is a random process, i.e. the Y-bearing pollen does not preferentially fertilized either the Y-bearing or y-bearing ovule. Both types of fusion are equally frequent because there are equal amounts of the two types of gametes. We can easily represent random fertilization by using the Punnett squares (designed by Reginald C. Punnett, 1875-1967). All the four boxes are equally possible in this case, and together constitute a unit.

Fig. 3.2 The Punnett Square

	POLLEN		
		Y	Y
EGG	Y	YY	Yy
	y	Yy Yellow	Yy Green

The genotype in each box is produced by the fusion of the corresponding gametes. The contents of the boxes represent the F_2 and they are equally visible. Mendel's actual results given earlier in Table 3.1 show that the ration of yellow: green in the F_2 was 3:1. The Punnett squares show the same type of ratio, and in addition, how the ratio was arrived at. It shows the genotypes contained in the two phenotypic groups.

The results produced by Mendel's assumptions and shown in the Punnett square allow the following predictions to be made:

1. The green F_2 will be pure breeding if they are either self fed or crossed to the pure-breeding green of the P-generation because they have the same genotype. (yy).

2. One-third of the yellow F_2 i.e. ¼ of all the F_2 will also be pure breeding for the yellow phenotype since they are YY in genotype.

3. Two-third of the yellow F_2 i.e. 2/4 of all the F_2 will yield the same results as the F_1 if they are self fed. They will give yellow and green F_3 in a ratio of 3:1.

You can convince yourself with respect to the fractions which are expressed in quarters by indicating the fractions of the gametic types i.e. ½ Y and ½ y. A fusion

event in the Punnett square is "like" an algebraic multiplication such that Y x Y YY (***NOT*** Y^2, that is why an ***arrow*** is used instead of =). If therefore you now include the fraction of the gametic type we shall have ½ Y x ½ Y ¼ YY.

Mendel tested these predictions and obtained the expected results, thus confirming the correctness of these assumptions – there are a pair of factors (alleles); there is segregation and there are dominant and recessive alleles.

We can re-summarise these and other facts as follows:

A diploid organism contains pairs of homologous chromosomes such that the numbers of each homologous pair separate into two cells during meiosis. A gene may occur as different forms of the same functional unit; the different forms are called alleles. A diploid organism contains only two alleles for any give phenotype, and the alleles may be identical as in YY or different as in Yy. Because there are only two of any alleles and because there is only a pair of any given chromosome type, we can say that one allele is on one chromosome and the other alleles is on its homologous partner. Recall the parallel behaviour of the genes and the chromosomes.

We can summarise Mendel's experiments with seed colour as shown below:

P Yellow x green

YY (cross) yy

Gametes (Y) x (y)

F1 Yy

x x = selfing

Gametes (Y), (y) (Y), (y)

F2 ¼ Y Y; 2/4 : ¼ yy

¾ yellow ¼ green

3 yellow : 1 green

Mendel derived the First law of inheritance, also called the Principle of segregation from these results. Mendel's First law of inheritance states that:

"In the formation of gametes, the members of a gene pair i.e. a pair of alleles, segregate from each other so that only one or the other member is contained in each gamete."

Although the law has been formally stated, it is not intended that you should memorise it. Rather, you should understand it and be able to apply it. As you can see, it deals only with gamete formation. If you cannot correctly derive the gametes then the offspring you derive would not be viable!

3.2 Some Definitions

3.2.1 Locus

This is the specific point on a chromosome, occupied by a gene. Thus alleles occupy the same locus on homologous chromosomes. We had said earlier, that genes do not normally move from chromosome to chromosome. The locus of a gene is constant. The only aspect that varies is the allele that may be at that locus on a particular chromosome.

3.2.2 Homozygous/Heterozygous

A genotype is said to be homozygous when both alleles are identical e.g. YY or yy, and it is heterozygous when the alleles are different e.g. Yy. Homozygous organisms are called homozygotes. By the same token heterozygotes are heterozygous individuals. From the definitions and the discussions above homozygotes are pure breeding types if self fed or crossed to similar homozygotes.

3.2.3 Backcross

This is a cross between an offspring and one of its parents an individual that is genotypically identical with one parental type.

3.2.4 Testcross

This is a cross between an individual whose genotype is not known and another individual who is known to be homozygous recessive for the trait in question. The testcross by its design makes it possible to determine the unknown genotype. For example we know that in the garden pea, axial flowers are dominant over terminal flowers. Suppose a plant had axial flowers and we had to determine the genotype of the plant. We would make a testcross.

i.e. Axial Flowers x terminal

7 x aa

The genotype which we give the plant with axial flowers will be determined by the types of progeny we get. The critical aspect of the test-cross however lies in the fact that the homozygous recessive parent (terminal flowers in our example) produces only one type of gamete and the gamete contains only recessive alleles. Because the allele is recessive, any allele from the other parent which it fuses with can be easily determined. Suppose our test-cross yielded two types of offspring as shown below:

Test cross: Anxial flowers x terminal

Genotype: 7 x aa

Gamete: (a)

Test cross: Anxial flowers x terminal

Genotype: 7 x aa

Gamete: (a)

F_1 Phenotype: Axial : terminal

Ratio: 1 : 1

Partial genotype -a -a

Since the recessive parent produces only one type of gamete half of the F_1 genotype is known, as indicated. In order to have a terminal phenotype, a recessive trait, there must be homozygosity for the recessive allele. Hence, that genotype is aa, and the axial parent must have contained "a" as part of its genotype. The axial F_1 also has "a" as part of its genotype but the phenotype is a dominant one, thus requiring that at least a dominant "A" allele be present. Such an allele could only have been contributed by the parent with unknown genotype which also has an axial phenotype.
Therefore, the genotype of the axial parent is Aa and the cross is

Axial x terminal

Aa			**x**		**aa**
Gametes:	**½**	**A**	**:**	**½**	**a**	**(a)**
		Axial			**Terminal**
		1			**1**
		½ Aa			**½ aa**

3.2.5 Phenotypic Ratio

This is the ratio of the different phenotypes in the progeny of a cross, based on the fraction of the different phenotypes. For instance in the testcross above, the phenotypic ratio is 1 : 1, but among the F_2 in Mendel's experiment the ratio was 3 yellow: 1 green.

3.2.6 Genotypic Ratio

This is the ratio of the different genotypes among the progeny of a cross. The genotypic ratio may or may not be identical with the phenotypic ratio. It depends on the parental genotypes.

3.2.7 Monohybrid Cross

This is a cross in which the parents differ with respect to only one trait which is controlled by only one gene (and its alleles). The example of Mendel's cross is a monohybrid cross. One pure breeding parent was yellow and the other green, but the trait was seed colour controlled by the one gene with the alleles Y and y. The F_1 combining the traits and alleles from both parents is a monohybrid. It is a hybrid with respect to one locus.

3.2.8 Genetic Symbols

As we found earlier symbols are used to designate the game responsible of a given trait. The same basic symbol may be modified to designate the alleles of that gene. We therefore use symbols to represent the genotypes of an individual.

The choice of symbols is somewhat arbitrary so you will sometimes find different symbols for the same gene in different books. There are however some common patterns which we shall adopt, except when convention demands something different.

Usually a single letter chosen from one of the phenotypes is used and the capital form represents the dominant allele while the lower case represents the recessive. It is often best to state which phenotype corresponds to a symbol, e.g. yellow = Y and green = y. Equally important is the need to ensure that the same letter is used for alleles since that is the only way of making it unambiguous that the phenotypes belong to the same gene. You would be correct if you use yellow = G and green = g, but I would mark you wrong if for the ***alternate*** phenotypes of yellow and green you wrote the allelic symbols as "Y" and "g" respectively. I would take it that these are alleles to two different genes occupying two different loci, so that a genotype such as Yg would not be taken as heterogenous. It would be taken as incomplete, since as we shall see later it represents a gamete carrying alleles from two loci.

One deviation from the above pattern is found in *Drosohila* genetics. By convention the wild type alleles (i.e. the most common type found in the wild) are written with a "+" as superscript e.g. "w^+." The less common allele is written as "w". The symbol implies neither dominance nor recessiveness. This aspect has to be stated.

4.0 CONCLUSION

We have covered very specific information as well as principles which apply equally to plants and animals. You are not expected to commit to memory whether a particular trait is dominant or recessive. On the basis of the facts you can easily determine that if you know the principles. In the example, yellow is said to be dominant because in the F_1 from a cross between pure breeding yellow and green was also passed on to the $_{F1}$.

I expect you to be able to give the genotypic and phenotypic ratio from a cross and also to be able to derive the types of offspring a cross between two parental types will produce as well as the converse i.e. to be able to derive the probable parental genotype given sufficient information about the offspring.

You would almost certainly have a lot of difficulty if you did not try to understand how results are obtained, you will never be able to memorise all the different situations. Yet you can quite easily master the principles for deriving gametes, hence offspring and parental genotypes. "F_1" or "F_2" do not designate any specific genotypes or phenotypes, nor does "backcross" imply a specific genotype. Yet a testcross must definitely include a homogenous recessive parent. You should memorise definitions but you should equally know how and when to apply them.

5. SUMMARY

Nuclear contribution by both gametes that form the zygote is equal, although the ovum has more cytoplasm than the sperm. Genes are the hereditary factors found on the chromosome and occur in pairs in diploid organisms. The predominant gene of the pair, where they are different i.e. heterozygous, is said to be dominant while the latent one is said to be recessive. Both the dominant and recessive genes are called alleles with the dominant being represented with capital letter (e.g. Y) and the recessive by small letter (e.g. y)

Self Assessment Question

1. Define the terms
   a) alleles b) genotype c) phenotype d) locus

2. Define the following terms with examples
   a) dominant b) recessive c) heterozygous d) homozygous

6.0 TUTOR-MARKED ASSIGNMENT

Using the Punnett square
a. show the offspring of a cross between Yy and Yy
b. explain the genotypes and phenotype of the offspring.

7.0 REFERENCE

Williams, G.O 2001, BIY 302 – Genetics –1, Module 5, Distance Learning Institute, University of Lagos.

Answers to Self Assessment Questions

1. **a.** alleles are modifications of the same genes, hence variations of the same symbols are used to designate them e.g. Y for yellow and y for green.

   b. Genotype stands for the genetic constitution of an organism e.g. an organism may be yellow but still bear the green allele; hence the genotype of this particular type would be Yy.
   c. Phenotype is the visible characteristics produced by the genes (genotype) present within an organism. E.g. Yellow seeds may have the genes Yy or pure YY; green seeds will be yy.

2. Dominant – is an allele that shows and overshadow the other counterpart in a pair. E.g. yellow (Y) overshadows green (y).

b. Recessive is the latent allele of a gene that is overshadowed, but remains unchanged, only to resurface in future generations.

c. Heterozygous is when the two alleles of a gene are different e.g. Yy.

d. Homozygous is when the two alleles of a gene are the same e.g. Yy or yy.

UNIT 4 PRINCIPLES OF INDEPENDENTASSORTMENT (MENDEL'S SECOND LAW OF INHERITANCE)

1.0 Introduction

1.0 INTRODUCTION

The Chromosome is a long twining chain of genetic materials. It has been established as the site where genes will be found. There are many genes to be found on one chromosome. For example in the human being the gene for tallness, and fair skin may be found on one chromosome. The father of a child may be tall and dark while the mother is short and fair-skinned. A child may take the father's height and the mother's fairness. This means that the two genes present on the same chromosomes have been assorted independently. This phenomenon could have been assorted independently. The phenomenon could have happened at the time of cross-over in metaphase stages of meiosis. Independent assortment, the thrust of Mendel's Second Law of Inheritance, may involve more than two genes on a chromosome.

2.0 OBJECTIVES

In spite of its importance as a basic law, the Principles of Segregation deals with the transmission of only one locus, in isolation from other loci. However, there are cases in which it is necessary to consider more than one locus at a time. The second law governs such situations. On completion of this topic, you should be able:

1. to state and explain the second law

2. to explain the fact that in spite of the apparent differences, the first law is implied and therefore, obeyed in the second law by each of the loci being considered together.

3. to determine the phenotypic and genotypic ratios among the progeny when two or more loci are involved in a cross.

4. to determine the gametic and offspring genotypes from given parents and parental genotypes from offspring genotypes or phenotypes and ratios.

3.1 Mendel's Second Law of Inheritance

Although Mendel's first law is a very important basic law, it deals with the pattern of inheritance of alleles at only one locus. However, it is very rarely

the case that two individuals differ at only one locus. Mendel recognized this fact and so performed experiments in which he studied the simultaneous inheritance of more than one phenotype. The simplest example of such a case is one in which there are two phenotypes, each controlled by one locus.

