B.A./B.sc Sem IV Paper 7 Unit I

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Human Genetics and Its Scope In Anthropology

Human genetics is the study of the inheritance of epigenetic traits among humans, notably but not exclusively traits of medical interest. The overarching goal of human genetics is to apply knowledge of human heredity to a better understanding of diversity in development and adaptation as "nature is nurtured." Another central goal of human genetics is the public health function of reducing dysgenetic burdens on individuals, families, and society at large. Although the boundaries of subdisiplines within genetics are not precise, the term anthropological genetics is used to distinguish general human genetics from more clinical applications, with the latter sometimes denoted specifically as medical genetics.

Humans, like all species, have many genotypic and phenotypic variations. Such variation is ultimately derived from mutations that affect proteomic expression. Genes encode for proteins that ultimately arrange and regulate all manner of biological structures and processes, from the intracellular level to organismic and even on the ecological. Thus, mutant genes disrupt proper proteomics processes, and disease results to the extent such disruptions are evident as defects (pathophenotypes). Many mutations have no pathological effect, but there are more than 6,000 known single-gene disorders, or about 1 of every 200 live births. Moreover, there may be manifold causes of phenotypically similar disease; for example, some 60 congenital forms of deafness are known, with some the result of environmental factors such as rubella and others due to genetic mutations. Genetic disorders, as caused by abnormalities in genetic material, occur in four basic types:

(1) single-gene
(2) chromosomal,
(3) mult factorial, and
(4) mitochondrial.

Single-gene (Mendelian or monogenic) defects are due to mutations of DNA at a single locus. Single-gene diseases arise in the classic familial patterns of inheritance: autosomal dominant, autosomal recessive, and X-linked. Major examples of such Mendelian diseases include cystic fibrosis, sickle cell anemia, Huntington's disease, pheylketonuria, alpha-1-antitrypsin deficiency, and hereditary hemochromatosis.

Chromosomal defects are due to abnormalities such as allelic deletions or redundancies; translocations of or even gross are evident on microscopic examination. Down's syndrome (trisomy 21) is a common disorder that occurs with a redundant portion of chromosome 21.

Multifactorial (complex or polygenic) defects are due to interactions of multiple alleles and the developmental environment. Many of the most common illnesses are multifactorial, including arthritis, cancer, diabetes, heart disease, and hypertension. Given such complexities of expression, multifactorial inheritance is more challenging to study.

Mitochondrial defects are due to mutations in mitochondrial DNA, which is distinct from the inherited nuclear-chromosomal genotype of the organism. Since mitochondria are the small organelles of cellular respiration in the cytoplasm of plant and animal cells, such anomalies can cause a variety of specific metabolic diseases.

Medical genetics historically developed in practical application for medical screening and advice for at-risk populations. Such screening requires not only adequate tests (valid, reliable, sensitive, specific) but also a sound grasp of the natural progression of and treatment options for the disease in question. A thorough family history augmented with a review of pertinent medical literature, preferably by an expert, is essential to inform families of the diagnosis and methods; identification of carriers; the phenomenology of the disorder, including complications; risk of recurrence for the patient and family; and therapeutic and reproductive options, including referral or support groups. This is a complex process of evaluation and education and carries considerable legal and ethic consequences.

Heterozygote screening is focused on susceptible populations with high rates of deleterious heterozygosity (for example, cystic fibrosis in Scandinavians, Tay-Sachs in Ashkenazi Jews, sickle cell anemia in Blacks, etc.). Prospective screening of parents, particularly where one is an identified heterozygote, allows more informed medical choices. Pre-symptomatic screening may be helpful within families with a history of Mendelian disorders. Such screening is most typical in certain dominant traits but can be very useful in other types of familial disease risk (for example, cancers of the breast and colon).

