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BIOLOGICAL EVOLUTION

EVOLUTION, in simple terms means 'change in progressive direction', 'change with modification' or 'change and adaptation'. In genetic sense evolution refers to change in gene frequencies.

THOUGH Darwin's theory of natural selection is generally accepted as the first scientific theory of evolution, yet Charless Darwin was not the first one to think on the lines of progression. Linnaeus (1707-1778) in the eighteenth century, in his *Systema Naturae*, for the first time, divided different plant and animal species into various groups based on the similarities and differences found in different species. In latter half of that century, Cuvier (1769-1832), considered the father of comparative anatomy, on the basis of the bones of extinct animals inferred that *"Catastrophism"* resulted in the destruction of old species and new ones came up. Hutton (1726-1797) in his *Theory of the Earth* (1788) observed that the landmasses of the earth were not static and they, because of a number of factors, keep changing. Lyell (1797-1875) in his *Principles of Geology* amply convinced the researchers regarding evolution of the earth's crust.

LAMARCK'S theory of evolution through adaptation (described later) received wide acclaim but it was Darwin who firmly explained the process of evolution through natural selection.

LAMARCKISM

LAMARCK synthesised various pre-existing ideas regarding organic evolution into a theory. Lamarck held that evolution is a result of constant striving by all living beings towards a state of perfect adaptation to the existing environmental conditions. He believed that living beings through the action of "internal forces of life", were capable of bringing about modifications or changes in their own physiological structure during the course of their life time, and that such "acquired changes" were inheritable and thus passed on to succeeding generations. The present diversity of life forms was a result of accumulation of such gradual changes over a very long period of time.

THE theory of evolution propounded by Lamarck has been expressed by the following four laws.

(i) Life, by its proper forces, continually tends to increase the volume of every body which possesses it, and to increase the size of its parts upto a limit which brings it about; In short, all living organisms grow due to the "internal forces of life".

(ii) The production of a new organ in the living body results from the supervention of a new want which continues to make itself felt, and a new movement which this want gives rise to and maintains. In other words, the growth of a new organ in living being, or the modification of an older one is need based.

(iii) The development of organs and their powers of action are constantly in ratio to the employment of these organs. In other words, use of an organ leads to its growth, while its disuse leads to its degeneration.

(iv) Everything which has been acquired, impressed upon, or changed in the organisation of individuals during the course of their life is preserved by heredity and transmitted to the next generation.

THOUGH all four of Lamarck's laws are very controversial, it is about the last 'law' that the controversy rages strongest, for it upholds the idea that acquired characters are inherited, now known as the *Lamarckian doctrine*.

A SOMEWHAT more specific statement of Lamarck's theory of evolution may be summed up in the following list of factors which he considered as playing an essential role in evolution.

(i) **Favourable Circumstances :** attending changes of environment, soil, food, temperature etc.; supposed to act directly in the case of plants, indirectly in the case of animals and man.

(ii) **Needs :** new physical wants or necessities induced by the changed conditions of life; Lamarck believed that change of habit may lead to the origination or modification of organs; that the changes of function also modify or create new organs. By changes of environment animals become subjected to new surroundings involving new ways and means of living.

(iii) **Use and Disuse :** (Naturally) to use an organ is to develop it; not to use it is to eventually lose it.

(iv) **Competition :** Nature takes precautions not to overcrowd the earth. The stronger and larger living beings destroy the smaller and weaker. The smaller multiply very rapidly, the larger slowly. A physiological balance is maintained.

(v) **Transmission of Acquired Characters :** The advantages gained by every individual as the result of the structural changes resulting from use or disuse are handed down to its descendents who begin where the parent leaves off, and so are able to continue the progression or retrogression of characters.

(vi) **Cross-Breeding :** If and when any peculiarity of form or any defects whatsoever are acquired, the individuals in this case, always pairing, they will produce the same peculiarities, and if for successive generations confined to such unions, a special distinct race will then be formed. But perpetual crosses between individuals which have not the same peculiarities of form, result in the disappearance of all the peculiarities acquired by the particular circumstances.

(vii) **Isolation :** Were not men separated by distance of habitation, the mixtures resulting from crosses would obliterate the general characters which distinguish different nations. This thought is expressed in Lamarck's account of the *Origin of Men from Apes*, and is not applied to living things in general.

LET US now have a critical appraisal of Lamark's theory. Lamarckism states that the living organisms, because of the internal forces of life, keep on increasing in size. Small animals, thus, with passage of time become large. It is true that large species are the descendants of small ones but it is not a rule. Of course man has developed to his present stage from small primates of eocene times. But it is not laways true that small species give way to larger ones, otherwise how could we explain the extinction of huge dinosaurs. During the course of evolution the other way round of what Lamarck envisaged has also happened.

NEW organs, we know today, do not appear in the way hypothesized by Lamarck. The need for a new organ can not direct the course of evolution, otherwise man, right from the day he became Man, has been thinking of flying but he has never developed wings.

LAMARCK'S third principle is only partially true. An anthlete can develop his leg muscles by jogging. If you keep thinking, you become wise but what if you run more than you can or tax your brain beyond limit. In either case you will be a looser.

LAST of the Lamarckian principles is probably the funniest because it states that acquired characters are inherited. We, even in the day-today life, find this principle being rediculed. If a person who, because of some accident, has to get the legs

amputated, he/she still bears normal children and not the lame ones. Indian females have a two thousand year old tradition of piercing ears and nose for ornamentation but we have never seen a child born with the holes in ears or nose. This last principle of Lamarckism brought the doom of Lamarck's theory. One basic drawback of his theory of evolution is that it lacks any convincing evidence and data to support it.

HOWEVER, despite all these severe criticisms, Lamarck's work still deserves to be commended. He gave his theory of organic evolution at a time when even the utterance of the term "evolution" in a favourable tone could be considered rebellious. Lamarck had to face social and academic ostracism for "deliberately misinterpreting the facts" but his theory created interest in the subject that lead to the development of modern scientific theory on the subject.

DARWINISM

DARWINISM may be defined as a certain causo-mechanical (hence not teleologic) explanation of the origin of new species. The Darwinian explanation rests on certain observed facts, and certain inductions from these facts.

Observed Facts

(i) THE increase by multiplication in geometrical ratio of the individuals in every species, whatever the kinds of reproduction which may be peculiar to each species. However, despite the very high fetility exhibited by living organisms, their total number remain (roughly) constant, generation after generation.

(ii) **Variations** : THE always apparent slight (to greater) variation in form and function existing among all individuals even though of the same generation or breed.

(iii) **Heredity** : THE transmission (with these inevitable slight variations) by the parents (to the off-springs) of a form and physiology essentially like the parents.

Inferred Facts

(i) A LACK of room and food for all these new individuals produced by geometrical multiplication and consequently a competition, (active or passive) among those individuals having any ecological relations to one another, e.g. those occupying the same locality or need the same food or needing each other as food.

(ii) THE probable success in this competition of those individuals whose slight differences (variations) are of such a nature as to give them an advantage over their conferers, which results in saving their life at least until they have produced off-springs.

(iii) THE fact that these 'saved' individuals will, by virtue of the action of heredity, hand down to the off-spring their advantageous conditions of structure and physiology (at least as the mode or most abundantly represented condition among the off-spring).

THE competition among individuals and kinds (species) of organisms may fairly be called a struggle. This is obvious when it is active and less obvious when it is passive. The struggle, is, or may be, for each individual, three folds in nature:

(i) AN ACTIVE struggle or competition with other individuals of its own kind for space in the habitat, sufficient share of food, and opportunity to produce off-springs in the way peculiar and common to its species.

(ii) AN ACTIVE or passive struggle or competition with the individuals of other species which may need the same space and food as itself or may need it or its eggs or young for food and,

(iii) AN ACTIVE (or more usually passive) struggle with the physico-chemical external conditions of the world it lives in, such as varying temperature and humidity, storms and flood and natural catastrophes of all sorts.

Observed Facts	Inferred Facts
Individuals multiply in geo-metric ratio. yet number of survivors remains roughly constant	Struggle for existence
Variation and heredity	Survival of the fittest natural selection
Survival of the fittest and continued changes in next generations.	Origin of new species

SOMETIMES for any individual or group of individuals any of these forms of struggle may be temporarily ameliorated,as in (i) the intraspecific struggle among the thousands of honebee individuals living together altruistically, in one hive or (ii) the inter-specific struggle, when two species live together symbiotically as the hermit crab (*Euplagurus*) and sea-anemone (Podocoryne) or (iii) the struggle against untoward natural conditions as in special times or places of highly favourable climate, etc. On the other hand, all forms of the struggle may be active and severe for certain other individuals or groups of individuals.

IT MUST be kept in mind that it is not just survival itself which constitute a "success" in the struggle for existence. The real point is "contribution to the next generation". Therefore, in the struggle, premium is placed both on characteristics that make for survival and on characteristics that make for high fertility. In other words, in the struggle for existence, individuals contributing the must offsprings to the next generation are the 'fittest' ones.

THE resultant of these existing conditions is, according to Darwin and his followers, an inevitable natural selection of individuals and of species. Thousands must die where some may live to maturity (at least upto the time of producing young); which some of the thousand shall live depends on the slight but sufficient advantage possessed by 'some' individuals in the complex struggle for existence due to the fortuitous possession of fortunate congenital differences (variations). The 'rest' with unfortunate congenital variations are extinguished in the struggle and with them the opportunity for the perpetuation (by transmission to their off-spring) of their particular variations. There are thus left 'some' to produce their advantageous variations.

THE off-springs of these 'some' will vary in their turn, but will vary around the new and already proved advantageous parental conditions. This repeated and intensive selection leads to a slow but steady and certain modification through the successive generations of the form and functions of the species; a modification always toward adaptation, toward fitness,toward a moulding of the body and its behaviour to safe conformity with external conditions. The exquisite adaptation of the parts and functions of the animal and plants, we see every day to our infinite-admiration and wonder has all come to exist through the purely mechanical, inevitable weeding out and selecting by nature (by the environmental determining of what may and what may not live) through uncounted generations in unreckonable time.

THIS is Darwin's causo-mechanical theory to explain the transformation of species and the infinite variety of adaptive modification. A regorous automatic Natural Selection is the essential idea of Darwinism atleast in Darwinism as it is held by the present day followers of Darwin.

Critical Appraisal of Darwinism

DARWIN'S theory of natural selection is based on large scale observations spanning over several years. As it is based on facts and inferences through the facts, Darwinism is credited with being the first scientific theory of evolution. Darwin was

intelligent enough to use the terms like '*struggle for existence*', '*natural selection*', '*survival of the fittest*' etc., which were quite in vogue during his times. Unlike his predecessors, he avoided the use of a new terminology to explain evolution. Yet based on facts though it was, Darwinism, in the light of modern scientific researches, is found wanting in certain explanations.

INCREASE in geometric progression, as inferred by Darwin, is not applicable to man. Many countries of the world today have now stablized numbers or even have negative growth rate. Again, for man, natural selection has to operate at a different level because man to an extent, has been able to control the negative effects of selection (for details please see: "Human Evolution - A Perspective"). Similarly, cultural advances in man demand a change in definition of the fittest.

DARWIN insisted that natural selection was good enough to explain the whole process of evolution. In other words, he ignored the contribution of mutation, genetic drift, inbreeding and hybridization. As we will see later, these factors too are very important for evolution to take place. At least the contribution of mutations (called 'sports' in his times) was then known, but Darwin insisted on the small fluctuating variations as the cause of evolution. Today we know that the small variations (of Darwinism) are non-heritable. He also did not distinguish between somatic and genetic variations. Further, Darwinism is silent on the issue of the origin of these variations and the factors that lead to such variations. It has also not been made clear that how small variations could initially be advantageous. If for example, the earliest fish who developed a fin had (say) only 0.1 mm of it, how could it be advantageous for its possessor compared to those who did not have it? Whether this minute variation is of any selective advantage? The objection can not be explained without the contribution of mutations in evolution.

SIMILARLY, a large number of characters which are as such useless or non-adaptive could not have arisen through the process of natural selection. It seems that the types of characters mentioned above may be essential in terms of correlated variability.

TO EXPLAIN the transmission of variations from one generation to the next Darwin put forth the theory of *pangenesis* which has been outrightly discarded by modern researches. Darwin felt that the variations in the body gave rise to *gemmules* (certain hypothetical structures) in blood stream which when carried to the germ cells became a part of heredity. Today we know that only the genetic mutations are inherited and the 'gemmules' are not formed for the purpose.

WHENEVER Darwin failed to explain evolution through natural selection he lapsed into Lamarckian explanations but otherwise he never acknowledged the contribution of Lamarckism in the formation of his theory.

ACKNOWLEDGING the pitfalls in the theory of natural selection, followers of Darwin (called neo-Darwinians) have modified the theory to one that has given due importance to other micro-evolutionary processes. However, natural selection still forms the core of this modified theory. The theory known as Synthetic Theory has been described and analysed later.

MICROEVOLUTION

EVOLUTION is referred to as change in genetic material or for convenience, changes in gene frequencies. Various hereditary traits are passed on over generations and heredity tries to maintain whatever has been existing hithero. Heredity is static and had heredity been omnipotent, there were no evoultion. But none of the so called hereditary traits is absolutely hereditary.

GENES find their expression in environment. There is always a continuing interaction between hereditary features and environment. Environment keeps changing. Different genes, therefore to find their expression, have to change. Recors are available to show that the genes who failed to change with changing environment are eliminated. Genes, to survive and spread, always keep adapting themselves and the resultant is evolution.

THE study of evolution has been divided into micro and macro evolution (some biologists have created a thrid category of megaevolution too which is not relevant for our purpose). Microevolution refers to the change within the species. A species is a group memebrs of which can potentially mate with each other to produce fertile offsprings. Further, microevolutionary changes are small-scale day-today changes that can be studied in living populations; whereas, microevolution results in gross morphological alterations that can be studied only through discontinuous populations. Man is one species because any man can marry any woman (at least theoretically) without threatening the existence of his race. Macroevolution refers to the evolutionary change that results in the formation of a new species. The change from *Homo erectus* to *Homo sapiens* should be called macroevolution. Mating between an ess and a mare results in a mule which is not fertile. Horse and donkey, therefore, belong to two different species and mule is the product of macroevolution.

THIS dichotomy has been devised for our convenience, otherwise there is no difference between micro and macro evolution. At least the nature does not distinguish between the two because evolution continues and that too through various microevolutionary processes.

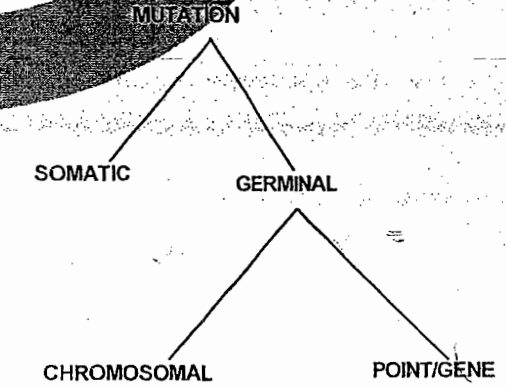
MICROEVOLUTION is not one process but is the aggregate of the effects of the action of different factors. These factors, called micro-evolutionary processes, five in number are:

Mutation
Natural Selection
Inbeeding
Hybridization
Genetic Drift

MUTATION

MUTATIONS are of two kinds: somatic and germinal. Somatic mutations bring changes in the general body cells and are not inherited. These are, therefore, not consequential in evolution. Germinal mutations are again categorized into chromosomal mutations and point mutations. Chromosomal mutations lead to gross alterations in the chromosomes. Their effects have been described later under the heading of changes in chromosome number. Point mutations are the ones which alter the functioning of a single gene. point mutations or gene mutations are the only source of new traits in man. As genetic recombination (described later) does not lead to any alternation in the gene structure, it does not, by itself, bring in any new traits in a population and therefore genetic recombination does not qualify to be called a point mutation. The discussion on mutation now onwards refers to point mutations only.

MUTATION refer to any sudden change in the genetic material., They do not arise to fulfill a need instead they are totally random. In other words, what ever changes occur are totally unrelated to any environmental demands that are being made



on the organism or its environmental experiences.

IT IS due to the random nature of mutation that most mutations frequently reduce the viability and fertility of their possessors. They are almost always deletrious for the individual who possess them. This is because the genetic material of all living beings is already so "well tuned" for adaptation to their environment, that any random change in it has a very high probability of decreasing the "adaptive fitness" of the living being vis-a-vis the prevailing environmental conditions.

THOUGH advantages mutations are definitely a rarity, however, many mutations are neutral for the individual, that is they neither confer any special advantage nor any disadvantage on their possessor. Such mutations, though they do not confer any great advantage on the individuals possessing them, are however crucial for the long term survival of the population or species. Such mutations create a greater genetic variability in the gene pool of the population, and this variability can be made use of to help the population adapt better to changed environmental conditions, if and when need arises. Higher the variability in the gene pool of the population, greater will be its capacity to withstand environmental change. Thus, though mutations are almost always deletious for the individual, yet they are necessary for the population survival. It must be kept in mind that ultimately it is the environment acting through the process of natural selection, that decides whether a particular mutation is harmful or not.

MUTATION may be spontaneous or induced but experiments have shown that only spontaneous mutations are relevant from the angle of evolutioanry mechanism. A mutation is a somewhat permanent change but a mutated gene may undergo a second or thrid or even a reverse mutation. Though mutations are sudden, the rate of change of genes by mutation is very slow. The table given on previous page, gives the rate of mutation for some of the human genes.

AS MUTATIONS are rare but recurrent, we can find the best evidence of mutation through family studies and pedigree analysis or (for lower species) in laboratary conditions. In the case of man, dominant mutations can be recorded easily as they instantly bring new phenotypes.

RECESSIVE mutations are, however, not easy to detect because a recessive mutated gene has no phenotypic expression. Such genes, as they have greater probability of expression by becoming homozygotes through consanguinous marriages and inbreeding, can only be studied in the small, inbread populations or consanguinous marraiges. Recessive X-linked mutations can be studied easily because these express themselves in the descendant males only. We can, for example, be almost sure that the Queen Victoria must have inherited the gene for haemophilia through female line only as none of her male ancestors contracted it while some of her male descendants did. Though most mutations have phenotype expression too, those concerned with physiological systems and metabolism do not produce any morphological alteration.

MUTATIONS may be caused by changes in temperatures, chemicals and radiation, the most potent mutagenic agent being the deep penetrating ionizing radiations (X-rays, gamma rays etc.), cosmic rays with a wavelength of less than 10-8 cm, as also the neutrons released in the nuclear reactors. Among the chemicals some aldehydes, nitrogenous compounds, acids, carcinogens and sulfure etc., can cause mutation. Changes in temperature are not known to cause mutation in man but studies have shown that radiations may cause mutation by the production of certain chemicals. It has also been seen that mutagenic agents can cause mutations only in the cells on which these are acting directly. Chemicals that cause mutation in plants do not effect man because in man chemicals are divided into components before they actually reach the cells. Radiations as mutagenic agents are not specific for any particular genes, some of the chemicals are. Incidentally, mutagens can cause mutation only in some of the genes. This is why mutations are not as common as these could have been.

Traits	Nature of Mutation	Mutations per 10^5 gametes
Huntington's Chorea	Autosomal dominant	1
Aniridia Autosomal dominant	5	
Retinoblastoma	Autosomal dominant	20
Haemophilia A	X-linked recessive	20-82
Muscular dystrophy (Duchenne type)	X-linked recessive	40-90
Achondroplasia	Autosomal dominant	40-90
Neurolibromatosis	Autosomal dominant	30-150

NATURAL SELECTION

NEW traits appear through mutations but they owe their existence to natural selection. The new characters, by themselves, are neither advantageous nor disadvantageous; it is for the natural selection to decide the importance of each mutation on merit. In other word, whether traits are malevolant or benevolant depends on the environment in which they appear and exist. This implies that increase in mutation rate for a particular gene may not lead to the higher frequency of mutated gene in a population without the generosity of natural selection. This is because mutation as a process occurs in individuals and it is for the natural selection to spread these mutated genes from the individual to the whole population.

IT WAS earlier held that selection operates in terms of survival, but this is not true. Selection operates in terms of fertility and fecundity, i.e. the mutations that are selectively advantageous spread faster because of greater fertility and fecundity of those who possess the mutant gene. Contrarily, the genes which are considered harmful are weeded out by the opposite or negative action of selection. How fast a gene will spread or be removed depends on the extent of advantage or disadvantage conferred by the concerned gene. By this understanding natural selection refers and results from the cumulative action of all forces tending to ensure that individuals possessing one genetic constitution shall leave a larger number of offsprings, than will individuals possessing some other genetic constitution.

IN OTHER words, natural selection is differential viability and fertility according to genetic constitution. It acts essentially on individuals and their gametes, only indirectly does it act on the genes and genotypes. If, however, an individual possesses some character which confers a great viability or fertility on him compared to other individuals of the population, then the genes controlling this character will be preferentially represented in the next generation in the greater than average number of offsprings of the individuals concerned. We then speak of the individual having a higher "Darwinian fitness", of the character being adaptive, and of natural selection being in favour of the responsible genes or gene combinations. The gene can be thought of as a unit of evolution, but the unit of selection is the individual.

IT MUST be kept in mind that individual fitness is a relative phenomenon, that is, some individuals are more fit than others. One also needs to considers simultaneously the environment,

for an individual who is relatively fit in one environment may be relatively unfit in another, or a gene that is *selected for* in one environment may be *selected against* in another environment. It is the environment which exerts the selective forces and pressures, and through this, organisms get better adapted to the environment in which they live.

NATURAL selection may act in different ways. When it acts to remove the unwanted genes, genotypes and phenotypes, it is known as *normalizing* natural selection. Whenever there is change in environment favouring a particular gene or genoytpe, the selection strategy is called *directional* natural selection. This is simply the opposite of normalizing selection, with selection favouring certain genes and genotypes rather than eliminating them What is seen from one viewpoint as selection in favour of a new gene (i.e. directional selection) can also be seen as a selection against its alternative allele (i.e. normalizing selection). Various plant and animal species, through directional natural selection have survived in otherwise hostile changes in environment. Adaptation in colour by wasps and bird species as also the adaptation towards insecticides by insects results because of changes in phenotype or genic changes in accordance with the changing environment. [In industrial areas, dark coloured species (e.g. of moths) can escape predation and survive.] At times certain gene modifiers bring large variations in phenotypes with little effect on nature of the gene concerned. Both (normalizing and directional) types of natural selection results in the reduction of genic and genotypic variability.

IN MANY species high proportions of an otherwise harmful gene are maintained through *balancing* natural selection that retains genic and genotypic variability and flexity in a population. Balancing selective forces may act in a variety of ways. The most important situation is that in which one allele of a pair is relatively advantageous in effect when in low frequency, but becomes relatively disadvantageous when in high frequency. This will happen automatically when the heterozygote is more fit than either homozygote. The classic example of this type of selection in man is sickle-cell gene. Sickle cell gene responsible for the formation of haemoglobin-S, is known to provide some kind of resistence against malaria. In malarial environment e.g. in a large belt in central Africa, the gene is important in selective survival of human species. Individuals with homozygote condition for normal heamoglobin have to face persistant attacks of malaria that becomes a threat to these HbA/HbA individuals. Sickle cell gene causes sickling of the red cells that causes problems for the oxygen transport. Individuals homozygotes for sickle cell gene (HbS HbS) therefore, can not survive to produce offsprings. Under these circumstances, heterozygote genotype HbA/HbS is best suited because it provides resistence against malaria without causing substantial damage to oxygen transport. May populations in the malarial environment of central Africa have almost 100 percent HbA/HbS surviving adults. A condition like this, where both types of gene survive because of the selective advantage conferred on the heterozygotes, is called *balanced polymorphism*.

IT IS not always that the heterozygotes are bestowed with favourable selection. A common example of selection against heterozygotes is the Rh factor whereby Rh+ve heterozygotes born to the Rh-ve mothers are selected out through *erythroblastosis foetalis*. Similarly, selection against heterozygotes in ABO and other blood groups is strong enough to cause changes in genotype and gene frequencies. Effectes on new mutations, heterozygotes and homozygotes lead us to the inference that selection operates on mutation, hybridization and inbreeding.

Evolution enigma

"SURVIVAL of the fittest" is the catch phrase of evolution by natural selection. While natural selection favours the most fit organisms around, evolutionary biologists have long wondered whether this leads to the best possible organisms in the long run.

A team of researchers at the University of Texas at Austin, led by Dr. Matthew Cowperthwaite and Dr. Lauren Ancel Meyers, has developed a new theory, which suggests that life may not always be optimal. The results of this study appeared on July 18, 2008 in the open-access journal PLoS Computational Biology.

GENETIC mutations create the raw material that natural selection acts upon. The short-term fate of a mutation is often quite clear. Mutations that make organisms more fit tend to persist through generation, while harmful mutations tend to die off with the organisms that possess them. The long-term consequences of mutations, however, are not well understood by evolutionary biologists. The researchers have shown that what may be good in the short run, may hinder evolution in the long run.

THE team developed computer models of RNA colecules evolving by mutation and natural selection. RNA mlecules, which are very similar to DNA, play key roles in essential life process and serve as the genetic material for some of our deadliest viruses, including influenza and HIV.

Their computer models show that the evolution of optimal organisms often requires a long sequence of interacting mutations, each arising by chance and surviving natural selection. As Cowperthwaite explains : "Some traits are easy to evolve formed by many different combinations of mutations. Others are hard to evolve — made from an unlikely genetic recipe. Evolution gives us the easy ones, even when they are not the best."

THE group's analysis of RNA molecules from a wide variety of species suggests that life is indeed dominated by the "easy" traits perhaps at the expense of the best ones.

INBREEDING

(or Non-random mating or Positive assortative mating or Isolation)

INBREEDING refers to the mating of member of a group to another member of the same group. The extreme expression of inbreeding is consanguinity whereby the spouses are very closely related (genetically) to each other. Inbreeding in general (and consanguinity in particular) has an important effect : it increase homozygosity and decreases hetero-zygosity, and consequently decreases genetic variability.

PLANTS with self fertilization as a rule provide ideal conditions for the understanding of effects of inbreeding. Let us assume a hybrid population (like the F_1 generation of Mendel) that remains constant in number (say N) over generations. The self-fertilization will lead to the coming together of alike genes ultimately increasing homozygosity as follows :

INBREEDING is deleterious in families or small groups with one or more lethal and/or semilethal genes. In the table given above the individuals in the right column (recessive homozygotes) will be constantly removed from the scene directly affecting the gene and genotype frequencies of the population. In F_1 generation both dominant (normal) and recessive (lethal) alleles are present in equal proportions with a frequency of 0.5 each. In F_2 generation one-fourth of the individuals will be recessive homozygotes who, because of the expression of lethal gene, would die. The genotypic ratios 1:2:1, therefore, assume the proportion of 1:2 for dominant homozygotes and heterozygotes resulting in the decrease in genotypic variability. Consequently, the frequencies of the alleles which were present in equal proportions in F_1 generations, also get altered with dominant becoming propotionately more frequent (66.67) than the recessive (33.33%).

INBREEDING, therefore, causes sudden changes in gene and genotype frequencies by eliminating the lethal and semilethal recessive homozygotes.

BUT is inbreeding always harmful? The answer is an emphatic 'no'. Various (almost all) populations of the world have practised inbreeding (and consanguinity) at different times in the history

Generation	Homozygotes (dominant)	Heterozygotes	Homozygotes (recessive)	Homozygosity %
F_1	0	N	0	00.00
F_2	N/4	N/2	N/4	50.00
F_3	3N/8	N/4	3N/8	75.00
F_4	7N/16	N/8	7N/16	87.50
F_5	15N/32	N/16	15N/32	93.75
F_6	31N/64	N/32	31N/64	96.87
Infinite	N/2	0	N/2	100.00

without endangering their own existence. Even today many societies of the world (and their number is large enough) permit marriage between as close the relations as first cousins, uncle-niece or even the individuals with one common parent. All such societies have survived (and are flourshing) without caring for the deleteriousness of inbreeding. Inbreeding is harmful only when there is a lethal autosomal recessive gene present, otherwise not. Besides it is really threatening only in small populations.

Is Inbreeding Harmful?

According to some scientists Inbreeding is harmful. To support their contention they give the example of Great Andamanis whose population according to Census of 1971 was reduced to 28 from about 300 a hundred years ago. Why Inbreeding is harmful? To answer to this question they say that if there is present an autosmal recessive, lethal or semi-lethal gene then it is harmful. As inbreeding increases homozygosity and autosomal recessive will also become homozygous and as it is lethal, its phenotype appears and it is removed through natural selection. As the recessive homozygotes keep dying, the population would face decline in numbes and will be eliminated in the end. So we have to deliberate whether inbreeding is really harmful.

(1) Those who say Inbreeding is harmful their statement starts with "if". It means that even they also agree that inbreeding by itself is not harmful. It is the presence of autosomal recessive lethal that makes difference.

(2) According to them as the recessive lethal homozygotes keep dying, the population would decline in numbers. But according to Malthus, living beings in genetal have enormous fertility. The survivors will produce many more than those eliminated.

(3) In Biological sciences it is generally said that smaller the numbers of genotypes greateer are the chances of elimination of population if environment changes. However, for Man there is neither any study not any evidence to prove that reduced number of genotypes can have any negative affect.

Inbreeding can be harmful only in one situation that the survivors do not have enough fertility to compensate the loss of recessive lethal homozygotes. As human beings in general have sufficient fertility, therefore, the issue of harmful effects of inbreeding in humans is only theoretical in nature. Here, we must remember that the issue concerns Population Genetics and not Human Genetics.

Hybridization

HYBRIDIZATION may be taken just opposite of inbreeding because contrary to effects of inbreeding, hybridization breaks down isolates to increase heterozygosity. Mating of two homozygous individuals for different alleles of a gene shoule be called hybridization. In a small isolate with high rate of inbreeding, individuals tend to have greater preponderance of homozygosity. When such two isolates come together in terms of sharing the gene pool of each other, hybridization should be said to have occured.

IT IS generally said that hybridization affects gene and genotype frequencies only indirectly. The statement is only partly true, because the dominant lethal or semilethal genes, wherever these are, are equally potent whether hybridization is there or not. The same is true for sex-linked recessive genes which express more frequently among the males under any circumstances. The autosomal recessive genes, through hybridization, get a chance to spread. With two populations coming genetically close, coming closer of the autosomal recessive lethal (and semilethal) genes is postponed at least till the time such alleles have spread enough to become homozygotes. Hybridization, therefore, delays the elimination of recessive harmful genes.

AS SAID earlier, hybridization results in sharing of the genes between two isolates. For hybridization to be perfect, the two interacting populations should have equal size of breeding population and if the mating between the members of two groups is random, it will take exactly one generation for the two groups to become one. With heterozygosity also increases the variability within the resultant population compared to that in each of its component groups before hybridization.

THROUGH the understanding of the process of hybridization can be understood the process of *gene flow*. Different populations of the world, settled away from their original homes, exhibit little to significant levels of gene admixture with their neighbours now. Americans of African descent, for example, exhibit much similarity with surrounding American populations more than they do with their parent group. But Gypsies of Hungary still have close resemblance with their ancestral Indian population. Through the process of gene flow, the genetic combinations that have evolved in one particular environment, get transferred to and find their expression in another kind of environment. As a result infra-group variability increases while inter-group variability declines.

GENETIC DRIFT

OR RANDOM Genetic Drift or Sampling Error : Mutation, selection inbreeding and hybridization can at the best be called pressures becuase the knowledge of these processes can lead to the understanding of evolutionary change. One way in which gene frequencies may change relatively quickly is by sheer chance or genetic drift. The probability of chance acting as an evolutionary factor had been mathematically developed by Sewall Wright and drift is often referred to as Sewall Wright's effect. Genetic drift is random aspect of evolution which refers to elimination or fixation of a gene in a population by sheer chance without the role of mutation or selection. To understand the effect of genetic drift let us take up a hypothetical case.

LET there be a population wth effective breeding strength of 100 with distribution of ABO blood groups as follows :

A = 30 (or 30%)
B = 10 (or 10%)
O = 60 (or 60%)

OUT of these hundred, some (say 10) opt to migrate. The group of individuals who opt for migration may not have the proportionate distribution of blood groups in them. Let various blood groups in the migrating subgroup be as follows :

A = 5 (or 50%)
B = 2 (or 20%)

O = 3 (or 30%)

THESE 10 individuals (or migrants) in an unknown place will marry among themselves and with passage of time would become a population whose blood-group frequencies will revolve around those of their migrant ancestors and not around those of the parent population. Thus, a new population has emerged. This phenomenon is also known as "*Founder's principle*", and it may have played a very significant role in determining geographical patterns of human variations.

HISTORY of mankind is full of such instances of genetic drift that lead to the formation of new populations. Dumker community of Pennsylvania who migrated to the United States in mid-eighteenth century exhibit much higher frequency of gene for blood group A (0.38) compared either to their ancestral group of Germans (0.29) or to their present American neighbours (0.26). Contrarily, the gene frequency of blood group O is much reduced compared to the other two populations. It is not necessary that migrants will exhibit large fluctuation in gene frequencies (compared to the population initially they belonged to). Many genes may have comparable proportions. It all depends on the frequency of different genes in the migrants.

FOUNDER'S effect is only one of the many ways in which drift occurs. There are thousands of others examples. For instance, the number of gametes produced is always large, but when populations are small, the number combined in zygotes is by definition also small and substantial deviations from expected proportion of gene frequencies can occur by sheer chance.

AGAIN, genetic drift can not be effective in all times or at all places. For the drift to be successful in resulting change, the following pre-requisites have to be met with: (a) The population size must be small. There is however no agreement on the limit of size to be called small. Yet, small the size of the group greater is the impact of drift felt by both segments (parental and migrant) of the population. As the size of a population becomes larger, the effect of drift becomes successively less meaningful. (b) There is considerable fertility differential. (c) The frequency of allele in question is low. (d) There is recurrent out-migration.

Humans evolving faster than ever

Humans are evolving more quickly than at anytime since the split with the ancestors of modern chimpanzees 6 million years ago, a team from the *University of Wisconsin* has found.

The study also suggests that human races in different parts of the world are becoming more genetically distinct although this is likely to reverse in future as populations become more mixed, said anthropologist *John Hawks*, who led the study.

The researchers analysed data from the International haplotype map of the human genome, and analysed genetic markers in 270 people from four groups : Han Chinese, Japanese, Africa's Youruba, and northern Europeans.

They found that at least 7% of human genes have undergone recent evolution. The changes include skin and blue eyes in northern Europe and partial resistance to diseases such as malaria among some African populations, according to the study in *Proceedings of the National Academy of Sciences* on Dec. 10, 2007.