Instead of using Mendel's example, we shall consider an example from the fruit fly, *Drosophila melanogaster*. This will give us a chance to use another series of genetic symbols. The term wild type is used to describe any phenotype which is most common in flies in the wild; such a phenotype may be either dominant or recessive. The wild type fly has red eyes and long bristles on various parts of the body. A mutant gene, purple, changes the eye colour to purple. This gene is represented by the symbol, pr, and its wild type allele for red eyes is symbolized as pr + the superscript "+" indicating that it is a wild type allele. Another gene, spineless (ss), drastically reduces the length of the bristles. Its wild type allele is represented as SS^{+}. Notice that the symbol is derived from the mutant and not the wild type. The reason for this is that there may be other non-allelic mutant genes which alter the same wild type feature. For instance, the red eye colour may be changed to white by the gene, w, whose wild type allele is w^{+}.

Coming back to the example we are considering we can make the following dihybrid cross i.e. a cross in which the parents differ with regard to two characters. Our initial cross is with two pure breeding parents as follows:

P: purple, spineless x wild type eyes and bristles

F_1: (Dihybrid) wild type eyes and bristles

The F_1 is described as a dihybrid because it is the product of parent who differs with regard to two characters. In future crosses, the wild type eye colour and bristles will be referred to as red and normal respectively. The wild type phenotype of the F_1 indicates that both purple and spineless are recessive, since they are not expressed when present in combination with their respective wild type alleles.

At this stage of our experiment, the result of our cross is not different from that of a monohybrid cross; all the F_1 have the same phenotype. (Review your monohybrid cross.) We therefore, do not know whether we are dealing with one or to loci. In order to answer the question we can cross the F_1 inter as i.e. cross to F_1. The result from such a cross using hypothetical numbers is shown below:

F_1 red, normal x red, normal

↓

F_2 red, normal; red, spineless; purple, normal; purple, spineless

	290	:	108	:	101	:	32
Approx. ratio	9	:	3	:	3	:	1

As shown above four phenotypic classes of F_2 are obtained. The numbers immediately below the classes show the number of each class of progeny. These numbers work out to a ratio (use the smallest number, 32, to divide all the numbers) of 9 : 3 : 3 : 1. Using the sum of the ratios as the denominator, 9/16 of the F_2 are red, normal, 3/16 are red, spineless e.t.c. This result looks very different from the F_2 of the monohybrid cross in which there were only two phenotypic classes in a ratio of 3:1.

A close examination of the distribution of the phenotypes among the F_2 of the cross above shows that there are 398 red and 133 purple, giving a ratio approximately 3:1. There are also 391 normal and 140 spineless and again the ratio is 3:1. Thus when we look at each trait separately, we find that it is behaving according to the first law of inheritance. We can therefore, re-write our experiment so far as two separate monohybrid experiments, shown below:

P	(1) red	x	purple		(2) normal	x	spineless	
		↓				↓		
F1		red				normal		
		↓				↓		
F2	red	:	purple		normal	:	spineless	
	398	:	133		319	:	140	
	3		1		3		1	

The fact that the dihybrid cross can be broken into two monohybrid crosses raises the question: "why does the F_2 ratio change when we look at both traits simultaneously?" The change, however, is only an apparent one since the 9 : 3 : 3 : 1 ratio is the same as the expression (3 red: 1 purple) (3 normal : 1 spineless). When that expression is expanded i.e. multiplied, it gives 9 red, normal : 3 red, spineless : 3 purple, normal : 1 purple, spineless. In other words the situation is such that what is inherited at on

locus does not prevent or determine what is inherited at another locus. There is a *random combination* of both loci in the progeny.

This conclusion is confirmed by examining a testcross. Recall that one of the parents in a testcross is homozygous recessive; in this case two lock are involved, as one parent is purple, spineless in phenotype. Notice that this testcross is also a backbone since the homozygous recessive parent is identical with one of the parents in the F generation of our cross. The testcross is as shown below:

Red, normal (F_1) x purple, spineless

↓

Red, normal: red, spineless; purple normal; purple, spineless

Ratio: 1 : 1 : 1 : 1

Here again as in the F_2 of our original cross, there are four phenotypic classes, but the ratio is 1 : 1 : 1 : 1. Recall that in the monohybrid testcross the ratio was 1 : 1. In order to account for the result of the testcross we must go back to determine the genotype of the F_1 which we used in the testcross. We found that purple was recessive to red and spineless recessive to normal bristle. We also found that the cross could be broken into two crosses and then recombines. Since the P generation parents were pure breeding our crosses and progeny are:

(1) red spineless x purple (2) normal x

(pr^+/pr^+) (pr/pr) (ss^+/ss^+) (ss/ss)

↓ ↓

Gametes pr+ pr ss^+ ss

↓ ↓

red normal

(pr^+/pr) (ss^+/ss)

The genotypes are listed under the corresponding phenotypes. When combined, the genotypes of the pure breeding parents are pr^+/pr^+, ss^+/ss^+, and pr/pr, ss/ss. The red, normal F_1 are pr^+/pr, ss^+/ss. Although we have derived the genotype of the F_1, one could still ask: what type of gametes did the F parents produce to give the F_1? At this stage it is pertinent to recall some of the relevant principles in answering the question.

1. According to the Chromosomes Theory, every type of chromosome must be represented in the gamete. Since the genes are on the chromosome, it follows that every gene/locus (two loci in that case) must be represented in the gamete.

2. According to Mendel's first law, there is a segregation of alleles, so only one member of a pair enters the gamete. Therefore there must be segregation at every locus present.

In each P – parent, the alleles at each locus are identical, so each parent produces only one type of gamete. The red, normal parent will produce ***pr*$^+$, *ss*$^+$** gamete and the purple, spineless will produce ***pr, ss*** gametes. Fertilization will produce the doubly hererozygous F_1 genotype (i.e. there is heterozygosity at each locus) derived above. The genotype conforms with the red, normal F_1 phenotype. On the basis of the preceeding, the genotype of the F_1 testcross parent is pr^+/pr, ss^+/s and that of the purple, spineless parent is pr/pr, ss/ss.

The next step is to determine the genotype of each of the four classes of the testcross progeny. We can easily determine one half of the genotype of each class of progeny because the purple, spineless testcross parent is (it has to be) homozygous for each of the two recessive genes. This parent will therefore produce only one type of gamete, having a genotype of pr, as we found with one of the P – parents. Since these two alleles which are contributed to all the testcross progeny are both recessive, they will not obscure the effects of the alleles contributed by the F_1 parent. Put differently we can say that the phenotypes of the testcross progeny will be determined by the genotypes of only the gametes produced by the F_1 parent. The testcross can therefore be represented as shown in the table below (Table 4.1)

Table 4:1 Testcross showing genotypes and phenotypes

(i)	Phenotype:	Red, normal (F1) x Purple spineless

(ii)	Genotype:	pr^+/pr ss^+/ss pr/pr ss/ss
(iii)	Phenotype:	Red, normal; red, spineless; purple, normal, purple, spineless
(iv)	F_1 Gamete:	pr^+, ss^+; pr^+, ss pr , ss^+ pr , ss
(v)	Other Gamete:	Pr, ss ; pr , ss ; pr , ss ; pr , ss
(vi)	Progeny Genotype	pr^+/pr, ss^+/ss; pr^+/pr, ss/ss; pr/pr, ss^+/ss; pr/pr, ss/ss
(vii)	Ratio	1 : 1 : 1 : 1

Note: gametes on lines (IV) and (V) are from the parental genotype in (ii).

We can derive the testcross progeny genotype shown above as follows: We already determined all the other lines except lines (iv) and (vi). Let us first determine the genotype of the red, normal class or progeny. From line (v) one now know that the other parent contributed pr, as which are both recessive. The phenotype, however, is dominant. Therefore, the F_1 parent must have contributed two dominant alleles in order to produce the observed phenotype. This contribution is represented in line (iv) under that phenotype. When combined, line (iv) and (v) give us the appropriate genotype for that class of progeny.

In the case of the red, spineless class, in order to have the red phenotype the F_1 parent must contribute the dominant alleles, pr^+ and for spineless, there must be homozygosity for the recessive alleles. Therefore in this case the gamete from the F_1 parent is pr^+, as in line (iv). You can go through the steps of determining the gametic contributions of the F_1 parent in the last two classes.

From the table above, it is obvious that the F_1 parent produced four types of gametes. The four types are possible because, as we derived, the F_1 are heterozygous at both loci. We can also see that with respect to each locus two of the four types of gametes contain one allele, e.g. pr^+ while the other two contain the other allele, pr, using the same example. Line (vii) shows that the four different (phenotypes) genotypes among the progeny are present in a ratio of 1 : 1 : 1 : 1. In other words each class represents ¼ of the testcross progeny. Since the phenotypes (and genotypes) which we obtained among the testcross progeny were in the final analysis determined by the gametic contributions of the F_1 parent, we have to conclude that (1) four different types of gametes are produced by the F_1 parent in a ratio of 1 : 1 : 1 : 1; (2) fertilization is a random process, determined only by the proportions of the different types of gametes present. In other words all the different types of gametes from the F_1 parent are equally likely to fuse with the gamete from the other parent.

We examined the test-cross in order to facilitated our understanding of the results obtained when two F_1 were crossed, and we obtained F_2 progeny in a

ratio of 9 red, normal: 3 red, spineless: 3 purple, normal: 1 purple, spineless. In our examination of the testcross we found that fertilization by the gametes from the F_1 is a random process, we can therefore, use the Punnett squares to diagram the gametic fusions when two F_1 are crossed. The gametes are as we derived earlier.

Gametes

	pr^+, ss^+	pr^+, ss	pr, ss^+	pr, ss
pr^+, $1ss^+$	pr^+/pr^+ , ss^+/ss^+ 1	pr^+/pr^+ ss^+/ss 2	3 pr^+/pr ss^+/ss^+	pr^+/pr ss^+/ss 4
pr^+, ss	pr^+/pr^+ , ss^+/ss	pr^+/pr^+ , ss /ss ////////////////////	pr^+/pr , ss^+/ss^+	pr^+/pr^+ , ss^+/ss ////////////////////
pr, ss^+	3 pr^+/pr $ss^{+/ss+}$	pr^+/pr ss^+/ss 4	//////////////////// pr/ pr , ss^+/ss^+ 7	3 pr/ pr $ss^{/ss+}$ /////////////////
pr, ss	4 pr^+/pr , ss^+/ss	6 pr^+/pr , ss /ss ////////////////////	pr/ pr , ss^+/ss 8	9 pr/ pr , ss/ss ////////////////////

Since there are four types of gametes from each parent, there would be sixteen possible fusions (boxes). In addition since the gametes are present in equal proportions each box represents 1/16 of the F_2. Therefore by counting the number of boxes corresponding to each phenotype we can determine the frequency of that class of progeny. The fourth phenotype classes are identified by different types of shading. For instance in order to have a dominant phenotype for each locus, there must be at least one dominant allele at each locus. This class of progeny is represented by the unshaded boxes which are nine in number. Therefore 9/16 of the F_2 are red, normal. Thus we find that the ratios obtained from the Punnett squares correspond to the observed results of the same cross split into two monohybrid crosses.

The genotypic ratio in the F_2 is different from the phenotypic ratio. The different genotypes among the progeny have been numbered in the Punnett squares. There are nine different genotypes in a ratio of 1: 2 :2 :4 :1 : 2 : 1 : 2 : 1. Make sure you understand how the genotypes correspond to the phenotypes. The fractions are in sixteenths like the phenotypic fractions and they add up to one.

From the above results we can conclude that the inheritance pattern (both in the formation or gametes and in the fusion of gametes) does not influence the pattern at another locus. The apparent discrepancy we found due to the independent behaviour of each locus. It is pertinent to emphasis that regardless of the method used to derive the F_2 frequencies, the sum of the

frequencies must be equal to 1 since together they constitute the F_2 progeny from a specific kind of cross.

Mendel derived his second law of inheritance (the Law of Independent Assortment) governing the simultaneous inheritance of genes at two or more loci, after analyzing the results of crosses similar to the one we have discussed. The second law may be stated as follows:

> *"In the formation of gametes, the two alleles of a given gene assort independently of the pairs of alleles of other genes on non-homologous chromosomes".*

You should not try to memorise the law as just stated. You should instead try to understand the meaning of the law so that you can explain it in your own words. The law as stated above is not in Mendel's words since Mendel did not know of chromosomes nor did he use the term alleles and genes.

