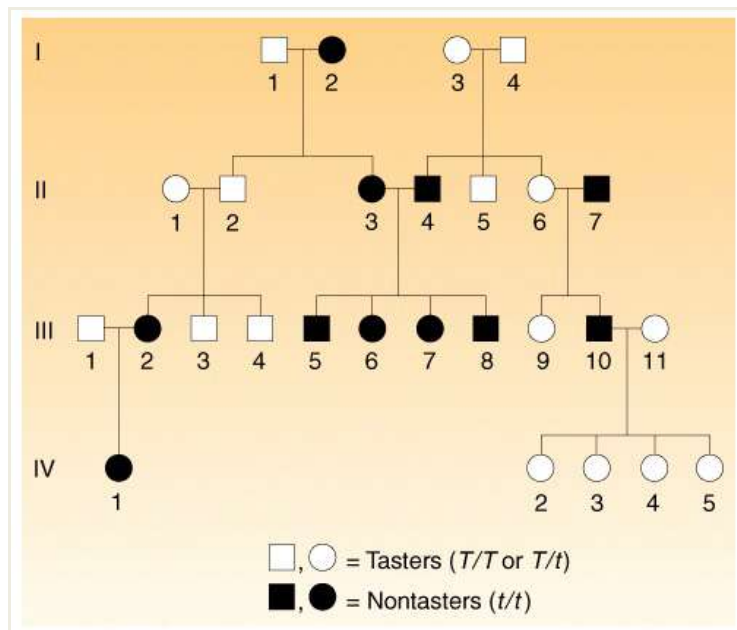


GENETICS

BIO 250 MODULE 3



Copyright

© Copperbelt College of Education 2012

No part of this module may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording or by any information storage and retrieval system, without permission in writing from the publisher.

Copperbelt College of Education

Science Department

P. O. Box 20382

Kitwe

Zambia

Email: cosetco@zamtel.zm

Acknowledgements

The Copperbelt College of Education, Science Department wishes to thank those below for their contribution to this module:

Editors

Zambia College of Distance Education Luanshya
(ZACODE)

Directorate of Distance Education (DODE) Lusaka

Authors

Mwale .M.: Lecturer CBCE

Lombe .A.: Lecturer CBCE

Contents

About this module	1
How this module is structured	1
Course overview	3
Welcome to Genetics BIO 250 Module 3.....	3
Genetics BIO 250, is this course for you?	3
Course outcomes.....	3
Timeframe.....	4
Study skills.....	4
Need help?	6
Assignments.....	6
Assessments	7
Getting around Genetics BIO 250 Module 3	8
Margin icons	8
Unit 1	9
Sex Determination and Sex Chromosomes	9
Introduction	9
Sex Determination.....	10
Morphology and Pairing of X and Y in the Lygaeus Mode	11
Using Karyotypes to Predict Genetic Disorders.....	16
Too many or too few chromosomes.....	16
How can cells end up with too many or too few chromosomes?.....	17
Nondisjunction and Chromosomal Abnormalities	19
Schematic of Nondisjunction in Meiosis I	19
Schematic of Nondisjunction in Meiosis II (or Mitosis)	20
Unit summary	24
Unit 2	25
Sex-Linked Inheritance.....	25
Introduction	25
Sex-Limited, Sex-Influenced and Linked-Traits.....	25
X-linked Inheritance.....	27
X-linked Recessive Inheritance.....	27
X-linked Dominant Inheritance.....	29

Unit summary	30
Unit 2 Assessment	30
Unit 3	31
<hr/>	
Pedigree Analysis	31
Introduction	31
Basic Principles	31
Dominant and Recessive Traits	32
Modes of Inheritance of Genetic Disorders	34
Using Probability	37
Unit summary	38
Unit 4	39
<hr/>	
Variation	39
Introduction	39
What is Genetic Variation?	40
Continuous Variation	42
Discontinuous Variation	43
Causes of Variation	44
Gene Pool	46
Unit summary	50
Assignment 3	51
References	53

About this module

This module is about Genetics. It is the second of three modules prepared for the course Bio 250. It has been produced by the Copperbelt College of Education. All Bio 250 modules produced by the Copperbelt College of Education are structured in the same way, as outlined below.

How this module is structured

The course overview

The course overview gives you a general introduction to the course. Information contained in the course overview will help you determine:

- If the course is suitable for you.
- What you will already need to know.
- What you can expect from the course.
- How much time you will need to invest to complete the course.

The overview also provides guidance on:

- Study skills.
- Where to get help.
- Course assignments and assessments.
- Activity icons.
- Units.

We strongly recommend that you read the overview *carefully* before starting your study.

The course content

The course is broken down into units. Each unit comprises:

- An introduction to the unit content.
- Unit outcomes.
- New terminology.
- Core content of the unit with a variety of learning activities.



- A unit summary.
- Assignments and/or assessments, as applicable.

Resources

For those interested in learning more on this subject, we provide you with a list of additional resources at the end of BIO 250 Module 3; these may be books, articles or web sites.

Your comments

After completing BIO 250, we would appreciate it if you would take a few moments to give us your feedback on any aspect of this course. Your feedback might include comments on:

- Course content and structure.
- Course reading materials and resources.
- Course assignments.
- Course assessments.
- Course duration.
- Course support (assigned tutors, technical help, etc.)

Your constructive feedback will help us to improve and enhance this course.

Course overview

Welcome to Genetics BIO 250 Module 3

Welcome to Genetics BIO 250 Module 2. In this module, you will further your knowledge about genetics. You will, among other things, look at how geneticists use statistics to determine whether experimental data fits into theoretical models of inheritance of specific traits, the effects genes have on each other and gene regulation, as well as how chromosome abnormalities or mutations arise and some disorders caused by mutations.

Genetics BIO 250, is this course for you?

This course is intended for people who are serving teachers and have passed BIO 110 and wish to do Biological Sciences at university level. You should have studied biology at Diploma level.

Course outcomes

Upon completion of Genetics BIO 250 Module 3, you should be able to:



Outcomes

- *Distinguish* sex-linked genes from sex-influenced ones.
- *Distinguish* sex-linked genes from sex-limited ones.
- *Show*, using genetic diagrams, how sex-linked disorders are inherited.
- *Describe* how primary non-disjunction occurs.
- *Explain* the effect of variation in chromosome number on the phenotype of affected individuals.
- *Use* a karyotype to identify disorders resulting from variation in chromosome number.
- *Interpret* a pedigree chart.
- *Construct* a pedigree chart given information about the incidence of a genetic disorder in a family.

Timeframe



How long?

This module is expected to take you a minimum of 80 hours to complete. This time should be spent on studying the module and completing the activities.

Study skills



As an adult learner your approach to learning will be different to that from your school days: you will choose what you want to study, you will have professional and/or personal motivation for doing so and you will most likely be fitting your study activities around other professional or domestic responsibilities.

Essentially you will be taking control of your learning environment. As a consequence, you will need to consider performance issues related to time management, goal setting, stress management, etc. Perhaps you will also need to reacquaint yourself in areas such as essay planning, coping with exams and using the web as a learning resource.

Your most significant considerations will be *time* and *space* i.e. the time you dedicate to your learning and the environment in which you engage in that learning.

We recommend that you take time now, before starting your self-study, to familiarize yourself with these issues. There are a number of excellent resources on the web. A few suggested links are:

- <http://www.how-to-study.com/>

The “How to study” web site is dedicated to study skills resources. You will find links to study preparation (a list of nine essentials for a good study place), taking notes, strategies for reading text books, using reference sources, test anxiety.

- <http://www.ucc.vt.edu/stdysk/stdyhelp.html>

This is the web site of the Virginia Tech, Division of Student Affairs. You will find links to time scheduling (including a “where does time go?” link), a study skill checklist, basic concentration techniques, control of the study environment, note taking, how to read essays for analysis, memory skills (“remembering”).

- <http://www.howtostudy.org/resources.php>

Another “How to study” web site with useful links to time management, efficient reading, questioning/listening/observing skills, getting the most out of doing (“hands-on” learning), memory building, tips for staying motivated, developing a learning plan.

The above links are our suggestions to start you on your way. At the time of writing these web links were active. If you want to look for more go to www.google.com and type “self-study basics”, “self-study tips”, “self-study skills” or similar.



Need help?



Help

If you have any pro study, please contact our Student Support Services on Phone 0212 239 003

Email: cosetco@zamtel.zm

Or write to:

Student Support Services Department,

Copperbelt College of Education,

P.O. Box 20382,

Kitwe.

During residential school, you will have access to the College library. It is located within the College campus. You will be oriented by a qualified librarian.

Assignments



Assignments

You are expected to submit at least one written assignment to your tutor each time you complete a module. This means that by the end of this module, you will write and submit one assignment. All written assignments are supposed to be sent, via your respective District Resource Coordinators, to:

The Director,

Directorate of Distance Education,

Copperbelt College of Education,

P.O. BOX 20382,

Kitwe.

You are expected to submit assignments in the order in which the modules are given to you.

Assessments



Assessments

At the end of each unit, you will find self-marked activities. These activities are meant to help you check your understanding of concepts presented in Module 3.

You will also write a Tutor Marked Assessment for this module. It is important that you do all the self-marked activities and Tutor Marked Assessment because these will help you check your progress. We recommend that you discuss the contents of the learning journal with your Tutor.



















Getting around Genetics BIO 250 Module 3

Margin icons

While working through this Module 3, you will notice the frequent use of margin icons. These icons serve to “signpost” a particular piece of text, a new task or change in activity; they have been included to help you to find your way around Module 3

A complete icon set is shown below. We suggest that you familiarize yourself with the icons and their meaning before starting your study.

			
Activity	Assessment	Assignment	Case study
			
Discussion	Group activity	Help	Note it!
			
Outcomes	Reading	Reflection	Study skills
			
Summary	Terminology	Time	Tip

Unit 1

Sex Determination and Sex Chromosomes

Introduction

The purpose of this unit is to introduce you to the concepts of sex determination and sex-linkage. While discussing these concepts, you will also look at nondisjunction and how variation in chromosome number causes genetic disorders. You may recall, from Module 2, that Sutton and Boveri's Chromosome Theory of Inheritance proposed in 1902; postulates that genes are located on chromosomes. Just previous to this (end of 19th century), biologists had discovered that half of all sperm cells carried a structure they called an X-body. In 1905 the X-body were determined to be chromosomes - X chromosomes to be specific. The Y chromosome was also discovered in 1905. Together the X and Y chromosomes are known as the **sex chromosomes** or **gametes**. You may also recall that all other chromosomes are called **autosomes**.

Upon completion of this unit you should be able to:



Outcomes

- *Define* what the phrase 'sex determination system' means.
- *Describe* at least two modes of sex determination in sexually reproducing organisms.
- *Describe* how nondisjunction occurs.
- *Explain* the effects of variation in chromosome number in humans.
- *Identify* chromosomal abnormalities by examining a human karyotype.



Terminology

Aneuploidy:	An abnormality in which a particular chromosome is present in too few or too many copies.
Gamete:	A cell which is the result of meiosis, having a haploid set of chromosomes.
Karyotype:	The entire chromosome set of an individual or cell as seen during mitotic metaphase.
Nondisjunction:	The failure of homologs or sister chromatids to separate properly during meiosis or mitosis respectively.
Ploidy:	This refers to the number of sets of chromosomes which a biological cell of an organism of a particular species carries.



Polyploidy:	Variation in chromosome number in which an organism has more than two genomes.
Chromosome abnormality:	[Term description]
Genome:	The complete chromosome set of an individual of a particular species.

Sex Determination

Let us begin this section by looking at what a sex determination system is. A sex-determination system is a biological system that determines the development of sexual characteristics in an organism. You may have noticed that most sexually-reproducing organisms have two sexes, that is, male and female. Occasionally there are hermaphrodites in place of one or both sexes. There are also some species that are only one sex due to parthenogenesis, which is the act of a female reproducing without fertilization.

In many cases, sex determination is genetic: males and females have different alleles or even different genes that specify sexual morphology. In animals, this is often accompanied by chromosomal differences. Genetic determination is generally through chromosome combinations of either XY, ZW, XO, or haplodiploid. Sexual differentiation is generally started by a main gene, a sex locus followed by a multitude of other genes in a domino effect. In other cases, sex is determined by environmental variables such as temperature or light, or social variables including the size of an organism relative to other members of its population.

You may have noticed that in almost all species, individuals are divided into two, depending on which sex cells are produced. For example, in humans, the 23 chromosome pair is called the **sex chromosome**. Sex chromosomes are responsible for the determination of sex. The presence of the Y chromosome in humans determines maleness, while its absence determines femaleness. So normal males are **XY** and females are **XX**.

Systems of Sex Chromosomes

Biologists have classified systems of sex chromosomes using different criteria. We will look at a few of these systems and which criterion is used in arriving at the particular system.