Some of the changes were tracked back to just 5,000 years ago, and "today they are in 30 or 40% of people because they (are) such an advantage," said Professor Hawks.

Many Chinese and African adults cannot digest lactose in milk, but across Europe a lactose-tolerance gene is now widespread.

One reason is though to be that at northern latitudes sunlight is weaker, so people make less vitamin D in their skin, Vitamin D is crucial for absorbing calcium, so being able to digest milk throughout life made people in clolder climes healthier.

The surge in global population had also led to faster evolution since more mutations occur, the researchers said.

They believe that in future, the tendency to start families later in life will drive evolution.

Evolution on fast forward

Human evolution has been moving at breakneck speed in the past several thousand years, far from plodding along as some scientists had thought, researchers said on Dec. 10, 2007.

In fact, people today are genetically more different from people living 5,000 years ago than those humans were different from the Neanderthals who vanished 30,000 years ago, according to anthropologist John Hawks of the University of Wisconsin.

SYNTHETIC THEORY

SYNTHETIC theory of organic evolution is the most recent, the most scientific of all the existing theories that states the best aspects of earlier hypotheses and combines or synthesizes them in a new and original manner. Exponents of synthetic theory also made use of such modern scientific knowledge as from cytogenetics, cytology, population genetics etc., and employed modern methods and techniques of research. The theory propagated by several neo-Darwinians including Stebbins, Fisher, Simpson etc., basically aimed to clear Darwinism off the drawbacks and criticism. As a result, Darwinian concept of selection still forms the core of synthetic theory. But other evolutionary processes too have been given the credit for the ongoing evolution. The basic features of Synthetic Theory can be summed up as :

1. "Mutation, Genetic Recombination, Natural Selection and Isolation form the most important processes of micro-evolution."
2. "Mutations only act as a potential source of variability and their role has previously been over-emphasized, the mutations which embrace large number of genes are more effective in microevolution than those which affect the single gene." In other words, though all new traits arise due to mutations (including genetic recombination and changes in chromosome numbers), however mutations only serve as a potential source of variability. The immediate source of variation in offsprings, on which natural selection acts, is the heterozygous combinations in the zygote. The mutations which are more effective in micro-evolution are those which individually have a slight effect on the phenotype and which collectively form the basis for polygenic inheritance.
3. "Natural Selection is the most vital process of microevolution and its role is more progressive and creative in bringing genetic variability."
4. "Isolation (Reproductive Isolation) as also geographic isolation forms strong base for the formation of new species. Reproductive isolation, to work effectviely, requires immense contribution of mutation, selection and geographic isolation." Thus, isolation forms the strongest basis for the formation of new species. When two populations get isolated from one another, each evolves in its own (slightly different) manner. If the isolation is prolonged over a sufficient period of time, then the genetic material of the two populations may get reconstituted, resulting in the development of some type of Reproductive isolating mechanism. When this happens, the two populations are incapable of successful reproduction with each other, even if the isolation is removed.
5. "New species are formed by the continuous action of micro-evolutionary processes over a long time-span, cutting through the geographical span."

ACCORDING to Synthetic Theory, evolution is the sum total of

the five essential evolutionary processes. These essential processes are :

1. Gene Mutation
2. Change in Chromosome Number
3. Genic Recombination
4. Natural Selection
5. Reproductive Isolation

FIRST three processes provide the essential genetic variability without which changes can not take place. Last two processes guide populations of organisms into adaptive channels.

IN ADDITION to above, three accessory processes affecting the working of evolution are:

1. Migration
2. Hybridization
3. Chance Factor

OF THE essential processes mentioned above, all except the two have been described previously. The remaining two, namely the change in chromosome number and genetic recombination are being described now.

Genic Recombination

GENIC recombination refers to the changes that may occur in a cell (genetic material) whereby chromosomes may become abnormal for the particular species. Then, though the total number of chromosomes remains the same, sequence of genes in one or more chromosomes changes. Inversion, deletion, duplication, and translocation are the typical examples of genic recombination.

DELETION is the simplest of all the above mentioned processes of genic recombination. It involves removal of a part from a chromosome. Parts of a chromosome without the centromere (during anaphase of meiotic cell division) break off from the parent chromosome without rejoining again. Deletion causes deficiency of genes in a germ cell. The most commonly known example of syndrome cause by deletion in chromosome pair number 5 and known as *cri du chat or cat-cry* is diagnosed by mental retardation, anomalies of heart, eyes, kidneys, skeleton etc., and severe malfunctioning of the larynx. Deletion can occur in any of the human chromosomes resulting in the severe anomalies in the body. Deletion in an X chromosome causes a Turner-like syndrome but those in the Y chromosome are not known to have any effect.

TRANSLOCATION involves two processes: firstly two deletions from non-homologous chromosomes, and secondly sharing of the broken parts by the concerned chromosomes. translocation is a very rare phenomenon. In man some cases of Translocation have been reported, most of which resulted in infant mortality. Surviving cases face acute mental retardation or the symptoms of Down's syndrome. A normal form of translocation but involving a homologous pair is crossing over that occurs in all diploid species during reduction division of a germ cell. Man too is no exception to this rule.

WHEN a part of chromosome is represented more than twice in a normally diploid cell, the situation known as *duplication* results. It may also be called half translocation whereby a part of one chromosome is represented thrice or more times at the cost of another cell that faces deletion.

INVERSION results when a part of the chromosome gets detached and then gets reattached to the same chromosome but in an inverted position.

ALL types of genic recombination result in the change in sequence of genes on a chromosome. The new arrangement, because of the new association of genes, may and does result in new genic expression resulting in new phenotypes. Inversion, deletion, duplication etc. are very common feature of plants and some lower species of the animals but as seen above, in man, such situations result in severe disabilities and even death. Genic recombination can be created artificially through radiation and study of genic recombination, if understood fully, may open up new vistas regarding future human evolution.

Changes in Chromosome Number

EACH species of living beings is known to have a particular number of Chromosomes. Some of such mammalian species have been listed in the table below:

Common Name	Species	No. of Chromosomes
Rat	Rattus norvigieus	42
Mouse	Mus inusculus	40
Rabbit	Sylvilagus floridanus	44
Horse	Equus caballus	64.
Ass	Equus asinus	62
Monkey	Macaca mullatta	42
Chimpanzee	Pan troglodytes	48
Man	Homo sapiens	46

CHANGE in chromosome number in the individuals of a species may or may not lead to the formation of a new species. CHANGES in chromosome number are of two kinds (i) *Euploidy* : when a whole set of chromosomes exists in multiple proportions compared to the specified ones for a species, (e.g. the individuals of a species with chromosome number of 2n may have 3n or 4n etc.) and (ii) *aneuploidy* : (loss or addition of single whole chromosomes, (e.g. 2n + 1 or 2n - 1 etc.). Both types of changes in chromosome number have been witnessed in plants and lower species of animals with or without the formation of a new species. While euploidy is somewhat rare in the animals, it has been estimated that more than two third of grass species have multiple sets of chromosomes.

EUPLOIDY occurs very rarely in man and the few cases known are still-births or spontaneously aborted foetuses. In all such cases gross malformations due to extreme genic imbalance are reported resulting is loss of all chaces of survival. According to an estimate of the total number of spontaneous abortions in man, about 15% are due to euploidy. Huskins (1920), Merchant (1963) and others have given enough evidence of the role of euploidy in species formation among plants. In man, as seen above, the situation can not be important in evolution because (i) it is a very rare event and (ii) such individuals don't survive to reproduce.

ANEUPLOIDY like the euploidy has been seen often in various plant species and is a potent source of evolution. In the case of man, it has been found to be more frequent than the euploidy.

THE most common cases of aneuploidy in man belong to the sex anomalies in the form of Turner syndrome and Klinefelter syndrome. Individuals with Turner syndrom with generally female phenotype have one X chromosome less (22 pairs of autosomes and a single X instead of 22 pairs of autosomes and XX in normal females) while the Klinefelters with a generally make of a pseudohermaphrodite phenotype have an additional X chromosome (22 pairs of autosomes and XXY). Cases with multiple number of X chromosome (XXX or XXXX) too are known in the medical records. Among the autosomal anomalies, the most commonly known condition is called Down's syndrome (or 21 trisomy) where either of the chromosomes of the smallest group (21 & 22) may occur in triplicate (instead of the normal duplicate). The frequency of this syndrome is as high as 1 in 600 live births.

A RELATIVELY rare condition with an occurence of 3 per 10,000 births is called Edward's syndrome and involves trisomy of chromosome 13; Patau syndrome with an occurence of 2 per 10,000 briths involves Trisomy–18. In all the above three syndromes, the total number of chromosome in an individual is 47 instead of the normal 46. All these syndromes result in severe mental retardation and/or serious physical disabilities leading to almost absolute restriction on the fertility of the individual. In majority of such cases the individuals do not survive to reproduce.

TO SUM up, changes in chromosome number in man do not entail any important viable situation for further human evolution.

As these are understood today, changes in chromosome number and genic recombination have highly strong negative selection value.

HOWEVER, for certain lower life forms of both plants and animals, chromosomal mutations do sometimes lead to the formation of new species. Since this kind of speciation takes place over just one generation, it may be thought of as a kind of "instant speciation".

SYNTHETIC theory is the best theory of organic evolution that combines all genuine elements of hitherto existing theories. Though the synthetic theory of evolution today is considered the best among the available theories of evolution yet it is not free from flaws. The theory in fact explains evolution as it occured in the past but fails to explain it in terms of its future direction. The factors of genic recombination and change in chromosome number (in man) do not warrent such importance as had been given to them in this theory. Especially change in chromosome number for 21st chromosome and sex chromosomes results in serious handicap for an individual in terms of his/her fertility and fecundity; all other chromosomes when found in single or triple condition, do prove lethal. Similarly, genic recombination in terms of inversion, duplication or deletion etc., also leads to lethal or semilethal situations in man. Crossing over, however, is as useful in man as it is in other animals or plants.

ROLE of Hybridization and genetic drift, in Synthetic Theory have been highly undermind. History of mankind as also recent experiments on plants and animals, clearly support the idea of large contribution of these factors. It is also true that through hybridization the whole great process of phenotypical change occurs.

MIGRATION as a process in physical term is meaningless unless it is followed by gene migration. Gene migration and genetic recombination can amply be explained in terms of hybridization and genetic drift. The inclusion of this factor in this theory is, therefore, superfluous.

FROM the foregoing discussion we conclude that the synthetic theory in its best possible form as applicable to man can be explained as the one that takes into account five processes of microevolution, namely

1. Natural selection
2. Inbreeding
3. Hybridization
4. Genetic Drift
5. Mutation
6. Conclusion

SYNTHETIC THEORY AND ANTHROPOLOGY

SINCE in anthropology there had been extreme reliance on typological thinking, orthogenesis, irreversibility and the importance of nonadaptvie characters, the synthetic theory devastated most of the structure of traditional anthropological thought. This can be seen most clearly in the study of human races. The majority of physical anthropologists had been busy dividing populations into types, and then manipulating the types in order to reconstitute racial history. Types similar to the existing ones were postulated to have existed hundreds of thousands of years ago; this notion of the fixity of the types of modern man goes along with the theory that modern man is ancient and almost all the fossils represent collateral lines which became extinct. Substitution of the variable Mandelian population for the type (composed of phenotypically similar individuals) simply destroyed the theoretical basis for the vast majority of anthropological thought. Many anthropologists believed in orthogenesis, that evolution proceeded from an internal momentum. The synthetic theory showed that no such process exists, and that trends are due to selection. Also the idea was common that evolution should be traced by nonadaptive characters. This point of view is seen in extreme form in the writings of Wood Jones, who, after giving an excellent comprehensive review of primate anatomy, attempted to determine evolutionary relationships on the basis of a few minorvariations in the patterns of sutures. According to the synthetic theory, selection is even more important than Darwin thought, and the explanation of characters should be sought in the understanding of their functions. These theoretical problems were by no means unique to anthropology, but the confusion of typological, pregenetic thinking was extreme in anthropology because of the emphasis on racial types, and the attempt to recreate his-

PUNCHUATIONISTS V/S EVOLUTIONISTS

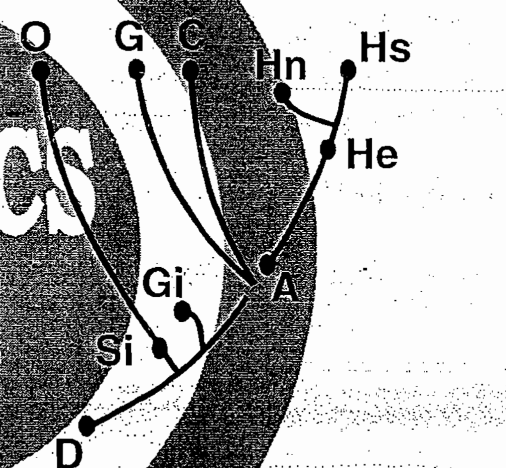
The publication of Darwin's "*Origin of Species*" 1859 scientifically established that evolution is a continuous process and applies to all the species. There were many objections to Darwinism, which were clarified by Neo-Darwanians in 1930's and 40's and the explanation was given the shape of Synthetic Theory. Church, however, till date is not convinced with the facts of evolution.

In 1972 Eldredge & Gould, on the basis of their study of North American Trilobites and Bermudan land snails, give the concept of "Punchuated equilibrium". According to them species remained unchanged for thousands of years and then changed suddenly into new species or are replaced by species from the neighbouring regions.

Towards the end of Mesozoic, Cretaceous period, the world was overcast by volcanic ash, converting the world into total dark that continued for several hundred years that resulted in sudden appearance of many new species and genera like flowering plants and primates, lending credibility to ideas of Eldredge & Gould.

The Synthetic Theory itself had made it clear that change in Chromosome number and genetic recombination can result in micro as well as macro evolution or speciatation in plants and lower species of animals, but not in higher species including man.

Evolution of man as shown in the evolutionary tree below —



shows a gap of 2.5 million years between Dryopithecus and Australopithecus, using Punchuationist logic Dryopithecus could have continued upto 5.5 million years ago or Australopithecus could have arrived early around 8 mya. Therefore, there must have been a quantum jump in evolution from knuckle walker Dryopithecus to bipedal Australopithecus. However the large scale changes in the anatomical structure resulting in bipedalism can not be an overnight process and therefore Punchuationists ideas are not applicable to human evolution.

However we can explain the changes undergone during this gap of 2.5 my with the help of our knowledge of biology and evolution.

tory without regard to the fossil record.

Human Evolution : A Perspective

WE HAVE, so far, discussed the evolution the way it has been as also the theories which attempt to explain evolution with difference on emphasis. The evolution has been there even without these theories and with changing environment, will override the most accurate theories of the past.

FROM human point of view evolution, in recent times, has drawn the attention of everyone. The environment during last couple of centuries has changed which must have a bearing on human evolution too. Man, to an extent, has manovered nature and the vagaries of selection have loosened their hold on Man. Advances in the field of science and technology have increased the longivity significantly. Infant mortality has been curbed resulting in population explosion. The individuals who could easily succumb to the pressures of erstwhile epidemics etc. now do survive and reproduce. Though the family-size has been on the decrease, the population has been increasing enormously because of the above mentioned factors. Such an increase in numbers without a proportionate increase in the source of survival, can, in not so distant a future, threaten the human existence as a whole.

TILL recently, it was the almost unimaginable to think in terms of the treatment of the genetic diseases. Thanks to the advances made in biochemical genetics, immunogenetics and molecular genetics, the spread of some lethal genes can not only be controlled but the affected individuals can be cured too. Genetic counselling and the treatment for phenylketonuric idiocy is a point in this regard but we must admit that the progress on the front of cure of genetic diseases is very slow. There is another facit of this problem. With the treatment of some genetic diseases are being preserved certain unwanted genotypes that would have been otherwise eliminated by natural selection.

OUR researches therefore, have benefitted individuals at the cost of human society. Preservation of harmful genotypes has resulted in the increase in genetic load in man. According to one estimate all of us have accumulated at least 4-6 harmful genes. But the situation, as yet, has not attained alarming proportions. Though there are not substantive studies undertaken, the evidence is conclusive regarding increase in mutation rate in recent times becuase of the ever-increasing nuclear activity in industries, nuclear reactors, tests of nuclear devices etc. The impact of this change is yet to be measured as also the operation and direction of natural selection. With the increase in the chances of survival, diseases of childhood have shown a steep upward spurt.

THE situation has posed a challenge to the scientists. There are three ways through which the situation can be improved or at least saved from further deterioration. *Firstly*, the expression of harmful genes be overriden. This practice in vogue has however resulted in accumulation of harmful genes, in terms of genetic load. Regarding how far the overriding of gene expression can be successful for humans, scientists present different viewpoints, some of which are quite optimistic, others are equally pessimistic.

THE *second* solution is direct recombination which is quite easy to perform, theoretically. Direct recombination refers to allowing reproduction of selectively advantageous genes. It also means a deliberate check on the fertility of those who possess harmful genes. But the question is : can it be performed at the global level? Who will set the rules? Whether it will be acceptable? Masses in general will opppose any law that stops them from reproducing even the defective offsprings. The selection of genes is however a practical solution whereby the required types of genes can be received from the sperm banks and egg banks. The way has been cleared for this kind of genic recombination but it is not expected to reach the common man at least in another few decades.

THIRD solution to improve the gene bank of man is genetic engineering. We are at a stage where genetic codes of some of the hereditary diseases have been understood but we are yet to remove the defects in these genes to make them normal. Scientists have been successful in making the synthetic DNA that has worked effectively in some lower species. Attempts are on to apply this knowledge to higher species and man.

THE day synthetic DNA can be utilized in the service of man, we may look towards a new direction of human evolution.

CONCEPTS OF EVOLUTIONARY BIOLOGY

DOLLO'S RULE (DOCTRINE OF IRREVERSIBILITY OF EVOLUTION)

MANY times during the long history of life, advanced organisms have returned to ancestral habits and modes of life. This gives selective value to adaptations similar to those of the ancestral species, and raises the question whether evolution might be reversible. Study of such cases shows that, due to commonality of environment and resultlant functional adaptation, always a gross similarity between ancestral and descended structures is achieved without any genuine reversal at all. Thus many reptiles and mammals have reverted to an aquatic mode of life. They have assumed a generally streamlined, fishlike form, and the limbs have become shortened, webbed, and finlike. Yet the skeleton of such flippers is always distinctly that of the class to which the animal belongs rather than that of a fish fin. Similarly, many angiosperms have returned to the water and assumed alga-like appearances, but their morphology is still that of flowering, vascular plants. The evidence indicates that major evolutionary steps, once taken, are never reversed. This is known as Dollo's Rule after Louis Dollo (1895) to whom the principle is ascribed. It even might be expected a *priori,* for major evolutionary steps are compounded of many smaller steps, each preserved by natural selection. That such a sequence, occurring by chance once, should by chance be exactly reversed would be a most extraordinary thing. If not impossible, it is at least most improbable for whole organisms. Attempts to apply Dollo's Law to individual characters have failed, for these are, indeed, reversible by mutation.

COPE'S RULE

A VERY common trend in evolution, sometimes called Cope's Rule, is one toward increasing size of individuals. The original studies of the phenomenon were made upon vertebrates, but comparable studies have shown the same tendency in many groups of invertebrates and plants. A review of the paleontology of almost any group shows that its largest representatives are not its earliest ones, though not necessarily its latest ones either. Newell has pointed out that species now living are the largest known representatives of the vertebrates, crustaceans, echinoderms, pelecypods, gastropods, cephalopods, and annelids. Yet the tendency toward size increase has been by no means universal. The rise of herbs and shrubs is a recent thing, and they have been derived from trees and other large plants. Hooijer has pointed out that progressive size decrease has been characteristic of many vertebrate groups during the Quaternary period, which is now in progress.

GAUSE RULE

COMPETITION may occur between populations within an ecosystem for any of the available resources, such as food, space, light or shelter. If two species occur at the same trophic level, then they are likely to compete with each other for food. Adaptive radiation by one or both species may then occur over a period of time with the result that they come to occupy separate niche within the trophic level, thus minimising the extent of competition. Alternatively, if the competitors occupy the same niche, or strongly overlapping niches, an equilibrium situation may be reached in which neither succeeds as well as it would in the absence of the competitor, or one of the competitors declines in numbers to the point of extinction. The latter

phenomenon is known as *competitive exclusion.* It is difficult to study in wild populations but some classic work on laboratory populations has been done, originally by the Russian biologist Gause in 1934 who worked on competition between several species of *Paramecium.* Some of his results are shown below

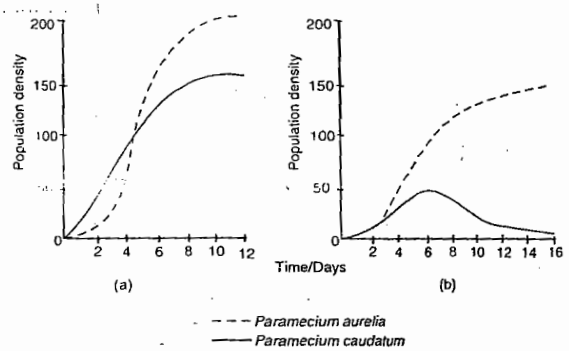


Fig.: Population growth of two species of Paramecium (a) Cultured separately, (b) Cultured together

WHEN the two species are cultured together *P. aurelia* has a competitive advantage over *P. caudatum* for gaining food and after five days the numbers of *P. caudatum* start to decrease until, after about 20 days, the species has become extinct, that it has been competitively excluded. *P. aurelia* takes longer to reach the stationary phase of growth than when grown in isolation, so is also affected adversely by the competition, even though it is more successful than its competitor. This helps to explain the selection pressure for competitors to adapt for separate niches. Under natural circumstances, the less successful competitor rarely becomes extinct but merely becomes rare and may even increase in numbers again before achieving an equilibrium position.

THE competitive exclusion principle (or Gausian exclusion principle) has since been confirmed in further animal experiments carried out by other workers. Competitive exclusions have been shown to occur in plant populations. In mixed cultures of duckweed (*Lemna*) species, *L. gibba* was capable of excluding *L. polyrrhiza*

THE study of natural populations is made more complex by the larger number of interacting populations and by the fact that the environmental variables such as temperature, moisture and food supply cannot be controlled.

PARALLELISM & CONVERGENCE

Similar structures, similar adaptive relationships, or similar behaviors occur in different groups of animals as the result of similar evolutionary opportunities. A fundamental principle of evolutionary biology is that, if there is a close similarity in the total morphological pattern of two organisms, there is a reasonably close phylogenetic relationship between them. The problem which this phenomenon of similarity brings up is whether such similarities are examples of parallelism or convergence, or whether they are evidence of evolutionary affinity between the organisms. Parallelism and convergence imply that a close phylogenetic relationship does not exist. We must emphasize that parallelism should not be indiscriminately invoked to explain similarities. If we constantly refer similarities to parallelism, the whole concept of evolution is rendered meaningless. Simpson has pointed out that parallelism, evident in detailed similarities in two groups, is usually both upon initial similarity of structure and adaptive type and upon subsequent recurrent homologous mutations. The term parallelism is usually restricted to the development of similar adaptive features in animals that are related, such as animals belonging to the same order. The parallel resemblances are, most likely, the realization of a genetic potential that is present in the entire group.

When two animal species or major groups that are not closely related develop similarities in adaptive relationships or structures, the two are said to converge. The exploitation of a volant way of life through the development of the wings of birds and of bats is clearly an example of convergence. The streamlined shape of marine mammals such as whales and dolphins is convergent to that of fish.

Not all cases of similarity are easy to classify as convergent or parallel. Many parts of the anatomy, many metabolic processes, even protein structures, are very much alike in different animals. If we insist that all similar cases are parallel developments, we are emphasizing the differences rather that the relationships between animals. It is always simpler to find differences between two animals than it is to demonstrate affinities. The examples presented in the following paragraphs are chosen to show some of the difficulties we encounter in attempting to categorize similarities.

There are two kinds of photoreceptors in the vertebrate eye, rods and cones. The rods are highly sensitive and function when there is very little light, but they have little power of discrimination. The cones are sensitive to higher intensities of light and make possible a high degree of discrimination of spatial relationships, colors, and textures. Rods have been found in the eyes of many nocturnal vertebrates —owls, bats, horses — and of those that must live in dim light —whales, cats, and some fish. The question is : In which of these animals are the rods convergent and in which are they parallel developments? The answer depends upon the definitions we give parallel and convergent and upon a detailed study of the rods in these various eyes. The rods in each of the various animals noted may have evolutionary derivations from very different structures (convergence). Or they may be derived from the same parts of the basic vertebrate eye (parallelism). In this latter case, the term parallelism refers to similarities that exist among animals separated at a much higher taxonomic level than that of the order.

The "song" or territorial call of *Indri indri*, a large. almost tailless arboreal, diurnal lemur of Madagascar, has some remarkable similarities to the hoot of the gibbon of southeast Asia. The similarities in the calls of these two primates include the social context in which they are used and the pattern made by the song when it is analyzed on a sound spectrogram. Because the gibbon and the indri are members of the same order, these similarities in vocalization are parallelisms. It is difficult to make a case for close evolutionary affinity between the indri and the gibbon, for little is known of the fossil lineage of the indri. At the same time a close affinity cannot be ruled out.

The incisor toothcomb of the "flying lemur" (order Dermopetra) and of the various prosimian primates is clearly a case of convergent evolution (fig.). All the living species, except two of the prosimian lineages have toothcombs formed by the lower incisors and canines. Brachiation, locomotion by swinging arm over arm through the trees, is highly developed in some monkeys of both the Old World and the New World and in certain apes.

These examples can be, and have been, interpreted either as convergences or parallelisms. The closeness of the postulated relationship between the animals is usually the deciding factor. What is important is the way these situations illustrate the opportunism of evolution. Similar environmental opportunities are exploited by different organisms for their long-range evolutionary advantage. The problems presented by the environmental pressure on the organisms lead to similar solutions. Argument about specifying these as parallel or convergent may obscure this important point.

The term homologous and analogous are often used to describe particular structures in animals. Homologous structures are those that are related by evolutionary descent and divergence. The wing of a bat and the forelimb of monkey are homologous — they are descended from the same ancestral

structure. The wing of a bat and the wing of a butterfly are analogous — they have similar functions and similar forms, but they are not related by descent from the same ancestral structure. Perhaps thinking of parallelism as homologous evolution and convergence as analogous would help us distinguish the two processes.

Adaptive Radiation

Adaptive radiation is the name we give to the rapid increase in numbers and kinds of any evolving group of animals. A group of animals —a species, a genus, superfamily— may take advantage of environmental changes and exploit a number of new places in the planetary living space. These places in the environment are called niches or econiches.

The mammals radiated into all parts of the earth as the climate grew cooler during the Palaeocene. The reptiles which had been the most successful group were at a selective disadvantage when compared to animals that could maintain a constant internal body temperature. Reptiles have a body temperature that is approximately that of the environment. They are poikilothermal (cold-blooded) animals. Thus, metabolism and all physological processes that are a function of temperature slow down when external temperature drops. Mammals have a complex system for maintaining constant body temperature. Their metabolic processes do not slow down when the temperature drops. They are homoiothermal (warm-blooded) animals. Most palaeontologists agree that the great reptiles died out and the warm-blooded mammals spread into almost every part of the living space on the planet as the worldwide climate grew colder. But it is not at all certain that it was the change in climate alone that limited further evolution of reptiles. The Darwinian fitness achieved by mammals, relative to reptiles, may have been decisive.

An adaptive radiation need not be a planet-wide event such as the example just cited. The spread of arboreal primates, the Old World monkeys, into trees of tropical forests is an example of a more limited but no less important radiation.

Adaptive radiation is said to have occurred when a group of organisms fits into a part of the planetary living space into which it could not have moved earlier, as a result of changes in the group's relationships to the environment. We deduce these changed relationships from two lines of evidence : morphology of the fossils we find and comparative studies of the living forms which are most likely descendants of these fossils.

One group of organisms may develop a relationship to the environment so that it has a reproductive advantage over another group or species which occupies the same environmental niche. This relative reproductive fitness was once called the "struggle for existence." The replacement of one species by another is the result of a reproductive advantage one has over the other. We usually are unable to reconstruct a very detailed account of the way in which a new adaptive radiation was achieved by a group of animals. However, inferences from the morphology of a fossil primate, for example, about, the way the living animal functioned behaved, lived, and adapted are possible and provide us with some basis for the evolutionary history of a group.

GENETICS

GENETICS is the science or study of hereditary characters. The term 'genetics' is derived from the Greek 'gen' which means to grow into something. Genetics, therefore, should include not only the study of inheritance of characters but also the factors which are responsible for the expression of hereditary characters.

IN THE case man it "deals with (all) those qualities present in all human beings that distinguish them from non-human beings, as well as with those qualities which characterize only certain groups of man, certain families or cetain individuals. Thus it is largely, a study of hereditary similarities and differences among human beings. It is concerned with the causes of those similarities and differences and the way in which they are transmitted from generation to generation (Stern, 1968).

MENDELISM

MENDEL is credited with being the father of formal genetics but he was not the first one to carry out genetic studies. In 1705s Maupertius; for the first time studied the polydactyly and described it as autosomal dominant. Otto (1803), Hay (1813) and Buels (1815) independently reached at the conclusions that heamophilia is inherited in X-linked recessive way. X-linked recessive inheritance of colour-blindness was first proved by Horner in 1876. Joseph Adams (1814) and Bemiss (1857) were amongst the first to describe the harmful effects of inbreeding. Galton (1876) was the first one to advocate the relevance of twin studies in genetics. Mendel is however, the right choice for the coveted position because he undertook extensive scientific observations as never before.

BEFORE the time of Mendel, it was known that life began from a single cell – the zygote. It was also known that in sexually breeding organisms, the zygote was formed by the fusion of two gametes, one from each parent. However, it was wrongly assumed that these two gametes thoroughly mix with each other to form the zygote. In other words, it was assumed that the offsprings inherited characteristics which were roughly the mean average of their parents. It was Mendel who finally cleared this misunderstanding.

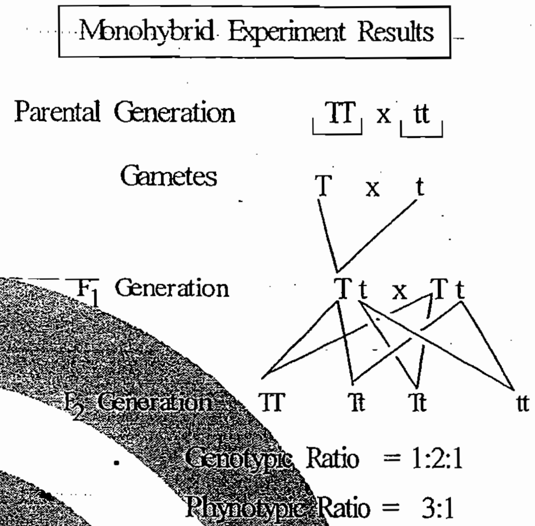
JOHN Gregor Mendel carried out various experiments on the garden pea plant (*Pisum sativum*) for roughly eight years. As a first step Mendel identified seven different traits, each of which occurred in two contrasting forms. These seven traits were as follows :-

Character (Traits)	**Varieties (Forms)**
1. Height of Plant	Tall; Dwarf
2. Colour of cotyledon	Yellow; Green
3. Shape of seed	Round; Wrinkled
4. Colour of seed coat	Grey; White
5. Shape of pod	Inflated; Constricted
6. Colour of pod	Green; Yellow
7. Position of flowers Axial;	Terminal

HE THEN isolated plants which were breeding true (when self-fertilized) for the two contrasting forms of all the characters. Mendel then performed cross breeding between these isolated pure plants, and arrived at certain conclusions which are today known as Mendel's laws of heredity.

IN ONE series of experiments (i.e. the monohybrid experiments), Mendel crossed two plants which were breeding true for two contrasting forms of one character. Let us assume this character to be the height of the plant. In that case, when Mendel crossed a pure tall (TT) plant with a pure dwarf (tt) plant, all the individuals of the next resultant generation or F_1 generation) were tall.

It seemed as if dwarfness was totally overshadowed by tall-



ness. However when the individuals of F_1 generation were self fertilized or crossed among themselves, dwarf plants reappeared in the F_2 generation in the ratio of 3 tall plants to every 1 dwarf plants (3:1). The dwarf plants of the F_2 generation when self-fertilized; produced only dwarf plants; in other words they bred true (to its character). Amongst the tall plants of F_2 generation, only 1/3rd bred true. The other 2/3rd when self pollinated, produced offsprings in the same ratio of 1 dwarf plant for every 3 tall plants (3 : 1). In other words, the phenotype ratios of F_2 generation were 3:1 (i.e. 3 tall plants for every 1 dwarf one), while the genotype ratio was 1:2:1 (i.e. 1 pure tall plant, two hybrid tall plants and 1 pure dwarf plant). On the basis of this experiment Mendel concluded the *law of segregation*. *Law of Dominance* has been given to explain segregation only. His third law (i.e. the *law of independent assortment*) was a result of another series of experiments known as the Dihybrid experiment.

IN THE Dihybrid experiments Mendel studied the mode of inheritance of two different characters (and not just one), simultaneously. Let us assume these characters to be height of the plant (i.e. tall or dwarf) and shape of seed (i.e. round or wrinkled). As a first step, Mendel isolated two sets of plants – one of which were breeding true for tall height and round seeds (TTRR), while the other were breeding true for dwarfness and wrinked seeds(ttrr). When he crossed these two plants with each other, all the individuals of the F_1 generation were found to be tall and having round seeds. When the individuals of F_1 generation were self-fetilized then the characteristics of individuals of the F_2 generation were in the following ratio :–

9 Tall plants with round seeds

3 Tall plants with wrinkled seeds

3 dwarf plants with round seeds

1 dwarf plant with wrinkled seeds.

This ratio of 9:3:3:1 is known as the *dihybrid ratio*, which is actually nothing but the product of two monohybrid ratios (i.e 3:1).

Law of Dominance : WHEN two parent types representing the contrasting strains of a single unit character are crossed the strain of one of the parents is expressed absolutely in the offspring (F_1 generation) while the one from the other paren

Dihyhybrid Experiment

Parental Generation TT RR x tt rr

Gametes TR x tr

F_1 Generation Tt Rr

Gametes of F_1 Generation = TT, tR, Tr and tr.

F_2 generation = ttRr

	TR	tR	Tr	tr
TR	TTRR	TtRR	TTRr	TtRr
	tR	TtRR	ttRR	TtRr
Tr	TTRr	TtRr	TTrr	Ttrr
tr	TtRr	ttRr	Ttrr	ttrr

[Dihybrid ratio = 9 : 3 : 3 : 1]

either goes unrepresented or its expression can not be seen with the naked eye. The strain that expresses in F_1 individual is called dominant while the one that fails observation is recessive. (Incidentally Mendel himself did not consider the law of dominance as a 'Law', the later studies only made it so.)