Given an individual whose genotype is AaBb, we can diagram the production of gametes using the second law as follows:-

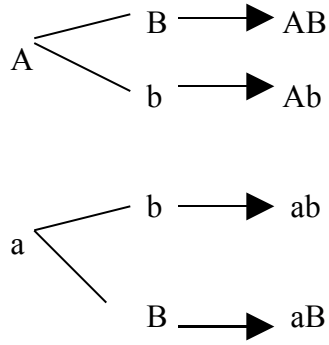
	B	AB
A	b	Ab
	b	ab
a		
	B	aB

According to the first law and each pair of alleles will segregate. But recall that meiosis-I leads to the production of only two cells. Therefore, the A allele has to go into the same cell with one of the alleles at the other locus. However, since the two loci assort independently, one locus does not influence the other. Hence, there are two equal possibilities of which allele will go into the same cell with A then b must go with a and vice versa. As shown in the diagram there are four equally possible combinations. (Diagram meiosis in a cell with two pairs of chromosome inserting one pair of alleles on one pair of homologous chromosomes – only one member of the pair of alleles on each chromosome).

4.0 CONCLUSION

We have seen so far that an individual heterozygous for one locus produces two types of gametes in equal frequencies. When two such individuals are crossed, four combinations (2 x 2 as seen in the Punnett squares) are expected among the progeny. The four types of gametic fusions really amount to three different genotypes in a ratio of 1:2:1. However, because of dominance only

two phenotypes are observed, in a ratio of 3:1. We have also seen the situation when there is heterozygosity for two lock – there are four types of gametes, sixteen (4 x 4) types of gametic fusions, nine different genotypes and four phenotypes. What happens when there is triple heterozygosity e.g. Aa Bd Dd? Gamete formation is as follows:



There are eight gametic genotypes, leading to 64 (8 x8) possible types of gametic fusions. In this case there will be 27 different genotype and eight different phenotypes if there is dominance. Below is a table showing the number combinations possible when two parents heterozygous for the same number of loci are crossed. Note the last column of the table applies only when there is complete dominance between a pair of alleles.

Number of pairs Of heterozygous Loci	Number of gamete genotypes from each parent	Number of gametic fusions	Number of different zygotic Genotypes	Number of different kinds phenotypes
1	2 or 2^1	4 or 4^1	3 or 3^1	2 or 2^1
2	4 or 2^2	16 or 4^2	9 or 3^2	4 or 2^2
3	8 or 2^3	64 or 4^3	27 or 3^3	8 or 2^3
4	16 or 2^4	256 or 4^3	81 or 3^4	16 or 2^4
n	2^n	4^n	3^n	2^n

As shown in the last line, the power in the expressions is the same as the number of heterozygous loci. Instead of merely memorizing the formula in the last line, you should learn to derive the expressions for one and two loci by understanding what they mean and why they are so.

5.0 SUMMARY

The first and second laws of Mendel are the guiding principles of Genetics. It is very important that you familiarize yourself with these laws and know their applicability. This will greatly ease your understanding of Genetics.

Self Assessment questions

BIO 201: GENETICS I

COURSE DEVELOPMENT

Course Developer:
????????.

Unit Writer:
???????

Programme Leader:
???????.

Course Coordinator:
???????
NOUN, Lagos.

NATIONAL OPEN UNIVERSITY OF NIGERIA

Module 2

UNIT 1 PROBABILITY

1.0 INTRODUCTION

We saw when discussing meiosis that, with regards to any pair of homologous chromosomes, an organism can produce two types of gametes. Thus when there are n-pairs of chromosomes, 2^n types of gametes can be produced. For instance, in man there are 23 pairs of chromosomes, therefore, every human being is capable of producing 2^{23} i.e. 8,388,608 different types of gametes, assuming that the two chromosomes which make a pair are different.. If every human being has the potential to produce such a large variety of gametes, it follows that even if the constitution of say the egg is kept constant, it would still be a matter of chance which one of the large variety of sperms would fertilize the egg. Thus in genetics there is a chance factor or probability to be considered with regard to whether a particular type of offspring will be produced by a given mated pair.

2.0 OBJECTIVES

From meiosis and the laws of inheritance it should be obvious that, depending on the genotype, a variety of gametes can be produced by any organism. Since fertilization is a random process it follows that it would be a matter of chance which types of offspring would be produced and in what proportions by any pair of parents. You should be able, on completion of this topic:

1. to explain and use the basic probability principles summarized at the end of this topic;

2. to appreciate the fact that genotypic and phenotypic rations correspond to probabilities when expressed as fractions;

3. to use the fact contained in No. 2 above to determine phenotypic and genotypic ratios from complex genetic crosses. In such cases the Punnett Squares are an ineffective tool because of their size.

4. to apply probability to simple human conditions.

3.0 MAIN CONTENT

3.1 General Principles

Before looking at probability as applied to genetics, let us consider an everyday example. A coin has two sides, a head and a tail. When the coin is tossed it will come up head or tail usually. If the coin is not loaded so that it is biased in favour of one side, we would expect that in a large number of trials, *approximately* 50% of the results would be head and 50% would be tails. The result of one toss does not influence the result of another toss. In other words the ratio of heads or tails would be *approximately* 1 : 1. Notice that I am not saying that exactly 50% of the result would be heads and 50% tails. The results could deviate from the ideal 1 : 1 ratio for any given set of trials. However, statistical tests would show that the deviations from expectation is insignificant i.e. we would be correct if we said that the ratio was approximately 1 : 1

The fact that we can draw the above conclusion means that we can also make the generalization that, when an unbiased coin is tossed the probability that it will come up heads is ½. By the same token the probability that it will not come up heads is ½, which is the same as saying that the probability it will come up tails is ½. State as a formula, we can say that the

$$\text{Probability of a Given event} = \frac{\text{Number of favourable occurences}}{\text{Number of possible occurences}}$$

Going back to our example, we would ask for the probability of a head. A coin has only two sides so there are only two possible occurrences and only one of them is favourable i.e. what we want. Therefore, the probability is ½. We could expand the numbers, as in the large experiment, in which case we would get a probability that is acceptable as ½.

3.1.1 First Law of Probability

In considering the probability of heads or the probability of tails we are considering the probability of single events. However, we could ask a different question; what is the probability that if we toss a coin, we shall get either a head or a tail? Since we have only two possible occurrences when a coin is tossed and both are favourable according to the question, the answer to the question is 1. It is certain that we shall get head or tail. Thus when it is certain that an event will occur the numerical probability is 1. Instead of using the formula above which would be 1+ ½ = 1, we could have arrive t the same answer by adding the probabilities of each of the two events i.e. ½ + ½ = 1. We can summarise this operation by saying that the probability of occurrence in one trial, of either of two mutually exclusive events is the sum of the probabilities of individual occurrence. The events must be mutually exclusive i.e. both cannot occur in one trial, it has to be one or the other as in the coin toss.

In the coin example we found that the sum of the probabilities of the different types of occurrences is 1. This principle applied even if the number of type of occurrences is greater than two. The reason is that in the formula given above "the number of possible occurrences" constitute both the numerator and the denominator. Put differently, for a given set of events e.g. throwing dice, it is certain that one possibility will occur. As we said earlier when an event is certain, the probability is one. It is important that you remember that the sum of all the probabilities for a given set of events is never greater than 1. Using this principle we could answer the question: "what is the probability that a coin will not come up head?" as follows:

Probability of not head = 1 – Probability of head i.e. 1 – ½ which is ½.

A dice has six sided which are equally possible therefore the probability that it will not show 6 when thrown is 1 – 1/6 which is 5/6. Notice that this is the probability that either 1, 2, 3, 4 or 5 will show. The converse of when an event is certain to occur is when it is impossible i.e. it cannot occur. The probability in such a case is 0. For instance we cannot come up with 7 when we toss a dice. Therefore if the numerator in our formular is 0 the fraction has to be zero. This in effect means that the probability of an event occurring can never be less than 0 i.e. it cannot be written with a minus sign. Therefore, the probability of an occurrence is greater than or equal to 0, and less than or equal to 1 but never greater than 1.

In the examples of the coin toss or the dice, the probability of obtaining a head is equal to that for a tail and the same is true for all the six sides of the die. However, such equality is not always true for all the possibilities of an event. Notice that the formula given above does not require such equality.

3.1.2. Genetic Considerations

The probabilities of the different possibilities depend on the type of event under consideration. For instance when two monohybrids are crossed, ¾ of the progeny have the dominant phenotypes while ¼ have the recessive phenotype. In simple terms then we can say that 3 out of 4 progeny would have the recessive. The reason as we saw from the Punnett squares is that there are 4 possible types of fusion between the parental gametes to give the progeny. Thus we could ask the question; what is the probability that the first offspring of two heterozygotes (monohybrids, Aa x Aa) will have the dominant phenotype?" The answer is ¾ since 3 out of the 4 possible gametic fusions will produce dominant phenotypes.

One important aspect of consideration of probabilities, is the fact that the answer is highly dependent on the phrasing of the question. Compare the last question with this one: "What is the probability that two monohybrid parents will produce an offspring having the dominant phenotype?" The answer is 1 because these parents are potentially capable of producing ***an*** (at least one) offspring with dominant phenotype. In the first question we were considering a particular offspring, the ***first***. In the same way the answer to the question, what is the probability that the first child of Aa x aa parents will have the recessive phenotype, is ½. The reasons are:

1. a particular child is indicated, and

2. there are only two possible genotypes and phenotypes, Aa and aa.

Earlier, we found that the sum of all the probabilities for a given series of events is always 1. We also know that from a cross of two monohybrid parents, ¾ of other progeny have the dominant phenotype. However, such progeny can be either AA or Aa in genotype. Among the progeny with the dominant phenotype, the two genotypes are present in a ratio of 1 : 2 respectively.

> **QUESTION**: "what is the probability that if a farmer put his hand ***in a bowl containing the yellow seeds*** from a cross of Yy x Yy,he would pick up a seed which is YY in genotype?"

The phrasing of the question eliminates the green seeds from the number of possible occurrences to be considered. The relevant seeds occur in a ratio of 1 : 2, therefore, the answer is 1/3. The probability of Yy would be 2/3; so again the sum of the probabilities for this series of events involving only yellow progeny is (1/3 + 2/3) equal to 1. (The answer to the question would have been ¼ if the question had been, what is the probability that the farmer would pick a YY seed from among the

progeny of a Xy x Xy cross?) It is important for you to remember that the sum of all the probabilities is one even if you have re-adjusted the total number of possibilities. The probability of occurrences of either of two mutually exclusive events in one trial is the sum of the probabilities of their individual occurrences.

> **QUESTION**: What is the probability of picking in one attempt, a seed with the dominant phenotype from a bowl containing the seeds from a cross of Yy x Yy?"

The question is the same as asking for the probability of either a YY or Yy genotype. The probabilities are ¼ and ½ respectively but both genotypes would give a dominant phenotype. Therefore the answer to the original question is ¼ + ½ i.e ¾. If the question had asked for homozygous genotype, the answer would be for either YY or yy i.e. ¼ + ¼. Which would be 1/2 .

3.1.3 Second Law of Probability

If two coins are tossed simultaneously, the appearance of a head or tail on one coin does not in any way influence what appears on the other coin. Thus we have the following possible combinations: HH, HT, TH and TT. All of these combinations are equally probable, assuming the coins were not biased. Using the probability formula, the probability that both coins would appear heads in a single toss is ¼. The same would be true for both coins appearing tails. However, the answer with respect to the situation where the coins show up differently will depend on the question asked. For example, "what is the probability that one coin will appear head and the other tail?" According to the possible combinations listed earlier, there are two favourable occurrences (combinations) which satisfy the condition HT and TH, therefore the answer is 2/4 i.e. ½. A different question is: "what is the probability that the ***first*** coin will be head and the ***second*** tail?" In this case the answer is ¼ because we have specified what we expect of each coin, making only the HT combination the favourable occurrence.

We can derive the probabilities for different combinations without listing all the possible occurrences. The probability of a head for each coins are tossed or one coin is true for tail. When two coins are tossed or one coin is tossed twice, the probability of an HH combination is ½ x ½ which is ¼ as we found earlier. The same is true for the other combinations. Note that there again, the sum of the probabilities for all the possible combinations is 1. The principle which we have discussed in this and the preceding paragraph may be summarized as follows:

4.0 CONCLUSION

The probability of the simultaneous occurrence of two or more independent events is equal to the product of the probabilities of their individual occurrences. This

principle applies only when one is dealing with independent events i.e. the outcome of one trial does not influence the outcome of the other trials. In the example we considered, one coin does not influence the outcome of the next toss of the same coin.

5.0 SUMMARY

Probability appears, at first hand, difficult but with careful reasoning you will be able to follow the principles involved. It is very applicable to Genetics, especially when considering Mendel's 2nd Law of Inheritance which states that two or more alleles segregate independently of one another. The same is true when throwing two dices or coins, each one of the coins can turn heads up regardless of what the other turns up.

6.0 TUTOR-MARKED ASSIGNMENT

1. An albino (aa) man of blood type MN marries a heterozygote for albinism (Aa) also of MN blood type. They plan to have 4 children. If you assume independent segregation, what is the exact probability they will have

   a) no albinos

   b) 2 non-albino children with MN blood type

   c) 3 children with M blood type?

