UNIT 4 APPLIED DIMENSIONS-II

Contents

Learning Objectives

It is expected that after reading, you would be able to understand the following applications of Human Genetics:

- paternity diagnosis;
- genetic counseling and eugenics; and
- DNA technology and its use in disease and medicine

4.1 INTRODUCTION

Genetics is the name given to the study of heredity, the process by which characteristics are passed from parents to offspring, so that all organisms including human beings resemble their ancestors. The central concept of genetics is that heredity is controlled by a vast number of factors called genes, which are discrete physical particles present in all living organisms.

> Branches of genetics are microbial genetics, mycogenetics, plant genetics, animal genetics, human genetics, population genetics, cytogenetics, biochemical genetics, molecular genetics, clinical genetics etc.

Since the present unit is on human genetics, the definition of human genetics is presented here. Human genetics is concerned with genetically determined resemblances and differences among human beings. In normal human being, the nucleus of each cell contains 46 chromosomes, which comprises 23 pairs. Of each of these chromosome pair, one chromosome is from father and one chromosome is from mother i.e., only one member of each pair is handed on through the reproductive cell (egg or sperm) to each child. Thus, each egg or sperm has 23 chromosomes (McGraw-Hill Science & Technology Encyclopedia, 2005). Twenty two of the 23 chromosome pairs, i.e., the autosomes, are alike in both the sexes, the other pair comprises of the sex chromosomes. A female has a pair of XX and a male has XY chromosomes. Further**,** Human Genetics has several applications**,** like Paternity diagnosis, genetic counseling and eugenics, DNA technology and its use in disease and medicine are discussed below.

4.2 PATERNITY DIAGNOSIS

Paternity Diagnosis helps to establish genetic proof whether a man is the biological father of an individual or not. This paternity test is carried out by using DNA analysis. The DNA analysis through DNA fingerprinting offers a more reliable way to determine the genetic parent. Before DNA fingerprinting came into existence, blood group polymorphisms like ABO, MN and Rh systems were most widely used. But using these blood group polymorphisms, a particular person can be excluded as the parent of a child. The exclusion of parentage can be determined with certainty.

But to determine parentage, DNA analysis is the most advanced and accurate technology. This paternity test compares a child's DNA pattern with that of the alleged father to check for evidence of this inheritance. The DNA fingerprinting technique assures the probability of parents to more than 99.9% if the alleged father is biologically related and the probability is 0% when the alleged father is not biologically related to the child.

Now let us briefly familiarise ourselves with the structure of DNA**.**

DNA: DNA (Deoxyribonucleic acid) is a chemical structure that forms chromosomes. A piece of a chromosome that dictates a particular trait is called a gene. The structure of the DNA molecule was proposed by James Watson and Francis Crick in 1953. DNA is a polymer (a large molecule containing repeated units) composed of a sugar, phosphoric acid and four nitrogen bases. Two of these nitrogen bases are purines, the other two are pyramidines. The purines bases are adenine (A) and guanine (G) and the pyramidine bases are thymine (T) and cytosine (C). The two strands of DNA are connected at each base. Each base will only bond with one other base, as follows: Adenine (A) will only bond with thymine (T), and guanine (G) will only bond with cytosine (C). The structure of DNA is presented below in Fig.4.1.