Law of Segregation (or Law of Purity of Gametes)

WHILE the body cells and the germ cells of the F_1 parent prior to reduction division involved in gamete formation contain the determiners (genes) of both alternative characters and are therefore hybid in character, a segregation of the alternative genes (allelomorphs takes place during maturation so that only one or the other gene comes to be present in any gamete. Thus, gametes are pure for any gene. A gamete has one or the other of a pair of allelomorphs and is never hybrid with reference to any single character. In other words, genes retain their purity and identity and express themselves whenever they get the chance. A dominant gene will express whenever it is present. The recessive can express only in the absence of dominant gene. The situation can occur only when an individual is recessive homozygous or hemizygous for a particular character.

Law of Independent Assortment (of different allelomorphs) : TO USE Mendel's own expression, "The relation of each pair of different characters in hybrid union is independent of the other differences in the two original parental stocks". This law can be discovered only when we try to follow the assortment and recombination of at least two pairs of allelomorphs upto the second hybrid (F_2) generation. If each allelomorph be studies by itself, it will show nothing more than the facts indicated in the first two laws, but as soon as we try to follow the modes of inheritance of more than one character simulatneously, we find that we are merely dealing with the independent shuffling and assorting of two or more genes.

THE concepts expressed in the above laws may be considered to have originated with Mendel. It must be remembered, however, that Mendel had no knowledge of chromosomes or of the chromosomal mechanism of maturation which now seems to be the mechine responsible for the regularities seen in the various Mendelian ratios and for segregation in general. It is remarkable, therefore, that Mendel foresaw a mechanism within the genetic apparatus of plants, which coincides in principle with that subsequently discovered. Among the great discoveries that have resulted from the use of Mendelian methods and procedures are the factor hypothesis, the chromosome theory of heredity and of sex-determination, linkage and crossing over, and the finer details of the hereditary mechanism. Though Mendel put forth his observations in the middle of the 19th century, it took nearly half a century for the rest of the world to understand their significance. His laws were "rediscovered" only in the beginning of 20th century.

UNIVERSALITY OF MENDEL'S PRINCIPLES

THOUGH Mendel's principles of heredity were based on a very wide range of observations, yet these are not free from flaws. The law of dominance is far from being universal. In ABO blood-group system, for example, a person may have blood group, A, B, AB or O. While gene for O blood group is recessive, the respective alleles for A and B blood groups are both dominant. In persons with AB blood group, both these alleles express themselves which is, as such against the law of dominance which states that one of the alleles must be recessive. The situation where both alleles express themselves is called *Co-dominance* or lack of dominance. *Co-dominance*, far from being an exception, is encountered quite frequently.

NORMAL individuals possess homozygous condition of normal haemoglobin (HbA/HbA). An abnormal haemoglobin, HbS, is known to provide some kind of resistance against malaria. The two alleles of HbA and HbS may have three genotypes of HbA/HbA, HbS/HbS and HbS/HbA. HbS results in deformation of red-cells. In HbA/HbA Individuals, all red cells are normal, disc type. In heterozygotes (HbA/HbS), only 8-15% cells are sickled, while in homozygoyte HbS individuals sickling is found in only 60-75% redcells. The sickle gene, therefore, does not follow the rule of dominance. Such conditions where gene expression has no specified proportion of genotypes are put in the category of *incomplete dominance*.

LIKEWISE, we have many cases of *intermediate dominance* too, whereby the expression of a harmful gene just doubles in the homozygous condition compared to the heterozygous state. The Glucose 6-Phosphate Dehy-drogenase deficiency gene (G-6-PDd gene) is a point in this regard. There are many lethal and semilethal genes which are considered. 'dominant' in their expression. If means could be devised to let these genes survive and reproduce, many of these genes may instead be found with intermediate dominance. It is too early to predict but speculations for this probability cannot be ruled out.

FURTHER, the cases of lack of dominance or co-dominance are more frequent with the *multiple alleles* about which Mendel said nothing. In a case of multiple allele gene, if (let us say) there are three alleles, two of them may be recessive or dominant, a situation never envisaged by Mendel. Also, for many genes the expression is not discrete (in the form of presence or absence) but is continuous (e.g. in case of height, skin colour etc. in man) and it is very difficult to identify an allele as dominant or recessive.

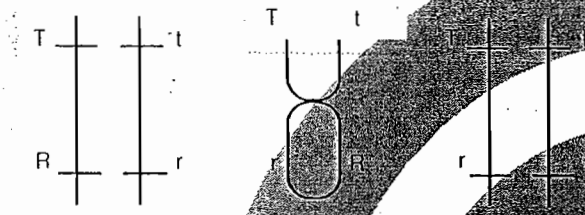
FOR certain phenotypic expression to appear the action of more than one gene is required, a condition known as *epistasis*. Under this situation, for a dominant phenotype to occur, dominants of two genes have to be present simultaneously in an individual. All other combinations will lead to the expression of recessive phenotype.

IN SHORT, the law of dominance is not the essential feature of Mendelian heredity, but the law of segregation is. In all plants, animals and human beings (where chromosomes occur in pairs) the law of segregation holds good. In fact, it might be called the ultimate discovery of Mendel, for it is almost unsurpassed among biological generalizations on account of its far-reaching applicability. The law has sometimes been called the law of the splitting of hybrids. Whether dominance is present or not, the law of segregation always holds.

THE law of independent assortment though proved mathematically, also does not have any universal applicability, and this was recognised soon after the rediscovery of Mendel's laws - when the phenomena of linkages came to the recognised Chromosomes carry many genes, and genes which are on the same chromosome, bound as it were in a common vehicle of hereditary transmission, tend to be inherited together Such genes are said to be linked and the phenomenon is

known as *linkage*. Morgan and Castle who were the first to put forward the "chromosomal theory of linkage" defined linkage as "the tendency of genes present in the same chromosomes to retain their original combination and enter together in the same gamete". Thus, theoretically at least, if two genes (each with two alleles) are linked, only two (and not four) types of gametes will be produced. However, in reality, linked genes are not inseparable, because exchanges between homologous chromosomes occurs during meiosis. Genetically, this phenomenon is referred to as *crossing over* and the main factor determining whether or not two gene loci are separated by it is their distance apart on the chromosome. Genes lying very close to one another are referred to as being highly linked, those far apart as loosely linked. In other words, the further apart two genes are on a chromosome, the greater the chance that they will cross over during meiosis.

Thus, it is the chromosomes which always assort independently and not the genes. The genes for eyeshape and eye colour, for example can not even be thought of existing independentally. Similarly, other genes that perform related functions are located very close to each other.



MENDEL could prove this law simply because either the genes for the seven characters were located on different chromosomes, or if any two genes were located on the same chromosome, the difference between the two was large enough to allow for separation during crossing-over. Members of a homologous pair of chromosomes are independent regarding their transfer into new cells during meiosis. In other words the chromosomes of a homologous pair can assort independently but not the genes.

APPLICATIONS OF MENDELISM

MENDELISM and later studies based on it have proved that the genetics has been much more useful to the life than any number of medicines available with us. Today we have a number of branches of genetics (Population genetics, Human genetics, Immunogenetics, Biochemical genetics, Molecular genetics, Medical genetics etc.) and all owe their rise to the applications of Mendel's laws. In the following paragraphs we briefly discuss the applications of genetics with particular reference to Man.

1. MEDICO-LEGAL APPLICATIONS

IN MATTERS relating to mixing up of new borns in the hospitals, paternity dispute and disputes relating to inheritance of property etc., Mendelism can fairly well serve the true judgement. With the help of the Laws of domianace and segregation, it can be known with fair amount of accuracy whether a child is the son or daughter of so and so. We can prove our point with the help of ABO blood group system.

A PERSON'S blood group is the result of antigens present on the red blood cells, e.g. a person with antigen H on his red cells will have blood group O. Four common phenotypes of ABO blood group system are A, B, AB and O which are the result of three alleles; of which alleles A and B are dominant while O is recessive.

A person with blood group B, therefore, may have a genotype of BB and BO. The same is true for blood group A. O blood group gene being recessive expresses itself only in the homozygous condition (OO). On the basis of this knowledge of ABO blood group system we can find out the possible blood group of a child as follows:-

FROM the above table it becomes evident that a man with blood group O can not be the father of a child with AB blood group (whatever be the blood group of the mother). Similarly

Blood group of Parentl	Parent II	Blood group of child Possible	Not Possibl
A	A	A, O	B, AB
A	B	A, B, O, AB	nil
A	AB	A, B, AB	O
A	O	A, O	B, AB
B	B	B, O	A, AB
B	AB	A, B, AB	O
B	O	B, O	A, AB
O	AB	A, B	O, AB
O	O	O	A, B, AB
AB	AB	A, B, AB	O

AB blood group person can not be responssible for the birth of an O child. Here we must remember that we speak in terms of paternity dispute only because paternity is only a blief while motherhood is an absolute certainty.

ABOUT 10-15% of the cases of medico-legal dispute can be solved merely with the help of ABO blood group system. For the rest we have to take the help of other genetic traits including various other blood group systems (MNSs, Rh or CcDEe, P, Kell, Duffy, Kidd, Cellano etc.) red-cell proteins (haemoglobins), serum or plasma proteins (haptoglobins and transferrins) and several enzymes. The mode of inheritance of all above mentioned genetic markers is known. We may, if need be, take the help of the study of tasting ability, secretor status, various genetic disorders etc. Dermatoglyphics too can be extremely helpful in solving the cases in question.

MEDICAL APPLICATIONS

THE study of the modes of inheritance of different types of histo-incompatibility and inborn errors of metabolism with the help of Mendelian principles has led to the development of cure for such abnormalities. The Rh-incompatibility between the two parents may result in what we know as the Haemolytic Disease of the New Borne (HDNB) or Erythroblastosis foetalis. The situation occurs where the expectant mother is Rh-ve, but the foetus (fathered by an Rh+ve man) is Rh+ve. Because, of the continuity between the foetal and mother's body systems through placenta, the foetal blood (Rh+ve) enters the mother's blood lacking in Rh-ve which, therefore, acts as an antibody for the mother's system. Mother's body, to destroy this foreign element, produces anti-Rh antibodies which, if allowed to pass through the placenta, can destroy the foetus. Fortunately, in normal circumstances it does not happen because placenta is a semi-permeable memberane that allows only small particles to pass through (antibodies are much larger in size than the antigens). If and when the placenta gets injured (e.g. if an expectant mother is involved in heavy physical labour or at the time of delivery when the child has to be detached from it), these anti-Rh antibodies enter the womb and destroy the subsequent foetuses. The study of such incompatibilities has resulted in prevention of hazards. In the case of Rh-incompatibility, for example, injection of anti-Rh Bovine to the mother within 72 hours after each delivery destroys all anti-Rh antibodies and removes all apprehensions regarding subsequen births. Incidentally about 85% of human population is Rh-positive, remaining being Rh-negative.

GENETIC COUNSELLING

GENETIC counselling or genetic advice is sought by the people

who themselves or their previous generation have a history of a genetic disease. Hundreds of genetic diseases are known today; some of them inherited in autosomal dominant way, others in autosomal recessive fashion; Some are sex-linked while in many others the mode of inheritance is not known. In the case of genetic disease with known inheritance, anyone with fair amount of such knowledge as also of the pedigree of concerned disease in a family, can advice for the benefit of advice-seekers. Generally two kinds of people seek such advice. Firstly, couples who have a long history of a disease in the family and want to go for a child. The second category comprises of those from different families (with history of some disease) who seek advice regarding marriage. Incidentally, a large number of persons for whom the advice is sought, are not affected. (This is more true in the case of autosomal dominant inheritance). In all cases of genetic advice, however, a geneticist has to act, not merely as a counsel, but also as a social reformer too. He has the responsibility of exposing the inhibition associated with certain diseases and bringing confindenc to the affected.

HYBRID VARIETIES

THIS application of genetics is beyond comprehension. But for the green revolution brought through the hybrid varieties of cereals, vegetables, fruit etc. the ever increasing world population could never be sustained. Not only that, rather Mendelism has saved this world from a certain holocast. Some of the species (including white tigers) which are essential for the maintenance of ecological balance in different areas of the world, have been brought back to the world from the verge of extinction. Though this application of genetics has its focus on plant and other animal populations, its uses for man are immense.

NOW the question is, if Mendel were not there? Then is it that we would have been deprived of all the benefits of genetics? The answer is a simple 'No'. The contribution of Mendel to the science of genetics was forgotton after his death. It was rediscovered about 30 years later when some scientists arrived at the conclusions which Mendel had reached before.

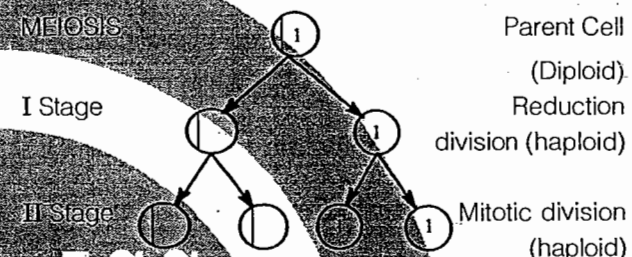
MOLECULAR BASIS OF GENETICS

IN ORDER to have an idea about the nature of genetic material, it is required to have at least some idea of the cell structure. All living cells are composed of a living substance called protoplasm. The two most important components of the protoplasm are the cytoplasm (where all cell activity occurs) and the nucleus (which is the main control mechanism of the cell). Within the nucleus occur the chromatin, which consists of long thread like structures called chromosomes. It is on these chromosomes that he genes are located. Since chromosomes occur in pairs, therefore it follows that genes also occur in pair. Each member of a pair of genes is known as an allele and alleles are present on the same loci on a pair of homologous chromosomes.

EVERY type of organism is characterised by a definite number of chromosomes. For man this number is 46. This number is represented in the female as 23 homologous pairs of chromosomes. In males there are only 22 pairs of homologous chromosomes, constituting the autosomes, and there are two chromosomes which are markedly different from each other, i.e. the X chromosome and the Y chromosome. These are the sex chromosomes and the X chromosomes is represented twice in females to make up the 23rd pair. During the formation of gametes, the two sex chromosomes segregate and enter different gametes. While females produce only one type of gametes (i.e. one having X+22 chromosomes), the males produce two types of gametes i.e. one having X+22 chromosomes and another having Y+22 chromosomes. During fertilization two gametes, one from either parent combine to form the zygote. The zygote will be a female or a male, depending on whether the male sperm which fertilizes the zygote contains an X-chromosome or a Y chromosome respectively.

THE question that arises now is that, why are there only 23 chromosomes in the human gametes and not 23 pairs (or 46 chromosomes)? The answer lies in meiosis. In all sexually reproducing organisms two kinds of cell division are found – namely mitosis and meiosis. Mitosis, which occurs only in the somatic cells, is a mere reproduction of one cell into two equal halves. Meiosis, which occurs only in the reproductive cells, is different. This type of cell division occurs in two stages. During the first stage, also known as reduction division, one parent cell having 23 pairs of chromosomes (i.e. diploid number of chromosomes) splits into two daughter cells. However, each of these daughter cells receives only one of each pair of chromosomes. Therefore two daughter cells, each having only half the total number of chromosomes (i.e. haploid number of chromosomes), are formed. The second stage consists of a simple mitotic division of the two daughter cells. Therefore, at the end of meiosis four gametes, each having haploid number of chromosomes (i.e. 23 in the case of man), are produced.

IT IS in meiosis that the physical reality of Mendel's laws is seen, because it is during meiosis that segregation, crossing



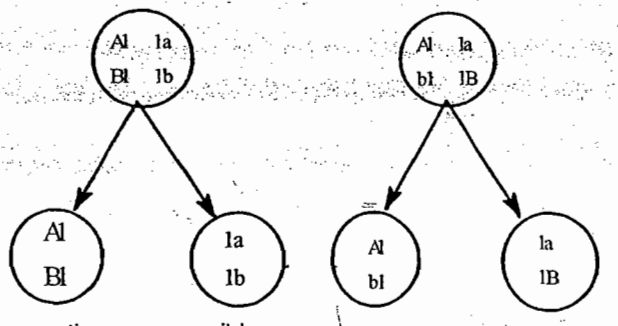
over etc occur. The evolutionary significance of meiosis lies in the following two facts :–

(i) It leads to the formation of gametes, each of which has only haploid number of chromosomes. It is this fact that ensures that the number of chromosomes for each type of organisms stays the same generation after generation. Since during fertilization two gametes (one from either parent) together, if the gametes did not have haploid number of chromosomes then the number of chromosomes in the zygote would be doubling with each successive generation. Thus, meiosis ensures that the number of chromosomes for a type of organisms stays the same generation after generation.

(ii) During meiosis gametes after gametes are produced, yet each gamete is unique. In other words, no two gametes are identical. All the variations that are found within a species are a result of this uniqueness of gametes. This uniqueness of gametes is due to a number of factors, such as :

(a) Shuffling of genes :– Any two pairs of chromosome can be oriented as two basic patterns, and therefore, 4 different types of gametes can be produced.

When all 23 pairs of chromosomes, as they exist in humans, are considered then 8.3 million possible combi-



nations are possible.

(b) During reduction division, at a certain stage the chromosomes align themselves along the equatorial plane of the cell. This alignment may take place in such a way

that more genes are inherited from one grand parent (say father's father) than the other (i.e. father's mother). This factor also immensely adds to the variations found between gametes.

(c) Besides, due to crossing over, individual chromosomes have genes from both parents. Since the amount of crossing over varies from instance to instance, therefore, the chances that two gametes will have the same genetic composition is very, very low.

THUS, millions and millions of genetic combinations are possible, and added to this are the effects of the environment. Thus, the possibility of two gametes being genetically identical are so low as to be near impossible.

WATSON AND CRICK MODEL

THE question that arises now is that how are the genetic elements to variability codified within the chromosomes? This puzzle was first solved in 1953 by J.D. Watson and F.A.C. Crick, who discovered the biochemical structure of the chromosome.

THE primary organic compound found in the chromosome is the nucleic acid. There are two kinds of nucleic acids – Deoxyribose nucleic acid (i.e. DNA) and Ribose nucleic acid (RNA). These nucleic acids are actually long chains of a basic unit, called nucleotide. Each nucleotide has three components:

(i) A 5-carbon sugar molecule. Ribose in case of RNA and Deoxyribose in case of DNA.

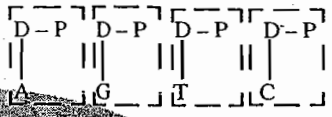
(ii) A phosphate unit.

(iii) A base molecule.

THE bases in DNA are of four kinds namely Adenine (A), Guanine (G), Thymine (T) and Cytosine (C). Adenine and Guanine are larger in size, and are together classified as Purines. The smaller Thymine and Cytosine are known as Pyramidines. RNA also has similar four kinds of bases, the only difference being that RNA has Uracil (U) instead of Thymine.

THE basic structure of DNA, the genetic material of all forms of life, consists of a pair of very long chains of polynucleotides. The nucleotide units in these chains are linked in such a way that a backbone of sugar and phosphate molecules is formed, from which the bases which are attached to the sugar molecule, stick out. These two chains are connected to each other due to the hydrozen bonding that exists between the bases. Since the distance between the two chains should be constant, and also since Purines are larger in size than the pyramidines, therefore, of the two pairs of base bonded together, One has to be a purine while the other is a Pyramidine. Besides due to the nature of the bonding, Adenine can pair with Thymine only, while Guanine can pair only with Cytosine. These are thus also known as "complementary pairs". Further, the two chains coil around each other to form a double helix.

Four Nucleotides of DNA



D = Deoxyribose sugar molecule

P = Phophate molecule

Simplified diagram of DNA structure.

THE base-sequence of each single strand of DNA contains the code for one or more genes. The differences between the genes are due to the difference in the sequence of the bases. The specifications of the DNA are coded in triplet sequences of nucleotides, known as codons. The credit this understanding of genes goes to Watson and Crick.

Serology in Reproductive Biology

The understanding of the role of cytology in reproductive biology involves the understanding of antigen-antibody relations

Antigen and Antybodies relationship in ABO blood group system

Blood Group	Antigen (in RBC)	Antibody (in Plasma)
A	A	Anti-B
B	B	Anti-A
AB	A,B	–
O	–	Anti-A, Anti-B

A and B antigens are formed in eighth month of pregnancy and immediately thereafter corresponding antibodies appear in blood plasma. Therefore, these are called Naturally Occurring Antibodies. Mixing of blood of mother and fetus can result the death of fetus (due to agglutination) if the two are incompatible. This occurr in only rare instances if the placenta ruptures.

Rh Blood Group System in Reproductive Biology

There are no naturally occcuring antibodies in Rh blood group system. If one is Rh^+, Rh antigen is present and if Rh^- then Rh antigen is absent (because there is no naturally ocurring antibody). Anti Rh antibodies are spontaneous antibodies which are produced at the time of need. If father is Rh^{+ve}, mother is Rh^{-ve}, and the fetus like father is Rh^{+ve} then only these antibodies are produced.

All fetal systems are continuous with those of the mother through placenta. As fetal blood enters the mother for purification, mother's blood reacts (as it has no Rh antigen and therefore it is a foreign body for her) to produce Anti-Rh antibodies. If these antibodies enter fetus (through placenta), these will destroy the fetus. Normally it does not happen because firstly these antibodies are very heavy (atleast 500 times heavier than antigens) and secondly, placenta is a semi-permeable membrane. However, in rare circumstances if there is any injury to placenta, these antibodies could enter the fetus and create complications. In normal circumstances, this does not happen but at the time of the birth of child the placenta has to be cut, the blood oozes out and the Anti-Rh antibodies preset get embeded in the walls of uterus. The baby is removed and is safe but all subsequent fetuses may result in spontaneous abortion.

POPULATION GENETICS

THE rediscovery of Mendel's laws led to a tumoil in the scholastic circles. Mendel's theory came into direct conflict with Darwin's idea of evolution. Mendel had identified the individual as the basic unit for evolutionary studies, while Darwin had identified the population. This conflict continued for nearly three decades, until it was finally realized that the proper unit for evolutionary studies is the common gene pool of the entire population and the evolution is the change in the frequency of genes in this gene pool. This realization gave birth to population genetics.

CENTRAL to population genetics is the concept of "Mendelian population", which may be defined as a group of people who share the same gene pool. In other words, it is a group potentially capable of successful reproduction. It is a distinct and closed genetic system, in other words a "breeding isolate". An isolate is a group of people which is now and has been for sometime past totally separated from other groups and is reproductively unstratified so that all the individuals share equally in the same gene pool. The concept of Mendelian population is not as simple as it seems at first look. This is because Mendelian populations exist in a series of hierarchies, depending upon the extent to which they share the common gene pool. In other words, each Mendelian population may contain (and often does), several other smaller Mendelian populations within it. The largest such population is obviously a species.

THE important thing about a Mendelian population is that it is a breeding isolate. This may be due to any number of factors such as geographical, cultural etc., the net result being that the members of the group mate within the group only. Due to this prolonged inbreeding, differences in gene frequencies between different populations arise, and continue to grow as long as isolation continues. In other words, the populations evolve in their own slightly different ways.

THESE changes in the gene frequencies of the gene pool of a breeding isolate can be determined with the help of the law of genetic equilibrium as put forth by G.H. Hardy and W. Weinberg. This law is founded on the premise that "given" certain conditions, the proportion of genotypes in a population will remain constant, generation after generation.

THE conditions specified by Hardy and Weinberg, under which populations will not evolve, are as follows :

(i) All matings should be random and equally fertile (i.e. there is no inbreeding nor hybridization).

(ii) Natural selection is not acting on the alleles under study.

(iii) The alleles under study do not undergo any mutation.

(iv) The population is infinitely large, so that there are no sampling errors (i.e. genetic drift) due to small population size.

OBVIOUSLY, no population can satisfy all these conditions, therefore there is no population which can stay in a genetic equilibrium. In other words, all populations have to evolve. A closer look at these four conditions reveals that, the net thrust of this equilibrium law can be summed up in the following statement :

A POPULATION will stay in a state of genetic equilibrium, provided microevolutionary processes do not act upon it."

THE significance of this law lies in the fact that, by being able to specify under what conditions a static genetic equilibrium will exist, one can see, measure and analyse change in the frequency of genes in the gene pool of the population under study. The genetic equilibrium may be thought of as forming a sort of inertia that has to be overcome, if evolutionary change is to occur. It tends to preserve gains made in the past and prevents too rapid a change. It also keeps a store of recessive genes continuously in existence, even though individuals homozygous for these rarely appear. These stored genes may be made use of, if and when the environmental conditions change.

HARDY WEINBERG EQUATION

According to Hardy Weinberg equation, "the proportion of genotypes of a gene is represented as the proportion of square of the sum of the allele frequencies. It means, if there are two alleles of a gene in the proportion of p : q then the genotype frequencies wil be represented as the proportion of

$$(p+q)^2 \text{ or } p^2 : 2pq : q^2$$

Similarly, if there are three alleles in the proportion of p : q : r, then the genotype frequencies would be represent as the proportion of

$$(p+q+r)^2 \text{ or } p^2 : q^2 : r^2 : 2pq : 2pr : 2qr$$

This Hardy Weinberg Equation has a number a applications in the study of population genetice as follows :

1. We can know about genetic structure of population as follows :

(i) One gene two alleles, a dominant and a recessive.

For example, tasting ability with respect to PTC. Here the 1st frequency of non taster gene (q) can be caluculated (i.e. q) by taking the underroot of the percentile of non taster i.e.

$$q = \sqrt{N}$$

As we know that $p + q = 1$

$$p = 1-q$$

(ii) One gene two alleles, both dominant as in MN blood group. Here just counting the total number 'M' & 'N' allele — 'M' is represented twice in blood group M, N is represented twice in blood group N while both are represented singly in blood group MN. The percentile of each of them represents its allele frequency.

(iii) One gene three alleles as in ABO blood group system where A & B both are dominant, O is recessive. The frequency of 'A' is represented by p, that of 'B' by q and that of 'O' by r.

O being recessive, r can be calculated by taking the underroot of the percentile of 'O'

$$r = \sqrt{O}$$

p & q can be calculated by following equations.

$$p = 1 - \sqrt{O + B}$$

$$l = 1 - \sqrt{O + A}$$

2. We can find out the direction of evolunionary change in a population in two ways

(a) Studying the population twice over a period of time. The difference in allele frequencies represents the direction of evolutionary change.

(b) Studying a total population, dividing into different age groups : children, adolescents, adults , middle age, old age. Calculate allele frequencies for each age group. The regular change in allele frequencies from old age to children represents the direction of evolutionary change.

3.We can findout the nature of a population i.e. whether it is a

Mendelian population or not. The first step in the this regard is to findout expected values of various phenotypes as follows :

$A' = (p^2 + 2pr)n$

$B' = (q^2 + 2qr)n$

$O' = (r^2)n$

$A'B' = (2pq)n$

Where n represents the total observed population size. The next step is to find the deviation of observed values of phenotypes from the expected values of these phenotypes. This is done with the help of a statistical tool $\sum \chi^2$ also known as the test of goodness of fit, as follows.

$$\chi^2 = \frac{(\text{Observed} - \text{expected})^2}{\text{expected}}$$

The value of χ^2 for each of the phenotypes is added as follows :

$$\sum \chi^2_{A',B,O,AB} = \sum \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$$

If the value of $\sum \chi^2$ is les than 3.84 (df = 1, $p < 0.05$) then we consider it to a random mating or mendalian population.

4. We can test the validity of a sample drawn from previously known Mendalian population. If $\sum \chi^2$ is < 3.84 then that is true representation of the population.

Hardy-Weinberg equation with its base in H.W. principle (1908) gives us the basics of all the population genetic studies.

METHOD OF GENETIC STUDY OF MAN

PEDIGREE ANALYSIS

THE genetic information collected on the family can be summarized concisely in a pedigree (family tree) and the inheritance pattern of a particular disorder in a family can be determined.

THE drawing up of a family tree or pedigree chart begins with the affected person first found to have the trait and through whom the family came to the attention of the investigation. This person is referred as *Proband,* or male as *propositus and female* as *propista* and indicated by an arrow. The next step is to ask whether any brothers or sisters (sibs) have been similarly affected and after careful questioning the health of all maternal and paternal relatives is carefully recorded.

A TRAIT which is determined by a gene on an autosomal ® autosomal trait (dominant or recessive). A trait on sex chromosome ® sex-linked.

Symbols used in Pedigree Charts

- □ → Normal male
- ○ → Normal Female
- ○—□ → Mating
- ○=□ → Consanguineous mating
- △○ → Dizygotic twins
- △□ → Monozygotic twins
- ◇ → Sex unspecified
- ② ③ → No. of children and Sex indicated

- ■ → Affected male
- ● → Affected female
- → Propositus (male or female)
- ◧ ◐ → Heterozygotes for Autosomal
- ⊙ → Carrier X-linked
- ⊠ → Dead
- → Abortion or still birth
- → Zygosity uncertain

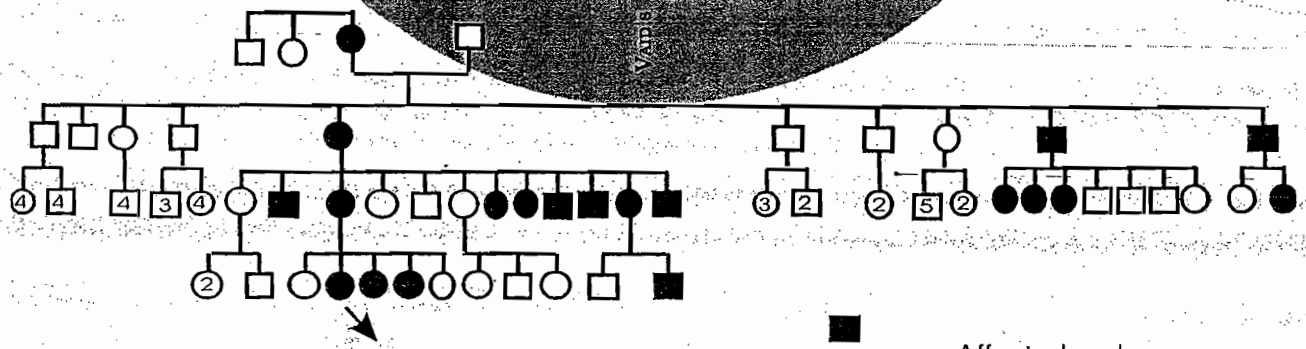
1. AUTOSOMAL DOMINANT TRAIT INHERITANCE

THE pedigree pattern of an autosomal dominant inheritance is characterised by the following features :

1. Each affected individual has an affected parent, to the point in the ancestry where the mutant gene arose by the fresh mutation.
2. Each offspring of an affected person (with one affected and one unaffected parent) and a normal mate will have a 50 : 50 chance of being affected.
3. Unaffected relatives of affected persons will not have affected offspring.

Eg.—*Cold urticaria* (carrier has skin blotches, chills and weakness due to cold).

PEDIGREE OF HEREDITARY *COLD URTICARIA*



PROBAND

■ → Affected male

② → Two unaffected females

♂ : ♀ = 8 : 12 = 2 : 3 Close to expected 1 : 1

POLYDACTYLY (small appendage on side of the hand), Achondroplasia (dwarfism), *Porphyria variegata* (metabolic disorder) etc.

Affected Parent (Aa)

↓

Gametes

Normal parent gametes →

	A	a
a	Aa (affected)	aa (normal)
a	Aa (affected)	aa (normal)

2. AUTOSOMAL RECESSIVE TRAIT

The autosomal recessive pedigree pattern is characterised by the following features :

(a) Almost never (if gene is rare) is disease present in the parents, ancestry or collateral relatives.

(b) The sibs of an affected child with normal parents have chance 1 in 4 of being affected irrespective of sex.

(c) The parents of affected children are more likely to be related to each other (consanguineous) than are parents of normal children, the rarer the disease, the greater the frequency of parental consanguinity.

(d) In small sibships the majority of cases will be *sporadic* i.e only one in the family.

Eg. *Cystic fibrosis* (damage of lungs etc.) Inborn errors of metabolism, deafmutism and hereditary blindness etc.

Normal Heterozygous Parent (Aa)

↓

gametes

Normal Heterozygous Parent (Aa)→

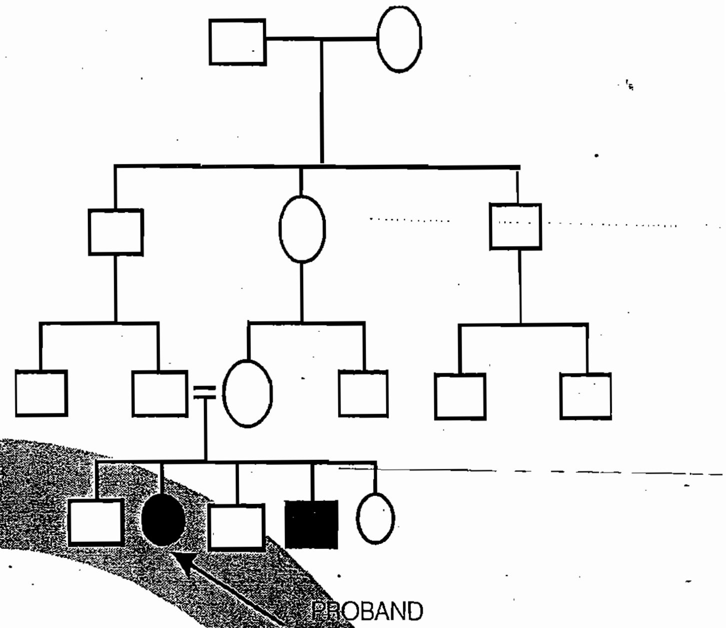
	A	a
A	AA (normal) Homozy.	Aa (normal) Heterozy.
a	Aa (normal) Heterozy.	aa (affected) Homozy.

3. SEX-LINKED TRAIT

The X-linked *recessive* inheritance shows the following pedigree characteristics, provided the gene concerned is rare :

1. The disease appears almost always in males whose mothers are unaffected by heterozygotes *carriers* of the mutant gene.
2. Each son of a carrier female has a 1 : 1 chance of being affected.
3. Each daughter of a carrier female has a 1 : 1 chance of being carrier.

Pedigree Pattern of an Autosomal Recessive Trait



4. Affected males never transmit the gene to their sons, but they transmit it to all their daughters, who will be carriers.
5. Unaffected males never transmit the gene. Eg. *Hemophilia, G-6PD deficiency, Duchenne muscular dystrophy,* Colour blindness etc.