2. After meiosis of the genotype Aa Bb in Neurospora you obtain 100 asci. If you assume independent segregation how many ascospores do you expect to have the following genetic constitution: AB? Ab plus aB?

7.0 REFERENCES

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UNIT 2 QUANTITATIVE/POLYGENIC INHERITANCE

1.0 INTRODUCTION

In our considerations so far we have dealt with phenotypes which can be clearly distinguished from one another regardless of:

1. the type of relationship that exists among the alleles at one locus – complete or incomplete dominance or codominance.

2. the complexity of the genotype, in terms of the number of loci involved and the type of interaction among the alleles at the different loci e.g. epistatic interactions.

Put differently every genotype or class of genotype has a distinctive phenotype. For instance, in the ABO blood group the blood types can be clearly distinctive classes of phenotypes and are described as QUALITATIVE traits. The genes are said to show DISCONTINUOUS variation is their phenotype.

2.0 OBJECTIVES

1. In this unit as in the earlier ones you should be able to recognize the fact that the basic principles of inheritance are still operative.

2. The difference in this case lies in how the genotype determines the phenotype.

3. In order to be able to appreciate No. 2, you have to be able to state and explain the assumptions which form the basis for all the discussion in this module.

You should be able to:

(i) to account for the shades of difference between the variety of phenotypes in a given polygenic trait.
(ii) to determine the number of genes controlling a trait
(iii) to determine the genotypes for various phenotypes and vice-versa, as well as the frequencies of various phenotypic and genotypic classes.
(iv) to use the probability method in the determination in (iii) above.
(v) to explain the fact that in some instances polygenic traits may have only phenotypes, produced by a threshold effect.

3.1 Continuous Variation

There are traits which flow – CONTINUOUS variation. The different phenotypic classes are small so that the classes are not sharply distinguishable or immediately obvious. For example, in a population not everybody is the same height; there seems to be somebody in every possible position from the shortest to the tallest. Weight and skin colour are other traits which also show continouos variation. The differences between the various classes of such genetically determined traits is therefore, described as *quantitative* inheritances.

Evidence from a number of experiments on quantitative inheritance show that more than one gene is involved in the phenotype that is produced. One can therefore talk of a trait controlled by *multiple genes* or *polygenes*. The latter term is used more widely. The roles of the alleles at the different loci in the production of the phenotype issuch that, on a simplified basis, one can recognise two types of alleles at each locus – CONTRIBUTING and NON-CONTRIBUTING alleles. These are merely terms adopted for convenience of description because it is highly unlikely that an allele has no effect. Thus a genotype with only non-controlling alleles still has a "basis" phenotype.

In order to facilitate the study of quantitative inheritance some simplifying assumptions have to be made. There are those who argue, with good reasons against some of the assumptions, but, be that as it may, we shall use them because they reduce the complexity of the problem. Also, in many cases valid predictions can be made using them. The assumptions are:

1. The effect of each contributing alleles on the phenotype is equal to the effect of any other contributing allele. Moreover, the effect is in addition to a base or minimum value. Thus, we may say that each

allele contributing to a height adds 2.5 centimeters to the minimum height of one hundred and fifty centimetres.

2. The effects of the contributing alleles are additive. Therefore, if we continued with the example in No. 1, we could consider a genotype with six contributing alleles. In this case the total effect of the contributing alleles would be 15 centimetres (i.e. 6 x 2.5) which would be added to the minimum height. Thus the total height would be 165 centimetres (i.e. 150 + 15).

3. There is no dominance at each locus; instead we recognise contributing and non-contributing alleles as mentioned earlier. In other words at any locus one allele does not obscure the effect of the other alleles and the effect of homozygosity for two contributing alleles is greater than that of heterozygosity for one contributing and one non-contributing allele. Yet when there is dominance, homozygotes and heterozygotes have identical phenotypes. The assumption of contributing and non-contributing alleles is also different from intermediate and codominance because in both of these cases as well as in dominance the other allele has a distinctive phenotype. The non-contributing allele is not ascribed a specific phenotype.

   One important consequence of the first three assumptions is that different genotypes will have the same phenotype is the total number of contributing alleles is the same in all the genotypes.

4. There is no epistasis. It is necessary to assume this condition in which the genotype at one locus does not mask the effect of the genotype at another locus because if that were not the case it would be difficult to assign a value for the effect of each allele. In the absence of epistasis there is a direct correspondence between the genotype and the phenotype.

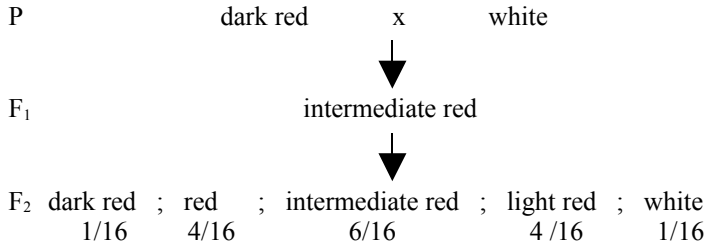
5. There is no linkage among the loci controlling the trait. Linkage, you will recall, is one of the factors which modifies the genotypic and phenotypic ratios and the modified ratios are difficult to calculate. As we shall see later there may be as many as four or more loci involved in some traits and that would of course increase the complexity of the linkage calculations.

4. The environment has no effect on the genotype. In other words the phenotype is entirely attributable to the genotype. Certainly this assumption is a great simplification of the true situation. You know from personal experience that most people will not attach their

potential maximum height and weight if they are under-nourished. In the same way various factors in the environment influence various traits in an organism. In spite of this obvious fact the environmental effect is not assigned any value because its true or even approximate value is variable and difficult to quantify consistently, ignoring it therefore, greatly facilitates quantification of the effect of the alleles involved.

I should emphasise the point that although the above assumptions are acknowledged as being merely for the purposes of simplification, conclusion based on them have been found to be very useful even in applied genetics.

The first significant breakthrough on the problem of quantitative inheritance was by Nilsson-Ehle in 1909. He worked on the colour of wheat kernel. The F_1 from a cross between pure-breeding dark red-kerneled and white-kerneled parents were all of an intermediate red colour. This type of F_1 from such a cross is consistently with incomplete dominance. The F_2 generation, however, forces a rejection of that hypothesis. In the F_2 generation, one-sixteenth (1/16) of the progeny has the same dark red colour of the P-generation parents. The same was true for white progeny in the F_2. The fact that the fractions of the different classes of progeny are in sixteenths, mean that the trait is controlled by two loci. But unlike what we found when considering the second law of inheritance with complete dominance, Nilsson-Ehle obtained Five phenotype classes among the F_2, instead of four. The presence of five phenotypic classes was also different from what is obtained when other types of genetic interactions are operative. The phenotypes in the crosses and among the progeny are shown below:



As mentioned earlier the fractions are indicative of two loci. The two types of alleles at each locus can be distinguished by a superscript. Thus we can assume that the A^1 and B^1 alleles contribute to red pigment production while A^2 and B^2 are non-contributing. The superscripts "1" and "2" as in "A^1" and "A^2" rather than capital and small letters such as "a" and "A" were chosen to distinguish the contributing and non-contributing alleles because capital and small letters have already been used to represent dominant and recessive alleles. We assumed that there is no dominance so it would be best to avoid any confusion in that direction. Much as you are advised to use the same

method of representation used in these modules, you would not be penalized as long as you clearly define whatever method you opt for.
Since the parents were pure breeding the dark red parent would be $A^1A^1B^1B^1$ and the white would be $A^2A^2B^2B^2$. The rationale for characterizing the dark red parent as being homozygous for only contributing alleles is that, that colour indicates the presence of the maximum amount of red pigment while white is due to the total absence of red pigment. Put differently the maximum number of contributing alleles any offspring can have is four if there are only two loci involved and four of such alleles would produce the maximum amount of red pigment.

Given the above parental genotypes, the F_1 would inherit a maximum of two contributing alleles, both from the drdk red parent. Since the contributing alleles have equal effects which are also additive, the F_1 with only two contributing alleles would have half as much red pigment as the parent. Hence its phenotype would be an intermediate red. The F_1 is heterozygous at both loci (doubly heterozygous) and independent assortment during gamete production would yield gametes with 2, 1 or 0 contributing alleles Random Fertilization would in turn yield F_2 progeny with 4,3,2, 1 or 0 contributing alleles. The phenotypes corresponding, would be different. Therefore, there would be five classes of F_2 as Nilsson-Ehle observed. The whole cross can be written as:

A^1 and B^1 = contributing alleles A^2 and B^2 – non-contributing alleles.

P :- dark red x white

$A^1A^1B^1B^1$ ↓ $A^2A^2B^2B^2$

F1 :- intermediate red

$A^1A^2B^1B^2$

Gametes: A^1B^1 : A^1B^2 : A^2B^1 : A^2B^2

Contributing alleles in gametes 2 1 1 0

F2 :- dark red	red	intermediate red	light red	white
$A^1A^1B^1B^1$	$A^1A^1B^1B^2$ $A^1A^2B^1B^1$	$A^1A^1B^2B^2$ $A^2A^2B^1B^1$ $A^1A^2B^1B^2$	$A^1A^2B^2B^2$ $A^2A^2B^2B^1$	$A^2A^2B^2B^2$
Fraction:- $\frac{1}{16}$	$\frac{2}{16} + \frac{2}{16} = \frac{4}{16}$	$\frac{1}{16} + \frac{1}{16} + \frac{4}{16} = \frac{6}{16}$	$\frac{2}{16} + \frac{2}{16} = \frac{4}{16}$	$\frac{1}{16}$

Contributing
Alleles:- 4 3 2 1 0

On the basis of the above and other experiment using larger numbers of loci it is possible to draw up the table below:

Table 2.1
Expectations in the F2 – Generation due to Polygenic differences between two homogenous Parents.

P-generation: Number of loci (pairs of polygenes) in which two parents differ	Fraction of F2 like either pure-breeding parents	Number of genotypic classes in the F2 - generation	Number of phenotypic classes in the F2 - generation
1	¼	$3 = 3^1$	$3 = 2 \times 1 + 1$
2	1/16 $= (¼)^2$	$9 = 3^2$ $27 = 3^3$ 59,049	$5 = 2 \times 2 + 1$
3	1/64 $= (¼)^3$		$7 = 2 \times 3 + 1$
10	$\frac{1}{1,048,576} = (¼)^{10}$	3486784401	21
20	$\frac{1}{1,099,511,627,776} = (¼)^{20}$	3^n	41
n	$(¼)^n$		$2n + 1$

From the table it is obvious that increases in the number of genotypic classes is not proportional to increase in the number of polygenes determining a trait. Rathe, the increase in the number of genotypes greatly outsripts the increase in the number of genotypes greatly outstripts the increase in the number of polygenes. The increase in the number of genotypes also results in an increase in the number of phenotypic classes, making it more difficult to distinguish between the phenotypic classes.

If two heterozygotes are crossed, the table shows that the number of genotypic classes is larger than the number of phenotypic classes wherever the number of loci at which they differ is greater than one. This means that there would be more than one genotype in a number of the phenotypic classes. In such cases it is necessary to know the number of genotypes in a given phenotypic class in order to be able to calculate the fraction of such progeny accurately. It is important that you bear in mind the fact that we are referring to number of genotypes not number of different genotypes. The

distinction is a fine one but nonetheless a very important one. The former category includes similar genotypes which occur more than once well as different genotypes. Thus in Nilsson-Ehele's experiment which we considered earlier, the class of F_2 progeny with intermediate red phenotype contains three different genotypes. Yet according to the distinction which we are trying to make, the number of genotypes in that phenotypic class is six, because the $A^1A^2B^1B^2$ genotype can occur in four different ways, making up 4/16 of the total F_2 progeny.

The above explanation makes it necessary to repeat what we are trying to accomplish: How to calculate the fraction of a given phenotypic class of progeny from a cross between two parents heterozygous for the polygenes under consideration. Suppose there are n loci involved. In any cross between two heterozygotes for one locus all genotypes occur in a fraction of ¼ i.e. Aa x Aa $\longrightarrow$ AA, Aa, aA, and aa. For n loci the fraction will be $(1/4)^n$. Recall that for two loci, there are 16 boxes in the Punnett squares, making the fraction of each genotype in the box, 1/16 which is the same as $(1/4)^2$. In other words n = 2. However, in order to get the correct fraction belonging to that class, $(1/4)^n$ must be multiplied by a coefficient which is the number of genotypes in that class. The coefficient may be calculated by either the binomial method or by the factorial method. I shall discuss only the factorial method. The formula for the number of genotypes in any phenotypic class is:

$$\frac{(2n)!}{X!\,(2n-X)!}$$

Where n is the number of loci (i.e 2n is the number of alleles in the genotype).

