
UNIT 2 HUMAN GENETICS AND SOCIETY

Contents

- 2.1 Introduction
- 2.2 Blood Group Polymorphism
- 2.3 Hemoglobinopathies
- 2.4 Genetic Counseling
- 2.5 Genetic Screening
- 2.6 Summary
- References
- Suggested Reading
- Sample Questions

Learning Objectives



It is expected that after reading Unit 2, you would be able to:

- discuss the importance of blood groups and the procedure in carrying out the ABO and Rh (D) blood group systems;
- understand and explain different abnormal hemoglobin's; and
- discuss what is genetic counseling and genetic screening and the processes of genetic counseling and genetic screening.

2.1 INTRODUCTION

As you know, physical anthropology is mainly concerned with human variation and evolution. However within physical anthropology numerous specialised branches arise such as human growth and development, genetic demography, population genetics, forensic anthropology, human genetics, molecular anthropology, physiological anthropology, applied physical anthropology etc. But applied physical anthropology is one of the major fields where the knowledge of physical anthropology can be practiced in the society. One such example is anthropometric measurements collected from different populations of the world are used in designing equipment, (furniture, head gear) garment industry, footwear industry etc. Nowadays the understanding of human genetics has turn out to be a central part of our society and the information of human genetics gained by physical anthropologists can be applied and practiced in society. Hence this unit focuses on some of the areas of human genetics namely, blood group polymorphism, haemoglobinopathies, genetic counseling and genetic screening. Physical anthropologists on gaining knowledge in these areas are able to practice them in the society.

2.2 BLOOD GROUP POLYMORPHISM

In blood transfusion the determination of blood group is very important. The determination of blood group is a part of the curriculum for the physical anthropology students. Hence it is indeed necessary to understand the blood groups. So we will provide a brief history of the blood groups and the procedure involved in the determination of ABO and Rh (D) blood groups, the two major blood group systems which are being used in the blood.

Karl Landsteiner discovered the ABO blood group system in 1901 and later on more than 20 distinct blood group systems have been identified. They are MNS, P, Rh, Lutheran, Kell, Lewis, Duffy, Kidd etc. However till now ABO is the major human blood group system which has four major blood groups: A, B, AB and O. All people can be placed into one of these four (A, B, AB and O) blood groups based on the presence or absence of two antigens and two antibodies. The antigens designated as A and B and the antibodies Anti-A and Anti-B. The antigens are present on the red blood cells while the antibodies are found in the plasma. The following table shows the antigens and the corresponding antibodies present in a blood group. AB blood group is considered as the universal recipient and O group as the universal donor.

Blood Group	Antigen	Antibody	Can Donate Blood to	Can Receive Blood from
A	A	Anti-B	A, AB	A, O
B	B	Anti-A	B, AB	B, O
AB	A and B	None	AB	AB, O
O	None	Anti-A and Anti-B	A, B, AB, O	O

Procedure for Identification ABO Blood Groups: Two methods are in practice one is porcelain tile/slide method and the other one is tube method.

Tile/Slide Method: Place one drop of Anti-A serum in one cavity of the slide/tile and same quantity of Anti-B serum in another cavity. Add one drop of 10% cell suspension already prepared from the collected blood sample in normal saline to each cavity and wait for 2 to 3 minutes and observe the agglutination reaction. If agglutination is observed in the cavity where Anti-A serum was added it indicates A blood group; if the reaction occurs in the cavity where Anti B is added it indicates B blood group. If the agglutination is observed in both the cavities the blood group is AB group while lack of agglutination in both the cavities indicate O group.

Tube Method: Take two small test tubes and add one drop of Anti-A serum into one tube and one drop of Anti-B serum into another tube. Add one drop of 3-5% cell suspension (already prepared from the collected blood sample) to each tube. Mix the contents gently and allow them at room temperature for few minutes. Then observe for the agglutination reaction. Interpret the results as stated for the tile/slide method.