Affected Male (X^hY)

↓

Gametes

Normal female (XX) gametes →

	X^h	Y
X	X^hX carrier daughter	XY normal male
X	X^hX carrier daughter	XY normal male

Carrier Female (X^hX)

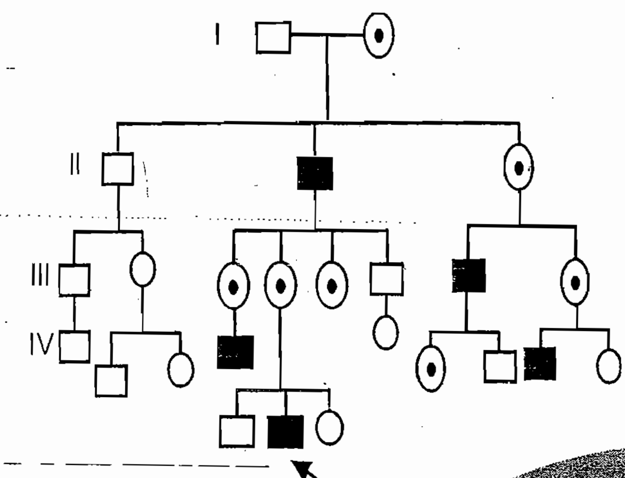
↓

Gametes

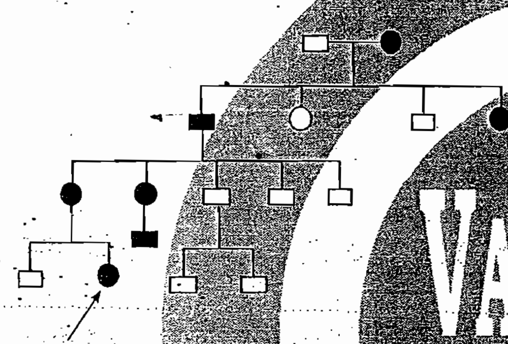
Normal male (XY) gametes →

	X^h	X
X	X^hX carrier daughter	XX normal daughter
Y	X^hY affected son	XY normal son

4. *Pedigree pattern of an X-Linked recessive trait*



5. *Pedigree of X-linked dominant trait*



An X-linked dominant trait is manifest in heterozygous ♂ aswell as in ♀ having the mutant gene on his single X-chromosome. An affected female transmits the disease to half her sons and to half her daughters and an affected male transmits the disease to all his daughters but to none of his sons. Eg. Vitamin D-resistant rickets, Xg blood group.

Y-LINKED inheritance (Holandric) implies that only males are affected and trait transmitted to his sons. Eg. hairy ears, webbed toes etc.

CHROMOSOMAL ANALYSIS

Basic prerequisites for analysis are :

1. Cells in metaphase stage.
2. Accumulation of sufficient cells
3. Preparation of a cellular suspension and fixation.
4. Slide preparation.
5. Karyotyping

PHYTOHAEMAGGLUTININ (PHA) is used to separate white blood cells from red blood cells and induce mitosis in circulating lymphocytes. A less toxic colchicine is added and treated the cells to prevent the formation of the spindle body and arrests the cells at metaphase. It acts to shorten chromatids, promotes contraction and widening of the chromosomes, and helps in accumulating cells in metaphase. Hypotonic solutions cause osmotic swelling of the cells and promote dispersing of metaphase chromosomes (sodium or potassium citrate, KCL). It facilitates counting and identification of chromosome. Fixation produces hardening of chromosomes (methanol/ethanol and glacial acetic acid mixture, ratio 3 :1). The slide is prepared by ruputtering cells by drying in a suspension. The slides are stained by using Giemsa stain, Feulgen etc.

FOR karyotyping, different banding techniques are employed as follows :

1. Q-Banding : A QUINACRINE mustard, a fluorescent alkylating agent, binds selectivily to the guanine residues in DNA. This banding characterises the brightly fluorescent segments of the chromosomal regions, identifies polymorphisms and Y-Chromosome.

POLYMORPHIC regions that can be distinguished by Q-Banding are :

1. The centromeric regions of chromosomes 3 and 4.
2. The short arms and satellites of chromosomes 13-15 and 21-22.
3. The distal long arm of Y-chromosome.

DISADVANTAGES

1. It needs a fluorescent microcope.
2. There is rapid quenching of fluorescence.
3. Not a permanent stain.
4. Fluorescence of minor bands and sub-bands is difficult to appreciate.

2. G-Banding : IN THIS method after the protease treatment (trypsin) Giemsa stain is used. It enchances the chromomere region and is simple and results in a permanent stain.

CHARACTERISTICS

(a) densely stained secondary constriction regions are seen in chromosomes 1, 9 and 16.

(b) Two small G-bands are seen in Y-chromosome.

3. R-Banding : In this, the DNA is denatured by different methods. In this, telomeric regions of chromosomes are stained.

4. C-Banding (Consistutive Heterochromatin Staining Technique)

IN THIS, chromosome preparations are treated with alkali solution followed by treatment with warm saline and stained with Giemsa. The characteristics are :

1. The centromeric area stained.
2. The short arms of the D (13-15) and G (21-22) group chromosome;
3. The secondary constrictions of chromosome 1, 9 and 16; and
4. The distal long arm of the Y-chromosome.

5. T-Banding : This technique is suitable for demonstrating small structural changes involving telomeric regions. It represents the bands of R-Bands which are resistant to treatment with denaturating agents.

FAMILY METHOD

A COMPREHENSIVE history is an important step in the analysis of any disorder. According to Childs (1982) *to fail to take a good family history is bad medicine and someday will be a criminal negligence*. It is an important method from geneticis to clinicians :

1. Helpful in diagnosis.
2. To find out whether the disorder is genetic in origin.
3. It can provide information about the natural history of the disease and about variation in its expression.
4. It can clarify the pattern of inheritance, indicate which other family members are at risk and allow the risk of occurrence in those persons to be estimated.

FOR an adequate family history, it should start with patient, about his relatives, cousins, parents, grand parents, uncles, aunts,. The informa-

tion should include names, date of birth and death, present and past medical conditions. Early infant deaths, still births and abortions should be noted. Consanguinity of the parents or grandparents and geographic or ethnic origin should be documented. If a patient is a child, information about the mother's pregnancy should be recorded with particular attention to very early events e.g. maternal infectious and metabolic disorders etc. and also obtain medical records if a family agrees.

IT IS useful to summarise the family history as a pedigree, which is essentially a method of recording genetic information in a form that can be rapidly and unambiguously interpreted.

FOSTER-CHILD METHOD

THIS method is particularly used to study the nature-nurture aspects, usually related to mental traits. If a group of children is randomly divided into several groups, then the average genetic endowment of the children in each sample should be the same in statistical sense. In case the children of one group are placed in adoptive homes of one kind and the children of another group into adoptive homes of the other kind, then each adoptive home will have some effect on the development of the children; which can be compared.

IN CHICAGO, the studies were carried out on IQ score in which the selective placement was minimal. The adoptive homes were classified as poor, average and good homes. The study revealed that the mean IQ scores of the adopted children were strikingly related to the quality of the adoptive homes.

Good homes : 45 adopted children scored 112 pts.

Average homes : 39 adopted children scored 105 pts.

Poor homes : 27 adopted children scored 96 pts.

THE above observation demonstrates the modifying influence of the home environment on the intelligence test behaviour.

A STUDY was conducted in Mineasota homes graded children in various ways in order to know if heredity plays any role in the determination of IQ performance. If so, then adopted children should be less similar to their adoptive parents than their biological parents (control group). It was observed that there was a continuous decrease in mean IQ (i.e. (113 to 103) with change of the occupational status of the father from the professional to unskilled, thus reflecting the environmental effect on test performance. A similar decline was in the control group (119-102) three times more), thus the upper occupational group scored higher score. The difference in score values between the adopted and in their own children are due to the fact that the latter resemble more their parents as they inherited part of their parents' genotypes.

THE studies strongly suggest that intelligence performance depends in part on the children's genetic endowment from their biological parents and is to a high degree independent of the educational status or the intelligence performance of their adopted parents.

OSBORNE (1951) stated the following essential requirements for using the foster child technique :

(a) Foster children must be placed in the adoptive home sufficiently early to be relatively uninfluenced by the environment of their original home.

(b) There must be little or no selective placement of the children.

(c) Adequate sample of adoptive home children at various social levels must be included in the survey.

(d) The foster children should form one population to eliminate ethnic sources of variation.

TWIN METHOD

TWIN study approach tends to under-estimate the extent of environmental variation. For the behavioural traits, it is difficult to accept that the environmental difference between two members of a twin pair is representative of that between two random individuals in the population. Paul (1914) said that the twin method is used in the assessment of genetic determination of a character. Siemens (1924) provided three-fold use of twins in genetic research :

1. Investigation of normal variability becomes possible.
2. Method for determination of zygosity.
3. The degree of genetic determination of a trait and its variability modified by the environmental influence are indicated by the similarity between MZ twins. In Dizygotic twins ½ degree of genes are common by descent, which provide a control.

WEINBERG'S differential method is used for the determination of frequency of DZ and MZ in a population.

Unliked sexed twins ® 2 separate Zygotes XX and XY

Liked sexed twins ® simple relation to that of the unliked sexed ones.

Secondary sex ratio 1 : 1 → DZ. ♂♂, ♂♀, and ♀♀.
¼ : ½ : ¼

Liked sexed ones ® ¼ + ¼ = unliked sex = ½

Frequency of DZ = 2 x DZ of same sex .

Frequency of MZ = Frequency of all twins — DZ

MZ are always of same sex.

SIEMENS and Von Verschuer argued that the MZ twins would be more alike in physical characteristics than the DZ twins. In MZ twins phenotypic identity = genotypic identity.

A MAJOR contribution of twin studies to genetics has been the estimation of for various quantitative characters. Since MZ twins are genetically alike, any differences between them must result from environmental variation. Thus, the measurement of differences between MZ twins provides a direct estimate of V_E. Differences between DZ pairs represent $V_G + V_E$. The heritability can be estimated from the frequency with which pairs are concordant (both affected) or discordant (only one affected). If the trait is determined in part by genes, the concordance rate will be higher in MZ than in DZ twins. The concordance rate C =

$$\frac{C + 2C}{C + 2C + d}$$

where C = No. of concordant pairs.

C = No. of concordant pairs in which both members were ascertained independently.

d = No. of discordant pairs. It signifies that when MZ concordance rate is low, it is quite high. In an individual whose genes place him near the threshold, relatively small environmental differences will place him on one side of the threshold or the other and determine whether he is affected or unaffected.

A NEW approach to the use of twins in genetic analysis compares the offsprings of monozygous twin pairs for the character being studied. The children of monozygous twins are full sibs, of course and also half-sibs of the children of the co-twin. Twins have proved useful in weighing the relative importance of heredity and environment in normal variation and in disease. Traits or disorders having important genetic component will be found in higher frequency in the co-twins of affected monozygotic (MZ) twins than in the co-twins of affected dizygotic (DZ) twins.

Eg. of Twin studies involving :

1. Chromosomal Aberrations,
2. Mutation in sporadic cases of disease,
3. Traits with complex inheritance : Heritability estimate (h^2) by the formula.

h^2 = [(Variance in DZ pairs – Variance in MZ pairs)] / Variance i DZ pairs

If $h^2 = 0$, the character is environmental

If $h^2 = 1$, the character is genetic.

4. *Diabetes mellitus,*
5. Cancer.
6. Behavior Genetics,
7. Congenital Malformations,
8. Cerebral palsy.

Limitations

1. The main drawback of the twin method is that though it tells something about the strength of the genetic predisposition to develop a disorder, it gives no insight into genes concerned, their mode of action or their pattern of transmission.
2. For many conditions studied even the MZ concordance rate is well below 50% indicating that environmental factors operative before birth are important in causing them.
3. Although twin method assumes that postnatal environment differences are constant for both types of twins this assumption may be unwarranted.
4. It is related to bias of ascertainment eg. in concordance rate indentifying concordant pairs etc.
5. Twin studies' results are only applicable to twins but not to whole of the population.

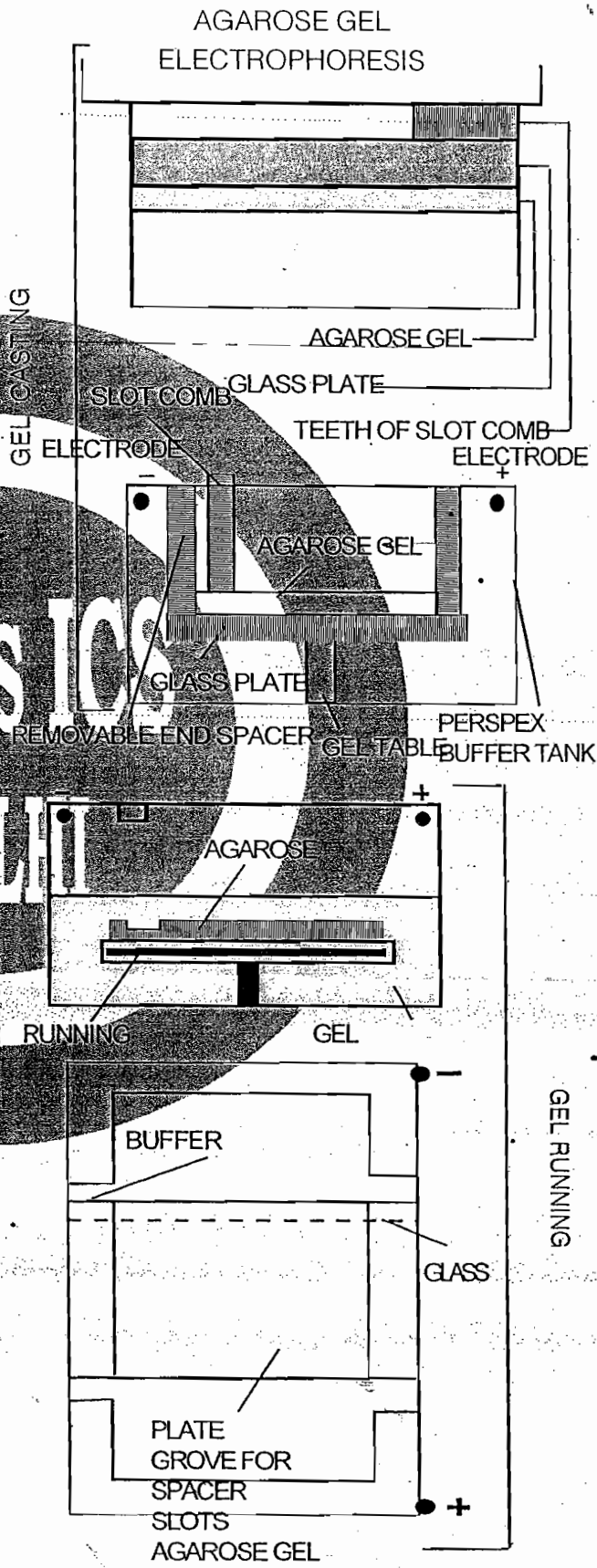
RECOMBINANT DNA

The term refers to the joining together of two pieces of DNA that are not normally found together usually involving DNA from two different species. e.g. when a small segment of DNA from the human genome is recombined with DNA from a small bacterial plasmid.

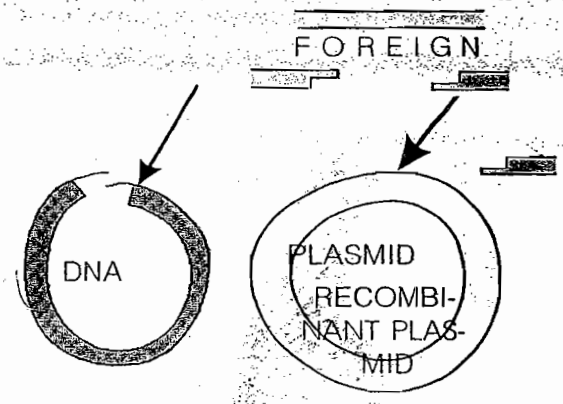
THE DNA is first digested with the appropriate restriction enzymes (is a nucleic acid clearing enzyme that acts upon DNA, cutting it into fragments at a specific sequence e.g. Eco RII Hind IV, etc.) After this gel electrophoresis is performed in an agarose or polyacrylamide gel. As they have a negative charge at neutral pH, DNA molecules migrate towards the positive terminal. Nucleic acids are loaded into slots in the gel and allowed to migrate towards the positive terminal. The pores in the gel act to sieve the molecules, so that the mobility of a particular nucleic acid species depends on its length. All the molecules of a particular size move at approximately the same rate through the gel, forming a band which gradually increases in width during electrophoresis because of diffusion. The size of the molecules in any band upon the gel can be deduced by running DNA molecules of known size in parallel track of an the gel. Polyacrylamide gel has a smaller average pore size than agarose and effective separating 10-1000 Kb.

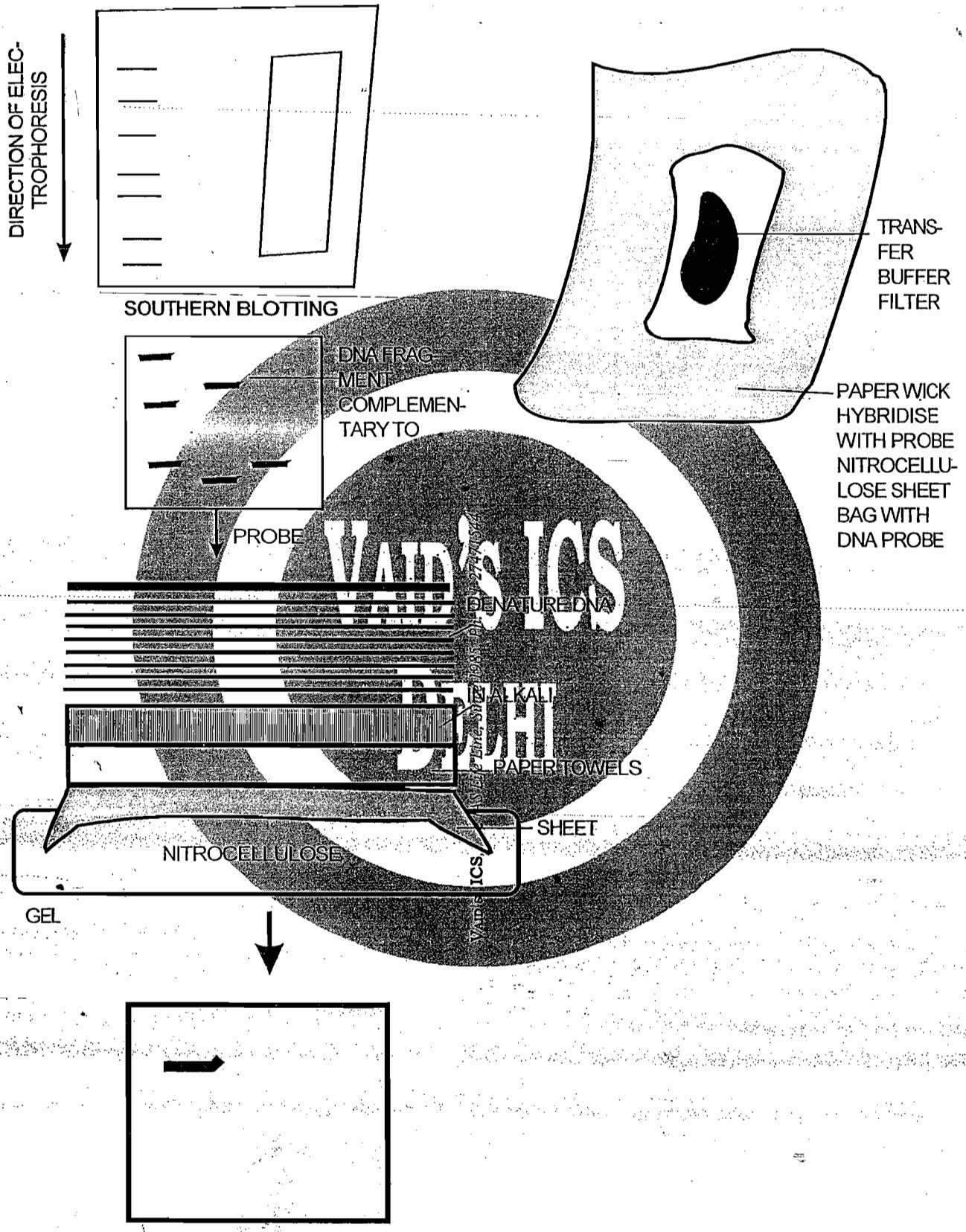
THE gel is stained by ethidium bromide to visualise the bands and can detect 5-10ng of DNA. DNA is denatured with alkali and then transferred to nitro cellulose sheet (southern Blot). It is called *blotting* as it is carried out by placing dry paper towels on top of a sandwich formed of the gel and nitro-cellulose sheet. This leads to a net movement of buffer solution from the gel into the paper towels through the nitrocellulose sheet. The DNA in the gel is carried along in the flow of buffer solution but becomes trapped on the nitrocellulose sheet.

FOR hybridization, the sheet is entered in solution with DNA probe (labelled) and recombinant DNA obtained.



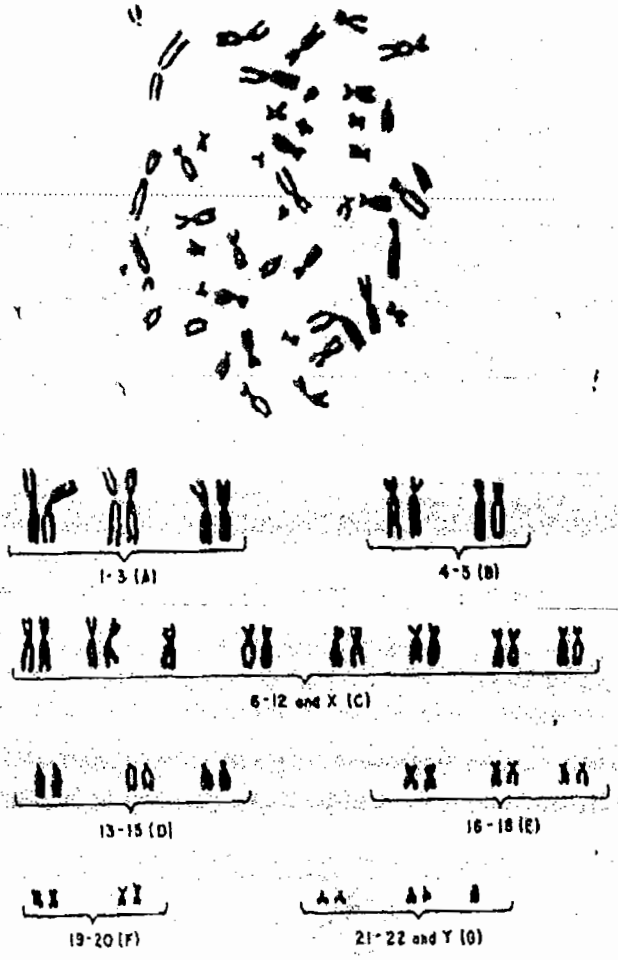
CONSTRUCTION OF RECOMBINANT DNA




DIRECTION OF ELEC-TROPHORESIS
SOUTHERN BLOTTING
DNA FRAG-MENT COMPLEMEN-TARY TO
PROBE
DENATURE DNA
IN ALKALI
PAPER TOWELS
SHEET
NITROCELLULOSE
GEL
TRANS-FER BUFFER FILTER
PAPER WICK
HYBRIDISE WITH PROBE
NITROCELLU-LOSE SHEET
BAG WITH DNA PROBE

KARYOTYPING

KARYOTYPING is a laboratory teachnique that has been applied by biological anthropologists in their own laboratories. This techniaue, which allows the inspection of the chromosomes and chromosome sets of human subjects, requires a modest amount of laboratory equipment but is labour intensive. It involves the culture of human cells, usually peripheral white blood cells, for several days in an artificial medium (Sutton, 1980). The process of division are thus held in relatively stable state of suspended cell division at a point where the chromosomes are in their most visible form. The cells are then immersed in a nypotonic solution. In such a solution, the salt concentration is lower than that of body fluids, including the intracellular fluid; therefore, water moves into the cells inflating them and spreading out the structures they contain. The chromosomes are spread out sufficiently to prevent them from clumping or stacking in the preparation to be examined. The cells are then transferred to a microscope slide and air-dried. As the surrounding fluid evaporates, the cells flatten out



A fixative is then applied along with a stain that is specifically attracted to the chromatin that makes up the chromosomes. The slides are then photographed and the photos enlarged. The photographs of the individual chromosomes are then cut out and arranged into the categories making up the total human karyotype.

Figure below shows aspread made from a lymphocyte culture and the subsequent arrangement of the photographs of the individual chromosomes into a complete human karyotype.

THERE are a number of fluorescent stains that are attracted to specific areas of chromosome. When a chromosome preparation is treated with one or more of these stains, a fluorescent banding pattern can be seen on the chromosomes. The bands, called *Q bands*, from patterns that permit chromosomes to be distinguished from one another with a high degree of certainity. It is also possible to treat the preparation with heat, acid, or alkali in order to alter or break down proteins and prevent the usual staining. By holding cells thus treated at a normal body temperature of *37°C* and at neutral *pH* fir a tune, it is possible to preferentially stain the regions alongside the centromeres and the secondary constrictions of certain chromosomes (1, 9, and 16), the distal long arm of the Y chromosome, and the satellites of the acrocentric chromosomes. When this procedure is used, the stained areas are called *C bands* (C is for consitutative heterochromatin).

EVEN finer resolution of chromosomes can be accomplished by variations in treatment of slide preparations prior to staining. For example, use of modified Giemsa stain can reveal bands that have been designated *G bands*. The application of heat can reverse the pattern of staining produced in G banding, creating dark bands where light ones would otherwise appear. This is called *R banding*.

THE analysis of chromosomes treated by a series of such techniques allows chromosomes and segments of chromosomes to be identified with a high degree of precision. A highly developed system of nomenclature has been adopted to designate chromosomes and chromosome segments using the banding pattern to identify landmarks and regions.

The cytogenetic techniques that have evolved through deelopment of these methods have proven valuable in the analysis of chromosomal variation within and between individuals and populations of living humans. They have also permitted the comparisions of the chromosomes and karyotypes of different species. The evolutionary relationships of the living primates have been a major focus of this line of research. The use of banding techniques to compare the chromosomes of the great apes, other primates, and humans has confirmed the close relationship between chimpanzees, gorillas, and humans and greater phyletic distance between orangutans, gibbons, and humans.

* * * * *

TWINS

EACH person has a unique genetic constitution different from every other living person and exception to it is that of identical twins. Francis Galton (1876) was one to assess the use of twins in nature-nurture problem study. He divided twins into two types

1. IDENTICAL (MONOZYGOTIC) TWINS

TWINS resulting from a single egg and sperm fertilised and give rise to two cells and each one differentiates into a single fetus.

2. FRATERNAL (DIZYGOTIC) TWINS

TWO eggs are fertilised by two sperms giving rise to two different fetuses.

DIFFERENCE BETWEEN MONOZYGOTIC AND DIZYGOTIC TWINS

	Monozygotic Twins	*Dizygotic twins*
1.	Arise from one egg and one sperm	Arise from two eggs which get fertilised by two separate sperms
2.	Same sex	Can be of same sex or of different sex
3.	They cannot be differentiated easily	They are genetically similar as any sib-sib pair.
4	It has always one chorion	They have two chorions

MZ-MZ correlations with sib-sib correlation provide a good measure of the extent to which a trait is genetically determined. Even the superficial observation of some traits in MZ twins gives an immediate feeling that the power of biological inheritance may be strong. The expected correlation between members of MZ twins pairs for a trait that is determined only genetically is one. The observed correlation between MZ twins is somewhat inflated measure of broad heritability.

SIEMENS (1924) provided three fold use of twins in genetic research :

1. Investigation of normal variability becomes possible.
2. Method for determination of zygosity i.e. to determine DZ & MZ pairs.
3. During study of behavioural traits DZ provide good control.

FACTORS INFLUENCING FREQUENCY OF TWIN BIRTHS

1. Maternal age & birth order : Twin birth that too DZ increase with maternal age due to increase in gonadotropin level (FSH) leading to polyovulation. DZ also increases with birth order also.
2. Genetic factors.
3. Differs in different races.

DETERMINATION OF ZYGOSITY

1. FETAL MEMBRANES

ON FOURTH day after fertilisation and subsequent cell division, a 16-cell solid ball formed is called morula and, on 6th day, blastula, in which outer layer is trophoblast and inner, cell mass. The outer develops into chorion forming fetal component. In the IInd week, fetal membrane forms amnion. MZ twins have : 2 placenta, 1 chorion (always) 2 amnions, while DZ have 2 chorions.

2. PHYSICAL SIMILARITY

IF TWINS are so much alike that they cannot be separated, then 95% probability is of their being MZ pair. If the pair differs in some genetically determined traits e.g. eye-colour, webbed toes etc., these ought to be DZ pair.

3. DERMATOGLYPHICS

THE finger pattern is determined largely by the genetic consistution. If the correspond-ing hands of twin pair are alike, then the pair is MZ, but in the case of DZ twin pair the pattern would be different as in sib-sib pair.

4. GENETIC MARKERS

MORE reliable method than physical or dermatoglyphic similarity is the use of genetic markers such as blood groups, serum proteins and, of course, sex. The more markers are the same, the higher the probability that the twins are monozygotic.

THE exact probability can be calculated if the genotypes of twins and parents are known. Consider a pair of twin boys who are both blood group MM and whose parents are group MM and MN respectively. A pair of twins has a priorichance of 7/10 of being DZ, as this is the proportion of DZ to MZ twins in the population. If the twins are DZ, they have 1 chance in 4 of being boys, 2 in 4 of being a boy and a girl, and 1 in 4 of being girls so the liked sexed chance is 1/2. The possible genotypes of DZ twins would be 1 in 4 of being MM—MM, 2 in 4 of being MM-MN and 1 in 4 of being MN-MN. So the chance of being alike in their MN groups is 1/2. Thus the probability of twins being DZ and alike for sex and MN blood group is IF THE twins are MZ they must be liked—sex and having same

$$\frac{3}{10}\times 1\times 1=\frac{3}{10}$$

blood groups. So the probability of these twins being MZ is

$$\text{Relative probability}=\frac{3}{10}:\frac{7}{40}=\frac{12}{7}$$

$$\text{Relative probability of being MZ}=\frac{12}{(7+12)}=\frac{12}{19}=63\%.$$

IF THE parental genotypes are not known, they can sometimes be deduced from those of their other children or their parents.

5. SKIN GRAFTS

THE grafted skin contains an antigen different from host cell and host produces artibody against and graft rejected. DZ twins are antigenically different since there are many alleles with several histoincom-patibility loci and will reject if graft differs. MZ will accept grafts from its co-twins, so it is an ultimate test for determination of zygosity.

6. WEINBERG'S DIFFERENTIAL METHOD

IT IS a statistical method conceived by Bertillon and Weinberg (1901) to detect how many twins in a population are MZ & DZ Unliked sexed twins are undoubtedly derived from two separate zygotes—one XX and other XY in consistution. Now, the

number of like-sexed dizygotic twins should bear a simple relation to that of the unlike-sexed ones. In a population in which the secondary sex ratio is 1 : 1, dizygotic twins of the ♂♂ & ♀♀ ♂♀ types should occur according to the chance frequencies of 1/4 : 1/2 : 1/4. This means that the number of like-sexed dizygotic male and female twin pairs 1/4 + 1/4, would be same as that of unliked sexed twins 1/2. Therefore the total number of dizygotic twins would be twice that of the observed number of unlike-sexed twins. The number of MZ twins is obtained by subtracting DZ from total number of twins.

THE sex ratio in most populations deviates from equality. Therefore, a more accurate use of the differential method employs, for the population under study, the specific values of p & q for the probability of male and female sex at birth. The fraction of unlike-sexed twins of all dizygotic twin pairs is given as

$$\frac{\text{Unlike Sexed Twins Pairs}}{\text{All DZ twin pairs}}$$

This yields, all dezygotic twin pairs

$$= \frac{\text{Unlike sexed twin pairs}}{2pq}$$

$$= \frac{2pq}{p^2 + 2pq + q^2} = \frac{2pq}{1}$$

7. SIMILARITY METHOD

SIEMENS and Von Verschuer (1924) argued that every trait has two loci which may be homozygous or heterozygous. Two parents are, in general, heterozygous for numerous genes. If, for a certain locus, one parent is heterozygous AA' and the other parent homozygous AA, the probability for two dizygotic twins being genetically alike is the sum of both of them being either AA or AA' which is 1/4 + 1/4 = 1/2. If both patents are heterozygous AA', the probability of genetic identity of dizygotic twin becomes 1/16 (both AA) + 1/16 (both A'A') + 1/4 (both (AA') = 6/16 = 3/8.

These probabilities for genetic identity of twins are also valid for phenotypic identity if the heterozygote has an intermediate or codominant phenotype and if penetrance of all genotypes is complete. If A' is dominant, then A'A' and A'A twins will appear alike and the probability for phenotypically alike DZ twins from two heterozygous parents becomes 1/16 (both AA) + 9/16 (both having at least one A' allele) = 10/16 = 5/8.

ALL these probabilities, 1/2, 3/8 & 5/8 are high, so that finding twins who appear alike in regard to the locus A will be fully compatible with their being regarded as dizygotics. If one considers that the two parents are both heterozygous not only for one locus, but for many, then phenotypic alikeness of two twins for many characters takes on a different aspect. For example, if ten loci with intermediate or codominant expression of heterozygotes are involved and one parent is homospories for some loci and heterozygous for other loci while the other parent is heterozygoses for the first and homozygous for the second group of loci, then the probability of two Dizygotic twins being phenotypically alike becomes $6/2)^{10}$, in dominance $(5/8)^{10}$ and in co-dominance $(3/8)^{10}$. These probabilities are lower and they become still lower with every additional locus taken into account. To classify as dizygotic twins who are alike in numerous traits for which their parents were heterozygous would, therefore involve an improbable assumption. On the other hand, if the twins were classified MZ then their genetic identity would correspond to single-egg origin

TWIN pairs are similar or dissimilar are scored for differences between twins by evaluation traits which are either present or absent—Twin pairs with similar traits as concordant and other as discordant. The correlation coefficient indicates that all coefficients are positively significant as both partners deviate in the same direction.

THIS method signifies that the differences based on genetic variation would exhibit greater resemblance in MZ and less in DZ.

THE environmental differences are more prominent in DZ.

LIMITATIONS OF TWIN METHOD

1. The results of twin studies can be only applied to twins but not to the whole population.
2. Twins are less frequent in the population and more common at high maternal age. They may suffer from abnormalities and mental retardation.
3. Their lower birth weight can only partly be attributed to the shorter duration of life.
4. The still birth rate and infant mortality in early life are considerably higher in multiple birth than in single ones.