1. XX-XO system (Protenor mode)

The Protenor mode of sex determination occurs in some insects like grasshoppers. The combination of chromosomes in organisms is:

- Female - **XX**
- Male – **X** (designated **XO**)

2. XX-XY System (Lygaeus mode)

The Lygaeus mode occurs in *Drosophila*, mammals, humans, and some plants, where:

- Female - **XX** (homogametic sex)
- Male - **XY** (heterogametic sex)

3. ZZ-ZW System

This system occurs in birds, butterflies and some fishes. This is similar to the system in humans, except that the sex chromosomes are in reverse order, that is:

- Female - **XY** (heterogametic sex)
- Male - **XX** (homogametic sex)

4. X-Y-XY System

This occurs only in organisms with alteration of generations in their lifecycle. This group of organisms include liverworts and vascular plants. The sex chromosomes are as follows:

- Male gametophytes - **Y**
- Female gametophytes - **X**
- Sporophytes – **XY**

Let us now take a closer look at the Lygaeus system, upon which sex determination in humans is based.

Morphology and Pairing of X and Y in the Lygaeus Mode

A closer look at this sex determination system reveals that each type of sex chromosome has two regions namely, the pairing region and the differential region. Each of these regions plays a specific role in organisms, namely;

a. Pairing region

- i. During Synapsis of Meiotic Prophase I, the pairing regions combine.
- ii. Some genes occur in these pairing regions.
- iii. These genes exhibit X- and Y-linkage.

b. Differential region

- i. Differential regions do not pair during Synapsis.
- ii. This region contains genes which are either X-linked or Y-linked.



Note that: Any gene whose locus (position) is either on the X or Y chromosome is said to be **sex-linked**. Let us now look at some examples of sex determination in specific species.

Sex determination in *Drosophila*

In *Drosophila* spp, the fruit fly, sex is determined by the ratio of the number of X chromosomes to number of autosomal sets, designated **A**, in individuals. The scheme is as follows;

- $X/A = 1.0$ - female
- $X/A = 0.5$ - male
- $X/A > 1.0$ – meta-female
- $X/A < 0.5$ – meta-male

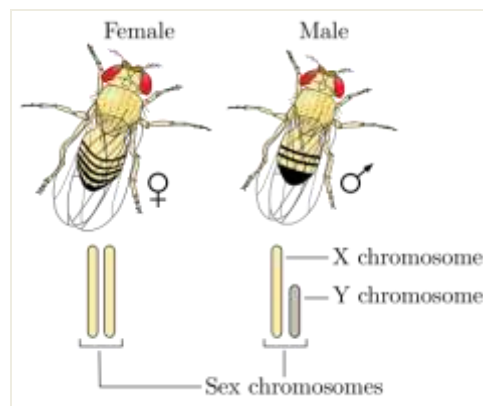


Figure 1: Sex Chromosomes in *Drosophila*

Autosomal sets can range from one, to more than one. Individuals are termed ‘meta’ if the autosomal sets are greater than one for female flies or less than one for male ones.

Sex determination in humans

You may recall that in placental mammals, including humans the presence of a Y chromosome determines sex. You may also remember that normally, cells from females contain two X chromosomes, and cells from males contain an X and a Y chromosome. Occasionally, individuals are born with sex chromosome aneuploidies, that is, sex chromosomes which occur in too few or in greater numbers compared to normal. In this case the sex of these individuals is always determined by the absence or presence of a Y chromosome.

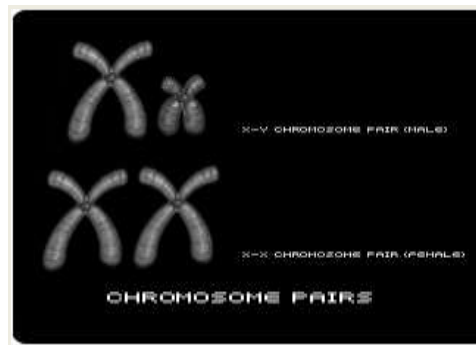


Figure 2: XY - XX Chromosome Pairs in Humans

The sex of an individual is determined by a combination of chromosomes. In the normal set of human chromosomes (genome) there are 44 (22 pairs of) ‘ordinary’ chromosomes, and 2 sex chromosomes. Figure 2 above shows that females have two identical chromosomes - ‘X’, whereas males have one ‘X’ and one ‘Y’ chromosome. If we extend the matrix system to include sex chromosomes: - **XX** and **XY** are different genotypes, and – ‘femaleness’ and ‘maleness’ are their corresponding phenotypes.

This means that individuals with 47, XXY or 47, XYY genotypes are males, while individuals with 45, X or 47, XXX genotypes are females. Cases in which an individual has less or more than 46 chromosomes are called ‘**supernumerary**’. Humans are able to tolerate supernumerary of sex chromosomes because of X inactivation and the fact that the human Y chromosome is quite gene-poor.

Let us now look at sex determination in greater detail. The presence or absence of the Y chromosome determines sex. A gene on the Y chromosome, called the sex-determining region Y (SRY) gene codes for the testis-determining factor.

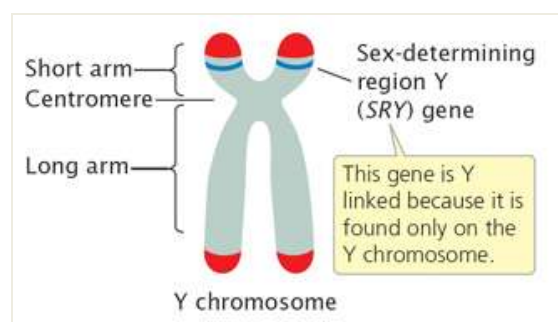


Figure 3: Location of the SRY Gene in Humans

Figure 3 above shows the location in humans, of the gene SRY on the Y chromosome. The Y chromosome, as you may recall, determines maleness in humans. In other species, including the fruit fly, the presence of two X chromosomes determines femaleness. Since the fruit fly, as well as other species which use the number of Xs to determine sex, individuals with an extra X are nonviable. SRY-reliant species on the other hand, can have conditions such as XXY and still live.



The SRY gene determines whether an individual develops male or female reproductive organs. The SRY gene works by inducing development of the medulla of the gonadal primordial, pairs of ridges on the embryonic kidneys into the respective organs of the appropriate sex. Consequently:

- i. **XY** individuals who lack the part of the Y chromosome with this gene are females.
- ii. **XX** individuals who carry a tiny piece of the Y chromosome with this gene on an X chromosome are male, though they are sterile.
- iii. The X chromosome contains what appears to be a homologous region, though the genes there are most likely pseudogenes.

Once the SRY gene is activated, cells create testosterone and anti-müllerian hormone to turn the genderless sex organs into male ones. With females, their cells excrete oestrogens, driving development down the female pathway. Note that not all organisms remain gender indifferent for a time after they're fusion of gametes occurs; for example, fruit flies differentiate into specific sexes as soon as the egg is fertilized. Let us now look at what happens when the X chromosome is inactivated.

Dosage Compensation of Genes

This phenomenon is due to either hypoproduction or hyperproduction. Hypoproduction is the result of the inactivation of one of the X chromosomes in homogametic females, which is observed in mammals, or hyperproduction caused by hyperactivity of the X chromosome in heterogametic males, as observed in *Drosophila*. Individuals with two different sex chromosomes are heterogametic, for example XY, and they are thus able to produce two types of gametes. Conversely, members of the homogametic sex (XX) can only produce one type of gamete. Dosage compensation in humans is due to;

- i. Inactivation of one X chromosome so that no cell has more than one functioning X chromosome, or
- ii. Regulation at some autosomal locus so that homozygous dominants do not produce twice as much product as heterozygotes do.

Another example of dosage compensation in humans, apart from X-inactivation is Barr bodies. In female mammals including humans, one X chromosome becomes highly condensed and becomes a Barr body early during embryonic development. The selection of chromosome becomes a Barr body is a random event. As a result, females are a mosaic of tissues that have one of the two X chromosomes inactivated.

a. Barr bodies; are densely staining masses presenting X chromosomes inactivated by dosage compensation. There are varying cases of presentation of Barr bodies, including:

- a. **XYAA - 0** Barr bodies
- b. **XXAA - 1** Barr body
- c. **X0AA - 0** Barr bodies
- d. **XXXAA - 2** Barr bodies
- e. **XXYAA - 1** Barr body

Let us now look at the alternative form of dosage compensation, which is the inactivation of one of the X chromosomes in greater detail. The Lyon hypothesis best explains how this takes place.

b. **Lyon hypothesis**; the phenomenon in which one X chromosome in each cell becomes inactivated early in an individual's development. Which X chromosome is deactivated is random. All cells derived from cells with a deactivated X chromosome will have that chromosome deactivated as well. This results in genetic mosaics, individuals who carry normal cells (XX) and cells with a deactivated X chromosome (X).

Examples of genetic mosaics are:

- a. Calico cats.
- b. Sweat gland distribution in females heterozygous for ectodermal dysplasia.
- c. Anhidrotic ectodermal dysplasia which results in no sweat glands in a hemizygous male as well as sectors of sweat glands.

Anomalies of Sex Determination

We now know that the sex of an individual is determined by a combination of chromosomes. In humans, homogametic individuals are female, while heterogametic individuals are male. In the normal human genome, there are 44 (22 pairs of) 'ordinary' chromosomes, and 2 sex chromosomes. Situations however arise where the genome is altered. We shall now look at some conditions arising from altered genome.

Hermaphrodites

These are individuals who have both female and male reproductive organs, that is, ovaries and testes. External genitalia are ambiguous and not easily distinguishable as being either male or female. Generally, true hermaphrodites are sterile, though not always. In 1978 (at The American Society of Human Genetics meeting in Vancouver, B.C.) a case was reported in which

- A 25-year-old hermaphrodite delivered a stillborn child after 30 weeks gestation.
- Earlier in life, this person had engaged in male sexual activity.

True hermaphrodites are genetic mosaics and have both XX and XY cells.

Pseudo-hermaphrodites

Pseudo-hermaphrodites have either testicular or ovarian tissue only, never both. The tissue is generally rudimentary or underdeveloped. External genitalia are also often ambiguous, as is the case with true hermaphrodites. Some are genetically female, but may look like males, while others are genetically male, but may look like females and lead normal female sex lives.

Activity 1

The following questions are meant to check your understanding of the previous section. You are advised not to spend more than 15 minutes on this exercise.



Activity



1. For humans, give the genetic sex of

- True hermaphrodites,
- Masculizing males pseudo-hermaphrodites,
- Feminizing males pseudo-hermaphrodites, and
- Female pseudo-hermaphrodites.

2. You are a geneticist and an infertile couple comes to you for genetic counselling. The man is relatively short, only 1.60m tall. He has no other obvious symptoms. Preliminary chromosome tests reveal that he has a Barr body in his nuclei. What is the likely cause of the couple's infertility?

*Refer to answers at the back of this module under answers for Unit 1. Well!!!
How did you do??*

Let us now look at how geneticists determine whether an individual has a genetic disorder or not using a karyotype.

Using Karyotypes to Predict Genetic Disorders

We will begin by first defining what a karyotype is. **A karyotype is a standard arrangement of the chromosome complement done for chromosome analysis.** A normal human karyotype has 46 chromosomes: that is, 22 pairs of autosomes and 2 sex chromosomes. For example, a normal human female karyotype would have 22 pairs of autosomes (non-sex chromosomes) arranged in numerical order beginning with 1, together with two X chromosomes. You may be curious to find out what happens when an individual has a different chromosome complement, such as:

- Too many or too few chromosomes?
- Missing pieces of chromosomes?
- Mixed up pieces of chromosomes?

Too many or too few chromosomes

To understand how our cells might end up with too many or too few chromosomes, you need to know how human cells normally get 46 chromosomes.

You need to understand Meiosis, which we looked at during Cell Division in BIO 110. Meiosis is the process that produces egg and sperm cells (gametes), which normally have 23 chromosomes each, that is, a haploid number (n). One may ask the following question: If eggs and sperm only have one set of chromosomes, then how do we end up with 46 chromosomes? During fertilization, when the egg and sperm fuse, the resulting zygote has two copies of

each chromosome needed for proper development, one copy of each chromosome from each gamete, giving a total of 46.

How can cells end up with too many or too few chromosomes?

A situation may arise in which chromosomes are incorrectly distributed into gametes during Meiosis. When this happens, one gamete may get two copies of a particular chromosome, while another one gets none. Supposing this gamete, with an abnormal number of chromosomes participates in fertilization? The result depends on how many chromosomes the gamete has. If a sperm that is missing a chromosome fertilizes an egg, the resulting zygote will only have one copy of that chromosome. This is called **monosomy**. If a sperm with an extra chromosome fertilizes an egg with a normal chromosome number, the resulting zygote will have 3 copies of that chromosome. This is called **trisomy**.

People who are born with an abnormal number of chromosomes often have genetic disorders because their cells contain too much or too little genetic information. Scientists can predict genetic disorders by looking for extra or missing chromosomes by putting together and examining an individual's karyotype. We already looked at what happens when chromosomes have missing pieces in Module 2. You are advised to look at the section of Module 2 dealing with this phenomenon.