Rh (D) Blood Group: This is another major blood group system which is also used in transfusion medicine. The Rh blood group system was discovered in 1940 by Karl Landsteiner and Weiner. This blood group system is based on the presence or absence of Rh antigen frequently called the Rh factor. The term “positive” or “negative” refers to either the presence or absence of the Rh D antigen. While blood grouping if the blood agglutinates in presence of anti-Rh D antibody, it indicates as positive and if the blood does not agglutinate, it indicates as negative.

Procedure for Identification of Rh D Blood Group: Place one drop of anti-Rh D serum in a micro tube and add 1 drop of 5% cell suspension (already prepared from the collected blood sample). Keep the contents at 37° C for minutes and then observe for agglutination reaction. If agglutination occurs in anti-Rh D serum, the Rh factor is positive; and if it does not, the Rh factor is negative.

2.3 HEMOGLOBINOPATHIES

This is another important area of human genetics, the information gained in this area may be practiced in the society by physical anthropologists. Before going into the details of Haemoglobinopathies, let us have a brief look on the normal Hemoglobin. Hemoglobin is a tetramer that consists of two α -like and two β -like globin subunits. Hemoglobin is an air-containing protein of the red blood cells. There are four kinds of hemoglobin: the ‘embryonic’ haemoglobin, the ‘fetal haemoglobin’ (HbF), Adult haemoglobin’ (HbA) and Hemoglobin A₂ (HbA₂). Under normal conditions, the red cell of an adult man contains approximately 98% HbA, traces of HbF and 2.0% of HbA₂. On the other hand Haemoglobinopathies are the inherited disorders of blood. Following is the brief account on Haemoglobinopathies.

The inherited disorders of hemoglobin comprise Hemoglobinopathy and Thalassaemias. Haemoglobinopathies comprise a major bulk of non communicable genetic diseases and one of the major public health problems in many countries including India. They are most widespread in ethnic populations from Africa, the Mediterranean basin and Southeast Asia. The vulnerable segments of the society like infants and children, adolescent girls, pregnant women, etc. are severely affected by these abnormalities and also cause a high degree of morbidity, moderate to severe hemolytic anemia. The most frequent mutations of hemoglobin which affect the beta globin gene and result in a hemoglobinopathies are sickle hemoglobin (HbS); hemoglobin C (HbC); hemoglobin D (HbD); hemoglobin E (HbE); hemoglobin O Arab (HbOArab). But in India Hb S, Hb E and Hb D are widely prevalent.

But Thalassaemias are hereditary disorders of hemoglobin synthesis characterised by reduced rate of production of normal hemoglobin due to absence or decrease in the synthesis of the amount of the globin chain produced. It can be divided into alpha Thalassaemias (α Thal) and beta Thalassaemias (β Thal). Beta-Thalassaemias is again of two types – Thalassaemias major and Thalassaemia minor. Thalassaemia major causes severe hemolytic anemia while the Thalassaemia minor causes mild anemia.

The diagnostic methods for hemoglobinopathies are discussed briefly.

Diagnostic Methods: The abnormal hemoglobin's or hemoglobinopathies can be identified by various laboratory methods which include haematological examination, electrophoretic techniques, estimation of fetal hemoglobin (Hb F), determination of hemoglobin A2 (HbA2), sickle cell examination, high pressure liquid chromatography (HPLC) etc. Hematological examination consists of determination of: total hemoglobin concentration (g/100ml), number of red blood cells ($10^6/\text{mm}^3$), and percent of packed cell volume (PCV) (haematocrit), naked eye single tube red cell osmotic fragility test (NESTROFT). Then calculation of different red cell indices such as mean corpuscular volume (MCV in μ^3), mean corpuscular hemoglobin (MCH in μg) and mean corpuscular hemoglobin concentration (MCHC in percent). For calculation of the red cell indices the following formulae are used:

$$\text{MCV} = \frac{\text{haematocrit (\%)} \times 10}{\text{RBC count (millins}/\text{mm}^3) \text{ blood}}$$

$$\text{MCH} = \frac{\text{haemoglobin (g/100ml)} \times 100}{\text{haematocrit (\%)}}$$

$$\text{MCHC} = \frac{\text{Hb (g)} \times 100}{\text{haematocrit (\%)}}$$

However these red cell indices can also be obtained through standard electronic cell counters.