HERITABILITY ESTIMATES

THIS a method to measure how much more closely the members of MZ pairs resemble than the DZ pairs and to determine the differences by employing various statistical methods. Twin-study approach to measure-ment of heritability tends to estimate the extent of environmental variation.

1. Mean Pair Difference

THE tendency of pairs (twins, sib-sib, parent-child etc.) to resemble each other can be measured as follows :

y = value for one twin

y* = value for its co-twin

= mean pair difference of n pairs

$= \Sigma (y - y^*)/n$

and smaller the value greater similarity—e.g. height, weight, IQ etc.

2. Variance (V) = (d^2)

SQUARING the difference of each value from the mean and summing the squared difference and dividing by number of observations is variance (V).

$$V = \frac{\Sigma d^2}{n}$$

The smaller V value indicates greater resemblance; i.e. pair is MZ.

3. Correlation

THE correlation coefficient for twins is defined as the variance of mean pair difference as compared to variance of population.

$$r = 1 - \frac{\frac{1}{2}V(y - y^*)}{V(y)} \qquad y = \bar{y} + g + e$$

A perfect correlation results when r = 1 and any quar titative character determined by additure genes for MZ pair, = 1 and for other pairs like DZ sib-sib it would be 0.5.

4. Partitioning of the Variance

THIS method is used to determine the degree of genetic

control character.

OBSERVED value of a character (y) for a particular individual will deviate from mean population (y) due to genetic (g) and environmental (e) factors.

$$\text{variance of y, } V = V_g + V_e$$

HERITABILITY (H) can be defined as the amount of variation resulting from genetic differences as a proportion of total variation.

$$H = V_G / (V_G + V_E)$$

If H = 1, then character is genetically determined;

and if H = O, character is environ-mentally controlled.

H can be estimated for characters determined by the genes and the frequency with which pairs are concordant (both affected) by the concordance rate.

$$C = \frac{C + 2C^*}{C + 2C^* + d}$$

C* = number of concordant pairs in which both pairs were ascertained independently, d = number of discordant pairs. C is greater in MZ twins is the trait totally controlled by genes.

$$\frac{V_G}{V_G + V_E} = \frac{V_{DZ} - V_{MZ}}{(V_{DZ} - V_{MZ}) + V_{MZ}} = \frac{V_{DZ} - V_{MZ}}{V_{DZ}}$$

H = 1 if character is of genetic origin.

THE difference in H values can be compared in twin pairs reared apart and reared together, for the study of role of the environment on the personality and characters expression.

$$\text{i.e.} \quad H = \frac{VT_{RA} - VT_{RT}}{VT_{RA}}$$

VT_{RT} = Variance in twins reared together

VT_{RA} = Variance in twins reared apart

If H = 1 then character is strongly determined by environment.

If H = 0 then it is strongly determined by genes.

APPLICATIONS

HERITABILITY estimates have great application in the study of quantitative and behavioural traits' expressions and what differences arise by change in the environment e.g. IQ, weight, stature etc.

THIRD TYPE OF TWINS?

Doctors have identified a third type of twins — somewhere between identical and fraternal — after performing extensive genetic tests on two young children.

They are referring to the pair as "semi-identical" — two sperm cells fused with a single egg — and said this is a previously unknown way for twins to arise.

With fraternal twins, the most common type, the mother contributes two eggs, each of which is fertilised in the womb by two different sperm cells from the father. They are genetically as similar as any ordinary siblings.

With identical twins, one egg from the mother is fertilised by one sperm from the father, and then very early in development the embryo splits and two foetuses grow. These twins are genetically very similar.

The new case came to light because one of the twins had an abnormality in sexual development — ambiguous genitalia — and was considered a hermaphrodite with both ovarian and testicular tissue. This child is being raised as a girl. The other twin is a boy.

Writing in the Journal of Human Genetics, *on March 28, 2007, researchers said the "semi-identical" twins are more genetically similar than fraternal twins, but less similar than identical twins.*

"This suggests the existence of other similar twins that have not yet been, and may never be, identified," they wrote.

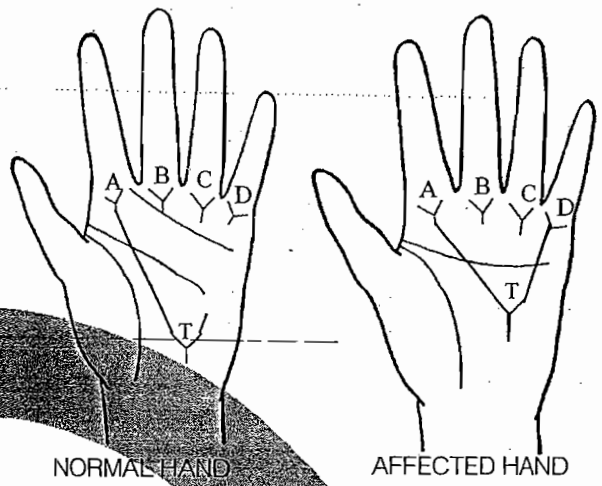
"I think the most important thing is that this shows that our understanding of how twining arises is probably something of a simplification," said Dr. Vivienne Souter, lead author of the study describing the twins.

SYNDROMES

DOWN'S SYNDROME

NON-disjunction of chromosomes during meiosis may result in change in chromosome number in multiples (euploidy) or singly (aneuploidy). Euploidy in humans results in spontaneous abortions of foetus, and therefore, such changes are not found in living humans. Aneuploids may survive even upto maturity but they suffer from severe mental retardation or infertility. The severity of the condition is a function of the size of the chromosome (or the number of genes involved).

DOWN'S Syndrome is the most common and the best known chromosomal aberration involving the trisomy of one of the smallest autosomal pairs, i.e. number 21. Also known as *Mongolism* (because of the presence of epicanthic fold in the affected persons and pseudo appearance of Mongoloid traits), it was first clinically detailed by Langdon Down, in 1866. Though its frequency at birth is $^{1}/_{700}$ in humans, it is found more frequently among the caucasoids where it frequency is $^{3}/_{200}$ of all live births. Besides, there is a direct correlation between the occurrence of syndrome and advanced age of mothers. Penrose has shown that the women who become mothers after 40 years of age, are more likely to have the



NORMAL HAND AFFECTED HAND

Syndrome in their offsprings compared to younger mothers. Further, mothers, with an affect offspring are more likely to

DISORDERS ASSOCIATED WITH AUTOSOMES

DISORDER	EXAMPLES OF KARYOTYPE	MATERNAL AGE	CLINICAL FEATURES
Down's Syndrome (1 in 700 births) Trisomy 21	47, XX, +21 47, XY, +21	Increased	1. Mental retardation 2. Flat facial profile 3. Epicanthic folds 4. Muscle Typotonia 5. Cardiac defects 6. Susceptibility to infection 7. Susceptibility to acute leukemia 8. Hyperflexibility 9. Abundant neck skin 10. Broad and/or short trunk 11. Dysplastic ears 12. Horizontal palmar crease 13. Dysplastic pelvis (on radiographs) 14. Dysplastic middle phalang (on radiographs)
Edwards' Syndrome (1 in 8000 births)	47, XX, +18	Increased	1. Mental retardation and failure to thrive 2. Prominent occiput 3. Micrognathia and low-set ears 4. Hypertonicity 5. Flexion of fingers (second and fifth digits over-lapping third and fourth) 6. Rocker bottom feet 7. Cardiac, renal, and intestinal defects 8. Short sternum and small pelvis
Patau's Syndrome (1 in 6000 births)	47, XX, +13 47, XY, +13	Increased	1. Microcephaly and mental retardation. 2. Scalp defect 3. Microphthalmia 4. Cleft lip and cleft palate 5. Polydactyly 6. Abnormal ears 7. Cardiac destroposition and inter-ventricular septal defect 8. Extensive visceral defects
Cri du Chat (Cat-cry) Syndrome 1 in 50,000 births)	46, XX, 5p— 46, XY, 5p—	Normal	1. Mental retardation 2. Microcephaly and round face 3. Mewing cry 4. Epicanthic fold

have the subsequent births with Down's syndrome.

PERSONS suffering from Down's syndrome exhibit short stature, mental retardation epicanthic fold, tendency for brachycephaly, round face, wide nostrils simian crease in the palm as also a wide ATD angle, stubby hands, large tongue in an open month. loose ankle joints.

LEJUENE was the first one to study the genetics of Down's Syndrome in 1959. He showed that the syndrome was caused by the trisomy of the smallest human chromosome pair, resulting in 47 (+21) chromosomes. Many individuals, suffering from this disorder may have only 46 chromosomes because the third 21st chromosome may get fixed up (translocated) on a chromosome of pair number 15.

THE affected persons can be trained in some basic mechanical skills to earn their own livelihood.

KLINEFELTER'S SYNDROME

KLINEFELTER'S syndrome is best defined as male hypogonadism that occurs when there are two or more X chromosomes and one or more Y chromosomes. It is one of the most frequent forms of genetic disease involving the sex chromosomes, as well as one of the most common causes of hypogonadism in the male. The incidence of this condition is approximately 1 in 850 live male births. It can rarely be diagnosed before puberty, particularly because the testicular abnormality does not develop before early puberty. The major clinical features are presented in table. Particularly characteristic are the eunuchoid body habitus with abnormally long legs, the small atrophic testes often associated with a small penis, and the lack of such secondary male characteristics as deep voice, beard and male distribution of pubic hair. The mean IQ is somewhat lower than normal, but mental retardation is uncommon. It should be noted, however, that this typical pattern is not seen in all cases, the only consistent finding being hypogonadism. Plasma gonadotropin levels, particularly FSH, are consistently elevated, whereas testosterone levels are variably reduced. Mean plasma estradiol levels are elevated by an as yet unknown mechanism. The ratio of estrogens and testosterone determines the degree of feminization in individual cases.

KLINEFELTER'S syndrome is the principal cause of male infertility. The reduced spermatogenesis is related to several patterns of morphologic change in the testis. In some patients, the testicular tubules are totally atrophied and replaced by pink, hyaline, collegenous ghosts. In others, the dysgenesis is manifested by apparently normal tubules interspersed with atrophic tubules. In some patients, all tubules are primitive and appear embryonic, consisting of cords of cells that never developed a lumen or progressed to mature spermatogenesis. Hyperplasia of the Leydig cells has been reported in all these variants. According to some authors, however, there is no true leydig cell hyperplasia but the leydig cells appear prominent owing to atrophy and crowding of the tubules.

THE classic pattern of Klinefelter's syndrome is associated with a 47, XXY karyotype (82% of cases). This complement has been explained by nondisjunction during the meiotic divisions in one of the parents. Advanced maternal age and irradiation of either parent have been suggested as relevant in the causation of this condition. In addition to this classic karyotype, some patients with Klinefelter's syndrome have been found to have a variety of mosaic patterns, most of them being 46, XY/47, XXY. Others are 47, XXY/48, XXXY and variations on this theme. Rare individuals have also been found to possess 48, XXXY or 49, XXXXY karyotypes. Such polysomic X individuals have further physical abnormalities, including cryptorchidism, hypospadias, more severe hypoplasia of the testes, and skeletal changes such as prognathism and radioulnar synostosis.

TURNER'S SYNDROME

THIS syndrome results from complete or partial monosomy of the X chromosome and is characterized primarily by hypogonadism in phenotypic females. In approximately 57% of the patients an entire X chromosome is missing, resulting in the 45, X karyotype. The remaining 43% have other abnormalities as described later. It should be emphasized that only about 3% of fetuses with the 45, X karyotype survive to birth. The surviving infants are severely affected, and unlike several other sex chromosomal aneuploidies, the diagnosis of the 45, X variant of Turner's syndrome can often be made at birth or in early childhood.

APPROXIMATELY 43% of the patients with Turner's syndrome do not carry the 45, X karyotype. Of these, (1) 10% have a complete deletion of the small arm of the X chromosome resulting in the formation of an isochromosome of the long arm X [46, X, i (X) (q)]; (2) 23% have a partial deletion of the small arm (Xp—), and (3) the remaining 34% are mosaics. It is important to appreciate the karyotypic heterogeneity associated with Turner's syndrome because it is responsible for significant variations in phenotype. In contrast to the patients with

DISORDERS ASSOCIATED WITH SEX CHROMOSOMES

DISORDER	EXAMPLES OF KARYOTYPE	APPROXIMATE INCIDENCE	MATERNAL AGE	CLINICAL FEATURES
Klinefelter's Syndrome	47, XXY 46, XY/47, XXy	1 in 850 male births	Slightly increased	1. Testicular atrophy and azoospermia 2. Eunuchoid body habitus 3. Increase in sole-to-os pubis length 4. Gynecomastia 5. Female distribution of hair
Turner's Syndrome (Gonadal Dysgenesis)	45, X	1 in 3000 female births	Normal	1. Short stature 2. Primary amenorrhea
Defective second X chromosome	46, XXp— 46, XXq—		Normal Normal	3. Infertility 4. Webbing of neck 5. Peripheral lymphedema 6. Broad chest and wide-spaced nipples 7. Low posterior hairline 8. Pigmented nevi 9. Coarctation of aorta.

monosomy X, those who are mosaics or who have deletions (e.g. 46, XXq—) may have an almost normal appearance and may present only with primary amenorrhea.

THE most severely affected infants generally present during infancy with edema (owing to lymph stasis) of the dorsum of the hand and foot, and sometimes swelling of the nape of the neck. The latter is related to markedly distended lymphatic channels, producing a so-called cystic hygroma. As these infants develop, the swellings subside but often leave bilateral neck webbing and persistent loosensess of skin on the back of the neck. Congenital heart disease is also common, particularly preductal coarctation of the aorta and aortic stenosis with endocardial fibroelastosis, anomalies that may account for some of the early deaths.

THE principal clinical features in the adolescent and adult are cited in Table. At puberty there is failure to develop normal secondary sex characteristics. The genitalia remain infantile, breast development is inadequate, and there is little public hair. The mental status of these patients is usually normal, but a few may exhibit some retardation. Of particular importance in establishing the diagnosis in the adult is the shortness of stature (rarely exceeding 150 cm in height) and the amenorrhea. To be noted, Turner's syndrome is the single most important cause of primary amenorrhea, accounting for approximately one third of the cases.

AS MENTIONED earlier, both X chromosomes are essential for normal development of the ovaries. To understand the pathogenesis of Turner's syndrome it is essential to review normal ovarian development. It has been said that "ovary is the most precisely doomed structure in the human body : it carries in its makeup the destruction of its own seeds. During fetal development, ovaries contain as many as 7 million oocytes. However, the oocytes begin to disappear *in utero*, so that by birth there are about 3 million left, and by menarche their numbers have already dwindled to a mere 400,000. Further loss continues after puberty, and when menopause occurs fewer than 10,000 remain. In Turner's syndrome fetal ovaries develop normally early in embryogenesis, but the absence of the second X chromosome leads to an accelerated loss of oocytes, which is complete by the age of 2 years. In a sense, therefore, "menopause occurs before menarche, and the ovaries are reduced to atrophic fibrous strands, devoid of ova and follicles ("streak ovaries"). The reduced estrogen output by the ovaries leads to elevated pituitary gonadotropin secretion.

GENETIC IMPRINTING OF HUMAN DISEASES

GENETIC imprinting is defined as the differential inheritance of genetic material from the mother versus the father. It is visualised that the male and female parental contribution to the genome is not fully equivalent and the function of a chromosome may differ depending upon whether it is maternally or paternally derived. The paternally derived genes control the early development of the placental tissues while the maternally derived genes play an important role in development of the embryo proper.

THE most expected theory for the mechanism of genetic imprinting is *selective methylation* of the genome. In females one of the two chromosomes is inactivated so that only genes on one X-chromosome are expressed. The methylation of the inactive X-chromosome is analogous to imprinting although it affects the entire chromosome and is not dependent upon the gender of parental origin. It inhibits the activity of transcription factors and is an important mechanism in controlling gene function.

THE concept of genomic imprinting suggests that in certain cases a genetic defect will only produce a phenotype if inherited from a particular parent. eg. a chromosomal deletion in a region concerned with placental development may have no effect if inherited maternally but may cause failure of placental development if inherited paternally.

THE good examples of the above are Pracler-Willi and Angelman syndromes. The Pracler-Willi syndrome is caused by deletion of Chromosome 15q. 11-13; characterised by hypotonia in infancy, developmental delay, obesity and hypogonadism. The individuals with this syndrome are always paternally derived. In the case of Angelman syndrome (deletion of 15, 11-13); the deleted chromosome is always maternally inherited.

THE characteristics of the disease are happy disposition, mental retardation, toxic movements, a large mouth and protruding tongue and seizures. When siblings have the same disorder but have phenotypically normal parents, it represents autosomal recessive trait; but imprinting techniques have represented chromosome regions of deletions, which have no effect in the parent, but since the imprinting status changes with meiosis, it does have an effect on the offspring.

IN CERTAIN autosomal single-gene recessive conditions there is a difference in the expression, severity or age of onset of the disease, depending upon the gender of the affected parent. eg. hereditary glomus tumour is seen only in the individuals who have inherited the disease from their father. The gene is presumably imprinted in female germ cell line so that it is not expressed in the offspring of affected mothers. In Huntington disease the age of onset of symptoms is lower in those who inherit the gene from their father than in those who inherit it from their mother, Myotonic dyotrophy is another disease in which severity varies with parental origin and occurs in the offsprings of affected mothers. Although this could be caused by some interaction between the affected fetus and the intrauterine increment of an affected mother, it is more likely to be an example of the effects of genomic imprinting.

THE differences between the maternally and paternally derived chromosomes appear to remain fixed through successive mitotic divisions. It is understood that imprinting affects a chromosome in a way which survives mitosis but not meiosis and at the meiotic division the chromosome must be newly imprinted depending upon the gender of its *host*. Genetic imprinting helps to know the effect of deletions in different sexes and the variation of the diseases according to the gender.

GENE THERAPY

THE ultimate achievement in the application of molecular biology is the technology to the treatment of disease by the replacement of mutated genes. The geneticists eagerly await to provide normally functioning alleles to persons suffering from genetic disease, thereby effecting a complete cure rather than merely treating the symptoms. If the germ cells of the affected person could also be changed from mutant to normal and extorted to future generations, it will be what is known as *gene therapy*.

THE disease in which most progress has been made in establishing gene therapy is adenosine deaminase deficiency (ADA). This causes severe immunodeficiency and patients must remain isolated because of their high risk of contracting infections. The patient's lymphocyte were infected with retroviruses carrying the ADA (gene) under the control of a retroviral promotor and periodically re-injected into their blood stream. It is not well established whether the *in vivo* supply of recombinant ADA protein will satisfy the patient's requirements and whether the therapy will have deleterious effects, but there is every cause for optimism that this will be an effective treatment.

THE sickle cell anaemia can be cured by removing some bone marrow (the site of haemoglobin synthesis) from a patient and inserting into these cells some normal beta-chain DNA in which the stretch of nucleotides coding for the 6th amino acid specifies glutamic acid rather than valine. Amongst the other target cells that are being investigated are muscle and liver cells. The muscle cells on gene therapy can be used to correct diseases like Duchenne muscular dystrophy (DND). It is difficult to have gene therapy in the case of genes requiring precise control eg. Over expression of b-thalassaemia could result in the clinical phenotype of a-thalassaemia in that patient and his on her offspring.

THERE is a need to find some controls to be exerted over transferred genes. If all of the controlling elements associated with a gene could be identified and transferred together with the gene itself, then it might be found that the inserted gene came under the same regulatory control as its natural homologue and was expressed only in the correct cells at the correct times.

THE problem in transferring the normal genes into the correct target cells is that the foreign genes introduced into potential embryonic cells or by some vector might enter the germ line as well as somatic cells. From an ethical point of view, transfer of genes into somatic cells of one individual is little different from organ transplantation, but modification of the germ line would probably represent an ethically unacceptable area for molecular biological technology.

THE major problem with gene therapy seems to be the effective introduction of the purified human genes into enough of the right cells so that the gene will be expressed at the right time at the right rate - neither too rapidly nor too slowly. The desirable DNA must not only enter the right cells and their nuclei but must be integrated quickly into chromosomal DNA of the host cell so as to avoid enzymatic degradation. Even if such methods become standard techniques for single-gene defect treatment, they would be totally ineffective against disorders caused by chromosomal aberrations or polygenic traits

Genetic Load

THE increase in homozygosity, due to inbreeding leads to a loss of fitness at those loci for which homozygotes are less fit than heterozygotes.

GENES which are deleterious when homozygous can belong to either of two major classes:

1. Genes that are not, or are only moderately, deleterious when heterozygous. The fitness of genotypes AA and Aa is then almost the same and genotype aa is at a disadvantage. Under such condition gene frequency of (a) will be kept very low by the balance between mutation and selection.
2. Genes for which the heterozygote is the fit genotype, and is therefore more fit than homozygote; such genes become polymorphic, so the allele can attain a relatively high frequency and is often called overdominant.

FOR both types of genes, homozygotes will occur with increased frequency in the progeny of consanguineous matings and thus the average fitness of the population will decrease with inbreeding.

Genetic load is a quantity, designed to measure the loss of fitness in a population due to selection.

GENETIC load is defined to be the relative decrease in the average fitness of a population, with respect to the fitness of all the individuals in the population who had the genotype that has maximum fitness (Crow, 1958)" In general, if W_{max} is maximum fitness and $\bar{W}$ the average fitness, the load is inferred by

WHEN the optimum genotype is assigned a fitness of one

$$\frac{W_{max} - \bar{W}}{W_{max}}$$

($W_{max} = 1$), then genetic load is simply equal to $(1 - \bar{W})$. The genetic load due to overdominant loci is often called *segregational load*. The aim of the study of genetic load is to distinguish the relative importance of two classes of genes which are deleterious recessive and overdominant.

GENETIC DRIFT

The gene frequencies may change relatively quickly by chance or genetic drift. Sewall Wright gave mathematical model for genetic drift; so it is also known as Sewall Wright effect.

IF TWO alleles A & A' are not produced in p & q frequencies the starting proportions of 50 : 50 deviate in 1st generation due to small population size. It is evident that a closed system which is small, will, eventually run to the fixation of one gene or the other. As a result, one population will have 100% of one gene and other population will have 50 : 50. The length of time for fixation, however, would vary from one population to another.

FOR the purposes of considering population size effects, one needs to take account of the fact that real populations contain representatives of a number of generations, individuals who don't reproduce, and chance variability in family size if a few marriages produce many offspring and others only a few—there is likely to be genetic heterogeneity. Among the offsprings then the total number produced by all different marriages make equal contributions; according to

$$\text{Wright} = L_T = L_0 e^{-T} / 2N_e$$

L_0 and L_T are number of unfixed gene in the initial and T gene. e = base of the natural logarthin.

IF POPULATION size in 100 then is 1/2 chance fixation after 139 generations

$$L_T/L_0 = 0.5 = e^{-1} / 200$$

THREE are two important processes where the chance factor plays an important role.

1. Affect the fate of a mutant gene; Deleterious or disadvantage gene can attain a high frequency by chance.
2. A gene will be absent by chance in small migrant population.

GENETIC EFFECTS OF MATING SYSTEM

A POPULATION which is inbred results in lowered viability and fertility. By Inbreeding, deleterious recessive genes, most of which are concealed in random or outbreeding populations, are brought to a state of homozygosity. Inbreeding depression is directly due to loss of heterozygosity and they have two different genes at a locus and a greater biochemical versatility than homozygotes. The particular nature of the genes and the ways they are integrated into a balanced genotype is the fundamental basis to the fitness of organism. When all the individuals are homozygous for the same genes, then the most desired phenotype or prevailing environmental conditions lead to low capacity of population to meet changing environmental demands.

A POPULATION with great genetic variability has a much better chance of evolutionary persistence for although the inevitable phenotypic variability means that fewer individuals have the most desired phenotype, the population is in a sense preadapted to environmental change. A variety of genes can be combined in a variety of ways. The major point at issue now however is that in outbreeding populations the majority of individuals will be heterozygous at many of their polygene loci and it is these individuals, rather than the rare homozygous ones, which will most closely approach the desired phenotype. Since the heterozygotes are common, natural selection can operate to build up in them efficient homeostatic mechanisms. It confers that heterozygosity confers high survival value.

GENETIC COUNSELLING

GENETIC counselling is the communication of information and advice about inherited conditions and a person seeking such an advice is known as a consultand. It usually begins with someone wanting to know whether a disease suspected of being genetic will reoccur in the near relatives of someone with the disease. Five stages are recognised in this process.

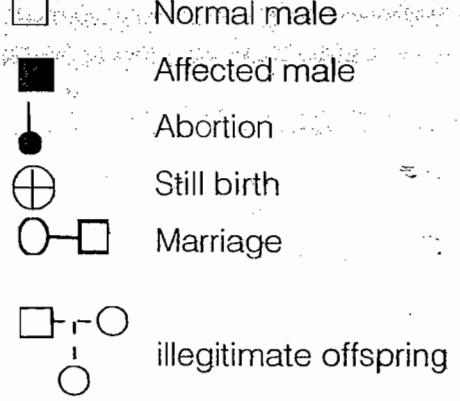
1. History and Pedigree Construction
2. Examination
3. Diagnosis
4. Counselling
5. Follow-up

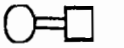
1. History and Pedigree Construction

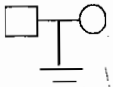
THE affected individual who caused the consultand to seek advice is called the proband, which is often a child. A standard medical history is required of the proband and of any other affected persons in the family.

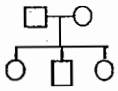
THE pedigree is constructed by employing standardised symbols.

THE male line is conventionally placed on the left, and all



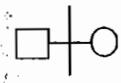

Consanguineous marriage


No offspring


Marriage, with three offsprings


Proband


Examined personally


Divorced


Normal Female


Affected female


Three unaffected females


Deceased


Sex uncertain


Pregnant


Non-identical twins


Identical twins


Twin of uncertain zygosity


Autosomal recessive Heterozygote


X-linked carrier female


Carrier of a balanced chromosomal structural rearrangement

Normal chomosome analysis.

members of the same generation are placed on the same horizontal level. Miscarriages, neonatal deaths, handicapped or malformed children and parental consanguinity might not be mentioned until required. Taking the family history involves constructing a pedigree and listing the patient's near relations by sex, age and state of health, particularly with reference to the occurrence of relevant diseases in the family. Depending on the nature of the disease involved, the counselor may want to amplify, the family history by doing special examinations or tests on particular family members.

2. Examination

A COMPLETE physical examination of the proband is essential. A dysmorphic feature is defined as the characteristic which is outside the range seen in normal individuals.

THE pattern of dysmorphic or other features is generally more important than a single sign, and as some of dysmorphic features are age-related, reexamination at a future date may be

3. Diagnosis

THE history and physical examination may permit a confident diagnosis or may indicate the need for further investigation reflecting the wide spectrum of genetic disease. It formulates a series of questions i.e.

1. Does the patient have a disease of clearly nongenetic origin e.g. infection or birth trauma ?
2. Does the baby have a disease of clearly genetic etiology e.g. haemophilia, an inborn error of metabolism or a chondrodystrophy ?
3. When a syndrome cannot be identified one must consider what further investigations are required.
4. In any case, the family history should be screened for clues to the possible genetic basis for the baby's problem.

THE most useful question to ask when taking the family history is whether problems similar to the present one have occurred in other members of the family.

FINALLY, one should ask about the possibility of parental consanguinity, since this can be a clue that the patient's problem is caused by a recessively inherited disease.

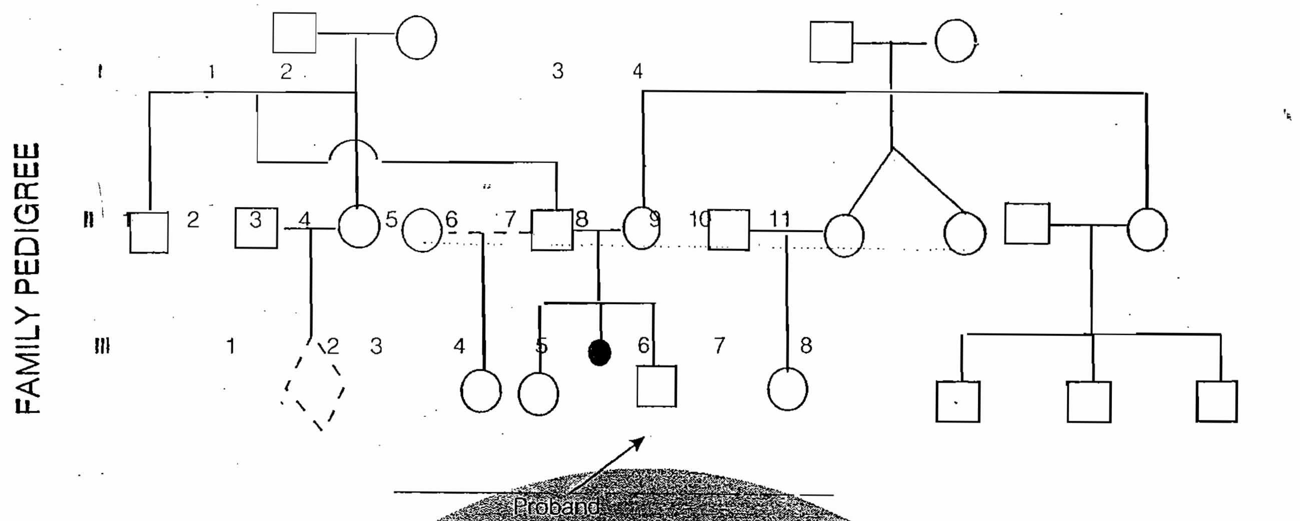
4. The Counselling Interview

ACCURATE diagnosis is of paramount importance for meaningful genetic counselling and thus counselling should never precede the steps involved in diagnosis.

BOTH parents should be counselled and adequate time allowed in an appropriate setting. It needs to include all aspects of the condition and the depth of explanation should be matched to the educational background of the couple. It starts by outlining the clinical diagnostic complications, natural history, prognosis and treatment/effective management of the condition and a recurrence risk calculated for the consultants. Common misconceptions about heredity are as listed between

1. Absence of other affected family members means that a disorder is not genetic and vice versa.
2. Any condition present at birth must be inherited.
3. Upsets, mental and physical state of the mother in pregnancy cause malformations.
4. Genetic diseases are untreatable.
5. If only males or females are affected in the family, it indicates sex linkage.
6. 1 in 4 risk means that the next three children will be unaffected.

THE possibility of prenatal diagnosis for the condition needs to be considered as this often encourages the couple to undertake a further pregnancy for which otherwise they right be



reluctant to contemplate.

COUNSELLING must be non-judgemental and non-directive. The aim is to deliver a balanced version of the facts which will permit the consultants to reach their own decision with regard to their reproductive future.

5. Follow-Up

MANY consultants can be fully counselled at one sitting, but some will require follow-up sessions. New opportunities arise (e.g. an improved carrier detection or prenatal diagnostic test). Consultants should be contacted and offered a return appointment through the regional genetic register.

PITFALLS AND PROBLEMS

1. No diagnosis in the proband.
2. Incorrect or incomplete diagnosis.
3. Genetic heterogeneity.
4. Non-penetrance.
5. Variable expression.
6. Inadequate knowledge of the literature
7. Previously undescribed disease
8. Gonadal mosaicism.

GENETIC SCREENING

GENETIC screening refers to the application of tests to groups of individuals for the purpose of detecting carriers of deleterious genes or chromosome rearrangements.

ITS goals are :

1. to identify individuals with genetic disease so that they may receive treatment to obviate the effects of the mutant phenotype (e.g. PKU).
2. to identify individuals or couples at increased risk for having offspring with genetic disorders.

ADDITIONAL benefits may be the collection of epidemiological data and expansion of our knowledge of these diseases. The choice of what groups to screen depends on the nature of the disease. If a counseler has a genetic disease or a near relative suffer with such a disease, the family becomes a group of individuals potentially at increased risk for having affected offspring e.g. Haemophilia, Duchenne Muscular Dystrophy, Tay-Sachs disease.

IT IS the systematic testing of newborns or individuals of any age, for the purpose of ascertaining potential genetic handicaps in them or in their progeny that may require treatment or prophylaxis.

TWO most important questions asked are :

1. Is corrective treatment available ?
2. How early the treatment can be administered ?

PKU can be determined at birth and other disease detected is galactosaemia, an inborn error of metabolism of the sugar, galactose. The disease can be detected by simple blood test of new born babies. The tests are technically reliable with a low proportion of false negatives or positives.

THE second question concerning the strategy of screening for a single genetic disease arises if corrective treatment is not available; then it is the condition that can be detected by amniocentesis in time for selective abortion ?

MODEL for Tay Sach's disease (a defect in the enzyme hexose aminidase (A) associated with death (3-5 years) and common among Jews of Central and Eastern Europe. It can also detected at fetal stage. The heterozygotes can be detected by simple blood test and the homozygotes by amniocentesis fluid. There are at least three questions about the advisability of all screening or a high proportions of pregnancies by amniocentesis.

LIMITATIONS

1. Possible risk of the procedure (still birth and abortions are low) and to be done by a competent practitioner.
2. The practice of institutionalizing children with Down's Syndrome.
3. The personnel and clinical and laboratory facilities are simply not yet available to undertake very widespread amniocentesis :

(a) Ultrasound techniques that accurately detect position of placenta and identify twins are a standard part of amniocentesis.

(b) Fetoscope visual inspection of fetus.

(c) The detection of substances released in amnioti fluid are markers for the abnormality.

THERE are a number of genetic diseases for which it is not possible to provide treatment or detected *in utero* e.g. Sickle Cell Anaemia, Thalassaemia and cystic fibrosis. Though Cystic Fibrosis can be detected at a very early stage of the disease, but it seems to make little difference to the prognosis of affected individuals.

GENETIC screening programmes and approaches to the treatment of genetic diseases are still limited in their applicability and are often coupled with need for abortion, which is still not desirable and against moral principles of people. To bear in mind long-term effects of such programs on attitudes are still awaited.

RECOMBINANT DNA TECHNOLOGY

DNA Structure

DEOXYRIBONUCLEIC acid is the single most important molecule in living cells and contains all the information that specifies cellular properties. Watson - Crick model described DNA as a double helix from two polynucleotides having complementary base sequences.

BASE composition is adenine, thymine, guanine and cytosine and

$$[A + G] = [T + C]$$

Purines = pyrimidines

THE two helical strands are present in DNA which are coiled about one another to form a double - stranded helix. The sugar phosphate backbones follow a helical path at the outer edge of the molecule and the bases are in a helical array in the central core. The bases of one strand are hydrogen-bonded to those of the other strand to form the purine to pyrimidine base pair A-T and G.C.