Medical genetics also entails other clinical procedures, such as prenatal diagnosis (sampling of chorionic villus tissue, umbilical cord blood, maternal blood sampling, or maternal serum, as well as fetal imaging via ultrasound or radiography). Prenatal screening is especially useful for prospective mothers over age 35 with family history of a condition diagnosed by prenatal tests, to evaluate abnormal maternal serum screening or some complications of pregnancy. Likewise, neonatal screening may be used to identify newborns in need of critical special treatments (special diets for phenylketonuria or replacement therapy for hypothyroidism).

Pedigree analysis is a classical technique of medical genetics by which a thorough family tree is depicted, with symbols for persons affected with known genetic disease. Thus is rendered a broad summary of inheritance patterns through generations that serves to clarify mode of transmission even for traits that may have identical phenotypes despite different causal genes (for example, cleft palate

can be Mendelian autosomal dominant, autosomal recessive, or X-linked recessive; other types are multifactorial as they run in families without clear patterns).

However, with this progress, an increasing number of gene tests are becoming available commercially, although the scientific community continues to debate the best way to deliver them to the public and medical communities, who are often unaware of their scientific and social implications. While some of these tests have greatly improved and even saved lives, scientists remain unsure of how to interpret many of them. Also, patients taking the tests face significant risks of jeopardizing their employment or insurance status. And because genetic information is shared, these risks can extend beyond them to their family members as well.

As the role of genetics is made clearer with respect to diagnosis, monitoring, and treatment of diseases, medical scientists continue to make rapid progress in the identification of genes associated with disease. A key long-range aim is to formulate new means to diagnose, treat, and even cure or prevent diseases. Epigenesis is a complex process that entails regulators (i.e., promoters and enhancers), actively expressed units (exons), unexpressed but intervening units (introns), and termination signals.

The field of human genetics has been dramatically bolstered by the Human Genome Project (HGP) and related studies that began in 1991. These constitute the new field of genomics that use techniques of molecular analysis to map all human genes to specific locations and thereby identify elements of genetic structures and functions. With this progress, medical genetics is expanding from a focus on diagnostics and counseling toward more active evaluation and treatment, including the prospect for procedures to directly repair dysgenetic cell lines. Similarly, human genetics has also progressed rapidly toward the elucidation of diverse issues in the phylogenetic history and geography of human populations

Scope of Human Genetics

As soon as fundamental principles of genetic inheritance were clearly established in the early twentieth century, anthropologists began using these principles and new empirical data to illuminate long-standing problems of human variation and primate phylogeny. Initially focusing on human blood characteristics, geneticists quantified regional differences in ABO genotype, and tried to correlate these differences with more traditional osteometric assessments of variation. Anthropologists were especially interested in alleles like the sickling trait, which had adaptive significance. When blood samples became available from other primates, in midcentury, it became possible to construct phylogenetic trees based on genetic data, and to compare these results with the fossil record. After World War II, field expeditions were organized by anthropological geneticists to collect far-flung samples of human genetic material, along with new cultural and linguistic data, in the hope of finding correlations, thereby detecting evolutionary trends and reconstructing human migration. With the addition of ancient DNA techniques to the anthropological repertoire in the 1980s, all four fields of anthropology – cultural anthropology, archaeology, linguistics, and biological anthropology – became

intimately involved in genetics research, both individually and in cross-disciplinary research. The immediate research agenda for anthropological genetics includes

(1) human origins;

(2) prehistoric migration;

(3) coevolution of biology, language, and culture; and

(4) variation and adaptation to modern environments.of person's life or identity (Nelkin and Lindee, 1995), which would run counter to the anthropological focus on culture. Normative human genetics after World War II, led by Theodosius Dobzhansky, James V. Neel, and Luca Cavalli- Sforza, tended rather to emphasize the complementarity of the two fields. Here, human genetics would form a foundation for the study of human microevolution, and its primary data would be biochemical 'markers' of ancestry, or intergenerational continuity. Within anthropology, then, normative genetic research came to incorporate four kinds of questions: (1) patterns of human variation; (2) the phylogenetic relationships among humans and other primate species; (3) the migration and adaptation of human populations, or microevolution; and (4) the relationships among biological variation and other kinds of human variation, especially in language and culture. Additionally, there are areas of overlap between genetics and humanistic anthropology, including medical anthropology (Taussig, 2009), economic anthropology (Pálsson, 2007), bioethics (Brodwin, 2005), and political ecology (Stone, 2010).