To diagnose hemoglobin abnormalities Electrophoretic technique is an easy and convenient method. This can be performed either on paper, in starch gel, on cellulose acetate, in agarose gel and in acrylamide gel. The fetal hemoglobin can be determined with the help of alkali denaturation, blood slide and electrophoretic methods. But hemoglobin A2 can be determined by using electrophoretic technique. Different methods are available to diagnose sickle cell anemia (Bhasin and Chahal, 1996) and they are Scriver and Waugh method, Bisulfite method and Sickledex method. But most common method to diagnose sickle anemia is Bisulfite method.

But recently high-performance liquid chromatography technique has been used for the diagnosis of haemoglobinopathies and thalassemias. Their advantages over other methods include sensitivity, resolution, and simplicity as well as speed.

2.4 GENETIC COUNSELING

Genetic counseling is an important area of applied human genetics which can be practiced in the society. The counselor should have adequate knowledge in the counseling process. The counselor is preferably a medical doctor or a profession who is having knowledge in human genetics. The duty of a counselor is to offer

the necessary genetic information and also the information about social, economic and psychological aspects related through the case.

Genetic Counseling, defined by Harper (1984), is “the process by which patients or relatives at risk of a disorder (that may be hereditary) are advised of the consequences of the disorder, the probability of developing and or transmitting it, and the ways in which this may be prevented or ameliorated”. However, the American Society of Human Genetics (1975) formulated the definition as “Genetic counseling is a communication process which deals with the human problems associated with the risk of occurrence of a genetic disorder in a family”. This consists of establishing an exact diagnosis and estimation of risks of recurrence or incidence in a family member. This process involves an attempt by one or more appropriately trained persons to help the individual or family to:

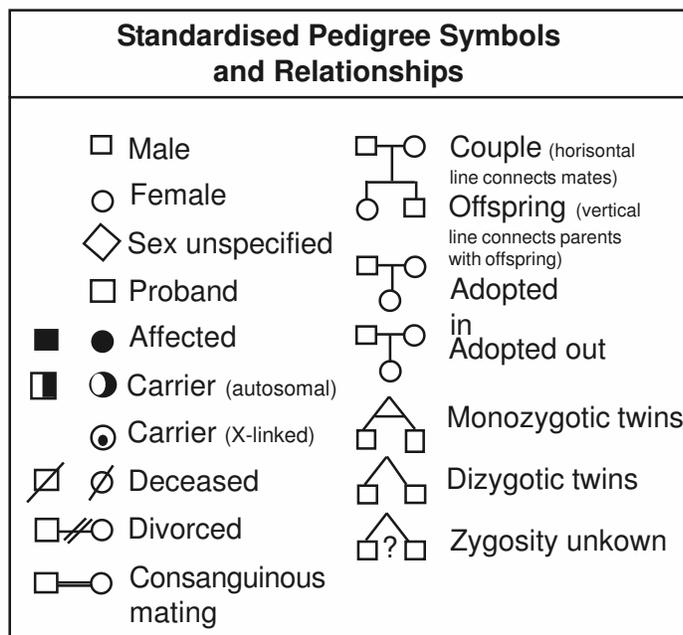
- 1) Know the medical facts including the diagnosis, probable course of the disorder, and the available management;
- 2) Understand the way hereditary contributes to the disorder and the risk of recurrence in specified relatives;
- 3) Appreciate the alternatives for dealing with the risk of recurrence;
- 4) Select a course of action which seems to them appropriate in their view of their risk, their family goals, and their ethical and religious standards and act in accordance with that decision; and
- 5) To make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder.