THE helix has two external helical grooves a deep wide one (major groove) and a shallow narrow one (minor groove). Base pair in DNA is peculiar i.e. base sequences of the two strands are complementary i.e. one is AATGCT, other TTACGA reading in the direction. The genetic information is stored in DNA. A ≡ T, G ≡ C Hydrogen bonds. There are four levels of coiling.

ONE of the main reasons why so much to known of the nuclear and phage DNA is that human genome is more complex. The term 'recombinant DNA' refers to the joining together of two pieces of DNA that are not normally found together usually involving DNA from two different species.

DEOXYribonuclease enzymes both endonuclease and exonuclease are used to cleave DNA strand.

[Endonuclease are the enzymes which cleave bonds within nucleic acid molecules.

Exonuclease are the enzymes which catalize the removal of nucleotides from the ends of a DNA molecule.]

POLYMORPHISMS can be detected as the appearance or disappearance of enzyme recognition sites resulting in different sizes of DNA fragments after digestion by restriction endonucleases as Restriction Fragment Length Polymorph-1 sms (RFLP) and are useful in :

1. Mapping the human genome
2. Prenatal diagnosis of hitherto undetectable genetic disorders
   a. A polymorphic site is closely linked to a human disease locus of the interest
   b. The phase of the locus and the RFLPS are established through family studies
3. Identification of carriers
4. Paternity testing and population studies.

PRINCIPLES

It has five steps :

1. The generation of DNA fragments.
2. The incorporation of these fragments into a suitable vector.
3. The introduction of the vector into a host organism.
4. Growing the host vector in culture medium and to produce clones and preparing multiple copies of DNA fragments.
5. The selection and harvesting of clones containing the relevant DNA fragment.

CERTAIN enzymes in particular microbes would cleave DNA at sequence specific sites → restriction endonuclease as they restrict the growth of infecting phage and act along the length of the DNA molecule rather then at terminal nucleotides as endonucleases. They always create double stranded breaks depending on the particular base sequence which is cleaved and staggered ends are produced e.g. ECORI.

—G A A T T C—
C T T A A G

Small → Blunt ends

—C C C : G G G—
—G G G : C C C—

EACH restriction endonuclease is designated according to the organism from which it was derived. Each cleaved DNA has staggered termini with complementary nucleotide sequences and referred to as 'sticky' since it will unite with complementary sequences produced by the same enzyme in the DNA of a suitable vector. The cohesive terrmini are held together by hydrogen bonding but are then sealed and stabilized with a ligase.

Enzyme	Organism	Cleavage site 5' 3'
Bam H I	*Bacillus*	G. GATCC
Hind III	*Haemophilus influenza*	A. AGCTT
ECORI	*E.COLI*	G. AATTC
Sal I	*Streptonyces albus*	G. TCGAC
Sma I	*Serratie narcescene*	G. TCGAC

VECTORS used are of three types :

1. Plasmids : It is small circular DNA duplex, capable of autonomous replication within a bacterium and confer resistance to antibiotics etc.
2. Phage : It is bacteriophage.
3. Cosmid : Plasmid DNA packaged *in vitro* into a phage.

PLASMIDS are stably inherited in an extrachromosomal state, and consist of a circular duplex of DNA. They have a limited number of specific restriction sites and carry resistance to particular antibiotics used to identify recombinant clones.

THE next step is to grow the host vector in culture to produce clones which contain the relevant DNA fragment. If the restriction enzyme used to insert the DNA fragment interferes with the drug resistance of the host cell, then it can be used for screening procedure.

Applications of recombinant DNA technology

1. Gene structure/mapping/function eg. globin gene.
2. Population genetics in relation to disease and population structure
3. Control of genetic disease, prenatal diagnosis, pre-clinical, carrier detection
4. Diagnosis and pathogenesis of disease.
5. Biosynthesis
   eg. insulin, growth hormone, interferon
6. Treatment of genetic disease, insertion of cloned normal gene
7. Agriculture
   e.g. nitrogen fixation

OF CONSIDERABLE practical importance : in medical genetics however has been the discovery of Restriction Fragment Length Polymorphisms (RFLPs). The changes in base sequences mean that the fragments produced by a particular

restriction enzyme will be of different lengths in different people and these genotypic changes can be recognised by the altered mobility of restriction fragments on gel electrophoresis and it has two points of importance 1. Genetic markers of use in studying the genetic structure of population similar to the way in which various blood groups and serum proteins and 2. in genetic lineage studies. It can be used for prenatal diagnosis (using DNA from uncultured amniotic fluid cells) or the detection of preclinical cases and female carriers of x-linked recessive disorders.

RECOMBINANT DNA technology can be used in the synthesis of biologically important molecules (A) & the replacement of defective genes in individuals with inherited disorders as gene therapy (B). The two approaches A & B can be used for the treatment of disease as shown in the table below :

Disorders	Probe	Approach
Cystic fibrosis	C-met	C-intergenic
	pJ 3.11	RFLPs
Diabetes	Insulin	A
Fragile X-mental retardation	Factor IX	C
Growth hormone deficiency	Growth hormone	A, B
Haemophilia A	Factor VIII-C	A, B
Haemophilia B	Factor IX	A, B
HbF persistence	b-globin	A
Phenylketonuria	Phenylalanine hydroxylase	B
Sickle Cell anaemia	b-globin	A
Thalassemia	a- and b-globin	A
	b-globin	B

RECOMBINANT DNA techniques are actively being pursued in attempts to improve plant and animal stock. Here the transfer of nitrogen fixation to cash crops, especially cereals, could have an enormous impact especially in the Third World.

PROBLEMS OF RECOMBINANT DNA TECHNOLOGY

NO ONE would argue that recombinant DNA technology has a very great deal to offer to medicine, but its potentially serious bio-hazards of the technology cannot be ignored. The main concern of DNA technology is that of producing organisms which might contain genes for cancer susceptibility e.g. or would remote their bacterial host immune to all known antibiotics.

THERE have been two main approaches to limiting possible hazards in DNA technology referred to as physical and biological containment. Thus from all points of view it may seem the hazards of genetic engineering have been perhaps overemphasised and the risksmore imagined than possible. Nevertheless great care will continue to have to be exercised in this field if for no other reason than to allay the fears of the general public.

CONTD.....

GENETIC COUNSELLING & MODE OF INHERITANCE

THE recognition of simple dominant or recessive inheritance of a given trait permits statements of practical value about the genotype of individuals. Persons affected with unfavourable traits and their close relatives, rightly wish to know whether their future children are likely to have the same traits.

GENETIC counseling makes use of a wide range of information on human inheritance. In the present chapter, counselling problems connected with simple single factor inheritance will be stressed, because only this type of inheritance has been covered in the preceding parts of this book. It may appear premature to discuss problems of genetic advisers before more facts have been presented; yet even at this stage of the discussion, it seems worthwhile to show how knowledge of human genetics can be applied to problems of individuals and of society.

DOMINANT TRAITS

THE answer to questions about the prospects of persons in families with affected individuals having affected children is simple when the trait is dominant. Event he closest relatives of affected individuals, as long as they are normal themselves, will not transmit the trait, either to their immediate offspring or to later generations. Affected persons will transmit the dominant allele to one-half of their children, although there is always a possibility that none or all will receive it.

THERE are numerous more or less serious defects that are transmitted in simple dominant form. For example, a pedigree of cataract is shown in Fig. The condition, opacity of the lens of the eye, is present in many members of this family group from childhood on. Blindness can be avoided by an operation, but even after the operation and after providing the affected individuals with special glasses, they are greatly handicapped. The trait is clearly dominant. Before having been advised by a medical geneticist, the members of this kindred were aware that the affliction was hereditary, but they did not know the rules of its transmission. They knew only that it was uncommon for all children of an affected parent to develop cataracts that all children of such a parent might be normal.

THE apparent irregularity of appearance had kept the members of the family group from realizing that cataracts never appeared among the offspring of parents who are both normal. The physician who drew up the pedigree on the basis of information willingly supplied by the family was able to explain to them why cataract appeared in only some children of a sibship and why, in some small sibships, all the children were defective or all normal. Having supplied this enlightenment, he could further assure normal sibs of affected persons that they did not need to worry about transmitting cataract to their children. This example shows that much harm may be avoided and much worrying relieved if consultants in human genetics become widely available to the public.

RECESSIVE TRAITS

ALTHOUGH the genotypes of individuals can be given with certainty if simple dominant inheritance of a rare condition is involved, some genotypes of rare recessive conditions are less easy to define. An affected person, of course, is dd, but nonaffected relatives are either DD or Dd. If they are phenotypically normal sibs of a dd individual, and if their parents were normal, their genotypes could be either DD or Dd, since both parents must have been heterozygous. The two genotypes, DD and Dd, occur in a ratio of 1 : 2, which makes the probability that a normal sib does not have the recessive allele 1/3, and that he is a carrier 2/3.

THESE two probability fractions may seem to contradict the expectation that Dd × Dd marriages will yield 1/4 DD and 1/2 Dd children; but they do not. The probabilities 1/4 and 1/2 express the frequency with which any child from two heterozygous parents may be expected to be DD or Dd, considering also that he may be dd. The fractions 1/3 and 2/3, on the other hand, are derived from the number of individuals who are phenotypically example: If two normal parents who have an affected child want to know the probability that their unborn second child will be homozygous normal, the answer would be 1/4, since he could be dd, Dd, or DD. If, however, the second child is normal, the answer to the same question would have to be 1/3, because his phenotype shows with certainty that he is not dd.

DETERMINATION of the probability that an affected individual or phenotypically normal relatives of such an individual will have affected homozygous recessive offspring has to take into account the various types of marriages possible, and also the frequency of the condition in the population at large. Marriages in which both partners are affected will, of course, result in affected children only. If one prospective parent is affected and the other normal and drawn from the general population, it is necessary to estimate the probability that a normal person chosen at random is heterozygous, i.e. a carrier. A FORMULA which permits such an estimate will be derived. the Hardy Weinberg Law. Here, it may be stressed that even very rare conditions that are due to a homozygous recessive constitution are quite often carried by heterozygous.

PROBABILITY OF AFFECTED OFFSPRING IF ONE PARENT IS AFFECTED

KNOWLEDGE of the frequent with which carriers occur enables a genetic consultant to predict the chance of affected offspring occurring in a marriage. For example, it has been estimated that about 1 in 70 persons is a carrier of recessive albinism. Consequently, the probability that an albino will marry a normally pigmented unrelated person who is heterozygous for the albino allele is 1/70. If enough children come from such a marriage to make it re reasonably certain that both genotypes, Dd and dd, will actually occur, the probability that an albino with a normally pigmented spouse will have some affected offspring is 1/70. Expressed in a different way: if prospective parents, one of whom is an albino, ask, "If our family is large, what chance is there of having albino children?" the answer is 1/70. Should, however, the couple ask, "What chance is there that our first child, or any specific child will be an albino?" then the answer is 1/2 × 1/70 = 1/140 since the probability of *dd* offspring from *dd* × *Dd* parents is 1/2.

PROBABILITY OF AFFECTED OFFSPRING IF ONE PARENT IS THE NORMAL SIB OF AN AFFECTED PERSON

IN marriages between normal sibs of affected persons and normal individuals who are not related to them, the probability that the sib is a carrier (which is 2/3) by the probability that the spouse is a carrier (which is 1/70 in albinism) and by the probability that the child will obtain *d* from each heterozygous parent (which is 1/4). Thus, 2/3× 1/70×1/4 = 1/420. This is a

rather small chance; yet it is much higher than that in a marriage of two normal individuals who have no reason to suspect the presence of the d gene in their genotypes. In the latter marriage, the chance that any specific child will be an albino is 1/70 ×1/70 ×1/4 = 1/19,600 ; the probability if one parent is a sib of an albino is almost fifty times as great.

ANY statement about the probability that an affected child will be born to normal persons is subject to change when new information gives more specific knowledge of the genotypes involved. If a normal sib of albinos and his normal finance should ask how probable it is that their first future child will albino, the best estimate possible it is that their first future child will albino; the best estimate possible is 1 in 420. Should the same couple them, the answer would be 1 in 4, since it would now be certain that both parents are heteroxygotes.

FURTHER PROBABILITIES OF BEING A CARRIER

IT is possible not only to determine the probability that individuals who are sibs of an affected person are heterozygotes, but also to calculate the probability of heterozygosity among individuals who are related to affected persons in the ways. These probabilities are consequences of the mechanism of genetic transmission and many can be found by applying the theorem that the probability of two or more events occurring together is the product of the separate probabilities. Let us give few example. (1) The probability that the normal child of an affected parent is heterozygous is 1 or certainty. (2) The probability that a normal parent of an affected person is a carrier is 1, while that for the affected's uncles or aunts is usually 1/2. This follows from the fact that a heterozygous parent himself almost always comes from a marriage of a normal homozygote and a heteroxygote and the chance that any offspring from such a marriage will be Dd is 1 out of 2. (3) The probability that the children of these aunts and uncles will be carriers is 1/2 that of their parents, or 1/2 of 1/2 i.e., 1/4. This last calculation does not take into consideration the rather rare chance that the spouse of the uncle or aunt may also be a carrier. All these probabilities are greatly increased when individuals from families with affected members marry close relatives.

THE INDEPENDENCE OF PROBABILITIES FROM PRECEDING EVENTS

IT is important to stress that, if the genotypes of the parents are known, the probability prediction for any one child is not influenced by the type of offspring already born.

"Chance has no memory!" The truth of Le Chatelier's remark is obvious to the geneticist, who knows that the formation of any one combination of genes at the conception of a child depends solely on the union of gametes. Thus, two parents heterozygous for a recessive allele that causes an abnormality have one chance in four that their first child will be affected. If the first child is affected, then the chance that the second child will also be affected is likewise one in four. However, the chance that two children will be affected is the product of the independent chances, or one in sixteen.

IN a relevant case reported by Mohr, a couple had a child who developed a paralysis causing death before it was a year old. Since it was known that the condition is due to a rare recessive gene, the parents were marked as heterozygiotes. They were informed that the risk was one in four that any other child would also be doomed. The couple greatly desired a healthy child and were willing to take the risk of another tragedy. They had a second child, and it too developed the deadly paralysis. When a third child was conceived, the dice of destiny determined finally that it was normal.

THERE are many trait for which a definite genetic interpretation is not available and, for these counselling cannot be based on theoretical ratios. However, the data that have been collected on a number of such traits show how often children or other relatives of affected individuals are similarly affected. Such *empiric risk figures* can be used in order to predict the probability of recurrence of the trait.

Human genetic counselling involves more than the statement of probabilities. Prospective parents may have to decide whether it is genetically desirable for them to have children and what the consequences will be both for their personal lives and for society at large.

HUMAN RACES

THERE is no doubt about the fact of human variability. The usual division of our species into races, however, often depends on a faulty perception of human differences. We rely on a simple visual appraisal to determine the distinctions between various groups. But even this simple appraisal suggests that *Homo sapiens* consists of a large number of diverse populations whose range of variability is enormous. Such variety causes one to ponder the composition of our species and its origin and casts doubt on any scheme which attempts to divide humanity into a few definite races or ethnic groups.

ONE of the biggest differences exists in the color of the skin, becuase people range in pigmentation from a very pale color - for example, northern Europeans - to an extremely dark brown - for example, the people of the Afrcian Congo or New Guinea. Human stature also ranges widely - from the 4½ feet pygimes in Africa and Oceania to the 6½ feet Nilotic peoples of East Africa. Europeans themselves vary from short (in southern Europe) to tall (in northwestern Europe). Hair form, another traits that attracts a great deal of attention, varies from straight and long to short and spiral shaped.

OTHER differences are not so rapidly identifiable but, with some care, can be measured. For example, the size and form of the human face differs considerably throughout the world, and the propotions of the lower limbs and the trunk vary over a broad range. Many more subtle differences between human populations, such as types and quantities of blood enzymes, blood groups, and other biochemical factors, can be determined only with the aid of laboratory instruments, but they exist nonetheless.

JUST why is *Homo sapiens* such an extremely polymorphic, polytypic species? That is, how can we explain the individual variability within a population (polymorphic) or the distinctions between the human groups we frequently call races (polytypic)? Why are these several characteristics of skin, hair, blood, and body size distributed among the world's peoples in the way they are?

HUMAN variability appears to be the result of a number of forces that have been at work throughout human prehistory. The influences that formed our species are part of the same complex of factors that gave rise to modern diversity. Each group reflects a number of elements in the environment which have been shaping the population through time. Evolution (change in genetic composition over time) is still proceeding and may give rise to future populations different from those of today. The composition of racial groups, as we define them now, will undoubtedly change considerably.

HOW have we become conscious of the distinct varieties of *Homo sapiens* and their place among living organisms in the world? This awareness developed gradually as a result of extensive explorations of the world by Europeans during recent centuries. Explorers brought back specimens of plants and animals unknown in Europe, and these, together with the stories of strange peoples, demonstrated the diversity in the living world - and challenged many of the Europeans' long-established beliefs. The idea that humans descended from an original pair was especially hard to accept after the discovery of such different kinds of people as the Hottentots, pygimes, and Melanesians. Aristotle's world view of idealized living form scaled to fit within eleven grades of development became most useful. With the arrangement of living creatures into a scale from lower to higher categories, from inanimate to animate, natural scientists were able to compromise the new discoveries with current religious dogma. The "strange" peoples were placed in subhuman categories and depicted as only partially formed *Homo sapiens*. This revival of Greek natural science applied the concept of life as a web or chain with many links to the discoveries of human variability. This "great chain of being" arrangement greatly simplified the study of human variability for the eighteenth century scientist.

THE "chain" concept fostered the belief that no two varieties of humans could occupy the same developmental level. So when the Hottentots and Bushmen were discovered, their appearance and language, which the European explorers considered to be like the chatter of monkeys - caused them to be placed in a lower category, nearly subhuman. Later, in the last half of the nineteenth century, when Darwin's evolutionary theory was gaining acceptance, the varieties of people were thought to represent past stages of development. But even before Darwin, there was a firmly held belief that many ancestral human pairs were created, each differing externally and internally in a way which suited them for a particular environment. These arrangements of our species into varieties were frequently complicated by the scientists' personal biases. They often felt that certain groups had been retarded in their progress towards civilization by environmental conditions. Naturally, because these schemes were proposed by Europeans, the Caucasians were considered to be thousnads of years ahead of the other races and far superior. Later, as studies of human diversity intesified in the nineteenth century, even European populations were divided into ethnic groups or races; the classic divisions were Nordic, Alpine, and Mediterranean.

DURING the ninteenth century several attempts were made to introduce scientific method into the study of human diversity in the form of mathematical analysis. For example, statistical methods were applied to the study of human variation in size, and the concept "average man" was introduced. But the notion that there existed an ideal, normal, or natural world has, for many hundreds of years, motivated us to seek patterns and to establish categories. These categories were organized and identified in terms of an ideal type of individual, supposedly representative of the group.

THESE "ideal types" work well for sorting out widely differing groups such as birds or butterflies or fish, though dealing with units or groups of similar organisms becomes more difficult. This difficulty increases when we search for forms that match notions of the ideal specimen, a factor which has caused many problems in studies of human evolution. Often the investigator has in mind an image of what the type specimen should look like and then searched until it was found. Kretschmer, who studied human body form (constitutional types), for example, emphasized in 1930 that this typological system was based on the most beautiful specimen, the rare and happy finds.

SUBJECTIVITY of this kind has plagued the study of human diveristy since the earliest times and still persists. The ensuing confusion of the multitude of typological systems has made it especially difficult to study our species and our position in the natural world.

OFTEN physical traits are confused with cultural habits of dressor language, and, though they may be useful devices for identifying human populations, they should never be applied as if they had biological meaning. A classic example was the term Aryan, which originally was applied to a group of languages (Indo-European) related to Sanskrit, the langauge of ancient populations of northern India. Many writers have persisted in using this term as if it described a biological unit, even though Aryan, the linguistic term, as used by Mueller,

included groups as diverse as the western Asians, Europeans, and Singhalese of Ceylon (Sri Lanka). Terms like Celtic, Teutonic, or Slavic are frequently applied to describe a biological unit though they more accurately distinguish between language groupings.

GROUPINGS of human populations or races are often socially or culturally determined. Even though these groupings are just as real to the observer as any biological fact, explanations of biological variability should not be offered on this basis. Regardless, racial divisions are often described by such popularized terms as Europeans, Negro, or Jewish; each includes many populations of numerous diverse characteristics. This mixing of units - the confusion between biological and social traits - poses one of the biggest problems for the anthropologists today. It is partially founded in the assumption that certain basic units of humanity are of great antiquity. The result is the many schemes that have been offered for sorting our species into groups.

HUMAN VARIATION AND ITS CLASSIFICATION

THE probles is not whether humans vary, of course we do. In fact, our species is very polymorphic and few arguments have been advanced against this fact. But this variation is not always in the ways that have described, because of the impressionistic means by which we usually perceived human differences. The problem lies in the degree of differences that exist and how they are to be evaluated. Human variation seems almost limitless and at times random, but there are limits, often within well defined boundaries. What are these boundaries and how do they relate to humans past and to human survival?

THE modern systematic study of human diversity begins with the classification of human races. Most depend on the system established by the Swedish botanist Linneaus. Linneaus classified approximately 4235 species of animals into a series of categories in ascending order. First published in 1735, the system underwent modification throughout several additions and provides the basis for the classification in use today. An abbreviated example of the modern version is well known in which it places *Homo sapiens* in the category of Order Primates with several other closely related species.

LINNEAUS based his classification system upon the assumption, current for his day, that species were of fixed type and number since creation. Species were seen as a unit of organisms which could interbreed only among themselves; an earlier description noted that a species could not spring from the seed of another, different species. All one had to do was to collect samples of the life forms and to classify them. This sharp distinction between species would greatly simplify the process. But, as it turned out, Linneaus was confronted with an ever-increasing variety of organisms, and with each new edition his categories had to be expanded and modified. This was especially true when modern human populations were discovered by European explorers. The discovery of monkeys and apes also presented challenges; where should they be placed? In the later editions Linneaus softened his stand on the fixity of species and allowed that certain varieties were unstable, a stand which suggested evolutionary change. Today, of course, biologists no longer consider the fixity of species but look to the fossil record and to the natural diversity as evidence of change, or of Drawinian evolution caused by a number of factors.

FOLLOWING Linneaus, other natural scientists turned their attention to human classifications. A German physician, Johann Friedrick Blumenbach the reputed "*Father of Physical Anthropology,*" gave us several of the racial terms in wide use today. He classified humanity into five races: Caucasoid, Mongoloid, American, Ethiopian and Malayan. To the usual criterion of skin color, Blumenbach added hair form and facial characteristics with special attention to the shape of the skull. The shape of the skull was supposed to be a significant racial trait and was regarded as highly resistant to environmental influences. Blumenback amassed a large number of human skulls from all over the world for study and, in keeping with the eighteenth century belief in ideal types, he searched to find the most perfect specimens. The skull that came closest to fitting this image of perfection was one that had been recovered from the Caucasus Mountains, in an area near Mt. Ararat. The Caucasoid eventually became a term applied to a major category which encompassed the European, north African, and Middle Eastern populations.

DURING this period of studies of human variety, our affinity to the lower primates did not go unnoticed. Peter Simon Pallas (1714-1811), a German naturalist and student of Linneaus, provided the first family tree diagramme used in biology. In a communication to Blumenbach, Pallas described a diagramme depicting degrees of morphological affinity between several animal groups. Recently, it has been suggested that this biological tree depicted what may have been Pallas' belief in organic evolution. It definitely showed close affinity between *Homo sapiens* and the lower primates, a relationship that was considered as a possibility by other naturalists; Buffon, a French naturalist (1707-1788), noted a greater resemblance between humans and orangs than between humans and baboons. His conservatism, however, prevented him from accepting human and primate affinities. Despite the similarity in anatomy between our species and other primates, *Homo sapiens* was set apart by Buffon on the grounds that only *Homo sapiens* had a soul.

BLUMENBACH, Buffon, Linneaus, and others in the eighteenth century were handicapped in their attempts to work out a classification more reflective of the actual nature of human variability. They lacked the insights possessed by later generations of scientists who had additional evidence and a clearer understanding of evolution. In addition, Blumenbach and his contemporaries assumed that the taxonomic groups of humanity were fixed and unchanging, as they believed species to be, and that there was a distinct boundary between each race established at creation. The biological diversity that was apparent within each group was presumed to be a variation around the ideal racial type. The characteristics of a European whose features and skull shape differed from the ideal Caucasoid type, would be explained as the result of climate, diet, or even social class. Such concepts and beliefs in racial diversity set the stage for modern studies of the human race throughout the nineteenth and most of this century.

AS DESCRIPTIONS of additional human populations were offered, explanations of the origins of their diversity were sought. Climate was most often described as a significant influence (the Ethiopian, blackened by the sun, was the usual example offered), but this oversimplification ignored the influence of heredity. As a critic of the environmental-influences theory, Leonardo da Vinci observed that the black races of Ethiopia were not the product of the sun's effects, because black parents produce offspring who are black. "Domestication of mankind," a process that supposedly accompained the development of civilization, was presumed to be another major influence on race formation and was described by James Cowles Prichard (1786–1848) in *Researches into the Physical History of Man.* However, in the second edition, published in 1826, Prichard rejected this domestication theory and described the environmental influences and the close correlations between climate and physical type.

IN ADDITION to the question of origins or causes of racial variation, the classification of races itself was called into question. Prichard recognized early the problems imposed by dividing humanity into only a few fixed species, and he rejected attempts to divide the human species into "principal families," which was a common practice followed when divisions were made on the basis of skull shape. "It is by no means evident that all those nations who resemble each other in shape o

their skulls, or in any other peculiarity are of one race, or more nearly allied by kindred to each other than to tribes who differ from them in the same particulars". Though he did reject such divisions, Prichard described major types of *Homo sapiens* based on head form and coloration. He argued that this was done only to facilitate comparisons independently of any design to ascribe common origins. He suggested that there was no such thing as a Negro race in the customary sense: "Among those swarthy nations of Africa which we ideally represent under the term negro, there was perhaps not one single nation in which all the characters ascribed to the negro are found in the highest degree". This insight, though strikingly modern, is seldom recalled today.

THE lack of correlation, when more than a single trait is used as a criterion, has been recognized again and again and renders any search for racial purity a futile and, often, silly excercise. Nevertheless, the attempt has been made repeatedly to work with idealized forms when a classification of our species is attempted. The notion of ideal type has persisted into modern times as illustrated by the fact that Otto Ammon (1842–1911), a German anthro-pologist who had measured thousands of human heads and had frequently discussed Nordic and Alpine types of Europeans, could not produce a perfect" specimen of either type. He confessed that he was not able to find a specimen perfect in all details.

WHAT IS RACE

HUMAN history records many contacts between peoples from all areas of the world. The frequent and free interbreeding of these populations, whether Hottentot with European, African with American Indian, or Polynesian with Chinese, to mention a few examples, is a matter of record. Such evidence has destroyed many of the myths of the last two centuries and has established that we all belong to the same species. This situation has probably existed for tens of thousands of years, ever since ancestral humans' mobility overcame geographical barriers. Despite this evidence confusion still occasionally arises over what are racial boundaries and how they can be identified.

THE term race was applied to varieties of *Homo sapiens* in the middle of the eighteenth century by Buffon, the French naturalist mentioned earlier. Prior to this time race was a term used to describe breeds of domestic animals. Since then the term has been used in a variety of social and biological contexts and has become encumbered with contradictory and imprecise meanings. Many people take for granted that they know what race means and assume that scientific investigation has long ago proved the existence of significant human racial differences. But each time the term is applied, a definition must be provided so that you will know what concept it represents. There is even a considerable conlusion over the number of divisions of humanity as few as three and as many as thirty-seven races have been described. Two carefully written studies published in 1950 listed six and thirty races respectively.

JUST what constitutes a race is a hard question to answer, because one's classification usually depends on the purpose of classification, and various approaches to taxonomy often have a built-in bias, especially when applied to humans. It is usually assumed that there is an actual structure or collection of organisms in the natural world awaiting classification. The sample definitions that follow give some idea of the confusion surrounding the race concept in biology as well as anthropology.

DEFINITIONS OF RACE

DOBZHANSKY : Races are defined as populations differing in the incidence of certain genes, but actually exchanging or potentially able to exchange genes across whatever boundaries (usually geographic) separate them. (1944: 252).

RACE differences are objectively ascertainable facts, the number of races we chose to recognize is a matter of convenience (1962: 266).

HULSE : .... races are populations which can be readily distinguished from one another on genetic grounds alone. (1963: 207).

BOYD : We may define a human race as a population which differs significantly from other human populations in regard to the frequency of one or more of the genes it possesses. It is an arbitrary matter which, and how many, gene loci we choose to consider as a significant "constellation".... (1950: 207).

GARN : At the present time there is general agreement that a race is a breeding population, largely if not entirely isolated repro-ductively from other breeding populations. The measure of race is thus reproductive isolation, arising commonly but not exclusively from geographical isolation (1960: 7).

MAYR : A subspecies is an aggregate of local populations of a species, inhabiting geographic subdivision of the range of the species and differing taxo-nomically from other populations of the species (1963: 348).

BAKER : It is concluded that race may be defined operationally as a rough measure of genetic distance in human populations and as such may function as an informational construct in the multi-disciplinary area or research in human biology (1967: 21).

BRUES : A race is: a division of a species which differs from other divisions by the frequency with which certain hereditary traits appear among its members. Among these traits are features of external appearance that make it possible to recognize members of different populations by visual inspection with greater or less accuracy. Members of such a division of a species share ancestry with one another to a greater degree than they share it with individuals of other races. Finally, races are usually associated with particular geographic areas (1977: 1.2)

BECAUSE of the prejudice surrounding the concept of human races, the following definition which substitutes ethnic groups for the term race was offered.

MONTAGU : An ethnic group represents one of a number of populations, comprising the single species *Homo sapiens*, which individually maintain their differences, physical and cultural, by means of isolating mechanisms such as geographic and social barriers. These differences will vary as the power of the geographic and social barriers acting upon the original genetic differences varies. (1954: 317)

THESE definitions, though they appear quite diverse, have in common certain factors that they emphasize. The first is an assumption about the role of geographic distribution in race formation. Primarily, the dividions are based on the sharing of a common territory or point in space. The second factor is that all agree on the importance of breeding populations in forming a collection of traits which sets the group apart. Beyond this there seems to be little agreement in terms or boundaries of human racial divisions. There are some opinions that dividing humanity into racial groups distorts the facts and forces the investigator into erroneous channels of thinking. The purpose for the classifications of human populations has continually plagued anthropologists for generations. But, regardless of the numerous ways of looking at human diversity or the evaluation of the utility of race groupings, the fact remains that many biological differences are real and cannot be described or explained away by simple statements. The concept of race is not merely a taxonomic problem of which group of populations fits together within a certain classification. It is a problem of the way in which one views *Homo sapiens* in an evolutionary perspective.

DISTRIBUTION OF RACIAL TRAITS AND RACE FORMATION

THE term race has been applied to units as small as local breeding populations (*demes*) or to large groups of populations occupying entire continents. Further confusion is added by the use of a variety of characteristics as sorting criteria; blood types are distributed differently throughout our species than, for example, skin color and body form. Race has also been used quite frequently to describe a cultural or political group (the Jewish, Aryan, English and so on). Another casual use of the term is shown by the phrase the human race, which has nothing to do with biological classification. The results of such varied and inappropriate usage have misled the reader and have obscured meaningful application. Further, the varied criteria used to delineate racial boundaries have added materially to the confusion over the need for race classification in studies of human biology.

THE question of how the human species should be divided for description and study is a difficult one, particularly because the majority of human alleles are shared by all populations. These factors, together with the reality of population variability, have caused several biologists to abandon the use of the race concept as a viable biological tool for the study of human diversity. Hiernaux, for example, observes: "In my opinion, to dismember mankind into races as convenient approximation requires such a distortion of the facts that any usefulness disappears." The facts to which Hiernaux refers are the many sources of evidence of human diversity, which include the several traits described later. The distribution of these traits is broader than generally appreciated and their distributions cut across population boundaries.

THERE is general agreement, however, that an understanding of human variation is basic to comprehending human adaptation. Some workers consider racial classification as a means of studying adaptation and thus a useful tool; other dismiss race as but an artifact of *Homo sapiens'* past. Many believe that traits should be considered individually and not as a group or cluster unless the resulting classification, based on one character, reflects the variability of others.

REGARDLESS of one's definition or application of the concept, we should remember the point raised earlier. There is no reason to assume there is now, or ever has been, a fixed number of races. If we keep this in mind, we can avoid the trap that so many nineteenth century naturalists fell into. "If races change, how do races come to be?" This logical impasse retarded the study of human biology for many generations. In fact, we are only now beginning to appreciate the complexity of our very polytypic species, whose variability is a result of a series of interactions between the social and biological systems.

HUMAN variability, as it is distributed through time and space, depends upon a multitude of factors. Several are the same factors that operate on any biological population, as described in microevolution. But humans are mobile and are able to manipulate the environment, and these abilities affect the elaboration of complex social systems which regulate behavior, particularly breeding behavior. The establishment of abstract boundaries or mating circles within populations and the custom of excluding outsiders are strong factors in directing gene flow and determine the shape of the new generation in an increasingly non-random way.

THE history of a population - how long it has lived in a given area, what selective forces have been acting on it, and what contacts it has had with other populations - helps determine the distribution of human variability. The effects of the European colonization dramatize the significance of mass movements of people. Smaller-scale, more gradual changes can also occur through interpopulation contact and through the establishment of sedentary populations, both of which occur as consequences of new technology or subsistence patterns such as agricultural activities.

IF WE take into account these factors that influence the distribution of our species, then any grouping of human variability into units, populations, races, or subspecies becomes a much more viable means of studying human diversity. The way in which we choose to group human populations depends, of course, on our purpose. We must keep this purpose in mind when working with these groups. For example, one should not establish races or ethnic units on the bases of sociopolitical criteria and then explain or interpret their existence in biological terms. The same stricture applies to groups established on the basis of geographical boundaries. The so-called natural boundaries do not prevent interpopulation contact, though distance does, of course, reduce gene flow.

HUMAN differences are distributed in some rather interesting patterns around the world. If we take a single trait or several traits together, we see that many population groups vary widely. The worldwide distribution of traits such as the ABO blood groups, Rh blood groups, abnormal hemoglobins, or the gene for taste sensitivity to phenylthio-carbamide show quite a wide difference between many populations. The fact remains, however, that these populations have been established because of conditions other than their gene frequencies. The combinations of genes in these populations are found there because of social, geographical, and cultural conditions that have constructed and maintained the biological unit which can be defined as a breeding population.