Let us now look at what happens in cases where individuals have variable numbers of chromosome sets. We shall begin by defining the number of chromosome sets in a species.

Ploidy is the number sets which a biological cell in organism of a particular species carries. Human sex cells (sperm and egg) have one complete set of chromosomes from either the male or female parent. Gametes fuse during fertilization to produce somatic cells. Somatic cells, therefore, have twice as many chromosomes as gametes. The haploid number (**n**) is the number of chromosomes in a gamete. A somatic cell has twice that many chromosomes (**2n**). Humans are diploid. This means that a human somatic cell contains 46 chromosomes: 2 complete haploid sets, which make up 23 homologous chromosome pairs. However, many organisms have more than two sets of homologous chromosomes and are called polyploid. It represents a genome containing chromosomes which are multiples of some basic number **x**, which is referred to as the monoploid number.

Polyploidy is the condition in which an organism has more than two genomes. Most plants that are polyploid, such as dandelions, are sterile but can reproduce by apomixis. This is reproduction without Meiosis or formation of gametes, or by other asexual means. Other polyploid plants are fertile, including, durum wheat (*Triticum turgidum durum*), which is used to make pasta and is tetraploid (it has four sets of chromosomes), while bread wheat (*Triticum aestivum*) is hexaploid (six sets of chromosomes). Polyploid plants, if viable, are often larger and more productive compared to their diploid counterparts. Plant breeders often deliberately produce such plants by crossing species or by other means. In the animal kingdom, polyploidy is abnormal and is often fatal.

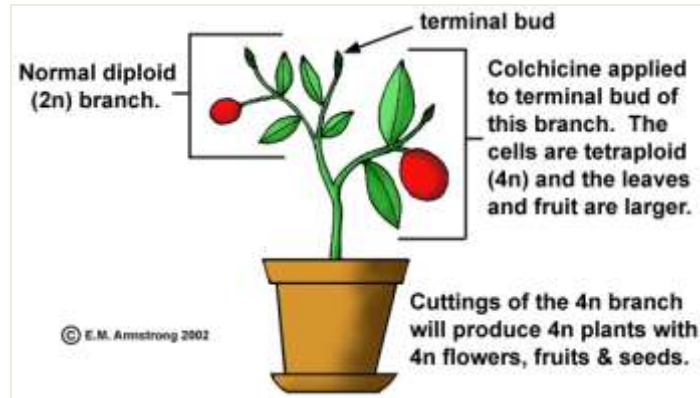


Figure 4: How to make a Fertile Polyploid Plant

The number of chromosomes in a single (non-homologous) set is called the monoploid number (x), and is different from the haploid number (n). Both numbers n and x apply to every cell of a given organism. Specific examples are;

- a. In humans x and n are the same. Therefore, $x = n = 23$, which can also be written as $2n = 2x = 46$.
- b. Bread wheat is an organism where x and n differ. It has six sets of chromosomes; two sets from each of three different diploid species that are its distant ancestors. The somatic cells are hexaploid, with six sets of chromosomes, $2n = 6x = 42$. The gametes are both haploid and triploid, with three sets of chromosomes. The monoploid number $x = 7$, and the haploid number $n = 21$.

Aneuploidy is another type of chromosome abnormality. This involves an abnormal number of chromosomes in which there is an extra or missing chromosome. It is a common cause of genetic disorders or birth defects in humans. Some cancer cells have also been found to contain abnormal numbers of chromosomes. Aneuploidy occurs during cell division, when the chromosomes do not separate properly between the two cells. Aneuploidy can therefore be defined as chromosomal set in which there is an additional chromosome or lack of one.



Note it!

It should be noted that since different species have different numbers of normal chromosomes, the term aneuploidy refers to the chromosome number being different for that particular species. In aneuploid sets, the balance of the chromosomes is disturbed so that aneuploidy can nearly always be detected by growth anomalies if it is not lethal from the outset. This can be illustrated by genomes which are variants of $2n$, for example, $2n+1$, $2n-1$, $3n+1$, $3n+2$, $3n-1$. These variants are referred to as monosomy or trisomy, depending on whether there is one less or one more chromosome.

Single additional chromosomes, or trisomies (sing. trisomy), cause the smallest damages. Such mutants have been found and characterized in nearly all cultivated species. Especially impressive are the disorders found in *Datura stramonium* (Thorn apple; $n = 12$). Every single chromosome of the set leads to abnormal changes in the shape of the fruit that are typical for the respective

chromosome. Chromosome abnormalities in humans occur in 1/160 live births. Most cases of aneuploidy in humans result in spontaneous termination of the developing foetus. However there can be cases of live birth; the most common being extra chromosomes among live births occur on chromosomes 21, 18 and 13. The most common aneuploidy that humans can survive past infancy is trisomy-21, also called Down's syndrome which affects 1 in 800 births. Trisomy-18 (Edwards' syndrome) affects 1 in 6,000 births, and trisomy-13 (Patau syndrome) affects 1 in 10,000 births. Ten percent of infants with trisomy-18 or -13 reach one year of age.

The next section of this unit looks at how errors in cell division cause chromosomal abnormalities, which result individuals with fewer or more chromosomes than is normal.

Nondisjunction and Chromosomal Abnormalities

The literal meaning of 'nondisjunction' is 'not coming apart'. It is the failure of chromosome pairs to separate properly during Meiosis I or II. The loss of a single chromosome ($2n - 1$), in which the daughter cell(s) with the defect will have one chromosome missing from one of its pairs, is referred to as a **monosomy**. The gaining of an extra chromosome, in which the daughter cell(s) with the defect have one chromosome ($2n + 1$) in addition to its pairs, is referred to as a **trisomy**.

It is important to stress that nondisjunction causes errors in chromosome number such as monosomies and trisomies. These include monosomy-X (Turners syndrome) and trisomy-21 (Down's syndrome). Nondisjunction could arise from a failure of homologous chromosomes to separate in Meiosis I, or the failure of sister chromatids to separate during Meiosis II or Mitosis. The failure of paired chromosomes to disjoin or separate during cell division means that both chromosomes go to one daughter cell and none to the other. This is because the resulting errors in a cell cause an imbalance of chromosomes. Such a cell is said to be aneuploid.

The diagrams below show two possible ways through which nondisjunction might occur during Meiosis:

Schematic of Nondisjunction in Meiosis I

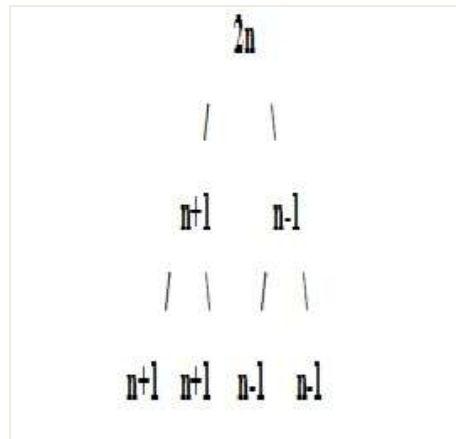


Figure 5: Nondisjunction during Meiosis I

There is chromosomes duplication in a diploid cell ($2n$). All the gametes are affected by nondisjunction in Meiosis I. Two gametes have one extra chromosome ($2n+1$), while the other two gametes are missing one chromosome ($2n-1$).

Schematic of Nondisjunction in Meiosis II (or Mitosis)

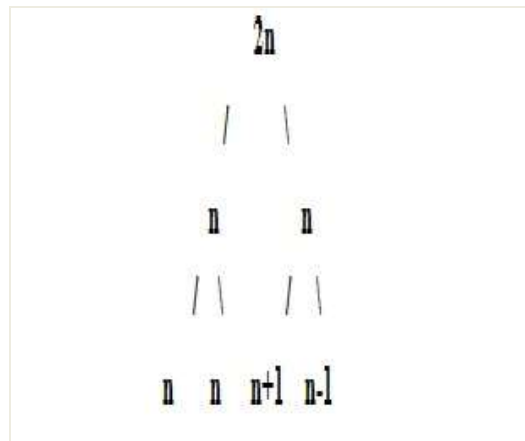


Figure 6: Nondisjunction during Meiosis II

There is chromosome duplication in a diploid cell ($2n$). Half of the gametes are affected by nondisjunction in Meiosis II and the other half are normal. One gamete has one extra chromosome ($2n+1$) and the other gamete is missing one chromosome ($2n-1$). In both instances, chromosomal abnormalities result, with effects which alter the phenotype of the affected individual.



Note it!

Remember that most chromosomal abnormalities are the result of nondisjunction in either the male or female parent, and in rare cases, both parents. We can therefore define nondisjunction as the failure of homologues (at Meiosis) or sister chromatids (at Mitosis) to separate properly to opposite poles of the cell. It results in various abnormalities, including monosomies, and trisomies. As explained earlier, monosomy is a chromosome complement having one less

chromosome ($2n - 1$), while trisomy is a chromosome complement having one extra chromosome to the set ($2n + 1$).

Let us now look at specific examples of human genetic disorders resulting from fewer or more than 46 chromosomes in the genome of an individual.

Turner's syndrome in humans (45, XO)

Turner's syndrome is a series of monosomies caused by nondisjunction either in the male or female parent. This results in the production of gametes with only one X chromosome in females. The incidence rate is 1/5000 live female births.

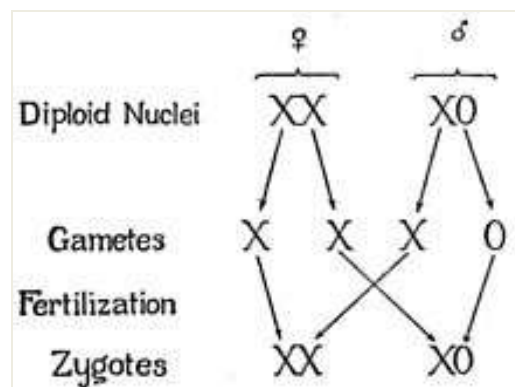


Figure 7: XO Sex Determination

Studies have determined that most spontaneous abortions are Turner's individuals. Some of the phenotypic features of Turner's syndrome include:

- Individuals are short in stature.
- Webbed neck, in which there is a web of skin between the neck and shoulders.
- Breast development is absent or nearly so.
- Some cognitive functions are affected, but intelligence is often generally normal.
- Pubic and axillary hair is reduced or absent.
- Genitalia are infantile.
- Individuals are usually sterile

Klinefelter's syndrome (47, XXY)

Klinefelter's Syndrome is also due to nondisjunction of the X chromosome in either the male or female parent. Incidences of Klinefelter's are 1/1000 live male births. Studies have shown that there seems to be maternal age effects at play as



well. Klinefelter's individuals have genotypes with two or more X chromosomes. The phenotypic features of Klinefelter's include;

- a. Unusually long arms.
- b. Breast development (remember Klinefelter's individuals are male!!)
- c. There is little or no sperm production.
- d. Testes are small or underdeveloped.
- e. Individuals are usually mentally retarded.

The karyotype below shows that this male individual has two, instead of one X chromosome, as in the case with normal males.

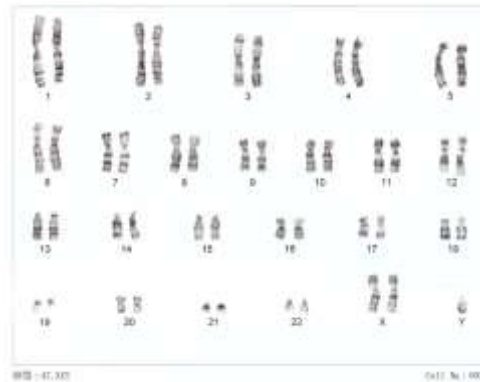


Figure 8: Karyotype of Klinefelter's Syndrome Individual

XYY Condition (Extra Y syndrome)

Extra Y syndrome is due to nondisjunction of the Y chromosome in the male parent. Incidence rates of extra Y are 1/1000 live male births. The phenotypic features of the syndrome include:

- a. Above average height (extra tall).
- b. Individuals are fertile.
- c. Sometimes the individuals are (but not always) mentally retarded.

Poly-X Females (XXX, XXXX, XXXXX, etc)

Poly-X females is due to nondisjunction during oogenesis primarily due to maternal age effect. Incidences are 1/1000 live female births. Some phenotypic features exhibited by poly-X females include:

- a. Infantile or underdeveloped genitalia.
- b. Underdeveloped breasts.
- c. Individuals are fertile.
- d. Sometimes the individuals are (but not always) mentally retarded.

For poly-X females, incidences of abnormal development increases with increasing number of X chromosomes.

Trisomy-21 (47, XX/XY, +21; also called Down's syndrome)

Trisomy-21 is the commonest chromosomal abnormality affecting humans; with incidences of 1/700 live births. The primary cause of trisomy-21 is nondisjunction of chromosome pair 21 during oogenesis. This becomes common with increased maternal age. Nondisjunction of chromosome 21 can also occur during spermatogenesis, though this does not appear to be associated with paternal age. Some phenotypic features of trisomy-21 include:

- Mild to moderate mental retardation.
- High risk of leukaemia
- Individuals are of short stature.
- The skull is broad and short, giving the individual a 'flat' appearance.
- Joints are unusually flexible.
- There is excess skin on the back of the neck.