Now let us see how genetic counseling is done

Firstly, it is necessary to identify people suffering from a genetic disorder; and this is relatively easy for a trained clinician. But, it is difficult to identify a carrier for genetic disease and in most cases, it is not possible. However, information on the likelihood of an individual being a carrier for a genetic disease can be obtained by the analysis of family history or pedigree analysis as detailed below. Thereafter, the prospective parents either suffering from or suspected to be heterozygous for some genetic disease are advised about the risk of their would-be children suffering from the same disease. By creating a suitable social environment, such parents may be encouraged to voluntarily abstain from producing children.

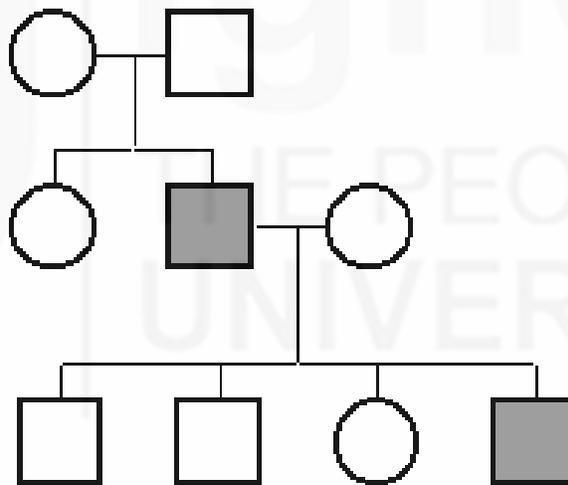
Pedigree analysis

Pedigree is a family history of hereditary condition or diagram of a family history representing the family members, their relationships to proband (the affected individual that brings family to medical attention), and their status with respect to a particular hereditary condition. While constructing a pedigree, following symbols can be used. The following diagram presents the standard symbols and relationships for Pedigree analysis. Males are represented by squares and females by circles. Mating is represented by a horizontal line connecting a male and a female. Children are represented by vertical lines which go downwards from the parents' line.



Source: Migeneticsconnection.org

The inheritance pattern of biological characters whether they are dominant or recessive for a particular genetic disease is determined by pedigrees analysis. The following diagram is an example of such a pedigree.



Source: Faculty.clintoncc.suny.edu

Pedigree analysis assists the counselor to decide if a trait is Mendelian. It also assists the counselor to establish the mode of inheritance. In pedigree analysis the first step is to observe the number and relationships of all individuals who express the same or similar clinical features. From this, we will be in a position to determine if the disorder is dominant or recessive, autosomal or X-linked by observing the typical patterns of inheritance.

After having known the inheritance pattern of the disorder, we can evaluate the status of family members in the pedigree. Then by examining the position of affected individuals, mutation carriers could be identified. With the data available, we can estimate the risk of carrier to other family members or the possibility that a couple may have an affected child.

2.5 GENETIC SCREENING

Genetic counseling is essentially a communication process that informs prospective parents about the nature of genetic disorders, about the risk of their having a genetically defective child, and about the options available to them in dealing with that risk. Or else they can opt to cope with the care of an existing genetically handicapped child. Genetic screening, in contrast, is a routine diagnostic procedure devised to detect those who are carriers of, or who are themselves affected by, a hereditary disease. Genetic screening applies to populations rather than to individuals. The most-widespread application of genetic screening in the United State is for phenylketonuria (PKU). All hospitals in the United States screen newborn babies for PKU by a blood test called Guthrie test.

After genetic screening, if both the parents are heterozygous for a genetic disease and the genotypes of both the prospective parents become known, then it is easier to work out the probability of their child (if they decide to have one) inheriting the disease. This can be done through amniocentesis about two months after conception; i.e. Through amniocentesis; the cultured fetal cells are used for determining their karyotype, levels of the critical enzymes and the restriction patterns of DNA. Such an antenatal diagnosis is now available for several genetic diseases and for a variety of chromosomal defects. Such a diagnosis can help the parents to opt for premature termination of abnormal fetus, if they so decide.