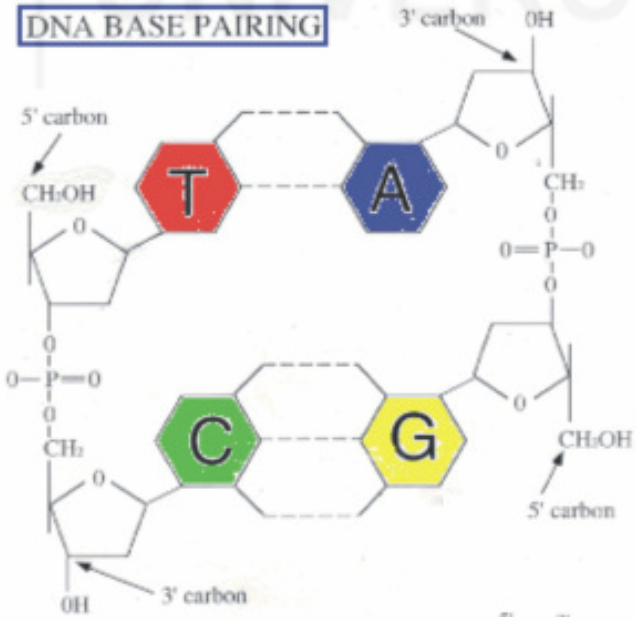

Fig.4.1: DNA Structure

Source: www.protist.biology.washington.edu

DNA Finger Printing: This is also known as DNA typing or Genetic Fingerprinting.

After knowing the DNA structure, we now briefly familiarise ourselves with the procedure adopted in DNA finger printing:

DNA samples can be extracted from blood, semen, hair roots, bone or saliva. The extracted DNA is then treated with restriction enzymes, which cuts the DNA into smaller fragments by cutting at specific sites. This DNA is then amplified by the technique of Polymerase chain reaction (PCR). By using alkaline chemicals this double stranded DNA splits into single stranded DNA. The DNA fragments are then subjected to agarose gel electrophoresis. The DNA bands so formed are transferred to nylon membrane. This is treated with a radioactively-labelled DNA probe which binds to complemental DNA sequences on the membrane. The excess DNA probe is then washed off. The radioactive DNA pattern is transferred to X-ray film by direct exposure. When developed, the resultant pattern is the DNA finger print.

4.3 GENETIC COUNSELING

Genetic Counseling, as 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 process involves an attempt by one or more appropriately trained persons to help the individual or family to: (i) comprehend the medical facts including the diagnosis, probable course of the disorder, and the available management; (ii) appreciate the way hereditary contributes to the disorder and the risk of recurrence in specified relatives; (iii) understand the alternatives for dealing with the risk of recurrence; (iv) choose 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 (v) to make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder (Fraser, 1974).

Now let us see how Genetic Counseling is done:

Firstly, it is necessary to identify people suffering from a genetic disease; 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 pedigree. 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 parent may be encouraged to voluntarily abstain from producing children.

Genetic screening

Genetic counseling is essentially a communications 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 States 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., in 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

- In vitro fertilization of egg
- Production of several copies of the normal allele of the defective gene
- Introduction of this DNA into the zygote or in the cells of the developing embryo and
- 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.

4.4 EUGENICS

The term Eugenics was introduced by Francis Galton in 1883. It refers to the improvement of a population by selection of only its 'best' specimens for breeding. This has been practiced both by plant and animal breeders since ancient times. The idea of eugenics was to improve society by screening out and sterilizing people diagnosed as genetically unfit. Those with desirable genes would be given incentives to reproduce. Regardless of the reasons in support of sterilization, restricting an individual's ability to reproduce is viewed as a violation of their constitutional rights. The science of eugenics can also be defined as a science of the well born, improving the inborn qualities of race and obtaining the better heritage of judicious breeding.

Eugenics is of two types, positive and negative:

Positive Eugenics: By encouraging desirable individuals to bear more children and also to produce genetically enhanced children i.e., give them genetic characteristics (genotypes) they ordinarily would not be born with (www.bioethicsanddisability.org). The positive eugenics can be increased by adopting the following measures:

a) Encouraging early marriages: It is a general observation that highly placed persons of the society and those who have high ambitions of the future life devote best part of their youth to achieve ambitious goals. Hence**,** they get married at a late age. Both**,** biological and psychological investigations have revealed that the aged persons often lack expressive warmth for the sexual behaviour and their germplasm also lose its strength. Hence**,** the young persons having the best hereditary traits should be encouraged for early marriages. For this**,** a few laws should be formulated to avoid the delayed marriages.

b) To fund the fit: Most of the well gifted persons in a society would like to lead a well planned and relaxed life. In order to lead a comfortable life and to avoid unnecessary difficulties in nurturing the children, they wish to have small number of children. Thus, the selected young men and women who have best eugenic value should be encouraged to have more children. H.J.Muller (1890–1967) has suggested that the persons who have best eugenic value should increase their family size. The persons who have best eugenic value besides increasing their family size can otherwise act as father to many more children, and this is possible through artificial insemination. The sperms and eggs of stupendous people should be stored for potential use.