RACE AS A BIOLOGICAL UNIT

EXPLAINING the arrangement of the varieties of organisms found in the natural world is as much a problem today as it always has been. With the newer techniques of taxonomy which utilize computer facilities, investigators can process thousands of items of information, many more than could the naturalists of previous generations could. But, rather than establishing and clarifying distinct boundaries between populations, this additional information raises new questions and often casts doubt on the validity of many older, accepted taxonomic units.

THE problem is not whether the earlier classifications were a true, accurate description of nature. The former methods merely had another way of looking at biological diversity, especially through those characteristics that were measured and considered significant at that time. Since the development of genetical theory and the description of DNA, life's diveristy is now seen somewhat differently. Groups of organisms appear as dynamic units, many of whose characteristics change from generation to generation. Types or averages are no longer considered a sufficient means to describe groups of individuals participating in a breeding population. It is this dynamic condition that makes it extremely difficult to establish any all-inclusive taxonomic unit. The older definitions of species as elementary units which are determined when collections of animals are sorted into groups are sufficient only as a first step. Even the description of a species as a reproductive unit, genetically isolated, has many exceptions when animals are studied under new conditions brought about by a change in habitats.

THE study of human diversity, especially the attempts to sort people into subspecies or races, is hampered by the disagreement over several aspects of this diveristy: its origin, its relation to the environment, and whether or not basic racial stocks are "real" and of great antiquity. Species are natural biological units held together by gene flow, whereas subspecies are divisions made on an arbitrary basis, and such vague criteria as "the 75 percent rule" are employed - a "good" subspecies is one in which 75 percent of the individuals examined can be recognized as belonging to that group. However, the number of individuals of a subspecies that we cannot classify ofter exceeds those that we can.

A SUBSPECIES is considered as a grouping of individuals o

populations who share a number of characteristics in common - no single one being sufficient to differentiate who share a close common ancestry and who have been subjected to similar selective forces. The existence of such conditions would result in a high degree of similarity between the genetic systems of these population groups.. According to many human biologists. the conept of race becomes much more useful if it is considered merely as a grouping of populations. Various definitions for race were listed in the beginning. These definitions took into account the many racial differences which appear to relate to the geographical histories of each group. Dobzhansky stated: "it is recognized that most living species are more or less clearly differentiated into geographic races, each race occupying a portion of the species distrbution area".

THE importance of geogrphy has often recognized in the definition of races. Garn used spatial distribution of human varieties as a means of establishing racialg roups. He provided us with geographical, local, and micro races. Microgeographical races and local races are smaller, less inclusive groups, comparable to the breeding populations used by many workers who study human variation. These basic units are subject to localized natural selection, and population size is also effective in causing differentiation between groups. The largest, most inclusive group - the geographical race - includes many diverse local groups. In a way, this category is misleading, because often, members of geographical races share only a few physical attributes. The geographical race conforms most closely to the older description of basic racial stocks or major races (usually the three Mongoloid, Caucasoid and Negroid).

EXCEPT for a superficial identification of the majority of the inhabitants of a continent, "basic stock" or geographical race tells us little about biological diversity or the interrelationships between breeding populations or the effect of the environment. which are the dimensions of the selective forces that act on the populations. "Basic stock" reveals little about gene combinations. "Geographical race" is merely a convenient label applied in a broad sense. In order to describe and study human variability, we must use a more restricted and precise grouping; because, otherwise important differences will be obscured.

MANY characteristics show a disrespect for classical time honored boundaries. This was recognized a number of years ago; Hooton, for example, observed : "There exists no single physical criterion for distinguishing race : races are delimited by the association in human groups of multiple variations of bodily form and structure". Another consideration is that race or any such label used to identify human groups is nothing more than an informational abstraction that provides us with a research tool to investigate biological variability. Such labels have no more reality than any of the others that we use to identify objects we encounter in our environment.

EACH geographical *Homo sapiens* contains numerous local populations whose characteristics make it difficult to place. What causes this diversity of our species? Several sources have been described. First, independent or special creation has been widely advanced as an explanation. Though once popular, this belief that races were of great antiquity lacks any supporting archeological evidence. Also, the diverse populations of our species have been linked together by gene flow and have maintained species continuity. This makes it difficult to support arguments for independent racial origins.

ANOTHER explanation of human diversity is that differing forces of natural selection caused the formation of relatively distinct groups. Before Darwin's theory of natural selection was published, a number of authors described the effects of climate and food on humans and suggested that these factors may have contributed to human variation. Buffon, for example, observed in 1791: Three causes .... must be admitted, as concurring in the production of those varieties which we have remarked among the different nations of this earth: (1) the influence of climate; (2) food, which has a great dependence on climate; and, (3) manners, on which climate has, perhaps, a still greater influence.

WE MUST consider yet a third factor : Human differences - especially those often used to establish racial groups - are not as extreme or as great as generally supposed. In fact, for a few characteristics, differences between male and female are sometimes greater than differences between races. Often the tendency is to exaggerate human variation, or in certain cases to be misled by similarities of a few characteristics. For example, Canary Islanders were thought to have a major Negro component in their make-up - an assumption based on morphological studies. More recent studies of haptoglobins and dermatoglyphics (dermal ridges or fingerprints) show little indication of such affinity, raising doubts about there being major Negroid elements in the populations.

INTRARACIAL variation is extensive in the major geographically determined races and is often overlooked. An example is the diversity found among the American Indians. Rather than matching their stereotype, they vary greatly in size and form from tall to very short. Some populations are composed of people of heavy build who are prone to obesity, like the Papago of southern Arizona. In contrast are the short, slender build people who dwell in the tropical rainforests of central and South America. Face form also covers a wide range from broad, heavy faces to small, gracile faces with long narrow noses, and head shape varies over the range of cephalic indices recorded for our species. Similar diversity is seen in several of the genetic markers of blood and taste sensitivity. Though American Indians share a close common ancestry as descendants of populations who migrated over the Bering Straits since approximately 40,000 years ago, their variability should not be obscured by broad racial classification.

AFRICAN peoples, commonly grouped into a Negroid race are another example of millions of peoples being treated incorrectly as members of a homogenous geographic race. There are wide differences between many of the tribal groupings and a careful study of breeding populations is necessary. Through several studies of each African peoples, Hiernaux, a French biologist, has shown significant differences in blood groups, stature and face form among several populations living in east Africa. Other studies over the past sixty years have recorded broad ranges of diversity among Africans south of the Sahara, a factor that is overlooked too often in racial classification.

THE principal causes of raciation are usually considered to be isolation, population size and natural selection in the local area of habitation. With the semi-isolation of a breeding population, or rather the reduction of gene flow, few new genetic materials are introduced, and the local selective forces have an opportunity to exert maximum selection. Certain gene combinations can then accumulate. However, some biologists consider that the importance of gene flow has been exaggerated.

BECAUSE of human polymorphism, humanity cannot be subdivided into one group with 0 percent and one group with 100 percent frequency of any characteristic (except for a very few monogenic traits), which makes it difficult to establish taxonomic units. Mayr described race as an artifact of evolution, not the unit that evolution act on. Other biologists have noted that classification of species variability does not produce new knowledge but is simply a means of organizing the existing information. If these statements are indeed correct, then what is the unit that evolution acts on and what is the most functional unit to investigate when studying human diversity?

THOUGH pure races do not exist today, racial classification of various human populations has been retained as a tool by physical anthropology. The concept is relevant and helpful in the study of various population differences as also the action and role of various micro-evolutionary processes in making of such populations or population groups.

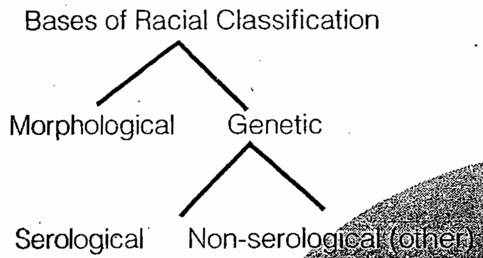
BASES OF RACIAL CLASSIFICATION

RACIAL classification has been a favourite subject of physical anthropologists since the beginning of present century. The criteria used for racial classification, as per our syllabus are morphological, serological and genetic. Serological criteria are however, themselves genetic in nature.

THUS, in reality there are only two major types of criteria used for racial classification, and these are genetic and morphological.

Morphological Criteria

HEREDITARY mechanism of morphological characteristics of man is quite complex. Such criteria are adaptive in nature,



and therefore, are at least to some extent easily influenced by environment. Some of them are morphoscopic (i.e. they have to be seen) while others are morphometric(i.e. they have to be measured). Eye shape, nose shape, eye colour etc. are example of the former while stature belongs to the latter group. Some of the commonly used morphological criteria for racial classification are:

$$\text{Cephalic Index} = \left[\frac{\text{Breadth of Head}}{\text{Length of Head}} \times 100\right]$$

(C. I.) is the earliest and most widely used criterion for racial classificatin. The classification of population groups into Dolichocephal (C.I. <-76.0), Mesocephal (76.0-80.9) and Brachycephal (^{3}80.0) for the Caucasoid, Negroid and Mongoloid groups of races respectively justifies the validity of morphological criteria.

$$\text{Facial Index} = \left[\frac{\text{Facial Length}}{\text{Facial Breadth}} \times 100\right]$$

GENERALLY broad face is associated with broad head and the narrow face with narrow head. Yet females invariably possess shorter and broader face. Three divisions of facial index are Europrosopic (<84.0), Mesoprosopic (84.0-87.9) and Leptoprosopic (^{3}88.0)

FACIAL and alveolar prognathism have also found place with morphological criteria. Alveolar prognathism is quite commonly found in Negroid populations.

$$\text{Nasal Index} = \left[\frac{\text{Nasal Breadth}}{\text{Nasal Length}} \times 100\right]$$

SUBJECTS with broad and short nose (African populations or Negroids, Negrito of South India, Australian aborigines etc.) are known as platyrrhine, Mongoloids are mesorrhine while Caucasoid rank as leptorrhine. Nasal Index is an indicator of adaptive mechanism of various populations during the course of their evolution. Root of the nose (broad or narrow), bridge of the nose (pointed or blunt) and nasal septum (directed downwards or upwards) are also sometimes utilized for the purpose of racial classification.

Eyes : A MONGOLOID eye can be distinguished from a non-mongoloid one simply by the presence of central, medial or lateral epicanthic fold. A typical non-mongoloid eye is wide open and generally straight.

Skin : SKIN colour is easily influenced by the environment. It, however, has some importance in classification of populations. In Leucoderms (white skinned people), the skin colour varies from pinkish white to light brown. Europeans, many western Asiatics, North Africans and Polynesians fall under this category. Yellow-skinned populations (Mongoloids) are termed as Xanthoderms while black skinned Negroids, Papuans, Pre-Dravidians etc. may well be called Melanoderms.

Hair : IN FORM, hair may be smooth (Leiotrichous, e.g. Mongoloids), wavy or curly (Cymotrichous e.g. Caucasoids) and wooly or kinky (Ulotrichous e.g. Negroids); colour of hair may vary from blonde (Europeans) to dark brown or black; texture may be fine (-56.9 m), medium (57-84.9 m Europeans) or coarse (^{3}85 m, Chinese, Japanese).

Stature : STATURE is the most varied and yet commonly used criterion for the classification of primary races. Stature is influenced not only by environment but also by nutrition and a host of other factors. In high altitude areas stature tends to be short as a mechanism of adaptation. The most common Haddon's scale for stature classification is: Pigmy (-148.0 cms), Short (148.0 - 158.0 cms), Medium (158.0 - 168.0 cms). Tall (168.0 - 172.0 cms) and Very Tall (172.0 - cms).

GENETIC CRITERIA

Blood Group : THOUGH the first blood groups were discovered as early as 1900, it was only in the third decade that the attempts to study population differences with respect to such criteria started. As compared to morphological criteria, serological criteria for racial classification have many advantages, and these are outlined by W.C. Boyd as follows :

(i) They follow the Mendelian prinicple of inheritance.

(ii) They are discret variables.

(iii) They are not easily influenced by environment, and hence are quite stable.

(iv) They arose quite early during human evolution.

ON THE basis of serological criteria Boyd classified humanity into the following six races; Early Europeans (represented by Bolsque), Europeans, Africans, Asiatic, Amerinds, and Australoids. This classification, however, had too many flaws to be taken seriously. Besides Boyd, Mourant *et al*, and Race and Sanger were others who made notable contributions in the use of blood groups as racial characteristics.

BESIDES the most commonly used ABO blood groups for racial classification, we have at our disposal several others including MNSs, Rh (CcDEe), Kell, P, Duffy, Celano etc. Unfortunately most of the developing countries lack facilities in such research so that the picture is not wide clear. From the work done on ABO blood groups the world over, some broad conclusions can be made.

IF WE recall, the mutation for blood group A occured in europe and that for B in Asia (or specifically India), the higher frequency of these groups in their respective environments can well be understood provided we do not forget about the advantage provided by these groups in specific environments.

DISTRIBUTION OF BLOOD GROUPS

OUR best information about the distribution of genes is for the ABO blood groups. The over-all world frequencies of these genes are estimated to be : G^o 62.3 percent, G^A 21.5 percent and G^B 16.2 percent but frequencies in different parts of the world are very unequal. The simplest condition is that of the American Indians, who in some areas have almost wholly G^o with little or no G^A or G^B. G^o is very common throughout the indigenous 'Amerindians', including the Eskimos (but the latter contain more A and B. G^o is common in western Europe but falls to its lowest, around 40-50 percent, in Central Asia. Yet, Asiatics, with Amerindians, are grouped in more classical terms as 'Mongoloid'. This shows the sort of problem that we encounnter if we try to make clear-cut divisions of people into

'races'. This example is not however, typical. There is in general some correlation between the distribution of blood group alleles and the major racial groupings.

THE distribution of the G^B gene is the inverse of G^o, being relatively common in Central Asia, but rare in indigenous populations of America. This gene shows a steadily decreasing frequency (cline) passing from Central Asia to western Europe and falling to its lowest value in the Basque population, where the frequency of O is very high and there is also (incidentally?) a highly distinctive language, not of the Indo-European type. Other populations with low G^o and high O are found around western Europe (e.g. in Ireland). There are also high frequencies of Rh negative genes among the Basques.

SUMMARY OF PRINCIPLE BLOOD GROUP DISTRIBUTION

ABO (including A_1 and A_2)	Type O most common, more than 50% of most individuals in a population. Type B nearly absent in American Indians and Australian aborigines. Type B present in up to 15% of Europe and 40% of Africa, Asia and India. A_2 limited primarily to Europe.
MNS-U	American Indians almost exclusively M; N most common in Australia and the Pacific. MS and NS absent in Australia. U-negative appears limited to Africa.
Rh (R_1, R_2, R_0, r, and others)	Rh negative (rr) rare or absent in most of the world, but found in 15% of Europeans. R_0 almost exclusively of African origin, found in 70% of Africans.
Duffy (Fy^a, Fy^b, Fy)	Most Australians and Polynesians and 90% of Asian populations. Duffy positive (Fy^a) 90% in India, 85% to 90% in American Indians, 65% in England and America, 27% in American blacks. Fy^a very low in Africa, but Fy gene is very common to about 86%.
Diego (Di^a, Di^b)	Diego-positive (Di^a) limited to American Indians, 2% to 20%, and Asians. Diego-positive is absent in Europe and Africa, and much of the Pacific and among Eskimos.
Kidd (Jk^a, Jk^b)	Jk^a (Kidd-positive) is most common in West Africa and among American blacks, 90%. Also found in American Indians, 70% to 90%, Europeans, about 70%, and is least common among Chinese, 50% to 55%.

DERMATOGLYPHICS

SCIENTIFIC studies on the dermal patterns started during the turn of last century and today dermatoglyphics form an important set of criteria for racial classification. Studies on finger ball patterns, toes, palms and soles have helped classifying various populations which could not be done so otherwise.

STUDIES reveal that of the finger ball patterns (arches, loops and whorls) Caucasoids exhibit the highest frequency of loops, while whorls are more preponderant among the mongoloids. The latter exhibit very small (1-2%) frequency of arches.

OF THE palmar main line formulae, 11, 9, 7, - finds favour with Caucasoids while 7, 5, 5, - represents Negroids. Mongoloids excel in 9, 7, 5, -.

BESIDES the above mentioned genetic criteria, some others (e.g. Secretor status, Tasting ability etc.) are also commonly used for racial classification of various human populations.

SO THEN, which is the best criterion for racial classification? At a first glance, it would seem that morphological criteria are excellent for racial classification. These are easy to notice or measure, besides there are a number of morphological characters which can be used for classification, and so a comprehensive racial classification should be possible.

HOWEVER, there are certain conditions which have to be fulfilled, before any criteria can be accepted for racial classification. These are conditions are as follows :–

(i) The mode of inheritance of the criterion should be known.

(ii) The trait must not be easily influenced by the environment.

(iii) Demarcations between variations of a single trait should be clear. In other words, the criteria should be a discrete and not a continuous variable.

BY THESE standards, morphological traits do not measure upto be good criteria for racial classification. Their mode of inheritance is still not clear, they are very strongly influenced by the environment and besides, most of them are not discrete variables. Thus it can be concluded that morphological traits are not very reliable criteria for racial classification.

HOWEVER genetic traits fulfill all these three conditions, and besides fulfilling these they have various other advantages also. Thus it would seem that genetic traits are excellent criterion for racial classification. However, in reality this is not true. On the basis of genetic traits, mankind just cannot be classified into races. In other words, on genetic basis races just do not exist.

THE distribution of Hb-S gene (i.e. the sickle cell gene) also goes to prove the contention. This gene provides some degree of resistance against *Malaria* and so is found in the highest frequency among the Negroid populations of central and east Africa (regions which have strong malarial environment). In fact, in many populations of central Africa, almost all the adult individuals are heterozygous for Hb-S gene. However, outside of central and east Africa, Hbs gene is not found in a significant proportion in any other Negroid population.

THUS, it is action of natural selection which determines the distribution of genetic traits, and their distribution has nothing to do with race.

IF GENETIC traits are also not reliable criteria for racial classification, than what are the good criteria for classification? No criterion can be considered as good for racial classification. This for the simple reason that pure races of mankind do not exist, and so how can any racial classification exist. Most scholars believe that any classification of mankind into fixed categories is useless, because the processes that constitute human variation are dynamic (and not static).

GENETIC similarities between man far out-weigh any racial differences. All living men belong to a single species and are

derived from a common stock. This goes to suggest likeness rather than differances. Populations differ from one another relatively (quantitatively), in respect of the frequency of genes and not in the kind of genes they contain. Segregation and recombination have gone so far in human population, that it is impossible to classify individuals by any other definition less complete than the total discription of their genetypes.

BEFORE ending the discussion on the criteria for racial classification one must embark on the UNESCO Statement on Race which concludes that the differences between various human populations are not absolute but are in degree only and higher or lower frequency of a trait in a population has no reflection on the capabilities of its subjects.

UNESCO STATEMENT ON RACE (1964)

1. All men living today belong to one species, *Homo sapiens*, and are derived from a common stock.
2. Pure races do not exist in the human species.
3. Differences ~~between individuals within a race~~ are often greater than the average differences between races.
4. From the biological point of view, it is not possible to speak of a general inferiority or superiority of a race.
5. Human races can not be compared at all to races of domestic animals.
6. It has never been proved that interbreeding between races has biological disadvantages for mankind as a whole.
7. The biological consequences of a marriage depend only on individual genetic make up of the couple and not on their race.
8. No biological justification exists for prohibiting inter-marriage between persons of different races.
9. There is no national, religious, geographic, linguistic or cultural group which constitutes a race, *ipso facto*, the concept of race is purely biological.
10. The people of the world today appear to possess equal biological potentialities for attaining any civilizational level.
11. Concerning the overall intelligence and the capacity for cultural development, there is no justification for the concept of "Inferior" and "Superior" races.
12. The biological data stand in open contradiction to the tenets of racism. Racist theories can in no way pretend to have any scientific foundation, and the anthropologists should endeavour to prevent the results of their researches from being used in such a biased way that they would serve non-scientific ends.

RESEARCHES have shown that different people today are the results of their respective environments. All of them have survived in varied environments because of the separate adaptive strategies followed by them in the past.

TODAY'S racial differences are the result of such adaptation only and have nothing to do with the capacities and capabilities (for culture).

ROLE OF HEREDITY AND ENVIRONMENT IN RACE FORMATION

HEREDITY refers to the genetic composition of an individual or group. It includes all the biological traits and parameters. Study of heredity is of vital importance whereby we can study various gene frequencies in different populations as also the process of gene migration. We can also study susceptibility to various genetic diseases and their influence on the gene frequencies.

ENVIRONMENT, on the other hand, refers to everything other than genetic. It includes climate, vegetation, nutrition etc. History of earth reveals that environment has never been static; climates have changed quite often and so have the flora and fauna. In recent times the evolution to man has resulted in tremendous artificial changes brought about by man.

FUNCTION of heredity is to retain, over generations, all traits that have been a part of genetic composition of an individual. It may however be at a discord for a persons with a definite genetic composition to live in a particular kind of environment. Individuals with normal hemoglobin HbA/HbA as also the individuals with HbS/HbS genotypes, for example, can not survive in the environment infested with malaria. HbA homozygous individuals in such environment can not survive because of persistent attacks of malaria resulting in successively decreased immunity. HbS homozygote individuals, on the other hand, loose the vital oxygen carrying capacity and therefore, can not survive. Malaria is an environmental disease while the presence of a particular kind of hemoglobin is purely of an individual's genetic make-up. The individual with genotype HbA/HbS is best suited to survive in this kind of environ

FROM the foregoing we conclude that specific genotypes are favoured or disfavoured in different environments. A genotype favoured by an environment will spread much faster while the ones not favoured by environment loose their existence gradually. Environment, therefore, has the direct bearing on genotypic structure. The expression of environment vis-a-vis heredity can best be understood in terms of micro-evolutionary processes discussed earlier.

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GENETIC MARKERS

THE BLOOD-GROUPS

BLOOD-GROUP variations obey Mendelian rules of inheritance with gratifying precision. They are therefore very valuable in paternity testing, in distinguishing monozygotic from dizygotic twins, and in work on genetical linkage. Since many blood-group variations have high, but variable, frequencies in different populations, they are also valuable in anthropology.

In 1968 Race and Sanger in their classic book listed 14 different blood-group systems, i.e. blood-group specificities or groups of specificities that appear to be controlled by independent gene loci.

THE A_1A_2BO SYSTEM

This system was the first to be discovered: in 1900 Landsteiner showed that the serum of some individuals agglutinated the washed red cells of certain other individuals. This discovery laid the foundation of safe blood-transfusion and also gave geneticists and anthropologists a set of simply inherited variations that are quite frequent in most populations, are easy to detect, and are virtually unaffected in expression by the sex, postnatal age, and environment of the individual. It was not in fact until 1924 that Bernstein established the mod. of inheritance of the ABO blood-groups. Red cells can carry either A or B antigens or both or neither so we have phenotypes, groups A, B, AB and O. Inheritance depends on 3 alleles A, B, and O, which segregate to form 6 genotypes, AA, AO, BB, BO, AB, OO. The presence of the A antigen can be detected by mixing the cells with serum containing anti-A, whereupon they agglutinate; the B antigen is similarly detected with anti-B. No true anti-O is known, and we are therefore unable to distinguish homozygous A or B from heterozygous A or B (AO and BO) by serological tests.

IT IS a striking fact that neither A nor B exceeds 50 per cent, whereas O reaches 100 per cent in some South American Indian tribes that have avoided intermixture. This suggests that there may be selective forces acting to limit the relative frequency of these alleles. We see in fact that O is above 80 per cent in most of the New World though the Alaskan and Canadian Eskimos in the far north have lower values. At the other extreme there is a broad zone of low O frequencies stretching from eastern Europe across much of central Asia and reaching part of the Pacific coast. In Europe we note that O frequencies in the British Isles are higher in the north west and in Ireland. Comparably high frequencies (75 per cent) are found in Iceland, which we know from written records was colonized from Norway in the ninth century. However, no region of Norway has a frequency above 66 per cent. Pockets of high O are also found in certain other peoples of Europe. such as the Basques, whose language is of obscure affinities, the Sardinians, Berber tribes of the Atlas Mountains, and people living in some parts of the Caucasus. We also see that O is relatively high in Arabia; however, Arabic-speaking tribes of Berber origin differ from the Arabians in other features of their blood-groups, apparently an example of a language spreading without much accompanying flow of genes. There is relatively high frequencies in northern Australia as compared with the rest of that country and with New Guinea. The island tribe, the Tiwi of the Gulf of Carpentaria has an O frequency of 95 per cent. This is no doubt an instance of genetic drift in a small community or of a founder effect; other examples of aberrant gene frequencies are known in various islands of this region.

The B gene map is to some extent the inverse of O; high frequencies are found in a large area of central east Asia with maximum of 25-30 per cent in the Himalayan region. In the New World and Australia, on the other hand, this allele is uncommon (5 per cent) or absent. The frequency tends to fall in passing from South East Asia to Indonesia, and there is a marked drop between New Guinea and Australia, where B is found, in low frequency, only in the Cape-York area. B is also rare or absent in Polynesia. Westwards from central Asia the gene frequency falls in an irregular cline and is notably low in the Basques. Presumably the Asiatic peoples who first entered the New World had low B frequencies, in contrast to the modern inhabitants of eastern Asia; however, at least one east-Siberian tribe, the Chuckchi, is known to have low B and A frequencies. In Africa B frequencies are low in Bushmen, but much higher in Hottentots.

TURNING to the A allele we see that frequencies are quite high in Europe with some unusually high patches, notably in Lappland and Armenia. In the New World the A pattern is to some extent the inverse of O. The gene is rate or absent in South and Central America, but much more frequent in North America, reaching 25 per cent or more in certain tribes such as the Blackfoot and Blood Indians. A is also frequent among Eskimos stretching from Alaska to Greenland. Again in Australia there is a resemblance of O and A patterns because the more southerly tribes, with low O have conspicuously high A frequencies reaching 40 per cent or more in some cases.

The subgroup A_2 has a much more restricted distribution that A. The frequency of this gene is around 10 per cent in much of Europe and Africa but falls to 5 per cent or less in India and South East Asia. In other parts of the world it is rare or absent. The A_2 gene is conspicuously frequent (25-37 per cent) in the Lapps, though varying in different Lappish groups; it is also relatively frequent in the Finns. This is one of several examples of deviant gene frequencies in the Lapps, a peoples whose origins still remains obscure.

IT IS also interesting to consider not only the local frequencies of an allele but where it occurs in greatest abundance. This means that population sizes have to be taken into account. Some Australian tribes have very high A frequencies but these genes contribute a negligible fraction of A in the world because these tribes are small. McArthur and Penrose worked out the average frequencies for various regions and found that for the world as a whole they were O = 62.5 per cent, A = 21.5 per cent, and B = 16.2 per cent.

THE RHESUS (RH) SYSTEM

IN 1940 Landsteiner and Wiener found that antisera obtained by immunizing rabbits with rhesus-monkey red cells agglutinated the cells of about 85 per cent of white Americans. Two phenotypes, Rh-positive and Rh-negative, could thus be distinguished, the former behaving as a dominant trait. Inheritance could be attributed to two alleles *Rh* and *rh*, which segreated to produce two dominant types, *Rh/Rh* and *Rh/rh*, and a recessive, rhesus-negative type, *rh/rh*. Subsequently antisera were discovered in the blood of pregnant women or in multiple transfused subjects that gave essentially the same results. We now regard these latter antisera, derived from humans, as detecting an antigen D which is different from, but related to, the antigen in rhesus monkeys. The Rh-positive genotypes can thus be rewritten D/D and D/d with d/d as the Rh-negative type.

IN 1943, noticing certain regularities in the serological results, Fisher put forward a scheme to explain the genetics of the system. He postulated 3 very closely linked gene loci, each of which could be occupied by one of a pair of alleles, D or d, C or c, and E or e. This would allow 8 types of gene triplet, or haplotypes on a chromosome as shown below :

Fisher-Race notation CDE CDe cDE cDe cde Cde cdE CdE

Wiener notation R_z R_1 R_2 R_0 r r′ r‴ r_y

FISHER thought that each gene produced its particular antigen and the corresponding 6 antisera would ultimately be discovered. This prediction was fullilled except that anti-d has not been found and may not exist.

THE Rh system with its 8 haplotypes and variety of alleles at each locus gives great scope for variation in which the frequencies in a selected range of populations. CDe(R_1), for example, ranges from less than 5 per cent in some African populations to over 90 per cent in many tribes of New Guinea. There is a tendency for this haplotype to be more frequent in the Mediterranean zone than elsewhere in Europe and for cde(r) to be correspondingly low. This trend, which is marked in the Sardinians, continues into northern India and in the Far East cde(r) is rare. An allele of the gene C, C^w, is unusually frequent in Lapps, Finns, and Latvians, cDE (R_2) is conspicuously frequent in American Indians and it is fairly high in Polynesia and South East Asia. cDe (R_0) is remarkable because the frequencies in Africa greatly exceed those in any other region. Frequencies of over 90 per cent have been recorded in peoples as physically contrasted as certain Nilotic tribes and the Bushmen. As we approach the Middle East, R_0 frequencies fall but are still 50-60 per cent in Ethiopia, 15-20 per cent in some tribes of the Yemen, and 10-16 per cent in the area south of the Caspian Sea. Moderately high R_0 frequencies have also been found in a few other scattered peoples such as Negritos of Malaya, and some tribes of northern Australia.

AMONG the rarer haplotypes we find that CDE (R_z) is relatively high among some of the so-called Veddoid tribes of India, and in some Australian tribes, though not among the Veddah themselves. The rare type cdE (r_y) is surprisingly frequent among the Ainu of northern Japan.

The Gm Groups

Immunoglobulins (Ig). The Gm factor is serologically detectable variations of certain antibody proteins (immunoglobulins) of the serum. The immunoglobulins are a physiologically very important but highly complex class of proteins.

THE Gm specificities, now some 20 in number, are due to variation in the H chains of IgG only. Four subclasses of IgG heavy chains can be recognized (gG_1, gG_2, gG_3, gG_4). Some of the Gm specificities are associated with gG_1, others with gG_3, one or two with gG_2 and none as yet with gG_4.

IF WE study the inheritance of simple Gm factors such as Gm(1) we find that Gm(1) positive and negative types segregate as expected for traits determined by a pair of codominant alleles. But if we test for several different factors we find that some of them are transmitted together in groups, a phenomenon we have already met in discussing Rh blood groups. In Europe, for example, the patterns Gm (1,17, 21), Gm (1, 2, 17, 21), and Gm (3, 5, 13, 14) are common and are inherited as units. We know that factors 1, 2, 3 and 17 are on gG_1, where 5, 13, 14, and 21 are on gG_3 and must therefore be produced by different loci.

THE number of populations that have been tested for as many as 9 Gm factors is still not very large but the data assembled in serves to show that there are some striking differences between the indigenous people of major geographical areas and in some cases between populations living in the same area. Certain haplotypes are frequent in some populations but rare or virtually absent in others. Gm (3, 5, 13, 14), for example, is common in Europeans (Caucasoids) but is infrequent or absent elsewhere unless there has been recent admixture with Europeans. There are 4 haplotypes that attain high frequencies in African Negroes or populations largely derived from them. It is interesting that about 10 percent of Gm (1,5,13,14,17) an African haplotype is found in Kurdish Jews of Iraq and about 2 per cent in Ashkenazi Jews. Bushmen have a deviant pattern, including one haplotype, Gm (1,5,17), that is peculiar to them and to peoples with whom they have mixed. They also have another haplotype, Gm (1,13, 17) that is found in eastern Asiatic peoples, but is not otherwsie characteristic of Africans.

Gm (1,5) occurs in many parts of the world, but, when additional factors are examined, it is seen to include 4 different haplotypes in Africa and a different combination again in eastern Asia and Oceania. It is an interesting fact that Gm (1) and Gm (5) segregate independently in Europeans.

IN WORK on Australian natives it was found that certain tribes of northern Queensland have appreciable frequencies of Gm (1,5,13,14), which is absent in tribes of the central and western deserts. This, and certain other Gm data, are consistent with gene flow to Australia across the Torres Straits. In New Guinea itself there is a good deal of local variation in haplotype frequencies. In the Markham valley area the frequencies of certain Gm haplotypes are correlated with the linguistic division between Melanesian-and non-Austronesian-speaking tribes and this evidence tends to support the view that the former came from South East Asia. The frequency of Gm (1, 15) has been used to chart Bushman—Hottentot admixture among the South African Bantu.

STEINBERG, who has been associated with much of the anthropological work on Gm factors, estimated the amount of Caucasoid and Khoisan (Bushman-Hottentot) admixture in Sidamo tribes of south-western Ethiopia and found 40 per cent and 12 per cent respectively. He also studied the Ainu of Hokkaido, Japan, who have one haplotype Gm (2,17,21) peculiar to themselves, and he concluded that his sample of Ainu had about 30 per cent of Japanese admixture.

THE HISTOCOMPATIBILITY (HL-A) SYSTEM

IT IS well known that skin and other tissues grafted from an individual to another usually evoke an immunological reaction leading to destruction of the graft. This graft-rejection is in general less severe if host and donor are closely related. Inherited differences in the HL-A antigens of the tissues are an important factor in these incompatibilities and the system has been intensively studied with a view to improving graft-tolerance by matching the antigens of donor and recipient. The HL-A antigens are detectable in most tissues but not on red blood cells.

THE HL-A antigens are determined by two different but closely linked loci, LA and 4. At least 14 different LA-locus antigens and 17 4-locus antigens are known in Europeans and they appear to depend on a series of alleles at each locus. Due to the close linkage of the loci certain pair of antigens such as 1(LA) and 8(4) and 11 (LA) and 5(4) are inherited together in a given population. We can refer to such combinations as HL-A haplotypes in the same way as we speak of Gm haplotypes. The fact that they have persisted suggests that there may be selective forces favouring certain combinations of alleles.

THE frequencies of some HL-A alleles show considerable geographical variation. Although most of the samples are quite small, and the standard errors of the allele frequencies correspondingly large, certain trends are apparent. Frequencies in Europe are fairly uniform but a few populations, such as Lapps Sardinians, and Basques, show deviations as they do for various other genes. Some alleles, such as 1, 3, 7, 8 and 12 are much less common in eastern Asiatic, Australasian, and American Indian populations than they are in Europe. On the other hand, 9 is conspicuously frequent in New-World Aborigines especially Eskimos. In general, African frequencies are less divergent from European values, though some antigens are now known that appear to be characteristic of this region. It should be noted that there is a good deal of variation between tribes in Australia and in New Guinea; such local variation is always troublesome when one tries to present the data in a compact form. The HL-A system, with its numerous polymorphic alleles, is outstandingly useful for the study of population

affinities.