X is the number of contributing alleles in that phenotypic class and 2n – X is therefore, the number of non-contributing alleles.

Therefore the fraction of a phenotypic class among the progeny is

$$\left[\frac{(2n)!}{X!\,(2n-X)!}\right] = (1/4)^n$$

3.2 Worked Example

Question

In human population the shortest height is one metre and the tallest is two metres. Five loci quantitatively determine height.

(a) What is the effect of each contributing alleles?

(b) If people of intermediate height marry

(i) What fraction of their children would be expected to be like their parents genotypically?

(ii) What fraction of their children would be expected to have the intermediate phenotype?

(iii) What fraction of their progeny would be expected to have intermediate height and be homogous for contributing alleles, A^1 and B_1 in their genotype.
(Assume the loci are A, B, C. D, and E)

Answer:

(a) Assume that the shortest height is homozygous for only non-contributing alleles and also that the tallest are homozygous for contributing alleles. Therefore the additive effects of the contributing alleles will account for the difference in height between the tallest and the shortest. Therefore the contributing alleles will account for one metre in height. There are five loci and the tallest are homozygous for only contributing alleles. Hence 10 equally additive alleles produce some metre or 100 cm.

. . The effect of each contributing alleles is

$$\frac{100}{10} = 10 \text{ cm}$$

(b) People of intermediate height would be 1.5 metres in height. The additional 50cm will be produced by five contributing alleles in addition to five non-contributing alleles in the genotype.

(i) Let us assume that the genotype of both parents is $A^1A^2B^1B^2$ $C^1C^2D^1D^2$ E^1E^2 (a number of other genotypes will produce the same effect).

If the parents are as sucy assumed the fraction of A^1A^2 from A^1A^2 x A^1A^2 is ½.

. . The fraction that is genotypically like the parents is:

$$(½)^5$$

(if you do not understand how this answer was arrived at, go back and review the lectures on Probability)

(ii) As mentioned above people of intermediate height have 5 contributing and 5 non-contributing alleles. It was also stated earlier

that the fraction (probability) of any given genotype from such a cross is ¼ at each locus. For the five loci, that would be $(¼)^5$ but there are a number of genotypes possible with five contributing and five non-contributing alleles. The formula for calculating this number or coefficient has been given. When applied, the expression to be solved is

$$\frac{10!}{5!\,(10-5)!} \times (¼)^5 \quad \frac{10!}{5!5!} \times (¼)^5$$

$$\frac{10 \times 9 \times 8 \times 7 \times 6}{5 \times 4 \times 3 \times 2 \times 1} \times (¼)^5$$

$$= 252 \times (¼)^5$$

(iii) Since the relevant progeny are both intermediate in height and homozygous for contributing alleles at loci A and B, four of the five contributing alleles have been determined. The fifth contributing allele will be due to heterozygosity at either locus C, D or E i.e. three different possibilities. The fraction of $A^1A^1B^1B^1$ from a cross of two $A^1A^2B^1B^2$ is $(¼)^2$ For the three other loci if there is heterozygosity for a contributing allele at the C locus, the two other loci must be homozygous for non-contributing alleles, giving 2/4 x ¼ x ¼ and the fraction for the full genotype would be

¼ x ¼ x 2/4 x ¼ x ¼

since there are three possibilities for genotypes at loci C, D and E, the fraction of this relevant type of progeny is:

$3 \times 2/4 \times (¼)^4$

3.3 Other Considerations

It is estimated that skin colour in man is determined by a minimum of three and a maximum of six additive loci. If we assumed that four loci are involved with the A^1, B^1, C^1 and D^1 alleles contributing to pigment production while A^2, B^2, C^2 and D^2 are non-contributing, a marriage between pure black and pure white would produce mulatto children with intermediate skin colour. Their genotype in this particular cross would be $A^1A^2B^1B^2$ $C^1C^2D^1D^2$. On the other hand, a marriage between two mulattoes would be capable of producing the while spectrum of skin colours. This is because both parents can produce gametes which contain only contributing (i.e. $A^1B^1C^1D^1$) or non-contributing (i.e. $A^2B^2C^2D^2$) alleles in addition to other gametic genotypes. The point being made here is that because of the way in which skin colour is

determined it is possible for a couple to have children who are either much lighter or darker in complexion than either of them. Infidelity on the woman's part therefore may not be the correct explanation when a child with a markedly different skin colour from the rest of the family is born.

Although the discussion of polygenic inheritance so far has characterized it as a condition in which there is a continuum of phenotypes that is not always the case. There are polygenic traits for which only two phenotypes are produced. For example, in the guinea pig the normal hind foot has only three toes, but there are some strains with four toes. Crosses between the pure breeding three-toed and four-toed strains produced F_1 which are nearly all three-toed. The F_2 from this type of cross consists of three-toed and four-toed individuals in a ratio of approximately 3 three-toed : 1 four-toed. This ratio suggests that we are dealing with a pair of alleles in one locus exhibiting complete dominance by the allele for three toes.

Pure breeding P three-toed x four-toed

↓

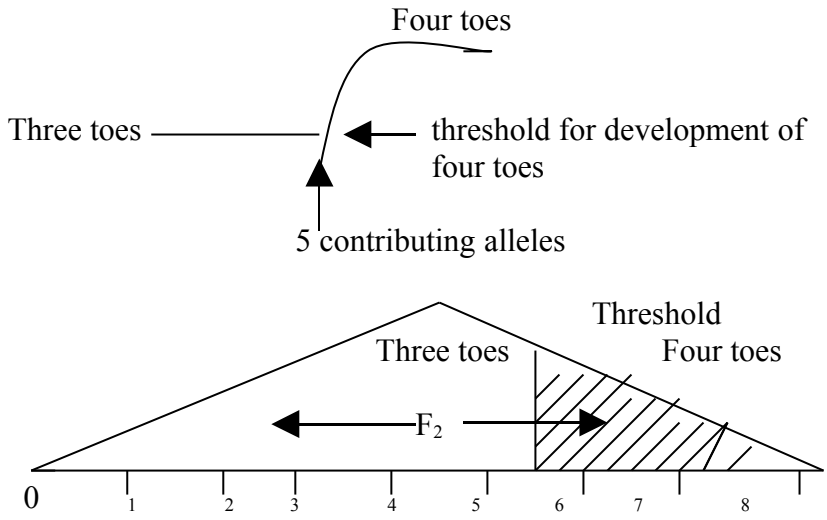
F_1 nearly all are three-toed

↓

F_2 three-toed : 1 four-toed

Crosses with the F2 however do not support the one locus hypothesis. Instead it is more reasonable to assume that there are approximately four additive loci involved, but that is not all. In order to have fur toes there must be at least about five contributing alleles present. If there are less than five contributing alleles then only three toes develop, but if there are five or more, four toes develop. In other words, there is a threshold or level which must be reached before there would be development of four toes. Any number of contributing alleles below the threshold produce only three toes.

In discussing this particular example of threshold effect on the phenotype, I have not gone into the ramification. The important point to bear in mind is that the alleles are additive. The effects of the different alleles must be added in order to reach the threshold at which the effect, in this case development of four toes, becomes visible. Equally important is the fact that once the threshold is re3ached the effect (phenotype) is the same regardless of the number of contributing alleles present. What we have discussed with reference to number of toes may be summarized by the following diagrams.



According to the hypothesis to account or the three-and four-toed phenotypes if A^1, B^1, C^1 and D^1 are contributing and A^2, B^2, C^2 and D^2 are not, then parents who are $A^1A^1B^1B^1C^1C^1D^2D^2$ would be pure-breeding for four-toes. The same would be true of $A^1A^1B^1B^1C^1C^1D^1D^2$ parents but of $A^1A^1B^1B^1C^1C^2D^1D^2$ parents. Try to explain why the statements are correct.

4.0 CONCLUSION

1. A trait is controlled by multiple genes or polygenes
2. Alleles appear in pairs and two types can be recognized – contributing and non-contributing alleles.
3. Certain simplifying assumptions have been made to facilitate the study of quantitative inheritance. Among these are

   (a) at any locus one allele does not obscure the effect of the other allele.
   (b) the effect of each contributing allele on the phenotype is equal to the effect of any other contributing allele.
   (c) the effect of the contributing alleles are additive.
   (d) there is no epistasin.
   (e) there is no linkage among the loci controlling the trait.
   (f) the environment exerts no effect on the genotype.

5,0 SUMMARY

Quantitative inheritance is the mechanism of genetic control of traits showing continuous variation. Many traits, especially those that are measured in a

"quantitative" manner, are affected by many genes, examples include Height, Weight, Yield in crops, Growth rate in farm animals IQ. In addition to quantitative inheritance, inheritance of these traits is often referred to as "cumulative gene action" or "polygenic-inheritance

6.0 TUTOR-MARKED ASSIGNMENT

How does polygenic inheritance differ from Mendelian inheritance?

Answer to TMA

Mendelian inheritance refers to the expression of inheritance of monogenic traits, that is traits that are controlled by one gene. We will use flower color as an example. Suppose we have two of the same kind of plant. Plant A has red flowers, and plant B has blue flowers. Red is dominant, and blue is recessive. Therefore the color genes for plant A are either AA or Ab. Plant B is bb. If we cross A with B, the color of the flowers will either be red or blue but not purple. The gene composition can only be AA, Ab, or bb. If it is AA, then the flowers will be red. If it is Ab, then the flowers will be red because the A gene will mask the expression of the b gene. "Ab" does not result in a purple flower. If it is bb, then the flowers will be blue.

However, when we consider polygenic inheritance things become more complicated. Polygenic inheritance refers to the expression of traits controlled by two or more genes and environmental interactions. Polygenic traits do not follow Mendelian patterns of dominance and recessiveness. Skin color is a good example. Not only do multiple genes affect skin color, but the environment does as well. Changing a specific gene or factor may result in only minor changes in the expression of the gene. Suppose one person has black skin and their mate has white. Their offspring may have black skin, white skin, or some shade in between.

7.0 REFERENCES

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UNIT 3 SEX DETERMINATION AND SEX LINKAGES

1.0 INTRODUCTION

Many men blame their wives for having only female children; some couple have only male children. Is it the fault of the woman for having only daughters? How exactly does a baby get to be a boy or a girl? This unit, among other things, examines this phenomenon.

2.0 OBJECTIVES

In many sexually reproducing organisms, especially in animals, the two sexes are distinct. There are a number of factors which determine the sex of an individual. The materials discussed should enable you to:

1. distinguish between autosomes and sex chromosomes;
2. account for the sexes produced by the chromosomal constitutions discussed;
3. explain the pattern of inheritance and expression of genes on the sex chromosomes;
4. explain the terms sex-linked, sex limited and sex influenced traits.

3.1 Sex Determination

One of the characteristics of living things is the ability to reproduce their own kind. The method of reproduction however, may be either of two kinds, although some organisms are capable of using both kinds. The two kinds of reproduction are asexual or vegetative reproduction and sexual reproduction. One major feature of sexual reproduction is the fusion of two types of gametes. In many organisms – all higher organisms have the two gametes

morphologically different. There is no fusion of gametes in asexual reproduction.

Sexually reproducing organism may be either *monoecious* or *dioecious*. In the former case one individual produces both kinds of gametes. In other words both male and female parts are present in the same individual. Dioecious organisms however, are characterized by the fact the sexes are separate; any normal individual is either male or female and therefore produces only one type of gamete. Put differently, among dioecious organisms, the primary sex difference is in the types of gametes produced. In addition, there are secondary sexual characters which distinguish the sexes. However, we will not be concerned with the secondary differences per se. Rather, our time will be spent in considering the underlying genetic mechanisms responsible for the differences. What is the genetic basis for the fact that one zygote develops into a male while another develops into a female?

In 1891, a German biologist, Hermann Henking (1858-1942), observed that in certain insects, the nuclei of half of the sperm contain an extra structure. He called the structure the "X-body" (similar usage of x in algebra to designate unknown quantity) because its role in the nucleus was not known. In 1902 Clarence Erwin McClung (1870-1946), an American biologist found that the somatic cells of female grasshoppers contain 24 chromosomes while male cells contain 23 chromosomes. In 1905, Edmund Beecher Wilson (1856-1939) and Nettie Maria Stevens (1861-1912), also Americans, identified Henking's X-body as a chromosome. They arrived at this conclusion after studying gametogenesis (oogenesis and spermatogenesis) in a number of insects. The X-body therefore, became known as the X-chromosome. In addition to the X-chromosome, another chromosome showing some similarities in behavior with the X was discovered. It was named the Y chromosome to indicate the closeness in behaviour.