c) Fitness and Education: In a society, the people should be educated about the basic ideology of wellbeing, ecology, human genetics, eugenics and sex. Hence, the children should be properly instructed about basic laws of health and they should be confident to develop a healthy, physically and mentally sound body. The children ignorant about the details of sex may do further harm to the society than others. Therefore, there is a need to have sex education to avoid unwanted behaviour which is not desirable for our country.

d) Wastage of germplasm: By following measures, one can avoid the wastage of best type of germplasm:

   i) We should select the marriage partners wisely,

   ii) The nuns and priests, because of religious commitment do not marry. This should be avoided. By allowing these persons to marry, the wastage of the best part of germplasm can be prevented.

e) Genetic counselling: Human being is benefited a lot through genetic counselling. The nature of mutant condition must be informed to the concerned persons. This is the duty of the genetic counselor to enlighten the affected persons. After knowing the problem, the probability of producing affected offspring can be calculated provided it is inherited in a Mendelian fashion. The ultimate judgment of taking a risk is exclusively the accountability of the person concerned.

f) Ecological surroundings and their improvement: To improve eugenically better persons, heredity and environment have played the most important role. Therefore, every individual in society should get better food, good existing circumstances, proper education and health assistance etc., so that his or her genetic behaviour may have the best improvement. This will help in producing fertile offspring.

g) Encouraging of genetic research: The existing knowledge on genetic diseases is not enough as we still have minute information on different human diseases. Hence, further research in the field of cytogenetics should be increased so that we can learn more and more about the man. Therefore, genetic research must be encouraged.

Negative Eugenics: Faulty germplasm from the people can be eliminated with the help of following measures:

i) Sexual disconnection: Colour blindness, night blindness, hemophilia, etc. are some of the sex-linked diseases possessed by the defective persons and these may be regulated by dominant or recessive genes. The defective traits in the population can be checked by sexual disconnection and keeping them away and separated from the public.

ii) Sterilization of the defective: Persons who have defective traits may be advised to go for sterilization. Through sterilization, without disturbing any of his usual functions, we can withdraw a person from his power of reproduction.

iii) Immigration and its control: The unwanted or faulty genes of different races and nationalities may intermingle with the normal germplasm of the people during immigration. The persons with unwanted hereditary traits must not

be permitted to migrate from one place to another. Some laws should be formulated to control the immigration of those persons who have defective genetic traits.

iv) Marriage regulation: The affluent or well placed persons (who, still, may have numerous faulty genetic characters), are more favored for marriages than those who have eugenically sound hereditary traits but have no money. Because of not having money the eugenically sound persons agree for marriage with the genetically defective people. These people fail to reach the uppermost status in the society due to lack of opportunities.

4.5 DNA TECHNOLOGY AND ITS USE IN DISEASE AND MEDICINE

Recombinant DNA (rDNA) technology, also known as genetic engineering, involves artificial modification of the genetic constitution of a living cell by introduction of foreign DNA through experimental technique. The DNA technology has made a significant contribution in the prevention, diagnosis and treatment of diseases. A few of the applications of recombinant DNA are discussed below:

i) DNA Probes: DNA probes are short segments of DNA that distinguish corresponding sequences in DNA and hence permit recognition of specific DNA sequences. This technique is mainly helpful in diagnosis. DNA probes can hybridize with specific DNA sequences and permit the recognition of specific parasites. Probes resultant by recombinant DNA methods are extensively used in prenatal detection of disease**:** for example, in detecting genetic disorders like cystic fibrosis, Huntington disease, sickle-cell anemia etc. In a few cases, probes resultant from the gene itself is used and, in extra cases, restriction fragment length polymorphisms genetically associated to the disease gene are engaged. If the disease gene itself, or a region close to it in the chromosome, differs from the normal chromosome in the positions of one or more cleavage sites for restriction enzymes, then these differences can be detected with southern blot i.e. with the use of cloned DNA from the region as the probe. The genotype of the fetus can**,** therefore, be determined since the restriction fragments present in its DNA. These techniques are very responsive and can be carried out as soon as tissue from the fetus-or still from the placenta – can be obtained. DNA probes have been developed for Leishmania, Trypnosoma, plasmodium, Schistosoma, Wuchereria and some additional human parasites. DNA probes can also be used to recognise viruses which were previously hard to culture.