The karyotype for trisomy-21 is shown below. It indicates that instead of two chromosome 21s, there are three.

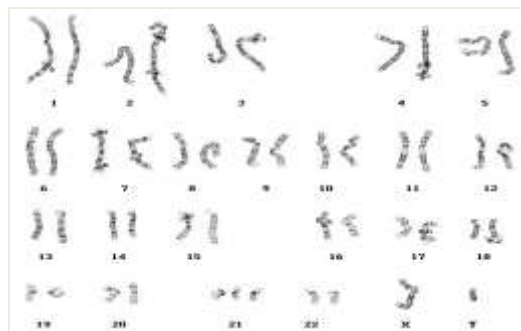


Figure 9: Karyotype of Human Trisomy-21

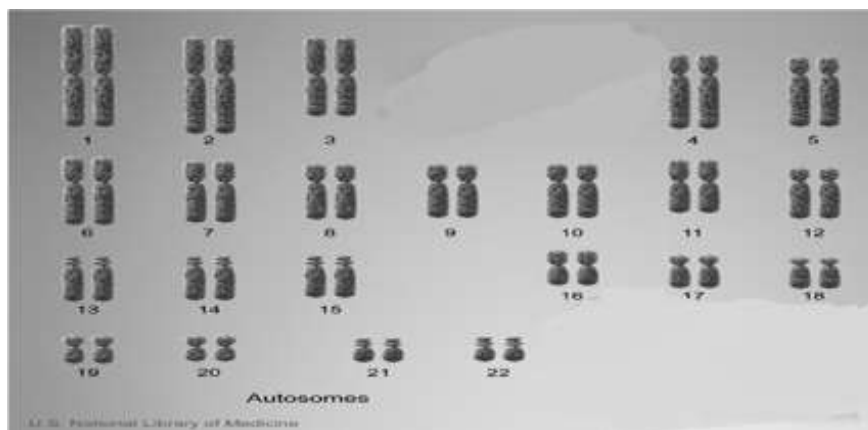
Activity 2



Activity

The following questions are meant to check your understanding of the previous section. You are advised not to spend more than 15 minutes on this exercise.

- Abyssinian oat (*Avena abyssinica*) is tetraploid with 28 chromosomes. The common cultivated oat (*Avena sativa*) is in the same series but is hexaploid. How many chromosomes does the common oat possess?
- Carefully examine the karyotype below and answer the questions which follow.



- i. State whether or not this karyotype shows a normal or an abnormal condition in humans. Explain your answer.
- ii. Explain how the karyotypes for individuals with the following abnormalities would differ from the one shown above
 - a. Monosomy-18.
 - b. Trisomy-21.

*Refer to answers at the back of this module under answers for Unit 1. Well!!!
How did you do??*

Unit summary



Summary

In this unit you have learned about how sex is determined in various organisms. You have also looked at chromosomal abnormalities in humans, how they arise as well as the effect they have on affected individuals. You also used karyotypes to identify normal humans and those with genetic disorders caused by nondisjunction.

Unit 2

Sex-Linked Inheritance

Introduction

You may have noticed that some diseases are more common in some families. You may also have noticed that some diseases are more common in males and not females. The purpose of this unit is to build up on the concept of sex-linked genes, which was introduced in Unit 1. You will look at how genes located on sex chromosomes are passed on from one generation to the next. You will specifically look at the concept of traditional patterns of inheritance of sex-linked genes.

Upon completion of this unit you should be able to:



Outcomes

- *Explain* what the phrase sex-linked means.
- *Distinguish* sex-linked genes from sex-influenced ones.
- *Distinguish* sex-linked genes from sex-limited ones.
- *Explain* the mechanism of x-linked recessive inheritance.
- *Explain* the mechanism of x-linked dominant inheritance.
- *Give* examples of x-linked diseases.



Terminology

- Sex-limited:** A trait which is expressed in one of the sexes only.
- Sex-influenced:** A trait in which dominance of an allele depends on the sex of an individual.
- Sex-linked:** A trait whose genes are located on the sex chromosomes.

Sex-Limited, Sex-Influenced and Linked-Traits

By now, you should be able to describe the location of genes on both autosomes and sex chromosomes. The traits carried on the sex chromosomes are carried either on the X or Y chromosome. Most traits carried are present on the X-chromosome only. This is because the Y-chromosome is smaller and gene-poor. This means that very few genes are located on the Y chromosome. Sex traits can be categorized into three types of inheritance: sex-limited, sex-linked, and sex-influenced. You may recall that we looked at sex-limited and



sex-influenced conditions in Module 1. Let us briefly explore how sex-limited and sex-influenced traits differ from sex-linked ones.

Sex-limited traits are traits that are visible only within one sex. Sex-limited traits are expressed in individuals of one sex only. For instance, barred colouring of chicken feathers, is normally only visible in the roosters. Another example is lactation, or milk production in mammals and humans. Although the genes for producing milk are carried by both males and females, only lactating females express these genes and produce milk. One can determine parental carriers of sex-limited traits can by using a pedigree. We will look at pedigree analysis in detail in Unit 3 of this module. Pedigree analysis is an effective method when determining the probability of an offspring inheriting a trait.

Sex-influenced traits are autosomal traits that are influenced by sex. Sex-influenced traits are expressed differently in the two sexes. If a male has one recessive allele, he will show that trait, but it will take two recessive alleles for the female to show that same trait. These traits are mostly conditioned by the presence of specific hormones. For example, though both males and females carry the gene which causes baldness, it is only expressed in males due to the high concentration of androgens. Under stressful conditions, females may exhibit male-type baldness due to excessive secretion of androgens.

As we saw earlier on in Unit 1, genes located on the X chromosome are called X-linked genes. There are very few genes located on the Y chromosome. Women have two X chromosomes; men have an X and a Y.

Sometimes, changes in genes prevent them from working properly and the gene is said to be faulty or mutated. The gene change can be either 'dominant' or 'recessive'. A woman who has a 'recessive' gene change in one of her X-linked gene copies while the other copy has the correct information is a carrier of the recessive faulty gene. The correct copy works as a 'back-up' so the individual will not be affected by the condition. Males have no working 'back-up' copy and so will generally be affected by the condition if they have the X-linked faulty gene. A woman who has a 'dominant' change in one of her X-linked gene copies and the other copy has the correct information, is a carrier of the dominant faulty gene and will generally be affected. The expression of genes on the X chromosome is also influenced by epigenetics, which involves 'switching off' most of one of the X chromosomes in women. This process ensures that women and men have the same number of X chromosome genes working in the cell. **Sex-linked traits** include colour blindness and haemophilia. They are said to be X-linked because more males (XY) develop these traits compared to females (XX). This is because females have a second gene on the second X chromosome, which will counteract the recessive trait. Thus, the trait is more likely to be visible in males.

Inheritance Patterns in Families of Conditions Due to Faulty Genes

You may recall that genes can be carried either on sex chromosomes or on autosomes. You may also recall that the genetic code itself can be altered through a mutation. Therefore, the inheritance pattern depends on whether the

- Faulty gene is located on one of the autosomes, that is chromosomes 1-22 or on the X or Y chromosome, which is one of the sex chromosomes.
- Change to the genetic code which makes the gene faulty, that is, whether the change is 'recessive' or 'dominant'.

The four most common patterns of inheritance of genetic conditions due to a change in a single gene in families are therefore described as:

- Autosomal recessive

- Autosomal dominant
- X-linked recessive
- X-linked dominant

Let us now look at specific examples of inheritance of the disorders caused by sex-linked genes.

X-linked Inheritance

X-linked inheritance refers to the pattern of inheritance of a condition caused by a faulty gene which is located on the X chromosome. The faulty gene may be recessive or dominant. Conditions that follow a pattern of X-linked recessive inheritance include haemophilia, Duchenne and Becker types of muscular dystrophy and fragile X syndrome. The chance that a child will inherit an X-linked recessive condition in every pregnancy is different for sons and daughters and depends on whether the mother or father carries the faulty gene:

- When the mother is a carrier of an X-linked recessive faulty gene there is 1 chance in 2 (50%) that a son will be affected by the condition and a 1 chance in 2 (50%) that a daughter will be a carrier like the mother.
- When the father is affected by a condition due to an X-linked recessive faulty gene, none of his sons will be affected but all of his daughters will be carriers of the X-linked recessive faulty gene, although they will generally be unaffected by the condition.
- There are very few conditions that have been shown to follow a pattern of X-linked dominant inheritance. Rett syndrome is one example.

It is important to note that parents can be tested for specific genes. Information regarding the appropriateness and availability of testing to determine if a woman is a carrier of an X-linked recessive faulty gene and testing in pregnancy where available and appropriate can be obtained from the local genetic counselling services.

X-linked Recessive Inheritance

Changes in genes on the X chromosome are more commonly 'recessive'. The pattern of inheritance of a condition due to a recessive faulty gene that is located on the X chromosome is called X-linked recessive inheritance. The effect of an X-linked recessive change in a gene that is part of the X chromosome is different in men and women.

Men who have the faulty gene copy on their X chromosome do not have a partner chromosome with a working copy of the gene and will not be able to send the right information to the cells to make the gene product. Men will therefore be affected by the condition due to the X-linked recessive faulty gene being expressed in the cells, even when the gene mutation is recessive. If the body can still work normally with the available gene product, a woman will generally have no health problems as a result of the X-linked faulty gene copy that she is carrying. The change making the gene copy faulty is thus hidden or 'recessive' to the unchanged information in the working copy of the gene. In some cases, however, women who are carrying a faulty X-linked gene will show the effects. This can be because the normal random process of 'switching off' one of the X chromosomes has been skewed strongly towards switching off the X chromosome carrying the working copy of the gene. As a result, more cells in the woman's body would contain an active X chromosome with the faulty gene copy. This would lead to less of the working gene product being available and the woman will show the effects of the faulty gene, though usually less severely than in men. Haemophilia, Duchenne and Becker types of muscular dystrophy and fragile X syndrome all follow a pattern of X-linked recessive inheritance.



Let us now look at some specific examples.

Examples of X-linked recessive inheritance

- The mother is a carrier of the faulty copy of the X-linked gene. The X-linked recessive faulty gene copy is represented by 'r'; the working copy by 'R'.

Phenotype:	Carrier x	Normal	
Genotype:	$X^R X^r$	x	$X^R Y$
Gametes:	X^R X^r		X^R Y
F1 Genotype:	X^R $X^R Y$	$X^R X^r$	$X^r Y$
F1 Phenotype:	$\frac{1}{4}$ female normal, $\frac{1}{4}$ male normal, $\frac{1}{4}$ female carriers, $\frac{1}{4}$ male affected		
F1 sex ratio:	$\frac{1}{2}$ (50%) females $\frac{1}{2}$ males		

- The father has the faulty copy of the X-linked gene. The X-linked recessive faulty gene copy is represented by 'r'.

Phenotype:	Normal x	Affected	
Genotype:	$X^R X^R$	x	$X^r Y$
Gametes:	X^R X^R		X^r Y
F1 Genotype:	$X^R X^r$ $X^R Y$	$X^R X^r$	$X^r Y$
F1 Phenotype:	$\frac{1}{2}$ female carriers, $\frac{1}{4}$ male normal, $\frac{1}{4}$ male affected		
F1 sex ratio:	$\frac{1}{2}$ (50%) females $\frac{1}{2}$ (50%) males		

Determining the History of the X-Linked Recessive Condition in a Family

You may have noticed that in some cases, the men of some families will be affected by a condition over several generations. An example is the British Royal family, which has a history of haemophilia affecting men. In other cases, a boy will be affected with a condition due to an X-linked recessive faulty gene, even though there is no family history of other male members being affected. The change making the X-linked gene faulty in the affected boy may, for unknown reasons, have occurred for the first time (a 'spontaneous' gene change) in a single egg cell, a single sperm cell, or during or shortly after conception.

The condition is described as being due to a new or 'spontaneous' mutation that makes the gene faulty. His mother is not a carrier of the faulty gene and for his siblings to be affected by the same condition would require a change to occur in the same X-linked gene in another egg. The chance of this happening is very low. The affected male could, however, pass on the faulty X-linked gene to his children as described in Figure 10.2. In other cases where there is no family history, the mother is a carrier of the faulty recessive gene on her X chromosome. The change making the X-linked gene faulty in the woman may, for unknown reasons, have occurred, either / or

- the egg or sperm from which she was conceived,
- at the time of her conception,
- in the first cell divisions following fertilization of the egg in early development.

Again, the gene change is new or spontaneous and she is the first in her family to carry the faulty gene and pass it on to her children. As she will generally be unaffected, she may never know she is a genetic carrier until she has an affected child. On the other hand, the change in the gene could have occurred in this way in a previous generation and have been passed down through the family but, by chance, no male family members inherited the faulty gene, or only females may have been conceived.