In general therefore, three types of chromosome can be identified, although not all the three are necessarily present in all sexually reproducing organisms. The three types of chromosomes are the AUTOSOMES, the X – and the Y – chromosomes. The number of autosomes is the same in both sexes of all but a few organisms. The X – and the Y – chromosomes are designated the SEX CHROMOSOMES because, although their number is constant (same as autosomes), for any member of a species, the number and types of sex chromosomes present depend on the sex of the individual (Table 6.1)

Table 3.1: The Chromosomes Number and Types in a Few Animals

		AUTOSOMES	SEX CHROMOSOMES		
			X	Y	2n
Fruitfly	♀	3 pairs	1 pair	-	8
(Drosophila melanogaster)	♂	3 pairs	1	1	8
Grasshopper	♀	11 pairs	1 pr.	-	24
(Zonocerus Variegatus)	♂	11 pairs	1	-	25
Man	♀	22 pr.	1 pr.	-	46
(Homo sapiens)	♂	22 pr.	1	1	46
Chimpanzee	♀	23 pr.	1 pr.	-	48
(Fantroglodytes	♂	23 pr.	1	1	48
Chicken	♀	38 pr.	1 z*	1	78
(Gallus domesticus)	♂	38 pr.	1 pr. of z	W -	78

* The choice of nomenclature is merely to underscore the fact that in some organisms it is the male which has two homologous sex chromosomes. This obviously is a different pattern. Some geneticists prefer the x-y nomenclature.

It is obvious that when the sec chromosomes are the same type they would behave like any pair of homologous chromosomes during meiosis-I, segregating to opposite poles. However, in spite of the differences in their nomenclature, the x (z) and the Y(W) behave like a pair of homologues in meiosis-I. Although we shall not discuss that aspect, there is in fact partial homology between the two chromosomes. Be that as it may, the net result of the meiotic behaviour of the sex chromosomes is that the individual with one pair of X- or z- chromosomes produces only X- or z- bearing gametes. On the other hand an XY or ZW individual will produce two types of gametes – X bearing and Y-bearing or Z- and W- bearing. The grasshopper male also produces two types of sperms X-bearing and O-bearing (pronounced zero-bearing i.e. no x chromosome). The sex which produces only one type of gamete is described as the *homogametic sex* while the sex which produces two types of gametes is called the *heterogametic sex*. Thus in man the male is the heterogametic sex but in the chicken it is the female.

From the table above, we can distinguish three different patterns of sex chromosomes distribution, the XX – XY, XX – XO and ZZ – ZW. Since these sex chromosomal constitutions are the basic differences between the chromosomal complements or the nuclei of the two sexes, it is reasonable to assume that the sex chromosomes are associated with sex determination. The assumption is not far fetched. Genes determine much of what an organism is. According to the Chromosome Theory, the genes are on the chromosomes and different chromosomes carry different genes. Differences in chromosomal constitutions should therefore, result in different phenotypes.

In the light of the information so far presented, the assumption regarding the significance of the sex chromosomes is a logical one. However, there are a number of questions which also require answers that would specify the role of the sex chromosomes. For instance, is the *Drosophila* female, a female because it carries two X-chromosomes, or is it a female because it carries two Y-chromosomes? We can ask similar questions about the male also. Is it a male because it carries one X-chromosomes or because it carries a Y-chromosomes? Are the autosomes involved in sex determination? Man and *Drosophila* are very different organisms yet they have the same pattern of sex chromosome distribution. Are the two systems of sex determination similar?

3.2 Sex Determination in Drosophila

Normally in meiosis-I homologous chromosomes go to opposite poles so that every gamete gets one of each pair of homologous pair. Deviations do occur however, such that both members of a pair go to the same pole. The condition where a pair of chromosome fail to separate during cell division (meiosis and mitosis) is described as NON-DISJUNCTION. Note that as defined non-disjunction can occur between a pair of homologues in meiosis-I or between sister chromatids (chromosomes) in meiosis-II and mitosis.

If non-disjunction of the X-chromosomes occurred during meiosis-I in the female Drosophila two type of eggs can be produced. In one case the egg will be XX, containing 5 instead of 4 chromosomes. The other type of egg will not contain any sex chromosome, there would be only three autosomes. If these eggs are fertilized by normal sperm, we would get the following sex chromosomal constitutions: XXX, XXY, XO, OY. The OY condition is very rear and the zygote dies in the egg, so the condition is lethal. The XXX and XXY conditions give rise to females. XXXY females are fertile and are phenotypically indistinguishable from XX females. On the other hand, the XXX female is frail and sterile, and dies quite early, sometimes in the pupil stage. The XXX female is known as a metafemale although some authors still use the original nomenclature, superfemale. Given the characteristics just described, the term superfemale is a misnomer. The XO fly is phenotypically indistinguishable from normal males but it is also sterile.

From the results just considered the mechanism of sex determination in the fly may be stated as follows: In the fly with a diploid number of autosome, sex is determined by the number of x-chromosomes present, such that the fly is a female if there is more than one x-chromosome present. It is however, a male if there is only one x-chromosome. The Y-chromosome does not play a role in sex determination, but it carries the genes which determine femaleness, the fact that the OY condition is lethal means that the x-chromosomes carries some genes which are necessary for viability.

The preceeding account of sex determination is *Drosophila* is only a part of the picture, hence the emphasis on the "diploid number of autosomes" in the paragraph above. The complete theory of sex determination in *Drosophila* as proposed by C. B. Bridges in 1925 involves an interaction between the autosome and the x-chromosomes, with great significance given to the ratio of x-chromosomes to complete sets of autosomes. The reason is that there is some evidence indicating that genes for maleness are distributed among the autosomes. I have opted not to discuss this aspect of the theory because we would almost invariably be considering only diploid conditions. But to reiterate the point made earlier, for the purposes of this course, it is sufficient to say that in conjunction with a diploid number of autosomes the sex of the fly is female when there is more than one x-chromosomes and male when there is only one x-chromosomes present.

The validity of the above conclusion is evidenced by flies known as gynandromorphs or gynanders. Such flies are made up of male and female parts. The male sections of the fly are smaller than the female parts since male flies are smaller than female. The male parts of the gynandromorphy are XO and the female parts are XX. The proof that the chromosomal conditions are as stated comes from the expression of recessive genes on the x-chromosome. The theory is that male parts have only one x-chromosome. Therefore, any recessive gene on that x-chromosome will be expressed. On the other hand female parts would not express such traits if they were heterozygous for the genes. Indeed, it is found when the appropriate experiment is done, that the parts which have the recessive phenotype are only the male parts. All the female parts have the dominant phenotype expected for a heterozygous genotype. A heterozygous genotype would be possible only if there are two homologous chromosomes, in this case two x-chromosomes, present in the same cell.

The evidence and the ensuing theory of sex determination in *Drosophila* indicated that it is the x-chromosome that is involved in sex determination. On the strength of this it is reasonable to conclude that a number of loci (genes) is involved in the determination of sex. All things being equal, that is the normal situation. However, there is evidence that single identifiable loci may play significant role in sex determination. For example, in *Drosophila melanogaster*. There is a recessive autosomal gene (i.e. a gene on an autosome as opposed to one on a sex chromosome) which when homozygous transforms XX-zygote i.e. female zygote into males which

are sterile. The effect is only XX zygotes. The gene, transformed I symbolized as ***tra.*** From what I have said so far, there are two possible types of males which are also homozygous for tar; they are ZY, tra/tra which are sterile males. The tra/tra genotype nullifies (i.e. it is epistatic) the effects of the female determining genes on the X-chromosomes present. I should emphasise the point that normally the recessive tra allele is not present, rather it is the dominant wild type allele, tra^{+}, which is present, and this allele has no epistatic effect on the pattern of sex determination.

3.3 Sex Determination in Man

Human males and females, as shown in the table earlier, are XY and XX in the sex chromosomal constitution. This is the same constitution found in *Drosphila*. A logical question that arises about this is whether the mechanism of sex determination in man is the same in *Drosphila*. Relevant places of evidence indicate that the mechanism is different.

As in *Drosphila*, evidence that help in the elucidation of the pattern of sex determination in man came from cases of abnormal sex chromosomal constitution. Available data from studies in the U.S. show that one in 500 – 800 (1/500 – 1/800) male births, i.e. babies recognizable as males, results in individuals affected with a condition known as Klinefelter's Syndrome. The condition was first described by Klinefelter's and the term syndrome indicates the fact that the condition is characterized by a member of specific abnormalities. In this case, some of the abnormalities are that although the external genitals appear normal, the testes are small and there is little or no sperm production; these males are therefore, sterile. The arms and legs are longer than normal. There is usually some enlargement of the breasts (a condition known as gynecomastia) and intelligence is often below average. Chromosomal studies show that Klinefelter males have 47 chromosomes instead of 46. The chromosomal constitution is made up of a normal complement of autosomes, i.e. 22 pairs, their sex chromosomal constitution is XXY.

Another major sex abnormally in man is Turner's Syndrome, occurring with a frequency of between one in 5,000 and one in 3,000 female births. Those affected with this syndrome, first described by Henry Ashby Turner (1932-2008), are recognizable as females but they are poorly developed; the same is true of the secondary sexual characteristics – breasts e.t.c. Affected females are shorter than average and have folds of skin on both sides of the neck. The condition is described as "webbing" of the neck because the folds are similar to those between the toes of a duck. Although there is often a degree of mental retardation there are a few Turner females who are anything but mentally retarded. Affected females have a normal complement of autosomes but only one X-chromosome making a total of 45 chromosomes. The sex chromosomal constitution is therefore XO as opposed to XX for the normal female.

The triple-X condition XXX is also known in man. These individuals have a normal complement of autosomes plus three X-chromosomes, making a total 47 chromosomes. They are female. Some are quite normal and most are fertile but others exhibit varying degrees of abnormality. Some have below average intelligence, some have poor development of the external and internal genitalia.

The OY condition has not been found in man, but it is known to be lethal in mice embryo. Therefore, it can be assumed to be also lethal in man.

The phenotype of the sex chromosomal constitutions descried so far indicate that in man as in *Drosophila,* the X-chromosome carries viability genes. Hence, at least one must be present if the embryo is to survive. However, the mechanism of sex determination in man is such that the Y-chromosome carries the male-determining genes but the X-chromosomes also carries some genes for femaleness. These constitutions are based on the fact that the XY and XXY constitutions are male and XO, XX and XXX i.e. no Y present are female. There is also the fact that there is development of some female secondary characteristic e.g. gynecomasty, in XXY males.

Further evidence in support of the male-determining effect of the human Y-chrosome is the observation that XXXY, XXYY, XXXXY are Klinefelter males. The logical conclusion is therefore, that the presence of a Y-chromosome, leads to a male regardless of the number of X-chromosomes present.

There is information regarding the distribution of the male-determining genes along the length of the Y-chromosome as well as the distribution of genes involved in sex-differentiation on both the X and Y-chromosomes, but will not be considered in this course.

One of the major points in the Chromosomes Theory of Inheritance is that a normal chromosomes complement is necessary for normal development. The cases of sex chromosomal imbalance which we have considered, underscore the point. Although there is some measure of normality in XXX females, XXXX and XXXXX females show increasing degrees of mental retardation.

XYY individuals are males as expected and are very rare in the population. They are generally above average height and in most cases are below normal in intelligence. There are no consistent major abnormalities associated with this constitution. However, the XYY condition is of social interest because there is some evidence that it might predispose such men to criminality. The emphasis is on predisposition because the evidence for a direct association with criminality is not conclusive. There are many XYY men who do not run into conflict with the law. However, it is pertinent to note that in some countries the XYY condition is considered in much the same way as the insane criminal.

Although in the normal pattern of sex determination in man, no specific gene is identified as having a specific role, there is evidence that might in fact be the case. In man there is a condition known as testicular feminization or male pseudohermaphroditism. Examination of those affected with this trait show them to be chromosomally XY but possessing female characteristics externally. Internally, however, they possess testes and lack ovaries and fallopian tubes. They behave as females and many are known to be married but are of course sterile. The only known effect of the gene for this trait on XX females is the absence of axillary and pubic hair in some carrier women. The gene also transforms XXY zygotes into sterile females. It has not been possible so far in man to determine whether the gene responsible is on an autosome or on the X-chromosome. If it is an autosomal trait, then it would have to be a dominant trait. Thus both carrier females and affected males would be heterozygous for the gene. On the other hand the gene could be either a recessive or dominant gene on the X-chromosome. The recessive gene would be expressed in all XY zygotes inheriting it since there is no other X-chromosome which could carry a dominant gene. Whatever the case, the gene is transmitted through only females and it overrides the male-determining effect of the Y-chromosome.

The pattern of sex determination in man is the same in most mammals. However, in mice the XO females are fertile although not as fertile as normal XX females. Also in mice the gene for testicular feminization is known to be located in the X-chromosome and it is dominant.