Human Variation

When laboratory techniques for studying Mendelian traits first became available, international anthropology had just emerged from a controversy over racial typology during which Franz Boas, recognized by many as the founding father of American anthropology, had repudiated to the satisfaction of most anthropologists the racial theories to explain civilization that had been popular in the late nineteenth century. Originally trained as a physicist, Boas presented data and arguments between 1910 and 1913 showing that 'race,' 'language,' and 'culture' were three independent phenomena that, he asserted, should all be studied by anthropologists, but using different kinds of theories and techniques.

Shortly after World War I, the earliest population genetic studies of human blood groups seemed to undermine the ideas about race that physical anthropology had traditionally employed, although it would be several decades before the meaning of this discordance became clarified (Marks, 2012). After World War II, as human genetics became increasingly redirected toward real genetically based medical pathologies (such as sickle-cell anemia), rather than imaginary genetically based social pathologies (such as feeblemindedness), it became clear that the simple rules of Mendelian inheritance applied only to the inheritance of biochemical variants and pathological conditions resulting from the breakdown of specific genes (the repository for medical genetic conditions is Online Mendelian Inheritance in Man, https://www.ncbi.nlm.nih.gov/omim). The interesting physical attributes of human variation (such as height, complexion, facial form, hair form, and body build), however, are all the result

of more complex hereditary and developmental physiologies, involving the coordinated activities of several genes and regulation of their products, in specific environmental, genetic, and cultural contexts.

For anthropologists, the major theoretical model that emerged to describe human genetic variation in this period was the cline, the gradual geographic change in the frequency of an allele, which also served to undermine further the idea of racial typology. Both physical form and genetic variation seemed to vary across the human species in a continuous, quantitative fashion.

Some patterns that emerged from the analysis of clines conformed to more general biological principles pertaining to other animals. It was found, for example, that Gloger's, Bergmann's, and Allen's Rules for variation within a mammalian species (pertaining to pigmentation, mass, and limb length, respectively) were also crudely valid for the human species, reflecting adaptation to the different latitudes, climates, and environments inhabited by local human populations. Since these traits were so clearly adaptive, it was suspected that other patterned traits, with definite clines, likewise reflected genetic adaptation to local conditions. Alternatively, they might be the track of large-scale migrations of ancient peoples.

Adaptation

The most forceful new example of human genetic adaptation was presented by Livingstone (1958) with his study of sickle-cell disease, especially as it existed in Africa. In addition to presenting convincing evidence of several types to prove that sickled blood cells were a long-term genetic response to the presence of malaria, Livingstone's work illustrated several other lessons in anthropological genetics. First of all, it was the heterozygote (a person with two different alleles for a specific gene) or carrier of hemoglobin S (HbS) who had the adaptive advantage, not the HbS homozygote (possessing two identical alleles for a specific gene), who suffered from sickle-cell anemia. The second lesson was that an apparent 'disease,' sickle-cell anemia, was on closer inspection actually a successful genetic solution to a largely human-made environmental problem, namely, malaria – stimulated by the widespread presence of mosquitoes, which in turn were attracted by large areas of standing water that were promoted by early agricultural practices. The story does not end in the past, however, as medical anthropology and history are now illuminating complementary anthropological aspects of sickle-cell anemia (Wailoo and Pemberton, 2006; Fullwiley, 2011).