X-linked Dominant Inheritance

We will now illustrate how X-linked dominant inheritance works by looking at whether it is the mother or the father carrying the faulty x-linked dominant gene. We will first consider the case of the mother carrying the gene, before considering a case where the father carries the faulty gene.

1. The mother carries the faulty X-linked dominant gene and is affected. The faulty copy of the X-linked gene is represented by 'D', the working copy by 'd'.

Phenotype:	Affected	x	Normal
Genotype:	$X^D X^d$	x	$X^d Y$
Gametes:	X^D X^d		X^d Y
F1 Genotype:	$X^D X^d$ $X^D Y$	$X^d X^d$	$X^d Y$

F₁ Phenotype: ¼ female affected, ¼ male affected, ¼ female normal, ¼ male normal

F1 sex: ½ (50%) females ½ males

2. The father carries the faulty X-linked dominant gene and is affected. The faulty copy of the X-linked gene is represented by 'D', the working copy by 'd'.

Phenotype:	Normal	x	Affected
Genotype:	$X^d X^d$	x	$X^D Y$
Gametes:	X^d X^d		X^D Y
F1 Genotype:	$X^D X^d$ $X^d Y$	$X^D X^d$	$X^d Y$

F₁ Phenotype: ¼ female affected, ¼ male normal, ¼ female affected, ¼ male normal

F1 sex: ½ (50%) females ½ males

Very few conditions have been shown to follow a pattern of X-linked dominant inheritance. Rett syndrome is one example.

Activity 1



Activity

The following questions are meant to check your understanding of the previous section. You are advised not to spend more than 15 minutes on this exercise.

In *Drosophila spp*, eye colour is a sex-linked trait. Red is dominant to white. What are the sexes and eye colours of flies with the following genotypes?



Refer to answers at the back of this module under answers for Unit 1. Well!!! How did you do??

Unit summary



Summary

In this unit you looked at inheritance patterns of sex-linked disorders. You also learned how they differ from sex-limited and sex-influenced ones.

Unit 2 Assessment



Assessment

The following questions are meant to check your understanding of Unit 2. You are advised not to spend more than 15 minutes on this exercise.

In humans, haemophilia is a sex-linked trait. Females can be normal, carriers, or have the disease. Males will either have the disease or not (but they won't ever be carriers).

- i. Show the cross of a haemophiliac male with a woman who is a carrier.
- ii. What is the probability of the couple having a male haemophiliac child?

Refer to answers at the back of this module under answers for Unit 1. Well!!! How did you do??

Unit 3

Pedigree Analysis

Introduction

In Unit 2, we looked at how x-linked diseases are passed on from one generation to the next. In this Unit, we shall look at how we can trace the transmission of genetic diseases from generation to generation using pedigree analysis.

Upon completion of this unit you should be able to:



Outcomes

- *Define* the phrase 'pedigree analysis'.
- *Determine* the mode of transmission of a genetic disease using a pedigree.
- *Interpret* a pedigree chart
- *Construct* a pedigree chart.



Terminology

Pedigree:	A family tree, which is drawn using standard symbols showing patterns of inheritance for specific phenotypic traits.
Pedigree chart (diagram):	A chart drawn to show how a specific trait is passed on across generations in a family.
Pedigree analysis:	The scientific use of pedigrees to trace or determine the incidences of genetic disorders in a family.

We will begin this unit by looking at the basic principles governing pedigree analysis.

Basic Principles

Consider the following: if more than one individual in a family is afflicted with a disease, it is a clue that the disease may be inherited. A doctor needs to look at the family history to determine whether the disease is indeed inherited and, if so, establish the mode of inheritance. This information can then be used to predict recurrence risk in future generations. A basic method of determining the pattern of inheritance of any trait, which may be a physical attribute like eye colour or a serious disease like Marfan syndrome, is to look at its occurrence in several individuals within a family, spanning as many generations as possible. For a genetic disease, a doctor has to examine existing family members to determine who is affected and who is not. The same information may be difficult to obtain about more distant relatives, and is often incomplete. Once family history is determined, the doctor will draw up the information in the form of a special chart or family tree that uses a set of standardized symbols. This is referred to as a pedigree chart. In a pedigree;



- males are represented by squares □
- females by circles ○
- an affected individual is represented by a filled symbol ■ or ●
- a horizontal line between two symbols indicates a mating □—○

The offspring are connected to each other by a horizontal line above the symbols and to the parents by vertical lines;

- Roman numerals I, II, III, etc. symbolize generations.
- Arabic numerals 1, 2, 3, etc. symbolize birth order within each generation.

In this way, any individual within the pedigree can be identified by the combination of two numbers, for example, individual II3 is the third offspring in the second generation.

The diagram below shows how these symbols may be used.

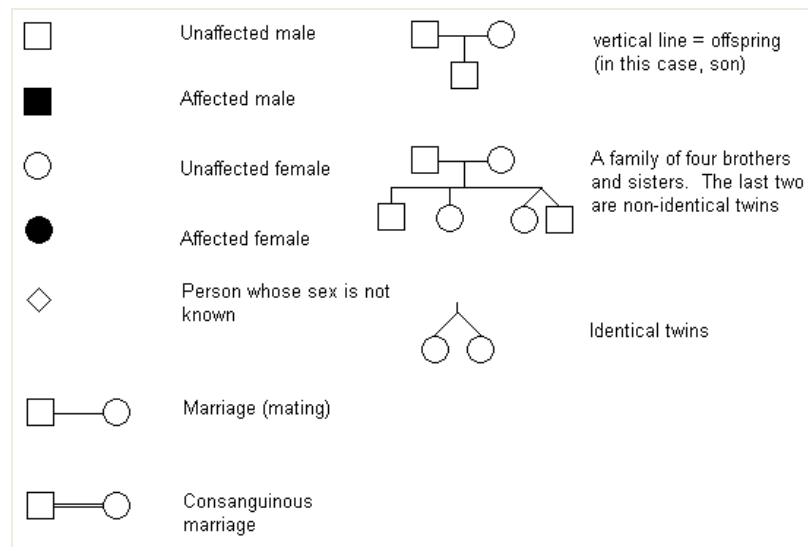


Figure 10: Symbols used in Human Pedigree Analysis

Dominant and Recessive Traits

The reason for the two distinct patterns of inheritance has to do with the genes that predispose an individual to a given disease. As we saw in Module 1, genes exist in different forms known as alleles, which are usually distinguished from each other by the traits they specify. Individuals carrying identical alleles of a given gene are said to be homozygous for the gene in question. Similarly, when two different alleles are present in a gene pair, the individual is said to be heterozygous. Dominant traits are expressed in the heterozygous condition. This means that one only needs to inherit one disease-causing allele from one parent to have the disease. Recessive traits are only expressed in the homozygous condition. In other words, you need to inherit the same disease-causing allele from both parents to have the disease. This means that some non sex-linked genetic conditions follow Mendelian patterns of inheritance, namely dominance and recessiveness. Let us now look at how dominant and recessive traits are passed on from one generation to the next.

Dominant Traits

Using genetic principles, the information presented in a pedigree can be analyzed to determine whether a given physical trait is inherited or not and what the pattern of inheritance it is. In simple terms, traits can be either dominant or recessive. A dominant trait is passed on to a son or daughter from only one parent. Characteristics of a dominant pedigree are:

- Every affected individual has at least one affected parent.
- Affected individuals who mate with unaffected individuals have a 50% chance of transmitting the trait to each child.
- Two affected individuals may have unaffected children.
- Each generation will have affected individuals.

This is shown on the pedigree diagram below.

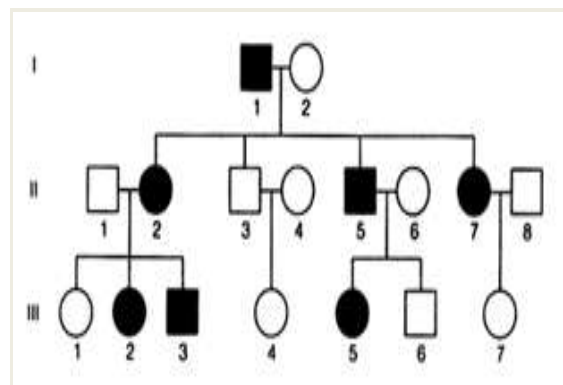


Figure 11: Pedigree showing Mode of Inheritance of Dominant Traits

Recessive Traits

Recessive traits are passed on to children from both parents, though the parents may seem perfectly normal. This is because for recessive traits, heterozygotes are not usually affected. Characteristics of recessive pedigrees are:

- An individual who is affected may have parents who are not affected.
- All the children of two affected individuals are affected.
- In pedigrees involving rare traits, the unaffected parents of an affected individual may be related to each other.
- Two affected parents cannot have an unaffected child.

This is illustrated on the pedigree diagram below.

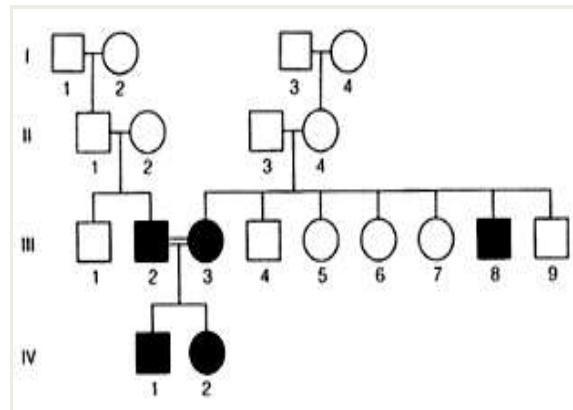


Figure 12: Pedigree showing Mode of Inheritance of Recessive Traits

Penetrance and Expressivity

You may recall, from Module 2, the concepts of penetrance and expressivity. We can redefine penetrance as the probability that a disease will appear in an individual when a disease-causing allele is present. For example, if all the individuals who have the disease-causing allele for a dominant disorder have the disease, the allele is said to have 100% penetrance. If only a quarter of individuals carrying the disease-causing allele show symptoms of the disease, the penetrance is 25%. Expressivity, on the other hand, refers to the range of symptoms that are possible for a given disease. For example, an inherited disease like Marfan syndrome can have either severe or mild symptoms, making it difficult to diagnose.

Non-inherited traits (Acquired Traits)

It is important to point out that not all diseases that occur in families are inherited. Other factors that can cause diseases to cluster within a family are viral infections or exposure to disease-causing agents, for example, asbestos. The first clue that a disease is not inherited but acquired is that it does not show a pattern of inheritance that is consistent with genetic principles. In other words, it does not look anything like a dominant or recessive pedigree.

We will now discuss the modes of inheritance of genetic disorders.

Modes of Inheritance of Genetic Disorders

You may have noticed that humans are usually not aware of the existence of genetic disorders, unless a variant form is present in the population. This is more so the variant form causes an abnormal (or at least a different) phenotype. This is because most human genes are inherited in a Mendelian manner. We can therefore follow the inheritance of the abnormal phenotype and deduce whether the variant allele is dominant or recessive by conducting a pedigree analysis. Let us now look at two ways through which genetic disorders are passed on from one generation to the next.

Autosomal Dominant

A dominant condition is transmitted in unbroken descent from one generation to the next. Most matings will be of the form $Mm \times mm$, that is, heterozygote to homozygous recessive. We would therefore expect every child of such a mating to

have a 50% chance of receiving the mutant gene and thus of being affected. A typical autosomal dominant pedigree might look like this:

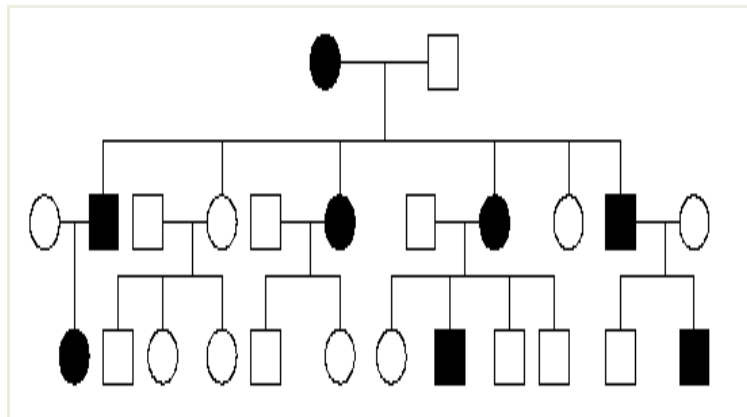


Figure 13: Autosomal Dominant Genetic Disorder

Examples of autosomal dominant conditions include Tuberous sclerosis, neurofibromatosis and many other cancer-causing mutations such as retinoblastoma.

Autosomal Recessive

You may recall that a recessive trait will only manifest in homozygous condition. If the condition is severe, it will be unlikely that homozygotes will live to reproductive age. Thus most occurrences of the condition will be in matings between two heterozygotes or carriers. An autosomal recessive condition may be transmitted through a long line of carriers before two carriers' mate. Then there will be a $\frac{1}{4}$ or 25% chance that any child of the two carriers will be affected. The pedigree will therefore often only have one sib-ship with affected members.