Genetic counseling and antenatal diagnosis provides definite relief to the possible parents 'at risk' and thereby reduce the frequency of genetically defective individuals in the population. However, it is unlikely that these measures would eliminate the deleterious alleles from a population. This is so because most genetic defects are recessive and heterozygotes for such alleles. Thus, even after a total ban on reproduction by the homozygotes for such recessive alleles, they would remain in the population through the heterozygotes, therefore, even such an extreme selection would lead to only a slow decline in their frequency. Further, it is not likely that all the couples in any society will willingly submit themselves, at least in the foreseeable future, to these procedures. But genetic counseling has become a routine aspect of medical practice in most developed countries.

It has been advocated that defective genes may be corrected through sophisticated genetic techniques either during the early stages of embryo development (embryo therapy) or in specific tissues of the adult patient (patient therapy); such an approach is referred to as genetic surgery. Embryo therapy involves

- 1) In vitro fertilisation of egg.
- 2) Production of several copies of the normal allele of the defective gene.
- 3) Introduction of this DNA into the zygote or in the cells of the developing embryo.
- 4) Integration of DNA, preferably in place of the defective allele, so that it may function normally.

The aim of patient therapy is to introduce the normal gene into the critical tissue of the patient that is affected by a genetic disease, i.e., the tissue where the concerned gene is required to express itself the most, e.g., pancreas in the case of

diabetes. The steps involved in patient therapy are similar to those in embryo therapy. But in this case, cells from the concerned tissues have to be treated in vitro to correct their genetic defects and then reintroduced into the tissue where they may function normally. Techniques for isolation, identification and multiplication of many human genes are now available, and for many others they are likely to be developed soon. The techniques for gene transfer in eukaryotes are being refined and it may not be a great problem in the near future.

A suggestion has also been made to use highly specific chemical mutagens that will correct the defect in the concerned gene. Such a directed mutagenesis, however, is a dream that may be more difficult to fulfill for the patient and embryo therapies through DNA mediated genetic modifications. Genetic screening and counseling may also lead to certain problems. The cases of mistaken paternity, the problem of confidentiality, delayed counseling are important among them.

2.6 SUMMARY

Practicing anthropology is one of the significant areas where the information gained by anthropologists is practiced outside academia. Since physical anthropologists have attracted towards human genetics and human genetics has turned out be a central part of society, the knowledge in some of the areas of human genetics gained by physical anthropologists can be practiced outside academia. Some of the areas consist of serology, hemoglobinopathies, genetic counseling and genetic screening. It is well known fact that the ABO and Rh (D) blood groups are being used in transfusion medicine. Hence the history and methodology of blood group polymorphism is presented. The inherited disorders of hemoglobin encompass Haemoglobinopathy and Thalassaemias. The hemoglobinopathies consist of sickle hemoglobin (HbS); hemoglobin C (HbC); hemoglobin D (HbD); Hemoglobin E (HbE); hemoglobin O Arab (HbOArab). But widely frequent hemoglobinopathies in India are Hb S, Hb E and Hb D. Genetic counseling is a process that seeks to assist affected individuals and other individuals at risk of getting an inherited condition; it also helps to understand the nature of the genetic disorder, its transmission and the options available for their management and family planning. On the other hand genetic screening is a regular diagnostic procedure worked out to identify the persons who are carriers of, or who are themselves affected by, a hereditary disease. Genetic screening concerns to populations rather than to persons.

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Sample Questions

- 1) Briefly discuss the applications of human genetics in the society.
- 2) What is genetic screening? Explain its process.
- 3) Write short notes on the following:
 - a) Genetic counseling
 - b) Haemoglobinopathies
 - c) Blood groups