Another highly visible connection between genetic variability, culture, and environment concerns the ability of human adults to digest milk and milk products from dairy animals, an ability that seems to be under genetic control. When mapped geographically, the alleles responsible for adult lactose tolerance in human populations seem to be correlated, in the Old World, with the present and past locations of pastoral peoples (Durham, 1991). Lactose tolerance has arisen in parallel in several different areas, and the most common mutation in Europeans probably spread with the descendants of early dairy farmers (Ingram et al., 2009).

Many correlations have been found between pathogenic diseases and genetic variations. None, however, has been established as firmly as the relationship between malaria and sickle-cell

anemia, and other related blood diseases. Different patterns of genetic variation among populations are explained as accidents of demographic history, or founder effects, rather than as adaptive responses of the gene pool. The most famous examples here are genetic diseases that are rare elsewhere but have attained an anomalously high frequency in a particular population, for example, porphyria variegata among the Boers of South Africa and Ellis–van Creveld syndrome among the Pennsylvania Amish – both of which have elevated frequencies because a single seventeenth-century immigrant was both a carrier of the genetic disease and an ancestor of the modern populations. In the absence of plausible and reliable physiology (as in the case of sickle-cell or thalassemia) or plausible and reliable historical records, most other diseases associated with genetic variants show more ambiguous patterns.

More generally, understanding the role that genetic variation may play in health care involves the analysis of risk factors and consequent probabilities (Terwilliger and Göring, 2000). Nevertheless, the presumption of a genetic basis for health disparities carries strong political implications and can hardly be taken at face value (Fullerton et al., 2012) Moreover, the saturation of medical genomics with modern capitalism may compromise the reliability of the scientific information it produces. BiDil, promoted as a cardiac medicine specifically for black patients, was actually supported by no valid evidence that it worked differently or better in blacks than in whites. Nevertheless, racializing the drug extended its patent protection. And far from being a public health service, BiDil's manufacturers charged their black patients far more than they needed to pay for it, since the drug itself was simply a mixture of two other generic drugs (Kahn, 2008).

Population Genetics

With increased funding for science in the United States after World War II, and increased access to field sites, anthropologists began to investigate isolated, small-scale human populations with renewed vigor, often including a biological anthropologist in the research team. The most visible of these joint enterprises was probably the comprehensive study of the Yanomamö, who live in the upper drainage of the Orinoco River in Venezuela and Brazil. In the 1960s, James Neel of the University of Michigan organized a comprehensive multidisciplinary series of field expeditions that investigated the environment, ecology, biology, culture, and social organization of these then little-known people. After a series of books and articles was published over the next two decades, the Yanomamö became not the least known, but one of the best-known tribal societies in the world.

For the genetic part of the research, Neel and Ward (1970) examined six blood systems relatively well known at the time (MNS, Rh, Kidd, Duffy, Diego, and haptoglobin) among 7 villages of Yanomamö, 7 villages of nearby Makiritare, and 12 other tribes of Central and South America. After comparing the different groups, the authors concluded that human evolution might have been proceeding at a pace '100 times more rapid' than previously thought, if these smallscale societies could be taken as analogs of earlier Pleistocene or Paleolithic human peoples.

In the same period, other biological anthropologists were proceeding with similar investigations elsewhere in the world. Working in the Solomon Islands from 1966 to 1973, Jonathan Friedlaender simultaneously undertook studies biological variability within the group, but low variability

among the groups, and that some traits, such as skin color, eye color, and hair form, were 'monotonous' on the island, while dermatoglyphic characteristics and some blood system alleles were discontinuous from village to village.

Those expecting that these early studies would provide fundamental insights into the mechanisms of human evolution were soon disappointed. Summarizing a widely shared consensus of opinion in 1974, Henry Harpending concluded that studies of the genetic structure of small populations have made particular and incidental contributions to formal genetics, to regional history and prehistory, to epidemiology, and to several other fields to which they are peripheral, but . they have not advanced our understanding of human evolution in a global sense. The sample sizes available have been too small to allow reliable inferences about natural selection; the extensive occurrence of what is presumably local random genetic drift has little or no consequence for evolution over long time periods over large areas; and the presumed selective agents in the various environments of these peoples differ greatly so that few of the generalizations which have been put forward hold for many groups.