Before we proceed to the next section, let us look at some examples of an autosomal recessive pedigree.

Examples of pedigrees of;

- a. A typical autosomal recessive pedigree, and
- b. An autosomal pedigree with inbreeding.

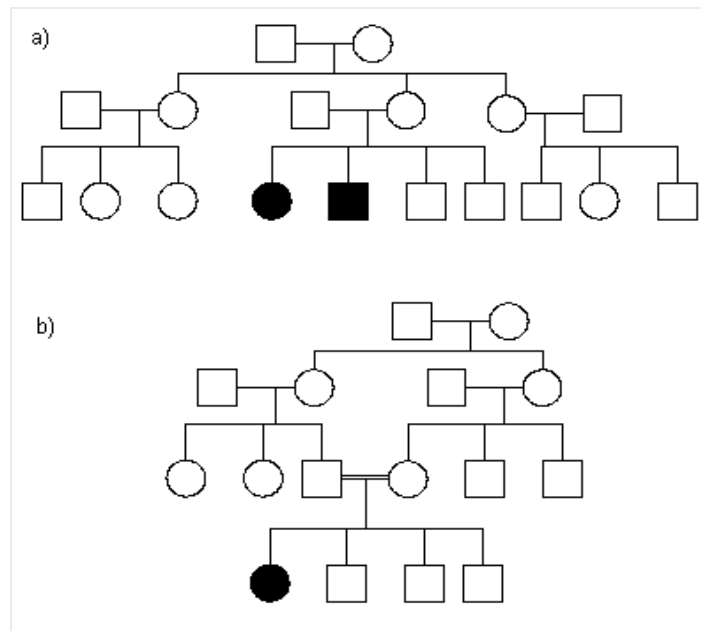


Figure 14: Autosomal Recessive Genetic Disorder

Though not common in humans, inbreeding is a major cause of occurrence of genetic disorders. If the parents are related to each other, perhaps by being cousins, there is an increased risk that any gene present in a child may have two alleles identical due to descent. The degree of risk that both alleles of a pair in an individual are descended from the same recent common ancestor is the degree of inbreeding of the person.

Let us examine pedigree **b**. in Figure 14 above in detail. If we consider any child of a first cousin mating, we can trace through the pedigree the chance that the other allele is the same by common descent. Let us consider any child of generation **IV**, any gene which came from the father **III3** had a half chance of having come from grandmother **II2**, a further half chance of also being present in her sister grandmother **II4**, a further half a chance of having been passed onto mother **III4** and finally a half chance of being transmitted into the same child we started from. This gives a total risk of

$$\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = \frac{1}{16}$$

This figure, can be thought of as either the

- Chance that both maternal and paternal alleles at one locus are identical by descent, or
- Proportion of all the individual's genes that are homozygous because of identity by common descent.

This is known as the 'coefficient of inbreeding' and is usually given the symbol **F**. The next section looks at using probability to predict incidences of genetic disorders in families.

Using Probability

The Punnett square, which you learned in Module 1, is a useful method of working out straightforward crosses. However, not all crosses are straightforward! Most of you have some background in mathematics and will have covered elementary probability. For those who need to revisit the concepts involved, reading *Advanced Statistics* by Crawshaw and Chambers (2004) is highly recommended as it covers probability in detail. The probability of an event is the chance or likelihood that it will happen. The probability of tossing a coin, for example, so that it lands heads up, is said to be $\frac{1}{2}$, as is the probability that it will land tails up. This means that

- The probability of an impossible event is 0; you will always get a heads or tails for a coin toss.
- The probability of a certain event is 1.
- If the probability of event **x** is **p** then the probability of '**not x**' occurring is **1-p**.
- The probability of two independent events occurring is the product of their two individual probabilities.

For example, in the example in Figure 14b above, about the coefficient of inbreeding of children from first cousin marriages, we considered a number of probabilities of $\frac{1}{2}$ which we multiplied together to reach a final probability of $\frac{1}{16}$ that any gene was homozygous by descent.

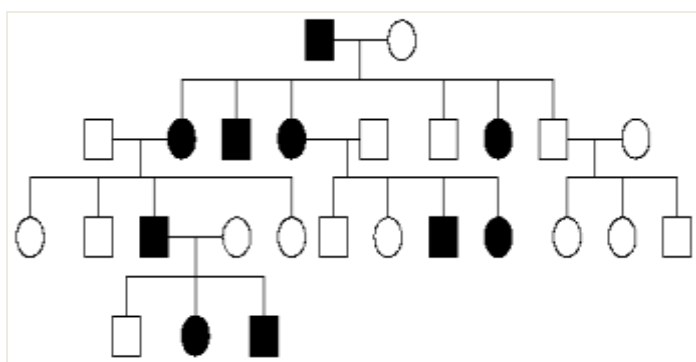
Activity 1



The following question is meant to check your understanding of the previous section. You are advised not to spend more than 15 minutes on this exercise.

Activity

The pedigree below could be the result of either the segregation of an autosomal dominant condition or of an autosomal recessive one. In the former case, what is the risk for individual III6 of having a child affected with this condition? In the latter case, who in the pedigree is an obligate carrier? Which other members of the pedigree are at risk of being carriers? Write down their risks.



Refer to answers at the back of this module under answers for Unit 1. Well!!! How did you do??



Unit summary



Summary

In this unit you at the concepts encompassing pedigree analysis. These include the standard symbols required to construct a pedigree chart or interpret one. This unit also introduced you to the use of probability in determining the degree to which an individual may inherit a genetic disorder running in the family.

Unit 4

Variation

Introduction

So far we have seen that Genetics is concerned with explaining how characteristics are passed one from generation to generation, i.e. heredity, or inheritance. However, it is important to also deal with some background information about the characteristics themselves in what is referred to as Population Genetics. This may then be tied in with evolution and the development of different species of living organisms. If you consider almost any characteristic, you will notice differences between various people, even within a family (or animals or plants) in a population. These differences are what we refer to as variation. Like most living organisms, humans show variation. You may recall from O' Level Biology that there are two forms of variation, namely continuous and discontinuous variation.

Upon completion of this unit you should be able to:



Outcomes

- *Define* variation.
- *Distinguish* continuous from discontinuous variation.
- *Explain* how variation is caused.
- *Explain* what a Mendelian population is.
- *Give* at least four examples of Mendelian population.
- *Define* gene pool.
- *Describe* variation with respect to human blood groups.
- *State* the Hardy-Weinberg principle.
- *Use* the Hardy-Weinberg principle to calculate the distribution of alleles in a population.



Terminology

Variation:	The differences among individuals in a population.
Continuous variation:	Characteristics showing a broad range, with many intermediate values between two extremes.
Discontinuous variation:	Characteristics falling into a few very distinct classes.

Gene frequency:	Ratio of the actual numbers of individuals carrying a specific allele to the total number of individuals in a population.
Gene pool:	This is a population containing the genetic units from which subsequent generations arise.
Hardy-Weinberg principle:	This principle states that the proportion of the different alleles in a gene pool only changes as a result of an external factor.
Mendelian population:	A group of sexually reproducing organisms with a relatively close genetic relationship
Polygenic inheritance:	The combined effect of many genes on the expression of a particular phenotype.

What is Genetic Variation?

We can define variation simply as the difference in genetic sequence among individuals of a population. This means that variation can be seen at every genetic level, that is, in the:

- i. DNA
- ii. Genes
- iii. Chromosomes
- iv. Proteins
- v. Function of proteins

Major Types of Genetic Variations

Mutations – changes at the level of DNA; one or more base pairs has undergone a change; change could be at random or due to a factor in the environment. These include structural changes to chromosomes - deletions, insertions, and genetic rearrangements, which can affect several genes or large areas of a chromosome at once.

Polymorphisms – differences in individual DNA which are not mutations. Single-nucleotide polymorphisms (SNPs) are the most common, occurring about once every 1,000 bases or so

Copy number variations – some DNA repeats itself (i.e. AAGAAGAAGAAG) and there can be variation in the number of repeats.

Understanding Human Genetic Variation

Scientists have noticed that most variation is ‘meaningless’ – it does not affect our ability to survive or adapt. A good example is ‘silent mutations’ in DNA, which change the DNA, but not the amino acid the DNA codes for. Other mutations may change the amino acid sequence of a protein, but not the overall function of that protein. This is true of many polymorphisms which do not seem to affect our survivability in any way.



Note it!

Please note that some variation is positive – it improves our ability to survive or adapt. For example, mutations in the **CCR5** gene provide protection against AIDS by making it harder for HIV to bind to the surface of cells and infect them. You may recall from Module 2 that individuals with sickle cell trait (i.e. carriers of the recessive gene) are less likely to die from malaria. This is because the genetic mutations which cause sickle cell anaemia have also been found to have a protective

effect. And, of course, some variation leads to disease. Single-gene disorders like cystic fibrosis and Huntington disease are two examples of diseases with devastating consequences on affected individuals, which are the result of variation.

Scientists are continually learning more about the contribution of genetic variation to more ‘common’ conditions, such as heart disease, cancer, diabetes, and psychiatric disorders like schizophrenia and bipolar disorder. It has been suggested that variation may give some individuals a predisposition to one of these conditions, though not the condition itself. For those mutations/variations which make us more likely to develop a condition such as diabetes, do not forget that environment plays a key role. Environment may be interacting with several different genes to cause a condition, instead of just one gene. Scientists now believe that genetics plays a part in virtually every condition.

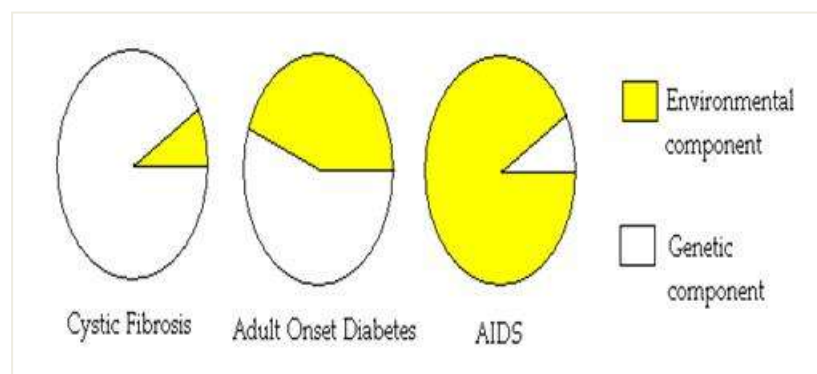


Figure 15: Environmental Interaction and Genetics = Phenotype

The Human Genome Project

One goal of the Human Genome Project was to provide the complete sequence of the human genome. Another goal of the HGP was to shed light on the extent of human genetic variation by providing a detailed picture of human differences and similarities on the genetic level. One of the conclusions the project arrived at was that any two individuals are 99.9% identical in their DNA. Looking at the differences among the human population, we can see that that 0.1% is VERY important in defining our differences. We, as humans, are all very similar, but all very different. Visitors to our planet would have a tough time telling us apart at first, but would slowly begin to notice the differences.



Note it!

The 0.1% of unique DNA, plus the interaction of genetic and environmental factors, is what leads to different phenotypic features observed in humans.

Distribution of Traits

Variation has enabled us to classify traits within a population according to various criteria. These categories into which variations have been grouped are;

- i. **Continuous trait:** no distinct categories; rather, there is a wide variety which covers a broad spectrum.
- ii. **Discontinuous trait:** distinct categories with no 'in-betweens'.
- iii. **Normal distribution** (e.g. the bell curve): majority of data points at an average point, with fewer and fewer data points as you move away from the average.
- iv. **Bimodal distribution:** a type of normal distribution with two peaks instead of one (may see a peak for two populations within one larger population).

Let us now look at Continuous and Discontinuous variation in detail.

Continuous Variation

You may have noticed that some characteristics differ in a general way, with a broad range, and many intermediate values between the extremes. As a matter of fact, if you consider a large enough sample from a population, perhaps plotting frequency as a histogram or as a frequency polygon, you will find that most of the values are close to the average (mean), and extreme values are actually rather rare. Such traits show continuous variation. Height is an example of a continuously variable characteristic; as long as you consider a consistent sample, for example, a large number of people of a particular age and sex. When plotted as a histogram, these data show a typical bell-shaped normal distribution curve, with the mean (= average), mode (= biggest value) and median (= central value) all being the same. This is illustrated in Figure 15 below.