The XX/XO system of sex determination is similar to that in *Drosophila* in that male have only one X-chromosome while females have two. Note, however, that the *Drosophila* male is different with respect to the fertility gene, which are located in the Y-chromosome.

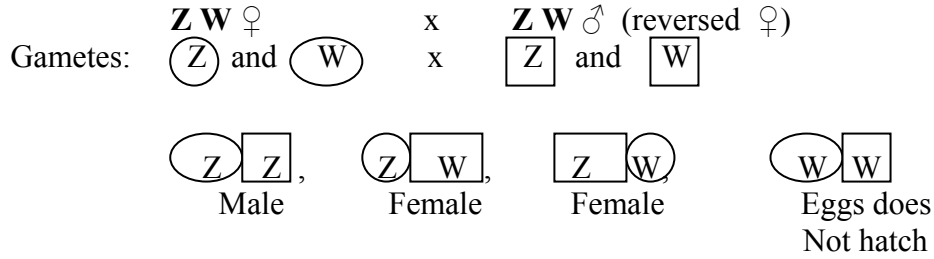
Using the term which I introduced early in this series of lectures, in the system of sex determination which we have considered so far, the female is the homogametic sex (all eggs contain an X-chromosome) and the male is the heterogametic sex, producing two types of sperm one of which contains an X-chromosome while the other contain either a Y-chromosome or no sex chromosome.

3.4 Other Organisms

The next system which I will consider is such that the male is homogametic and the female heterogametic. For this reason, the sex chromosomes are often designated differently; they are represented as Z (the equivalent of the X) and W (= Y). In this system the male is ZZ and the female is ZW or ZO in some animal. This system is found in the chicken; males are ZZ and females are ZW. One interesting aspect of sex determination in the chicken is the fact that sex reversal without chromosomal

change is possible in females. Normally only one, the left, of the two presumptive gonads develops into an ovary. The other is essentially rudimentary or better still dormant. If the left gonad i.e. the ovary is destroyed, the chicken even as an adult is transformed into a fertile ZW male.

Such a reversed female would be a heterogametic male. When this male is mated to a normal female, the cross would be:



The observed ratio of two females to one male instead of the expected 1:1 ratio among the progeny of this cross is proof that the male was a revered female with a ZW sex chromosomal constitution. (Diagram a normal ZW x ZZ cross to convince yourself that the expected sex ratio is 1 female : 1 male).

The chromosomal system of sex determination is not restricted to animals. For instance, in the dioecious plant, *Lychnis* XX plants are female and bear only pistillate flowers. There is, however, evidence to show that the type of flower produced is dependent on the ratio of X to Y chromosomes. When the ratio is 4X : 1Y the plant produces mainly perfect flowers (i.e. hermaphroditic flowers with stamen and pistil) but occasionally there are some staminate flowers. Therefore, it is possible to suppress the male determining effect of the Y-chromosome by increasing the number of X-chromosomes.

Sex chromosomes also play a role in sex determination in some haploid organisms. For instance, in liverworts meiosis in the sporophyte, the diploid asexual generation, results in the production of two types of gametophytes (gamete producing plants). The one bearing the X-chromosomes develops into the archegonium which produces the egg cell. The one bearing the Y-chromosome develops into the antheridium and will produce the sperm. Fertilization will restore the XY constitution of the diploid asexual sporophyte.

In the hymenoptera – base and wasps – the system of sex determination does not depend on sex chromosomes. In the honey bee, for example, workers and the queen bees are females. Chromosomal analysis shows that they are diploid (2n = 32). Male bees (drones), develop by parthenogenesis i.e. from unfertilized eggs and are haploid, with 16 chromosome. Thus on a generalized basis one can say that the 2n condition leads to femaleness while the haploid condition leads to maleness. Careful

studies have however, shown that a large number of genes are involved and more specifically it is the extensive heterozygosity for the large number of genes which leads to a female bee. By the same token homozygosity for a large number of the genes leads to a diploid male. For our purposes however, it would be sufficient to generalize the mechanism in terms of chromosomes number.

The patterns of chromosomal sex determination which have been discussed can be summarized as shown in the table below:

FEMALE	MALE	ORGANISMS
*AAXX	AAXY	Man and other mammals; some dioecious anglosperms (plants): *Drosophilia***
AAXX	AAXO	Grasshopper, Cockroach and many orthoptera and hemiptera.
AAZW/ZO	AAZZ	Birds, reptiles, some amphibia, some fishes and lepidoptera.
AX	AY	Liverworts (plants)
AA	A	Hymenoptera.

*A = one haploid set of autosomes.
** Drosophila technically does not belong in this group since the Y is not sex determining.

Self Assessment Questions

1. What is the diploid number of chromosomes in humans?

2. Explain how (a) a boy (b) a girl is formed at fertilization.
3. What is (a) heterogametic sex
   (b) homogametic sex

4. What are (a) autosomes (b) sex chromosomes?

5. What are the sex chromosomes in man?

4.0 CONCLUSION

Reproduction is one of the general characteristics of all living organisms. Sexual reproduction is a more advanced form of reproduction than asexual reproduction and involves the fusion of sex cells or gametes which are quite distinct from one another.

A sexually reproducing organism may be *monoecious* in which case an individual produces both types of sex cells or gametes, or *dioecious* in which two distinctly different individuals in dioecious organisms are designated male or female. The chromosomes that determine the sex of an organism are known as *sex chromosomes*; others within the cell are known as autosome. In man, there are 22 pairs of *autosomes* (i.e. 44 autosomal chromosomes) and one pair (i.e 2) sex chromomoses. The sex chromosomes are designated X and Y. The Y chromosomes determines maleness.

5.0 SUMMARY

Sex chromosomes are important in the formation of distinct sexes in living organisms. They are also responsible for some sex-linked diseases in organisms e.g. haemophilia and colour blindness in man. Some of these will be discussed in the next unit.

6.0 TUTOR-MARKED ASSIGNMENT

1. Discuss Klinfelter's Syndrome.
2. Discuss Down's Syndrome.

7.0 REFERENCES

Williams, G.O 2001, BIY 302 – Genetics –1, Module 5, Distance Learing Institute, University of Lagos.

Herskowitz, I. H. 1973, Principles of Genetics. The Macmillan Co. New York.

Answers to Self Assessment Questions

1. There are 23 pairs or 46 chromosomes in the human cell.

2. (a) A boy is formed when a Y chromosome sperm fuses with the ovum to form XY.

(b) A girl is formed when an X sperm from the father fuses with the ovum to form XX.

3. (a) An heterogametic sex is one that contains differing sex chromosomes e.g. XY as in a boy.
   (b) A homogenetic sex is one where the sex chromosomes are the same.

4. (a) Autosomes chromosomes within a cell other than those that can determine the sex of the individual.
   (b) Sex chromosomes are those that can determine the sex of the organism.

5. The sex chromosomes in man are the X and Y chromosomes.

UNIT 4 SEX LINKAGES

1.0 INTRODUCTION

The sex of an organism is determined by the sex-chromosomes. These are designated by the letters X or Z for females and Y or W for males. The remaining chromosomes are called autosomes. The sex chromosomes carry some genes which are responsible for certain traits. Some genes are predominant on the X-chromosomes while some are linked to the Y-chromosomes. Such traits as night-blindness, colour blindness, haemophilia, deep/soprano voice and hairy chests are all linked to the sex chromosomes.

2.0 OBJECTIVES

At the end of this unit you would be expected to:

1. Know about the discovery of the Barr Body.
2. Understand the term holandric genes linked with the Y-chromosomes.
3. Give examples of sex-linked traits
4. Give examples of sex-influenced genes.

3.0 MAIN CONTENT

3.1 Sex Linkage

From the preceding series of units we have found that the basis of chromosomal sex determination is the fact that one chromosome or a pair of non-homologous chromosomes does not occur in the same numbers in both sexes. These chromosomes are therefore, named the sex chromosomes and

symbolized as X and Y in some organisms or Z and W in others. In all our considerations of the transmission of genes hitherto, no attempt has been made to specify the sex of each parent. This was because the genes being considered are on the autosomes which you will recall are present in equal numbers in both sexes. That is not the case with the sex chromosomes. Hence, it is pertinent to inquire into the pattern of transmission and expression of genes on the sex chromosomes. The term linkage you should recall is used to describe the occurrence of genes on the same chromosome. By convention however, sex "linkage" refers to genes on the X- or Z-chromosome, even though the Y- and the W- chromosomes are also sex chromomoses. The reason for such a usage of the term is the fact that in most organisms no specific loci on the Y- or W- chromosomes have been identified as being responsible for particular traits. With regard to the Y or W, one almost invariably refers to a group of genes rather than single genes as being responsible for say, fertility or determination of sex.

One of the most clear-cut pieces of evidence illustrating sex-linked inheritance was reported by Morgan in 1910 from crosses with *Drosophila melanogaster*. The crosses are shown below:

P red-eyed ♀ x white-eyed ♂

↓

F_1 all ♀♀ red; all ♂♂ red

½ ½ i.e 1:1 ratio of ♀♀:♂♂

↓

F_2 all ♀♀ red; red ♂♂ ; white ♂♂

½ : ¼ ; ¼ i.e 2:1:1

also 3 red : 1 white

Backcross:

P red ♀ (F1) x white ♂

↓

F1 **red** ♀♀ ; white ♀♀ ; red ♂♂ ; white ♂♂

¼ ¼ ¼ ¼

From the F1 of the original cross, one would conclude that the white-eye phenotype is recessive to the wild type i.e. red eye. The evidence that the eye-colour trait is probably controlled by one locus is the fact that there is only one pair of alternative phenotypes – red or white. The next question is

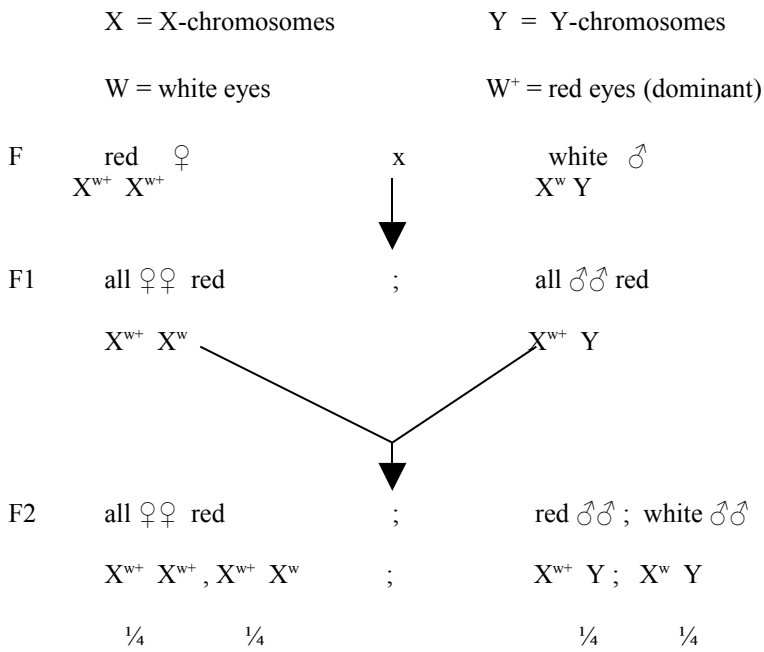
whether the trait is due to an autosomal gene. If trait were an autosomal trait we would have expected both the male and female F_1 in the original cross to be heterozygous for the pair of alleles, since both sexes have the same numbers of each autosome. If that were so we would then have expected in the F_2 a ratio of 3 red to 1 white. *BUT* with the sexes evenly distributed between the two phenotypic classes. Instead, we find that one-half of the males are white and the other half red but all the females are red-eyed.

In the backbone, one half of the F1 are white and the other half red. Furthermore, one half of the white are females and the other half males. The same is true for the red-eyed class. These ratios of 1 red : 1 white and equal numbers of males and females in the two classes are similar to what one would expect with an autosomal trait. However, the fact that the results of the original crosses were so different from what would be expected for an autosomal trait made Morgan to seek other explanations. It is necessary to note here that my attempt to explain sex linkage based on the results of Morgan's crosses is not strictly along the same steps. For example, Morgan based his hypothesis on the results of the backbone using his hypothesis. Instead I have chosen to discuss all the crosses and in the process explain sex linkage.

The result of the P-generation cross indicates that the white eye phenotype is recessive. If this were an autosomal trait white-eye flies would have to be homozygous. On the other hand if the locus of the gene were on the X-chromosome only white-eyed female need be homozygous for the recessive allele because they have two X-chromosomes. By the same token red-eyed females would be either homozygous dominant or heterozygous.