ii) Gene Therapy: The hereditary disease in particular can be treated with Gene therapy. Gene Therapy is the insertion of genes into an individual's cells to treat a disease. Gene therapy normally aims to supplement a faulty mutant allele with a functional one. In the majority gene therapy studies, a normal gene is inserted into the genome to supplement an abnormal disease causing gene. A carrier**,** called a vector**,** must be used to deliver the therapeutic gene to the patient's target cells. Presently, the most widespread vector is a virus that has been genetically changed to carry normal human DNA. The vector unloads its genetic material containing the therapeutic human gene into the

target cell. The creation of an efficient protein product from the therapeutic gene restores the target cell to a normal state.

iii) Production of hormones and Proteins: Using DNA technique, the genes responsible for the production of hormones and proteins can be introduced into bacteria by vectors. These genetically changed bacteria produce greater amounts of these substances. The hormones like insulin, human growth hormones, somatostatin, erythropoietin etc. are being produced using this DNA technique. The most important application of genetic engineering is the production of large quantities of particular proteins that are otherwise hard to acquire. Urokinase, are industrially produced today using this DNA technique.

iv) Production of vaccines: The conventional vaccines are inactivated germs or their antigens. There is always a danger of contamination to use such kind of vaccines. However the synthetic vaccines are produced by separation of pure antigens using mono-clonal antibodies. These are specific antibodies produced by Lymphocytes when they hybridize with the concerned cell. The resulting hybridoma (of Lymphocyte and the cell) can produce antibodies constantly. In diagnosis, therapy and also in prevention such antibodies can be used. Synthetic vaccines can also be produced by transferring genes for certain antigens into bacteria. Bacteria produce antibodies in large quantities which can be used as vaccines. The vaccine for Hepatitis virus is manufactured in this manner.

v) Diagnosis of Infectious Diseases: Several diseases are diagnosed by conducting definite tests. The diseases like TB and cancer are being diagnosed using Recombinant DNA technology. The other diseases like measles, small pox and hepatitis can also be diagnosed through these tests. In the diagnosis process, certain pathogens are isolated and identified, and then diagnostic kits are produced (when the genome of the specific pathogen is known to kill it or block its pathogenic activity).

This DNA technique is also used in the diagnosis of AIDS diagnosis, prenatal diagnosis, understanding the molecular basis of diseases like sickle cell anaemia, thalassemia, familial hypercholesterolemia and cystic fibrosis.

4.6 SUMMARY

Genetics is primarily concerned with the understanding of biological properties that are transmitted from parents to offspring. Human genetics is the study of the inherited characters of human beings. The applications of human genetics are many; for instance, paternity diagnosis, genetic counseling, eugenics, DNA technology in disease and medicine. DNA profiling popularly known as DNA fingerprinting is used to establish paternity and distant relationship by tracing their ancestors. 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. Eugenics deals with the application of the laws of genetics for the improvement of human race. The recombinant DNA technology has revolutionized modern biology. It is used in the efficient production of useful proteins, derivation of DNA probes for diagnosis

and in the production of vaccines. Gene therapy is another important application of human genetics, which is useful in introduction of functional genes in individuals suffering from non-functioning of some of their genes. Some infectious diseases, AIDS diagnosis, prenatal diagnosis, molecular basis of diseases, like sickle cell anaemia, thalassemia, familial hypercholesterolemia and cystic fibrosis are also diagnosed through this DNA technique.

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Sample Questions

1) Define Human Genetics and briefly discuss the applications of Human genetics
2) What is DNA Finger Printing? Explain its application in Paternity Diagnosis.
3) What is genetic counseling? Explain its process
4) Write a note on DNA technology in disease and medicine
5) Write short notes on the following
   a) Eugenics
   b) DNA Finger printing
   c) Genetic counseling