Evolution of Primates

Early in the twentieth century, it was appreciated that the relations of primate blood appeared to replicate the relations of primate bodies; that is to say, animals who appeared more similar physically tended to have more similar biochemical properties discernible in their blood. Further, the blood of humans was especially similar to the blood of apes; indeed, by the 1920s, human blood was known to be even more similar to chimpanzee blood than horse blood was to donkey blood.

In the 1960s, Allan Wilson and Vincent Sarich (1967) showed that the biochemical variation distinguishable immunologically in the blood tended to track the time since the species being examined diverged from one another, rather than their degree of adaptive physical difference from one another. In the ensuing decades, this generalization has held up remarkably well over diverse kinds of genetic comparisons. Consequently, genetics tends to show how similar humans are to chimpanzees, not how different we are. The reason is that we do not know how to build a four-dimensional body (an organism) from a one-dimensional set of instructions for it (the DNA). Absenting that information, detectable DNA changes are largely uncorrelated with the adaptive physical variations that characterize the 'major features' of the history of life. Consequently, we know rather a lot about how similar genetically we are to chimpanzees, but almost nothing about the genetic basis of bipedality, language, evaporative heat loss, cooperative breeding, or any of the other significant ways in which we differ strikingly from the apes.

Sarich and Wilson (1967) used the primate molecular data in the 1960s to demonstrate convincingly that Ramapithecus, considered to be on a human line 14 million years ago, on the basis of teeth and jaw fragments, was about three times older than the human line itself was, and therefore could not be on the human line. Morris Goodman invoked the genetic similarity of humans and chimpanzees to argue for classifying them together as members of the genus Homo (Wildman et al., 2003). This would involve privileging the genetic relationships (in which chimpanzees and humans are

extremely similar) over anatomical, behavioral, cognitive, and ecological relationships (in which they are considerably less similar).

The most fundamental tools used in genomic comparisons involve (1) the acquisition, isolation, manipulation, and amplification of genetic sequences to be studied; (2) the qualitative and quantitative assessment of patterns of similarity among the samples, for example, inferring the kinds and numbers of mutations needed to transform one DNA sequence into another; and (3) an explanation for the patterns in the history of the organisms.

The study of the human genome has revealed that traditionally defined genes (containing the DNA code for a specific protein) constitute only a small percentage of the total DNA in a human cell. About 90% of the human genome is intergenic, that is to say, lying between genes and thus not classically functional. Moreover, most of a gene itself does not actually code for a protein; it may be transcribed into RNA without being translated into protein. Two obvious conclusions are (1) our classical ideas about the functions of DNA were too narrow and (2) there are some interesting structural features of noncoding DNA. Some noncoding DNA is localized, and consists of simple sequences repeated side-by-side millions of times. Other repetitive DNA is interspersed among the genes, and consists of millions of sequences, each one hundreds or even thousands of bases long, and shot through the genome in apparently random places. This redundancy is characteristic of the genome. Genes themselves are commonly found in clusters, the ancient products of a 'rubber-stamp' process of gene duplication, followed by the mutation-mediated inactivation or alteration of the duplicate gene. Other sites in the genome differ from person to person in the number of segments of a short repetitive motif that may be present. These polymorphisms are known as variable numbers of tandem repeats (VNTRs) and are particularly valuable in forensic contexts, where a match of several highly variable sites can provide a statistical basis for identifying the person that a particular DNA sample came from.