The heterozygous female would produce two types of eggs – one containing the X-chromosome with the dominant allele and the other containing the X-chromosome with the recessive allele. Both types of eggs can be fertilized by a Y-bearing sperm. If the egg with the dominant allele is fertilized the eye colour of the resulting male offspring is of course red because the dominant allele is present. However, one can only deduce the basis of the phenotype in the case of the egg with the recessive allele fertilized by a Y-sperm. The phenotype has to be white because there is no other X-chromosome present which could possibly carry a dominant allele. Even though the X and the Y segregate like a pair of homologues they are not homologous chromosomes. In other words there is no locus corresponding to the white locus of the X and Y. Therefore, the male fly has one set of sex-linked genes. The sex which has only one X or Z chromosomes and therefore, only one set of sex-linked genes is described as being HEMIZYGOUS for that set of genes. To underscore the point, one can say that when an individual is hemizygous for any gene, that gene will be expressed regardless of whether it is recessive or dominant.

Based on Morgan's deductions one can assign genotype to the parents and progeny in the crosses. In writing the genotypes, each allele will be written as a superscript on a capital X denoting the X-chromosomes. This is merely to remind you of the sex chromosomal constitution of the individuals. You need not include the X if you can keep track of male and female genotypes.



Ratio of red white is 3 : 1

Notice, however, that all the females are red!

The genotypes assigned to the parents and progeny in the crosses adequately account for their phenotypes. The genotypes are of course a consequence of the hypothesis that the eye colour gene is located on the X-chromosome with no corresponding locus, and therefore no alleles, on the Y-chromosome. In the crosses above the white-eyed P male is hemizygous and his X-chromosome (designated by the heavy type) is transmitted to his daughters only. Thus some inherit their X-chromosome exclusively from their mother. Mothers can transmit either of their X-chromosomes to both sons and daughters. Since a father transmits his X-chromosomes to daughters only, only some of his grandsons by his daughters will inherit his X-chromosome. Thus under normal circumstances, an XY male never transmits his X-chromosomes to his sons. This transmission of the P-generation's male X-chromosome to F_2 sons via the F_1 daughters is sometimes referred to as "crisscross" inheritance.

(Assign genotypes to the backcross parents and progeny as was done for the original cross).

Morgan's postulate has the following implications:

1. A cross of white-eyed females with white-eyed males will yield only white-eyed progeny.

2. Heterozygous red females will always produce and expected proportion of 50% red-eyed and 50% white-eyed male progeny regardless of the type of males to which they are mated. However, only matings of these females to white males will produce white daughters in a proportion of 50% red-eyed and 50% white-eyed. (Recall the backcross).

3. F1 males from white ♂ x red ♀ (pure breeding) will produce only red-eyed females; but all sons from the cross will be white-eyed.

4. F2 females from a P cross of pure-breeding red ♀ x white ♂ will all be red but of two genetypes : ½ W^+/W

5. Reciprocal crosses for sex-linked genes will yield different results, contrary to what is found with autosomal genes:

red ♀ x white ♂	white ♀ x red ♂
red ♂♂ x	all ♂♂ white, all ♀♀ red

The reason for the differences is the fact that the male is hemizygous for sex-linked genes.

Results from different crosses prove that these implications are correct and that they also apply to other sex-linked genes. Hence Morgan's sex-linkage hypothesis is a valid one.

Another demonstration of sex-linked inheritance in *Drosophila* is as follows. There is an X-chromosome which is ring-shaped instead of rod-shaped. During the early cleavage stages in development there is a tendency for the chromosome not to be included in some nuclei. The loss of the ring X-chromosome from some nuclei in an XX embryo results in a condition in which some cells retain their original X condition and other cells would be XO. The latter types of cells would be hemizygous for the genes on the remaining rod X-chromosomes.

Since the XO constitution is male determining, the parts of the fly containing the XO cells would give rise to male structures while the XX cells would develop into female structures. The extent of the mosaicism of male and female parts would depend on the distribution of the two types of cells and the relative numbers of the two types of cells. We have already characterized this type of fly as a gynandromorph.

With respect to sex-linkage, there is recessive allele which makes for yellow body chitin and bristles. Another recessive allele makes for twisted bristles. The embryo could be made heterozygous for the two loci such that the normal X-chromosomes carries the two recessive alleles while the ring X-chromosomes carries the dominant alleles for normal colour and straight bristles. Under such circumstances the male parts of the gynandromorph would be recognized by the fact that in addition to being smaller than the female parts, they would be yellow and would have twisted bristles. Such phenotypic differences between the XO male parts and the XX female parts bear testimony to the facts that the genes are on the X-chromosome and that the male is hemizygous for X-linked genes. The XO phenotypes for the genes are no different from the phenotypes in XY moles. Note that the phenotype in the gynandromorphy are further proof that the XO constitution in Drosophilia leads to male development.

Inheritance of the X-chromosomes of man follow the same pattern as in Drosophila. Therefore, with respect to X-linked traits sons are never like their fathers, instead they are more like their mothers! It is only daughters won inherit their fathers's X-chromosome. It is equally interesting to note here, that the sex of the child is determined by which of the father's two types of sperm fertilizes the egg. All things being normal it is a matter of chance, 50%, which type of sperm fertilizes the egg. Thus a family of six daughters is not highly improbable – $(½)^6$ i.e. one out of sixty-four families of six children.

A number of sex-linked traits are known in man and they follow the same patterns of inheritance as sex-linked traits in *Drosophila*. Most of the known sex-linked traits in man are recessive. These tratits are rare in the population but males are more frequently affected than females. The reason in that the male is hemizygous, therefore any male who inherits the recessive allele from his mother will be affected. On the other hand female who is affected must have an affected father and a mother who is either heterozygous (called a "carrier") or affected. Put differently, if she inherited the abnormal recessive allele from one parent she might inherit the dominant normal allele from the other parent. In mathematical terms if the frequency of affected males in the population is q, the frequency of females would be q^2 because they have to be homozygous. q^2 is less than q because q is often in the range of 1/1000 or

even much less than that. A few examples of recessive x-linked traits are night blindness, hemophilia in which the affected cannot distinguish between red and green, deficiency for the enzyme glucose-6-phosphate dehydrogenase and ocular albinism.

The inheritance of sex-linked genes in XX/XO organisms follows the same pattern as in the XX/XY types which we have discussed using the *Drosophila* example. In ZZ/ZW animals the only difference is in the fact that it is the female which is heterogametic, therefore daughters never inherit Z-linked genes from their mothers.

3.2 Barr Body

One interesting aspect of sex-linked inheritance in mammals is connected with the presence of a dark staining body – the Barr body (named after the discoverer) – found in the interphase nucleus of most female somatic cells. The Barr body is one of the two x-chromosomes in the female. Furthermore it is not the same X-chromosomes which occur as the Barr body in all cells. Mary Lyon and others proposed the Lyon or inactive-X hypothesis about the Barr body. Very simply the hypothesis states that the genes in the X-chromosome forming the Barr body are inactive. Therefore, every female somatic cell is technically hemizygous. Since it is not the same X-chromosome which is inactive over the entire body, a female who is heterozygous for a trait would have the two phenotypes of her body. She would be a mosaic. For instance, in man the condition known as anhidrotic ectodermal dysplasis has as one of is characteristics, the absence of sweat glands in the skin. A woman who is heterozygous for this trait two types of patches on her body – no sweat glands and sweat glands. Although the Lyon hypothesis is clearly applicable to many x-linked traits, there are some which deviate from the hypothesis.

3.3 Y-Linkage

The y-chromosome does not occur in mammalian females or occurs only under special circumstances in *Drosophila* females. Therefore, any traits present on the Y-chromosome will be transmitted from father to son only. In other words the genes and their corresponding traits will occur in only one sex. Such genes therefore, would be described as holandric genes. The occurrence of an unusual amount of hair on the ear rims of some men was once thought to be holandric but the absence of the expected hairs in some males has cast some strong doubts on a Y-linked explanation. In man only two traits – a testis – determining factor and Y-histocompatibility – are known definitely to be Y-linked.

3.4 Sex – Limited Traits

Sex-limited traits are also referred to as sex-limited genes. However, I prefer the former term because as we shall see, the genes occur in both sexes although it is not expressed in one. One example which is of agricultural importance is the production of milk in cattle. The bull chosen to sire the dairy cattle is just as important as the cows because the genes controlling high milk production also occur in males but males do not produce milk because they are not equipped (differentiated) to do so. Other examples are the size and shape of the penis in males, breast development in women, heavy beard development in men and testicular feminization.

3.5 Sex – Influenced Genes

Sex-influenced genes are also described as sex-controlled or sex-modified genes/traits. These are genes which are expressed in both sexes, unlike the genes for sex-limited traits. However, in this case the type of expression is different in the sexes given the same genotype. One common example is "pattern" baldness, which has a genetic basis. In the population there are many more males than female affected with this trait. The reason is that affected males are either homozygous or heterozygous i.e. BB or Bb but only homozygous BB females are bald. In other words although the trait is dominant men, it is recessive in females. Another sex-influenced trait in man is singing voice in which low bass males and high soprano females seem to have the same genotype.

4.0 CONCLUSION

Sex chromosomes are designated by X and Y in some organisms or by Z or W in others. Genes on the autosomal chromosomes are present in equal numbers in both sexes. However, the sex chromosomes do not carry equal numbers of genes.

By convention sex-linkage refers to genes on the X or Z sex chromosomes and not the Y and W chromosomes. This is because for most organisms the genes on the Y and W – chromosomes no specific genes have yet been identified; rather, one refers to a group of genes as being responsible for, say, fertility or determination of sex.

The Barr body is a dark staining body found in the interphase nucleus of most female somatic cells. It is one of the two sex (x) chromosomes in the female. The Y chromosomes determine maleness in mammals and are not found in the females. The Y chromosome bears such genes (holandric genes) responsible for at testic-determining factor and Y-histocompatibility.

Sex-limited traits or genes are responsible e.g. for high production of milk in cattle, size and shape of the penis in males, breast development in women, heavy beard development in men and testicular feminization.

Example of sex-influenced genes/traits is pattern baldness which has a genetic factor. Affected males are genetypically BB r Bb but only homozygous BB females are bald; hence the trait is dominant in men that another sex-influenced trait in man is singing voice in which low bass males and high soprano females seem to have the same genotype.

5.0 SUMMARY

We started with the knowledge that the nucleus controls the activities of the cell. We narrowed the control center to the chromosome which carries information on themselves. The set of information is called genes. Genes are responsible for the characteristics/traits that are shown by the organisms. Genes occur on all sets of chromosomes – both autosomes and sex chromosomes. The genes on autosomal chromosomes are common in all cells but those on the sex chromosomes are not; this gives rise to sex-linked, sex-limited and sex-influenced genes/traits.

6.0 TUTOR-MARKED ASSIGNMENT

i A lot of yellow and red tomatoes were crossed. Matings were not necessarily between true-breeding lines, but only between the phenotypes indicated. Determine whether yellow or red is dominant, and give your reasoning

Type of mating	# red offspring produced	#yellow offspring produced
red x red	73	0
red x yellow	28	66
yellow x yellow	33	185

Answer to TMA

Recessives breed true, thus red is recessive. Yellow x yellow can give some red, because some yellow x yellow matings were Aa x Aa. Some red x yellow matings can give red, because some matings were of Aa x aa. However, red = aa, so aa x aa only gives aa red offspring.

ii Recently, a study was made of fruit flies with plum-colored eyes. It was found that two plum colored flies mated together produced 145 plum-eyed offspring and 71 red-eyed offspring. What phenotypic proportions are expected from the mating of a plum-eyed and a red-eyed individual? Give genotypes and phenotypes of all individuals used to get your answer.

Answer to TMA

145:71 is what kind of a ratio? Well, it looks like a 2:1 ratio (140 is twice 70, so 145 is about twice 71). 2:1 ratios imply lethal alleles, where a cross of two heterozygotes would give a ¼:½:¼ ratio, except that one of the ¼s is lethal. So, plum is the heterozygote, red is one homozygote, and the other homozygote is lethal. Best to use codominant symbolism. A_1A_1=red, A_1A_2=plum, A_2A_2 = lethal. Remember, lethal is not another color, it simply means that that genotype doesn't exist.

7.0 REFERENCES

Williams, G.O 2001, BIY 302 – Genetics –1, Module 5, Distance Learing Institute, University of Lagos.

Herskowitz, I. H. 1973, Principles of Genetics. The Macmillan Co. New York.

Self Assessment Questions

1. What letters are used to symbolise the sex chromosomes?
2. In man which of the sex-chromosomes is responsible for maleness?
3. What is a Barr body

Answers to Self Assessment Questions

1. The letters X or Z and Y or W
2. The Y sex chromosome is responsible for maleness in man (i.e. XY)
3. The Barr body is a dark staining body found in the interphase nucleus of most female cells and it is one of the two X-chromosomes.