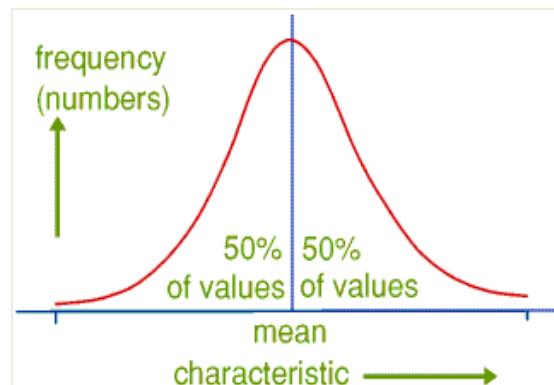


Figure 16: Distribution of Characteristics Exhibiting Continuous Variation

The list below gives other examples of human characteristics which show continuous variation.

- Weight,
- Foot length, or
- Any measurable dimension.

As you will find out later, it is usually difficult to give a straightforward explanation of the genetic basis for these continuously variable characteristics. This is because they are the result of two factors: 1. genes that are inherited by an individual; 2. effect of environment on the individual, such as the availability and type of food, diseases and climate. Other examples of continuous variation include:

- Hand span,
- Shoe size, and

- Milk yield in cows

Continuous variation is the combined effect of many genes; that is **polygenic inheritance** and is often significantly affected by environmental influences. Milk yield in cows, for example, is determined not only by their genetic make-up but is also significantly affected by environmental factors such as pasture quality and diet, weather, and the comfort of their surroundings.

Discontinuous Variation

You may have noticed that some characteristics fall into a few very distinct classes or categories. The ability to roll the tongue, attached ear lobes, eye colour, gender and blood groups, are examples of such traits. These traits show discontinuous variation. They can be explained much more easily by simple rules of genetics as they are less likely to be affected by other factors, including environmental ones. This is because discontinuous variation is the result of inheritance only; your blood group won't change no matter what kind of whether you're exposed to or type of food which you consume. Figure 16 below shows how one such trait, blood group, is represented on a histogram.

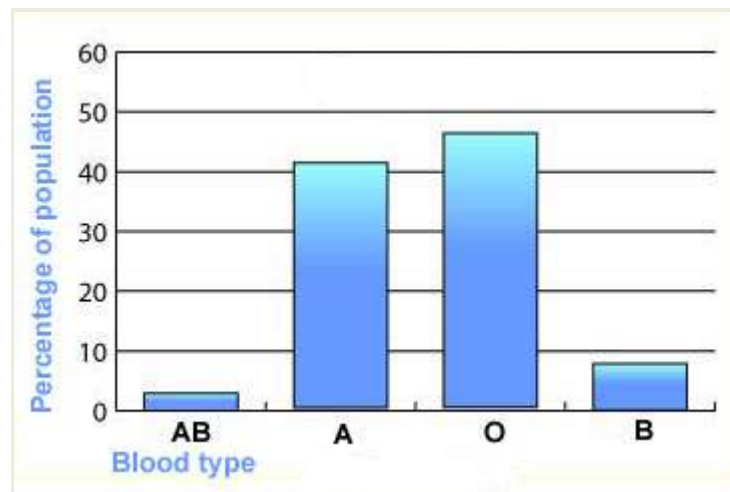


Figure 47: Distribution of Characteristics Exhibiting Discontinuous Variation

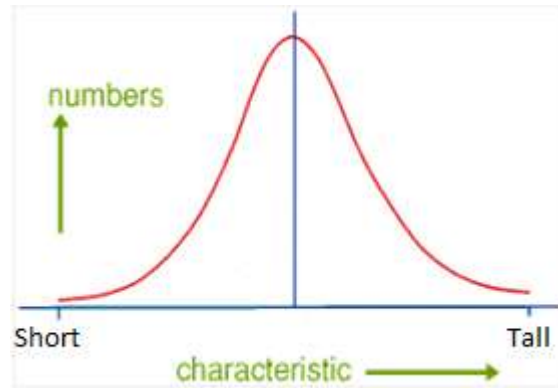
Activity 1



Activity

The following questions are meant to check your understanding of the previous section. You are advised not to spend more than 15 minutes on this exercise.

1. Carefully study the figure below and answer the questions which follow.



- i. What type of variation does this show? Give a reason for your answer.
 - ii. In what way is this type of variation affected by environmental factors such as nutrition.
2. Answer the following with respect to characteristics which vary discontinuously.
- i. For tongue-rolling ability, how many classes are there?
 - ii. How many classes of blood group are there?

Refer to answers at the back of this module under answers for Unit 4. Well!!! How did you do??

Let us now look some of the factors which may cause variation in a population.

Causes of Variation

1. Inheritance

You may have noticed that some of the characteristics possessed by an individual in a population run within families and can be said to be inherited - i.e. derived from previous generations. These characteristics are passed on, in a fairly predictable way, as a result of sexual reproduction. Sexual reproduction also introduces an element of randomness, so that variation is brought about in a population. These two almost contradictory factors - dependable inheritance of characteristics from parents, and variation within the population - are essential to an understanding of the process of evolution.

Below are some examples of characteristics which may be inherited by a child from his or her parents.

- hair colour
- eye colour
- skin colour

The examples often give the impression that inheritance covers only trivial features, such as the shape of the human chin, or ear-lobes. However, an extremely wide range of characteristics are known to be passed on in this way. In fact, practically every aspect of normal human body functioning is under hereditary (genetic control), because there are many examples of fairly rare conditions which can be inherited in exactly the same way as hair or eye colour.

Remember that there are also diseases which cannot be transmitted from one person to the next, but which are caused by defective functioning of certain cells. These inherited forms of 'disease' may also be called 'inborn errors of metabolism'. The list below is an example of some human conditions which may be passed from one generation to the next;

- Sickle cell anaemia.
- Huntington's chorea.
- Cystic fibrosis.
- Haemophilia.

2. Acquired

You may have noticed that some traits seem to appear from nowhere and affect individuals, and do not run in families. Such characteristics are said to be acquired during an individual's lifetime (non-inherited). These may also be caused by environmental effects. Some examples of acquired human characteristics are;

- Scars.
- Fillings.
- Ability to speak other languages.
- Ability to ride bicycle etc.



Note it!

It should also be noted that some characteristics probably have both an inherited and an environmental basis, such as (possibly) I.Q. - intelligence quotient? The balance between them is the answer to the 'nature versus nurture' debate. Similar considerations apply in all living organisms; for example, different plants grown in different conditions of light or temperature may show differences in growth rate and vigour, and understanding the causes of this variation is quite fundamental in controlling or increasing agricultural and horticultural productivity. From an experimental point of view, how may the effects of these environmental factors be shown, as distinct from effects due to different genetic make-up of the plant in question? One may consider the following;

- use a clone of plants,
- from cuttings, etc

3. Mutation

You may recall how mutations, covered in Module 2, occur. You may also recall that there are two basic types of mutations depending on where the mutation occurs, that is, either at the gene or at chromosome level.

A Gene Mutation is a very rare event. A mutation in a single inheritable characteristic (gene) is usually less likely than one in a million, but once it has happened, it may be passed on to the next generation, along the same lines as other inherited characteristics. However, not all individuals carrying mutations survive; most have been found to be harmful, so that the organisms carrying them are at a disadvantage. In the wild, such organisms are unlikely to survive. Nevertheless, some (beneficial) mutations confer an advantage, and others (neutral?) cause neither advantage nor disadvantage - at least until there is some reason for selection of adapted types to occur. This may be another reason for variation within a population. In fact, the few different forms resulting from mutation which are beneficial can spread through a population by natural selection, and this may have the eventual effect of changing a population so much that it differs from its original form - resulting in the evolution of a new species.

Chromosome Mutations may result in change in the number of chromosomes incorporated into sex cells. A child produced as a result may have, for instance, an extra chromosome, or an extra part of a chromosome attached to the normal set. Down's syndrome is caused by having 47 chromosomes instead of the normal 46 per cell.

Mutations as described above may occur 'naturally', though it has been shown in the laboratory that they may be caused (more efficiently) by other means. Similarly, various factors in the environment may increase the chance of mutations occurring. The risks associated with some lifestyle activities are known, and exposure to most of these is avoidable. For instance, chemicals in tobacco include mutagens, and several types of ionizing radiation have mutagenic effects, as you may recall from Module 2.

Below are some examples of diagnostic/medical treatments which may cause mutations;

- X rays.
- Gamma rays.
- Ultra-violet rays.

You may have noticed that these are in fact similar to the causes of cancer. This means that the idea of 'natural' causes for mutations (and cancer?) is probably rather dubious.

Gene Pool

Let us now turn our attention to the concept of a gene pool. A gene pool is the total number of alleles (**note, not genes!**) in a breeding population. Put simply, a gene pool is a breeding population. For example, the human population will have 3 alleles for blood groups, that is, I^A , I^B , and I^O . Since every human must have at least one of each of these alleles, the total frequency must be **1.0** and the frequency of each allele can then be expressed as a decimal of this total. In the above case, the frequencies vary greatly amongst different ethnic groups. This variation of blood groups among humans is shown in Table 1 below.

Table 1: the Distribution of Frequencies of the Alleles for Blood Groups amongst Different Ethnic Groups

Population	I^A	I^B	I^O
African	15	10	75
Caucasian	30	15	55
Oriental	20	22	58
American Indian	0 - 55	0	45 - 100
Australasian	50	0	50
Europe	22	11	67
Worldwide	22	16	62

In Module 2, we saw that geneticists use statistics to determine whether the results of a specific cross fit genetics theory. Geneticists also use other mathematical models to calculate the results of the modes of inheritance of genes in a given population. One such model is the Hardy-Weinberg principle.

The Hardy – Weinberg principle

This principle states that the proportion of the different alleles in a gene pool (that is a breeding population) only changes as a result of an external factor. Thus providing the following assumptions are met, each generation will be the same as the present one:

- Large population.
- No migration – either in (immigration) or out (emigration).
- There is random mating.
- No mutations occur.
- All genotypes are equally fertile.

The Hardy-Weinberg formula, proposed by Hardy and Weinberg, is widely used in population genetics. In its application, one assumes that both gene frequencies and genotype frequencies remain constant from generation to generation within an infinitely large inbreeding population in which mating is random and there is no selection, migration or mutation. The formula is given as

$$1 = p^2 + 2pq + q^2$$

Where **p** = the proportion of dominant alleles and **q** = the proportion of recessive alleles.

$$\text{And } p + q = 1$$

Since both **p** and **q** are decimal fractions, both will therefore be less than 1.0.

Let us look at a couple of examples showing how this principle may be used. See if you can give accurate answers to the questions before going through the solutions provided to each question.

Example 1

In a population containing 2 alleles, **T** and **t**, three genotypes will exist – **TT**, **Tt** and **tt**. If **T** is a dominant allele, then it is impossible to tell which individuals are **TT** and which are **Tt**. It will also be impossible to tell the relative proportions of these two genotypes. The Hardy-Weinberg equation allows us to calculate that.

Solution

Follow the stages laid down to perform the calculation accurately:

First define the alleles:

Let the proportion of **T** alleles = **p** and the proportion of **t** alleles = **q**

This means that:

$$p + q = 1$$

Note that both **p** and **q** are decimal fractions, and therefore both will be less than 1.0.

That means that the proportion of the different genotypes is:

TT individuals are p^2 ;

Tt individuals are $2pq$; and

tt individuals are q^2

Since that is the whole population, it follows that:

$$1 = p^2 + 2pq + q^2$$

In applying the Hardy-Weinberg formula in population genetics, one assumes that both gene frequencies and genotype frequencies remain constant from generation to generation within an infinitely large inbreeding population in which mating is random and there is no selection, migration or mutation.

Now, we can see, and count, those individuals that are **tt** (double recessive). So:

1. Work out the proportion (as a **decimal fraction, i.e. 5% = 0.05**) of **tt** individuals in the whole population. The question will give you this data, so just use your calculator!
2. Take the square root of that number. That gives you **q**.
3. Since **p + q = 1**, you can now calculate **p, which is (1 - q)**.
4. Substitute the values you now have in the equation **1 = p² + 2pq + q²** to give you the decimal fraction of each of the genotypes.
5. If the question asks you to calculate 'how many individuals in then population are....', then multiply the number you have (for the required genotype) by the total population. Remember that you cannot have a fraction of an individual, so round up/down to the nearest whole number.
6. Easy isn't it!

Example 2

The four human blood types – A, B, AB and O are determined by a multiple allelic series having L^A or I^A , L^B or I^B and L^O or i . A geneticist collected and summarized the frequencies of the four blood types in a sample of 23, 787 persons taken from Rochester, New York in the table below.