We can generally measure the intensity of selection on a particular genomic region by its rate of change. Noncoding sequences invariably are more different across species than coding sequences are. The simple reason is that coding sequences are expressed as phenotypes, and have evolved by natural selection to produce a functioning body. Any random change within them (mutation) is far more likely to make that body run worse than better. Consequently, mutations that occur in coding sequences are far more likely than mutations in unexpressed DNA sequences to be 'weeded out' by selection. Establishing the background extent of genetic difference between two species helps to identify regions that are evolving 'too slowly' and may thus be under selective constraints. More rarely, a genomic site may be of interest for evolving 'too fast' and thus possibly be related to the adaptive differences that arose between the species.

Various branches of human genetics

· **Classical genetics**- consists of the technique and methodologies of genetics that predate the advent of molecular biology. A key discovery of classical genetics in eukaryotes was genetic linkage. The observation that some genes do not segregate independently at meiosis broke the laws of Mendelian inheritance, and provided science with a way to map characteristics to a location on thechromosomes.

· **Quantitative genetics**- is the study of continuously measured traits (such as height or weight) and their mechanisms. It can be an extension of simple Mendelian inheritance in that the combined effects of one or more genes and the environments in which they are expressed give rise to continuous distributions of phenotypic values.

· **Biochemical genetics**- the study of the fundamental relationships between genes, protein, and metabolism. This involves the study of the cause of many specific heritable diseases

· **Cytogenetics**- is a branch of genetics that is concerned with the study of the structure and function of the cell, especially the chromosomes

· **Behavioural genetics**- is the field of study that examines the role of genetics in animal (including human) behaviour

· **Developmental genetics** is the study of the process by which organisms grow and develop

· **Conservation genetics**- is an interdisciplinary science that aims to apply genetic methods to the conservation and restoration of biodiversity

· **Ecological genetics** is the study of genetics in natural populations.

· **Evolutionary genetics**

· **Genetic engineering** is the direct manipulation of an organism's genome using biotechnology. New DNA may be inserted in the host genome by first isolating and copying the genetic material of interest using molecular cloning methods to generate a DNA sequence, or by synthesizing the DNA, and then inserting this construct into the host organism.

o Metagenics- is the practice of engineering organisms to create a specific enzyme, protein, or other biochemicals from simpler starting materials. The genetic engineering of E. coli with the specific task of producing humaninsulin from starting amino acids is an example.

· **Genomics** is a discipline in genetics that applies recombinant DNA, DNA sequencing methods, and bioinformatics to sequence, assemble, and analyze the function and structure of genomes (the *complete* set of DNA within a single cell of an organism

· **Human genetics**- is the study of inheritance as it occurs in human beings. Human genetics encompasses a variety of overlapping fields including: classical genetics, cytogenetics, molecular genetics, biochemical genetics, genomics, population genetics, developmental genetics, clinical genetics and genetic counselling.

· **Medical genetics**- is the specialty of medicine that involves the diagnosis and management of hereditary disorders. Medical genetics differs from Human genetics in that human genetics is a field of scientific research that may or may not apply to medicine, but medical genetics refers to the application of genetics to medical care.

· **Microbial genetics**- This involves the study of the genotype of microbial species and also the expression system in the form of phenotypes.It also involves the study of genetic processes taking place in these micro organisms i.e., recombination etc

· **Molecular genetics-** is the field of biology and genetics that studies the structure and function of genes at a molecular level. Molecular genetics employs the methods of genetics and molecular biology to elucidate molecular function and interactions among genes. It is so-called to differentiate it from other sub fields of genetics such as ecological genetics and population genetics.

· **Population genetics**- is the study of allele frequency distribution and change under the influence of the four main evolutionary processes: natural selection, genetic drift, mutation and gene flow. It also takes into account the factors of recombination, population subdivision and population structure. It attempts to explain such phenomena as adaptation and speciation.

· **Psychiatric genetics**- is a subfield of behavioral neurogenetics, studies the role of genetics in psychological conditions such as alcoholism, schizophrenia, bipolar disorder, and autism. The basic principle behind psychiatric genetics is that genetic polymorphisms, as indicated by linkage to e.g. a single nucleotide polymorphism (SNP), are part of the etiology of psychiatric disorders