Phenotype	Number	Frequency
A	9, 943	0.418
B	2, 379	0.100
AB	904	0.038
O	10, 561	0.444
	23, 787	1.000

Solution

Ignoring the sub-types let the following be used in gene frequency analysis;

p = frequency of I^A

q = frequency of I^B

r = frequency of i

Therefore $p + q + r = 1$

The genotypes in the population, under random mating will be given by

$$(p + q + r)^2$$

We can calculate the frequency of each allele from the data in the table and gene frequency analysis values given above, remembering that we let p , q and r represent the frequencies of genes I^A , I^B and i respectively. The value of r , that is gene i , is immediately evident from the figure given;

$$r^2 = 0.444$$

$$r = \sqrt{0.444}$$

$$\mathbf{r = 0.6663 (= frequency of i)}$$

And the sum of A and O phenotypes is given by

$$(p + r)^2 = 0.418 + 0.444$$

$$(p + r)^2 = 0.862$$

Therefore $p + r = \sqrt{0.862}$

$$p + r = 0.9284$$

$$\text{So } p = (p + r) - r$$

$$p = 0.9284 - 0.6663$$

$$p = 0.2621 \text{ (= frequency of } I^A \text{)}$$

$$\text{Since } p + q + r = 1$$

$$\text{Then } q = 1 - (p + r)$$

$$q = 1 - 0.9284$$

$$q = 0.0716 \text{ (= frequency of } I^B \text{)}$$

Using these allelic frequencies, we can now calculate the genotypic frequencies, as shown in the table below;

Phenotype	Genotype	Genotypic frequency	Population based on	Probability samples
O	ii	r^2		0.4440
A	$I^A I^A$	p^2	0.0687	0.4180
	$I^A i$	$2pr$	0.3493	
B	$I^B I^B$	q^2	0.0051	0.1005
	$I^B i$	$2qr$	0.0954	
AB	$I^A I^B$	$2pq$		0.0375
				1.0000

Unit summary



Summary

In this unit you learned about what variation is and how it is caused. You have also looked at the concept of a gene pool and the application of the Hardy-Weinberg formula.

Assignment 3



Assignment

Instructions:

1. Read each question carefully.
2. Answer **ALL** the questions in this Assignment.
3. Show all the steps in any genetic crosses you perform.
4. You may type your assignment (font: **Times New Roman**; size: **12**; line spacing: **1.5**; alignment: **justified**).

Due Date: May, 2012

1. In *Drosophila*, the X chromosomes may become attached to one another (X-X), such that they always segregate together. Some flies contain both an attached X chromosome and a Y chromosome.
 - a. What sex would such a fly be? Explain your answer.
 - b. Given the answer in i. above, predict the sex of the offspring that would occur in a cross between this fly and a normal one.
 - c. If the offspring just mentioned in ii. above were allowed to interbreed, what would the outcome be?

2. A son with Klinefelter's syndrome is born to a mother who is phenotypically normal and a father who has the X-linked skin condition called anhidrotic ectodermal dysplasia. The mother's skin is completely normal with no signs of the skin abnormality. In contrast, her son has patches of normal and patches of abnormal skin.
 - a. Which parent contributed the abnormal gamete?
 - b. Using the appropriate genetic terminology, describe the meiotic mistake that occurred. Be sure to indicate which division the mistake occurred in.
 - c. Using appropriate genetic terminology, explain the son's skin phenotype.

3. Albinism in humans is inherited as a simple recessive trait. For each of the families listed below, determine the genotypes of the parents and offspring. When two alternative genotypes are possible, list both.
 - a. Two normal parents have five children, four normal, and one albino.
 - b. A normal male and an albino female have six children all normal.
 - c. A normal male and an albino female have six children, three normal and three albino.
 - d. Construct a pedigree diagram of the families in b. and c. Assume that one of the normal children in b. and one of the albino children in c. are the parents of eight children.

4. Tay-Sachs is caused by loss-of-function mutations in a gene located on chromosome 15 that encodes a lysosomal enzyme. Tay-Sachs is inherited as an autosomal recessive condition. Among Ashkenazi Jews of central European ancestry, roughly 1 in 3,600 children is born with the disease. What fraction of individuals in this population are carriers?

END OF ASSIGNMENT

References

1. Brad Field, P., Dodds, J., & Taylor, N., (2002). *A-Level Biology*, Pearson Education Limited: Essex, UK.
2. Clegg, C.J., & MacKean, D.G., (2002). *Advanced Biology: Principles of and Application*, John Murray Publishers Limited: London, UK.
3. Crawshaw, J. & Chambers, J. (2001). *Advanced Level Statistics*, 4th Edition, Nelson Thornes Limited Cheltenham, UK.
4. Kent, M., (2000). *Advanced Biology*, Oxford University Press: Oxford, UK.
5. Genetics Home Reference Handbook ; Help Me Understand Genetics, Reprinted from Genetics Home Reference at <http://ghr.nlm.nih.gov/>
6. Robert, M.B.V., (1991). *Biology: A Functional Approach*, John Murray Publishers Limited: London, UK.
7. Robert, M.B.V., King, T., & Reiss, M., (1994). *Practical Biology for Advanced Level*, Nelson Thornes Limited: Cheltenham, UK.
8. Simpkins, J., and Williams J.I. (1994) *Advanced Biology*, Collins Educational Publishing Limited: London, UK.
9. Taylor, D.J., Green, N. P. O. & Stout, G. W. (1997). *Biological Science*, 3rd Edition, Cambridge University Press: Cambridge, UK.
10. Toole, G. and Toole, S., (1995) *Understanding Biology for Advanced Level*, Nelson Thornes Limited: Cheltenham, UK.
11. Verma, P. S. & Aggarwal, V. K. (2003). *Cell Biology, Genetics, Molecular Biology, Evolution & Ecology*, S. Chand & Company Limited: New Delhi, India.
12. Verma, P. S. & Aggarwal, V. K. (2005). *Genetics*, S. Chand & Company Limited: New Delhi, India.

ANSWERS TO UNIT ACTIVITIES

UNIT ONE

Activity 1

1. For humans, give the genetic sex of

- True hermaphrodites,
- Masculizing males pseudo-hermaphrodites,
- Feminizing males pseudo-hermaphrodites, and
- Female pseudo-hermaphrodites.

2. You are a geneticist and an infertile couple comes to you for genetic counselling. The man is relatively short, only 1.60m tall. He has no other obvious symptoms. Preliminary chromosome tests reveal that he has a Barr body in his nuclei. What is the likely cause of the couple's infertility?

Solution

1. In humans, sex determination follows the XX-XY System. Therefore the presence of X and Y chromosomes determines whether is male or female. This means;

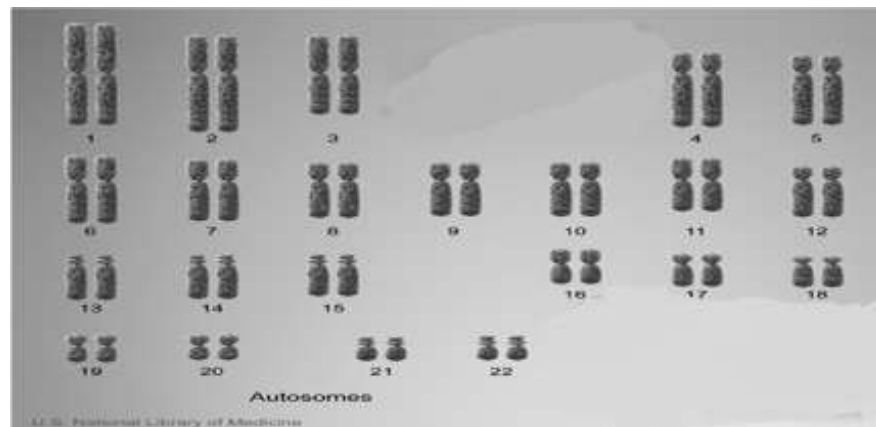
- True hermaphrodites - XX
- Masculizing males pseudo-hermaphrodites - XY
- Feminizing males pseudo-hermaphrodites - XY
- Female pseudo-hermaphrodites - XX

2. Perhaps the husband is an XX male. His karyotype should be examined more closely. DNA tests for the presence of Y chromosome and the SRY gene should be carried out in order for more conclusive results to be obtained.

Activity 2

1. Abyssinian oat (*Avena abyssinica*) is tetraploid with 28 chromosomes. The common cultivated oat (*Avena sativa*) is in the same series but is hexaploid. How many chromosomes does the common oat possess?

2. Carefully examine the karyotype below and answer the questions which follow.



- iii. State whether or not this karyotype shows a normal or an abnormal condition in humans. Explain your answer.
- iv. Explain how the karyotypes for individuals with the following abnormalities would differ from the one shown above
 - c. Monosomy-18.
 - d. Trisomy-21.

Solution

1. 42 chromosomes

2. This is a normal human karyotype. The karyotype shows a total of 46 chromosomes, arranged in 23 pairs and a total of two sex chromosomes.

- a. Monosomy-18 results when there is one less chromosome on chromosome 18.

The individual's chromosome complement is $(2n - 1)$, that is 45.

- b. Trisomy-21 occurs when there is one extra chromosome on chromosome 21.

The individual's chromosome complement is $(2n + 1)$, that is 47.

UNIT TWO

Activity 1

In *Drosophila spp*, eye colour is a sex-linked trait. Red is dominant to white. What are the sexes and eye colours of flies with the following genotypes?

 $X^R X^r$ $X^R Y$ $X^r X^r$ $X^R X^R$ $X^r Y$

Solution

$X^R X^r$ female, red-eyed $X^R Y$ male, red-eyed $X^r X^r$ female, red-eyed

$X^R X^R$ female, red-eyed $X^r Y$ male, white-eyed

UNIT 2 ASSESSMENT

In humans, haemophilia is a sex-linked trait. Females can be normal, carriers, or have the disease. Males will either have the disease or not (but they won't ever be carriers).

- iii. Show the cross of a haemophiliac male with a woman who is a carrier.
- iv. What is the probability of the couple having a male haemophiliac child?

Solution

First identify the genotypes of individuals, both male and female. Specify which individuals will be normal, carriers and affected.

$X^H X^H$ = female, normal

$X^H Y$ = male, normal

$X^H X^h$ = female, carrier

$X^h Y$ = male, haemophiliac

$X^h X^h$ = female, haemophiliac

Then cross the two individuals with the appropriate genotypes as specified in the question, as shown below:

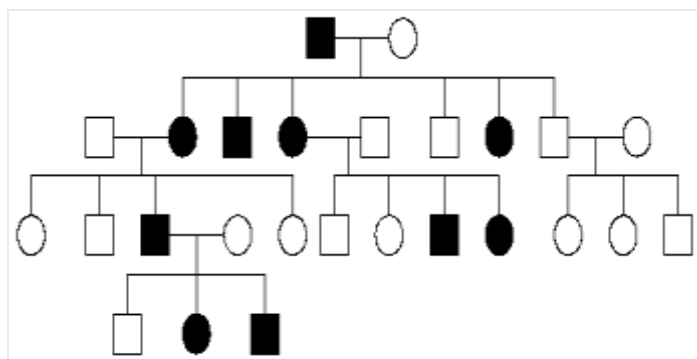
Phenotype:	Female, heterozygous	x	Male, haemophiliac
Genotype:	$X^H X^h$	x	$X^h Y$
Gametes:	X^H X^h		X^h Y
F ₁ genotype:	$X^H X^h$	$X^H Y$	$X^h X^h$ $X^h Y$
Ratio:	Sex; $\frac{1}{2}$ female	:	$\frac{1}{2}$ male
	Haemophiliac; $\frac{2}{4}$ or $\frac{1}{2}$		

Probability of a male haemophiliac child (P) = $\frac{1}{2} \times \frac{1}{2}$
 $P = \frac{1}{4}$

UNIT THREE

Activity 1

The pedigree below could be the result of either the segregation of an autosomal dominant condition or of an autosomal recessive one. In the former case, what is the risk for individual III6 of having a child affected with this condition? In the latter case, who in the pedigree is an obligate carrier? Which other members of the pedigree are at risk of being carriers? Write down their risks.



Solution

If dominant, then the chance that III6 will have affected children is almost zero, with the exception of just a chance mutation occurring.

If recessive then obligate carriers are:

I2,
II1, II5, II6, II8,
III1, III2, III4, III5, III6, III7,
IV1

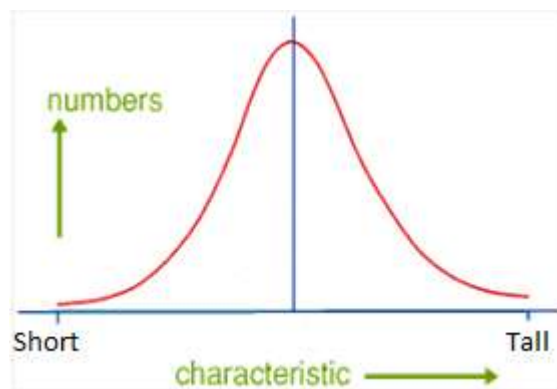
The following are at risk of being carriers:

III10, III11, III12 all with chance 50%

UNIT FOUR

Activity 1

1. Carefully study the figure below and answer the questions which follow.



- iii. What type of variation does this show? Give a reason for your answer.
 - iv. In what way is this type of variation affected by environmental factors such as nutrition.
2. Answer the following with respect to characteristics which vary discontinuously.
- iii. For tongue-rolling ability, how many classes are there?
 - iv. How many classes of blood group are there?

Solution

1. Continuous variation.

Reason:

2.
 - 2; rollers and non-rollers only.

- 4, that is A, B, O, and AB.