HAEMOGLOBIN (Hb) VARIANTS

A LARGE number of Hb variants are known today. The first of these variants to be discovered, sickle-cell Hb, is specially interesting for population genetics as an example of a mutation held at high frequencies in some places by selective forces.

Sickle-cell haemoglobin (Hb-S) : The beginning of the story was the recognition of a severe type of congenital anaemia in a West Indians in 1910. It was called sickle-cell anaemia (SCA) because blood-films showed that many of the red cells were distorted into an elongated, curved shape. Work on American Negro and African families established that this disease is simply inherited, the SCA cases being homozygous for an allele Hb^S. Most of these homozygotes die prematurely unless advanced medical care is available, so that most cases arise from a mating of two heterozygotes who both carry a sickle cell and a normal gene (genotype Hb^A/Hb^S). This heterozygous phenotype, known as 'sickle-cell trait' (SCT) is not usually harmful though it can cause trouble at high altitudes when there is oxygen deficiency.

HAEMOGLOBIN is a protein of moderate size with a molecular weight of 64,000 and is composed of 4 subunits. These are of two kinds, the a-and the b-chains which differ at 57 per cent of their amino-acid sites but are folded in a closely similar way. The subunit compositions can thus be written a_2b_2. A third type of chain, g, found in Hb-F (a_2g_2) and a fourth, d, in the minor component, Hb-A$_2$ (a_2d_2) that is almost always present in normal adult red cells.

MORE than 130 structural variants of Hb are known but only three of them, Hb-S, Hb-C, and Hb-E, are found in fairly large areas of the world at heterozygote frequencies of 10 per cent or higher. Many populations in the wet tropical belt of Africa have 20-30 per cent of the sickle-cell trait and comparably high values occur in a few Mediterranean localities and in various peoples of India it was almost certainly absent in the New World before the advent of African slaves. Hb-C is frequent in a somewhat restricted area of West Africa centring on Upper Volta and Norther Ghana, while Hb-E is remarkably common in Thailand and adjacent countries but fades out in Bengal and at the margins of Australasia.

IN EAST Africa the gene is infrequent or absent in Nilo-Hamitic pastoralists. Possibly certain Liberian tribes have low sickling frequencies because they represent such an ancient forest population, but it is worth noting that sickling is frequent among the Efe Pygmies of the Ituri forest. In India the highes frequencies of *Hb^S* are found in some of the tribal peoples, who are hunters and slash and burn agriculturalists, and also in certain lower Hindu castes that may be partly derived from them. Patches of high sickling, as in parts of Greece and certain Southern Arabian oases, may be correlated with locally intense malaria.

IN GENERAL the Hb^S frequencies in American Negroes are around 5 per cent which is about half that in many West-African populations; but there are some more or less isolated groups in which the gene frequency reaches 10 per cent.

THE gene Hb^C has a focus of high frequency (10-15 per cent) in a limited area of West Africa.

A FEW other variants attain heterozygote frequencies around 5 per cent locally, e.g. Hb-D in the north-west of the Indian subcontinent, Hb-K in parts of West and North Africa, and Hb-O Indonesia in Celebes. The great majority of Hb variants are rare and do not reach a gene frequency of 1 percent, which is sometimes taken as the arbitrary lower limit defining a polymorphism.

ENZYMES

Glucose 6-phosphate dehydrogenase (G6PD) variants

THE mature red cell gets energy for its limited metabolic activities by anaerobic breakdown of glucose to lactate. G6PD catalyses the conversion of glucose 6-phosphate to 6-phosphogluconate in the presence of the coenzyme NADP, which is reduced to NADPH in the process.

IT WAS noticed in the Korean War that many American Negro soldiers had episodes of haemolysis when given the antimalarial drug, primaquine. This primaquine-sensitivity was later traced to an inherited X-linked deficiency of G6PD activity. Electrophoretic screening of haemolysates, using specific stains to reveal the position of G6PD, shows that in many tropical African peoples two variants of the enzyme are remarkably frequent (about 20 per cent each).

A MORE severe type of G6PD deficiency, known as Gd-Mediterranean of Gd(B—), is frequent (15-20 per cent) in parts of Greece, Sardinia, the Midle East, and eastwards to India. The highest known frequency (50-60 per cent) is in a Jewish isolate that formerly lived in Kurdistan, but frequencies in European Jews are much lower.

A THOROUGH study in one region of Greece, where the overall frequency of severe deficiency was about 20 per cent showed that Gd Mediterranean accounted for 70 per cent of the cases but that 3 other variants causing severe deficiency, 3 causing mild deficiency, and 3 with normal activity were also present at low frequencies. G6PD deficiency is found in about 5 per cent of southern Chinese; it is due to at least three different variations, the commonest of which is Gd Canton. Another variant, Gd Markham, seems to be fairly common in lowland areas of New Guinea.

RED-CELL ACID PHOSPHATASE (AP)

THIS enzyme splits phosphate including phenolphthalein phosphate. Some of the commoner phenotypes, which can be accounted for by segregation of 3 alleles are now denoted as ACP_1, ACP_2, and ACP_3, and the common alleles become ACP_1^A, ACP_2 and ACP^C.

IN GENERAL ACP^B is the most frequent allele, ranging from about 60 per cent to 80 per cent while ACP^C is the least frequent. The latter is commonest in Europe (4-9 per cent) and less frequent in most other populations. The European range for ACP_1^A is about 35-5 per cent, with rather higher values for some Lapp populations but in Africa, as far as the evidence goes, frequencies of this allele are considerably lower. IN New World Aborigines freguencies of ACP_1^A seem to vary widely (25-67 percent). A number of rare alleles have also been described.

6-PHOSPHOGLUCONATE DEHYDROGENASE (6PGD)

THIS enzyme follows G6PD in the HMS pathway, oxidising 6-phosphogluconate to ribulose 5-phosphate and thereby generating NADPH.

The frequency of PGD^C varies around 3 percent in Europe but appears to be rather higher in some African and Far East populations. Quite high frequencies have been reported in Bhutan (21 per cent) and amongst South African Bantu (15 per cent).

ADENYLATE KINASE (AK)

The enzymes is present in various tissues besides red cells and catalyses the conversion of adenosine triphosphate to adenosine diphosphate and monophosphate. In the standard starch-gel procedure the commonest phenotype (AK1) appears as a series of bands decreasing in strength towards the anode. A variant allele, AK^2 produces a more cathodal type with is generally seen in heterozygous form (AK^{2-1}) because this allele is infrequent in most parts of the world. AK^2 frequencies are around 2-5 per cent in most European populations but in Africa and in many Asiatic populations this allele is less common. However, frequencies of about 10 percent have beer

reported in several Indian populations.

PHOSPHOGLUCOMUTASE (PGM)

THIS enzyme, which catalyses the conversion of glucose 1-phosphate to glucose 6-phosphate, is also found in various tissues. It is produced by three loci which are not closely linked. The products of the loci PGM_1 and PGM_2 appear as two distinct sets of isozyme bands when haemolysates are examined by standard methods. The products of the third locus PGM_3 are not, as a rule, detectable in red cells but can be seen as a set of even more anodal bands in extracts of tissues such as placenta. A number of variant alleles at each of these three loci are known but only a few of them are common. Show the phenotype patterns associated with the common PGM_1 alleles PGM_1^1 and PGM_1^2. The frequency of PGM_1^1 in England is 76 per cent and (if we exclude a few aberrant frequencies in small isolates) most values for other populations lie between 65 per cent and 85 per cent, with a tendency for high levels in African and American aborigines. The frequency of this allele in Lapps is sometimes low (45-79 per cent) but varies between Lapp groups. The rare variants PGM_1^6 and PGM_1^7 were found at frequencies of 1 per cent each in a Chinese sample. None of the four or more variant alleles of the PGM_2 locus seems to be common; PGM_2^2 has been detected at frequencies around 1 per cent in a number of African samples.

ADENOSINE DEAMINASE (ADA)

THE three commonest phenotypes of this enzyme are known. The frequency of the allele ADA^2 is about 5 per cent in much of Europe, but apparently rather high in Italians and Greeks and higher still (11-14 per cent) in various Jewish groups and in those Indian populations that have been tested. Again the Lapps, with ADA^2 frequencies of 10-16 per cent, diverge from most other Scandinavian peoples though this allele is also relatively common in Finns (10 per cent). A number of African populations have been found to have low ADA^2 frequencies (0-3 per cent), and the values for Greenland Eskimos and Japanese are also low (3 per cent).

SERUM PROTEINS

Haptoglobin (Hp)

HAPTOGLOBIN is an a_2 globulin which has the property of binding free oxyhaemoglobin. Three simply inherited phenotypes are found in virtually all populations, though in very varying frequencies. Type 1 is the homozygote for the allele Hp^1 and shows a single band. Type 2, the homozygote for the allele Hp^2, has a series of more cathodal bands. The heterozygote, 2-1, has a weak band at the HP_1 position together with a series of more cathodal bands that differ in position and relative strengths from those of type 2.

HP^2 gene is found in man throughout the world suggests that it was already present in quite early human ancestors. Another phenotype which looks like a type 2-1 with weak cathodal bands is fairly frequent (10 per cent) in Africans and is known as 2-1 modified (2-1M).

HIGH frequencies (60 per cent or more) of Hp^1 are found in many tropical African peoples, in Central and South America, New Guinea, and Polynesia, while a zone of relatively low frequencies stretches from the Middle East to India and South East Asia, and includes Australia. Haemolysis due to malaria and other diseases is common in Africa, where Hpa^1 frequencies tend to be high, but is equally prevalent in parts of Asia where the frequencies of this allele are conspicuously low.

TRANSFERRIN (TF)

TRANSFERRIN (molecular weight 70,000) is a b globulin that transports iron from sites of red-cell destruction and from the intestine to the bone marrow where Hb is synthesized.

About 20 inherited variants have been distinguished by differences of electrophoretic mobility. The commonest type, TfC, appear as a single band on gels while heterozygotes for one of the slow (D) variants or one of the fast (B) variants have an additional band.

A slow (cathodal) variant, TfD_1, is quite common in African populations gene frequency 1-5 per cent) and also in Australia, New Guinea, and adjacent islands. In some Australian aboriginal groups the gene frequency is as high as 20 per cent. Peptide analysis (finger-printing) shows that African and Australian TfD_1 have the same amino-acid substitution. Whether the same mutation occurred independently in these two regions and then increased in frequency due to selection or drift in each or whether both received it from some remote common ancestor is uncertain. Another variant, TfD_{ohi}, with an electrophoretic mobility very much like that of TfD_1, was first described in Chinnese and has been found in various populations of South East and East Asia, in the Veddahs of Ceylon, in some Indian tribes, and also in a number of American Indian populations. Most of the B variants are infrequent, but Navajo Indians of the south-western USA were found to have 8 per cent of TfB_{0-1}.

HUMAN PHYSICAL GROWTH

ALL living beings survive on other living beings. They, for their survival, have to intake some substances that, in lay man terms, we calls as nutrition. These substances after their intake, pass through the process of breaking down and resythensis so that these can well be digested and assimilated into the body. After assimilation, they help in the further existence of the individual by becoming the source of energy. In fact, nutrition refers to the energy requirements of a living body and these substances which are the source of energy or those which help in the release of energy are the nutrients. Proteins, carbos, lipids, vitamins, minerals etc. are all nutrients. Of these vitamins are themselves not the source of energy but help in the release of energy of other nutrients.

DIFFERENT types of nutrients are interconvertible. Many proteins, in the hour of need can be converted into carbos and vice-versa. Similarly, fats (the stored energy) can be converted into carbos, the instant energy. It is generally considered that the forms of nutrients - proteins, carbohydrates and lipids are interchangable among the adults, except for the three fatty acids - oleic acid, linoleic acid and linolenic acid, which have to be taken in the form available in vegetative food only and can not be created out of the other types of nutrients.

A LOT many details are known about various types of nutrients, the sources of these nutrients, their functions, the effects of their higher or lower intake than the required, their deficiency diseases etc. etc. All these details can be made available through a reading of any book on everyday science and are also contained in the G.S. books meant for the aspirants of Civil Services. We shall, therefore, save our time and space to talk of the real issue.

AND the issue is : what is the effect of nutrition on human body, especially on the growth of the body. To understand these effects of nutrition, we should have a brief knowledge of human body growth.

THE growth of foetus/embryo is quite fast compare to the early days after birth. The individual registers a regular growth after birth, upto the age of six or seven years. Thereafter, there is a sudden spurt in growth (say height) for about three years. This spurt may or may not be marked in all the individuals alike. This spurt is known as the *juvenile growth spurt*. After this spurt the growth of body again is consistant till about thirteen of fourteen years when, again, their is a spurt in the growth of the body; and this time more marked than the juvenile growth spurt. This spurt is known as *adolescent growth spurt* and lasts for three to four years. After the adolescent growth spurt is completed, the growth declines, and say, height generally attains its maximum limit by the age of late teens or slightly later.

THERE are two accepted ways to study body growth known as cross-sectional method and longitudinal method. In the latter a few individuals are measured at regular intervals (of say, six months or one year) throughout or through most of their growth period (say from birth to 20 years) and through their study, the growth standards of the population to which they belong can be known. This is quite a cumbersome method and one researcher may not be that patient, or he may not have enough resources to continue this long or his age/health may deter him from carrying out such patient work. Besides, there are many other limitations imposed on the researcher by the longitudinal method and the method is not very popular in its use.

IN CROSS-sectional method the researcher takes the anthropometric measurements on a large number of growing and fully grown individuals of a population through the random selection of the individuals. It is a one time job. The growth standards of a population can be known through this method by plotting a graph by taking the average measurements of the individuals in the same age-group. This method is not very accurate but saves considerable time and energy.

REALISING the pit-falls in the two standard methods, a combination of the two (known as the semi-longitudinal method) is more commonly used whereby a significant number of individuals of a population chosen by random selection, are measured for a limited period (say three to five years), periodically.

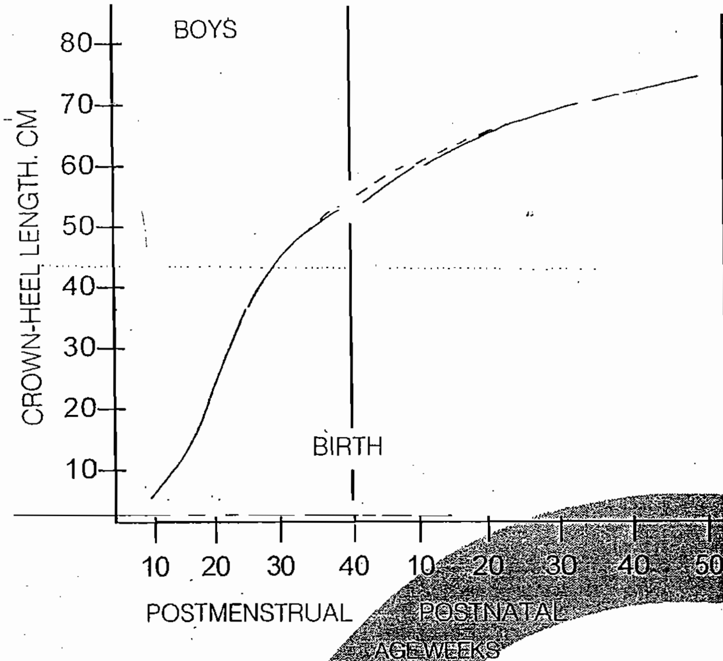
THE two growth spurts - juvenile and adolescent - have genetic disposition and can not be seen in the absence of hereditary component. They, however, get their fullest expression only if one is getting proper nutrition throughout the time period of spurt. In conditions of malnutrition or undernutrition throughout the spurt period, the individual will not grow to his full hight and his growth will be stunted. If however, he starts getting proper nutrition midway through the spurt, the spurt picks up and the individual may attain his expected hight/ growth.

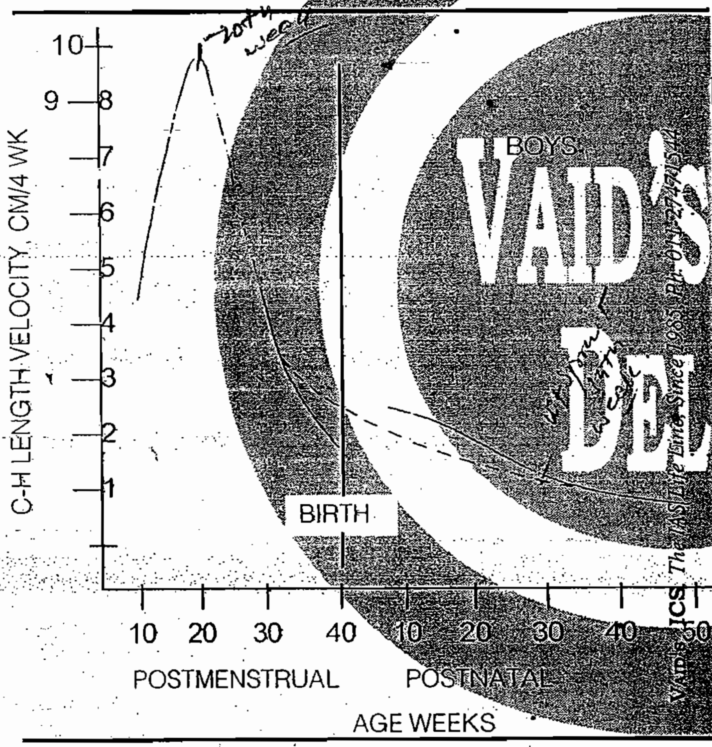
PRENATAL GROWTH

THE velocity curve of growth in height begins a considerable time before birth. Graph below shows the distance and velocity curves for body length in the prenatal period and first postnatal year. The peak velocity of length is reached at about 18 weeks post menstrual age. (Age in the foetal period is usually reckoned from the first day of the last menstrual period, an average of 2 weeks prior to actual fertilization, but as a rule the only locatable landmark.)

GROWTH in weight in the foetus follows the same general pattern except that the peak velocity is reached later, usually at the 34th post-menstrual week. From about 36 weeks to birth (at 40 weeks), the rate of growth of the foetus slows down particularly, due to the influence of the maternal uterus, whose available space is by then becomes fully occupied. Twins' growth slows down earlier, when their combined weight is approximately the 36 week weight of the singleton foetus. Birth weight and birth size in general, reflect the maternal environment more than the genotype of the child. The slowing-down mechanism enables a genetically large child developing in the uterus of a small mother to be delivered successfully. Directly after birth the growth rate increases again, particularly in genetically large children, and in weight reaches its peak approximately 2 months after birth.

THE velocity of growth in length is not very great during the first 2 months of foetal life. This is the period of the embryo. During this period, differentiation of the originally homogeneous whole into regions, such as head, arm, and so forth, occurs ('regionalization'), and also histogenesis, the differentiation of cells into specialized tissues such as muscle or nerve. At the same time each region is moulded by differential growth of cells or by cell migration into a definite shape. This process, known as morphogenesis, continues right up to adulthood, and indeed, in some parts of the body, into old age. But the major part of it is completed by the eighth post-menstrual week and by then the embryo has assumed a recognizably human or child-like appearance.



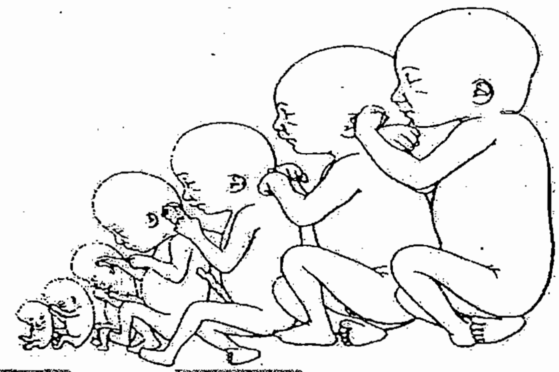


Growth of the Human Embryo and Fetus

Age	Length Crown to Rump	Total Length	Weight
60 days	30 mm	40 mm	5 gm
90 days	55 mm	70 mm	20 gm
120 days	100 mm	150 mm	120 gm
150 days	150 mm	228 mm	300 gm
180 days	200 mm	300 mm	635 gm
210 days	230 mm	350 mm	1,220 gm
240 days	265 mm	499 mm	1,700 gm
270 days	300 mm	450 mm	2,240 gm
280 days	310 mm	470 mm	3,000 gm

BIRTH

AT the end of the gestation period, birth (parturition) occurs. The factors that lead up to the initiation of labour are not fully understood, but it is generally believed that both the mother and the infant participate in the process through the production of chemical messengers that signal the end of the fetal period of life. The size of the fetus, the increase in intrauterine pressure, and limitations in the diffusing capacity of the placenta are all thought to play a part in the termination of pregnancy. The onset of labour itself is the result of increased levels of oxytocin released by the neurohypophysis (the posterior part of the pituitary gland).



Development of the Human (3-8 months) foetus

THE TRAUMA OF BIRTH

FOLLOWING explusion from the uterus, the fetus is forced to make a number of major physiological adjustments in a very short time. The lungs must fill with air and the umbilical veins and arteries are lost, terminating the flow of oxygenated blood from the placenta. With the increased flow of blood to the lungs, the work load of the heart, particularly the part of the heart that supplies the lungs, increases. Because oxygenated blood begins to flow to the heart from the now functional lungs, the separation of oxygenated from nonoxygenated blood becomes important. In normal births, the opening between the atria, or blood-collecting chambers of the heart, is cloased, and the membrane covering the opening (the roramen ovale) ultimately fuses permanently to the interatnal wall. Also, the blood vessel that had, during feal life, short-circuited the flow of blood from the heart to the lungs, the *ductus arteriosis*, is closed off by the first surges of blood into the expanded lungs. These fundamental physiological changes are, not surprisingly, accompanied and in part fiacilliated, by the baby's first cry.

NEONATAL LIFE - THE FIRST 4 WEEKS

REFLEXES

THE newborn human is helpless in many respects, but it enters the world equipped with a set of reflexes that help it to survive. These reflexes are conventionally checked by the attending physician to assess the infant's neurological development (Lowrey, 1978). One of the earliest reflexes to appear is the infants and in all but the smallest premature infants. Newborns will not only suck vigorously on a fingertip placed in their mouths, but they will also turn their heads in the direction of a light touch on the cheek. This is called the "*rooting reflex*", which combined with the sucking reflax allows the newborn to find and feed from the mother's breast. Another reflex present by the end of a normal gestation is the *Moro reflex*, which is an embracing motion of the arms in response to removal of support for the head when the baby is lying on its back. Newborns also reflexively "walk" when supported vertically with the soles of the feet on a flat surface and moved slowly forwards. If the outside of the sole of a full-term infant's foot is stroked from heel to toe while the baby is lying on its back,

rooting reflex | moro reflex

the big toe will curl downward. This is called the *Babinski reflex*. An object placed in the hand of a full-term newborn will stimulate a grasp sometimes so strong that the baby can be lift into the air while holding on to an adult's tuhumbs. Normal newborn can also blink, sneeze, cough, and gag, all reflexive responses that can protect them from eye damage, choking, and asphyxiation.

1. Infancy

At birth, the average human infant weights about 3-3.4 kilograms (7.5 pounds) and is about 51 centimeters (20 inches) long. Full-term females are somewhat lighter and slifhtly shorter than full-term males. Its proportions differs from those of any later time in life. Its head and neck make up 25% normally seen in the adult. The newborn's arms are weak and poorlyl developed, and its legs are even more poorly developed. Whereas the lower limbs represent about half of the total length of the adult, they are only about a third of the newborn's length, and their tendency to be drawn up against the baody makes themappear even shorter. Approximately 72% of the newborn's weight is water, as compared to about 60% in the adult. Of the total body water, the newborn has 37% inside its cells, compared to 58% in the adult. Extracellular fluid decreases continuously throughout the growth process. Table below shows the relative sizes of body parts at several ages upto adulthood.

Percent of Total Body Length of Major Sectors at various ages

Age	Head and Neck	Trunk	Upper Limbs	Lower Limbs
Birth	30	45	10	15
2 yrs	20	50	10	20
6 yrs	15	50	10	25
Adult	10	50	10	30

THE human newborn's disproportionately large head reflects the greater maturity of the head, or cephalic end, of the embryo and fetus compared to teh tail, or caudal end. This difference in maturity, called the cranial-caudal gradient, is an important aspect of preantal human growth since it results in the presence of a large and relatively well-developed brain early in life. At birth the brain represents from 10 to 12% of the total body mass compared to 2% of the total body mass at adulthood. The newborn's brain is a rapidly growing organ that will double its weight during the first year of life and will approximate adult size (about triple its wieght at birth) by around age 10. Under normal circumstances, the infant's total body weight will double in the first 5 months, will have tripled by the end of the first year and will be about ten times birth weight by around age 10.

Postnantal growth of the brain takes place through the increase of cell size with virtually no increase in cell number. Important changes in brain function arise from the lengthening of cell processes of the nerve cells (neurons) and the establishment of connections (synapases) between neurons. One of the features that distinguishes the human brain from that of other mammals is the large number of synoptic connections present and the development of major associative areas where information derived from several sensory channels and from memory is integrated and processed through numerious synpases. In addition to the increase in the length of neurons and the establishment of complex areas of association, the brain also grows by the addition of insulating sheaths of myelin, a fatty substance produced by specialized cells. The myelinization process therefore enables the increasingly sophisticated areas of association in the maturing brain to receive more information faster than would be possible if neurons were unshealthed.

OTHER organs besides the brain grow rapidly during the first year of life. Most impressive is the growth of the thymus, a gland located in the chest behind the sternum, or brease bone. The thymus achieves about 40% of its adult weight in the first year of life. It will continue to grow rapidly untill about the age of 12 years, when it is usually about double the size it will be at age 20. The thymus gland is a very important component of the developing immune system, playing a major role in the "education" of T-cells, which are crucial to the defense against many infections as well as cancers.

DURING the first year of life, both head circumferences and chest circumferences will increase by about one third. In a normal, well-fed baby, chest circumference will exceed head circumference for the first time at around the sixth month. In poorly fed or sickly babies, this may not happen until much later, a fact that is often used to assess the nutritional status of infants.

HEIGHT or length increases by about 50% during the first year of life, although the rate of heifht increase (growth velocity) actually declines from shortly after birth until the onset of the adolescent growth spurt. The most rapid increase in length had occurred in mid-gestation, when for a short time the fetus was growing at a rate of 11 centimeters a month.

CHILDHOOD

CHILDHOOD for the most part is characterized by rapid neurological development and gradual increases in organ sizes, height and weight. Following the attainment of upright posture at around 1 year of age, the infant progresses to the toddler stage during which neuromuscular control improves steadiyl. Learning to speak is also a major milestone for the toddler. Some students of human growth and development believe that the refllexes present at birth form the foundations for both neuromuscular and intelectual development, with the increasing recruitment of neurons and the addition of synapses underlying both processes. There is little doubt that the human child processes, stores and analyzes a remarkable amount of information each day. One aspect of that processing, the acquisition and use of language, is an impressive accomplishment that is still not fully understood.

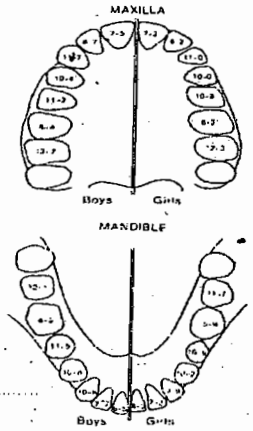
THE rate at which neurological development takes place varies considerably from one individual to another, just as physical growth does. It also appears that the process can be retarded, perhaps with long-term consequences, when serious deprivation, trauma, or disease intrudes. As mentioned previously, the human brain attains adult size by about 10 years of age. In this area of growth, as in al others, the average female is closer to the completition of growth than the average male of the same age. This sex difference in maturity is already present at birth and remains about 10% up to and including the occurence of sexual maturation and the final cessation of growth. Thus, the part of the life cycle that we have designated "*childhood*" is of greater duration in boys than in girls. Differences in size and proportion that characterize male and female adults are largely the result of the longer period of childhood grown that boys experience.

Vocabulary Development of Children upto 6 year of age

Year	Month	Number of Words
1	0	3
1	3	19
1	6	22
2	0	272
2	6	446
3	0	896
3	6	1222

4	0	1540
5	0	2072
6	0	2562

The most noticeable changes that childhood growth produces are those of increased height and increased length of the legs. Children grow by increasing the length of the long bones of the legs and arms and by increasing the height of individual vertebrae. Growth is called epiphyseal growth because it involved the presence of epiphyses, the growing ends of long bones separated from the shaft by a cartilanginous plate.



Eruption times (in years and months) of the permanent dentition of girls and boys

Eruption times (in years and months) of the permanent dentition of girls and boys

Although the predominant factor in the increase in height during childhood is the growth of the long bones of the lower limbs, the spine increases in length as well. Each vertebrae increases in height through growth occuring at the annualr epiphyses. This aspect of grown is slow and persistent, and the last epiphyses to close are generally those of the thoracic vertebrae. As a consequence of the sequencing of epiphyseal closured, growth of the spine persist after growth of the legs has stopped, and the sitting height will make up a larger proportion of total height in the adult than was the case in the childhood.

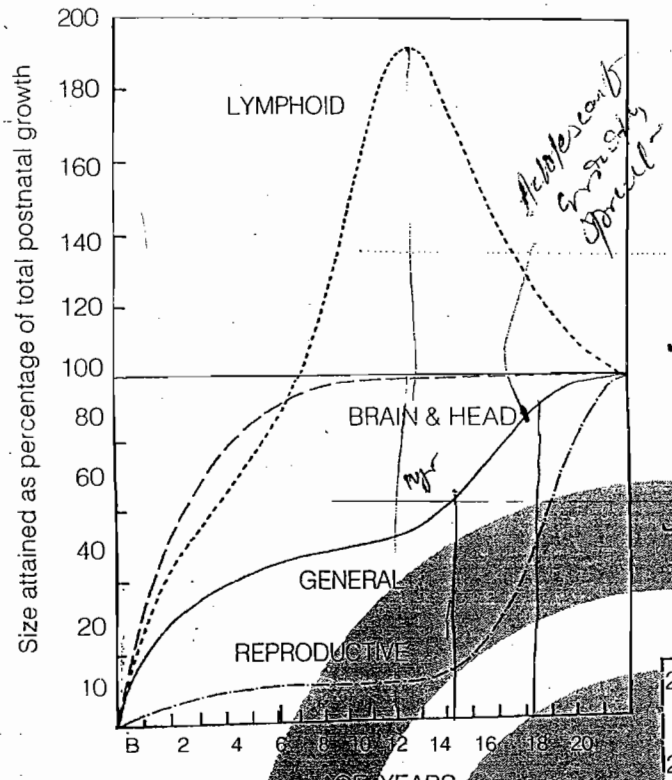
THE skull, mandible, and dention also undergo major changes during childhood growth. By age 10, the size of the skull is nearly that of an adult, but much change will take place in the face and jaws later. The eruption of the decidous (or milk) teeth begins during the first year of life, and some of the permanent teeth (the 6-year molars) appear in mid-childhood.

GROWTH OF DIFFERENT TISSUES AND DIFFERENT PARTS OF THE BODY

MOST skeletal and muscular dimensions follow approximately the growth curve described for height. So also do the dimensions of organs such as the liver, spleen, and kidneys. However, there are other tissues which have curves sufficiently different to need description. These are the brain and skull

Pattern of Normal Language Development

Age	Vocalization and Speech	Response and Comprehension
1 month	Much crying and whimpering; produces some vowel and few consonant sounds.	Smiles; decreases activity; startles at loud sounds.
3 months	Different cries for pain, hunger, and discomfort; decreased crying time;some repetitive sounds ("*ga, ga, ga*"); coos and sighs	Vocal gurgle in response to soothing voice, some imitative response to speech.
5 months and	Bables; vocal play; many repetitive sounds; all vowels, m, k, g, b and p; laughs out loud	Imitative response to speech decreased; turns looks to sound; recognizes familiar voice; voccalizes displeasure.
7 months	Considerable variety in babbling, loundness and rhythm of all vocalizations; adds d, t, n, and w to repertory of sounds; talks to toys.	Gestures increase as part of vocal responses to stimuli; response to sound is increasingly influenced by visual factors.
9 months	Cries to get attention; increasing variations in pitch; "*mama*", "*data*"and "*baba*" part of vocal play but not asociated with a person or object.	Retreats from strangers, often accompanied by crying may limitate hand clapping.
11 months	May use one word correctly; imitatives sounds and correct number of syllables; little crying.	Comprehends "no no"; responds to "bye-bye" or "pritty-cake" with appropriate gestures.
1-2 years	Much unintelligible jargon; all vowels present; improves articulation so that 25% of words intelligible; names many objects by 24 mo; much echolalia.	Recognizes 150-300 words by 24 months responds correctly to several commands, ("sit down", give me that", stand up", come here", and so on).
2-3 years	Tries new sounds but articulation lags behind vocabulary; 50-75% of words intelligible; often omits final consonants; jargon nearly absent.	Comprehends 800-1,000 words by 3 years, responds to many commands using "on", "under", "up" and so on.
3-4 years	Speech nears 100% intelligibility; faulty articulations of l and r frequent; uses 3-4 worlds in sentences; uses a few	Recognizes plurals, sex differences, adjectives and adverbs; comprehends complex sentences.



the reproductive organs, the lymphoid tissue, and the subcutaneous fat.

THE graph below shows the size attained by various tissues, as a percentage of the birth to maturity increment. Height and the majority of body measurements follow the 'general' curve. The reproductive organs, internal and external, follow a curve which is perhaps not very different in principle, though strikingly so in effect. Their prepubescent growth is slow and their growth at adolescence very rapid; they are less sensitive than the skeleton to one set of hormones and more sensitive to another.

THE brain, together with the skull covering it and the eyes and ears, develops earlier than any other part of the body. It thus has a characteristic postnatal growth curve. At birth it is already 25 percent of its adult weight; at age 5 years, 90 percent; at age 10 years, about 95 percent. Thus, if the brain has any adolescent spurt at all it is a very small one. A small but definite spurt occurs in head length and breadth, but all or most of this is due to thickening of the skull bones and the scalp together with development of the air sinuses. The face follows a curve midway between that of the top portion of the skull and the remainder of the skeleton. At birth it is nearer its mature dimensions than is body-length, but it has still a considerable adolescent spurt, which is greatest in the mandible. Thus, the head as a whole is more advanced than the remainder of the body, and the top part of it, that is, the eyes and brain, are more advanced than the lower portion, that is, the face and jaw.

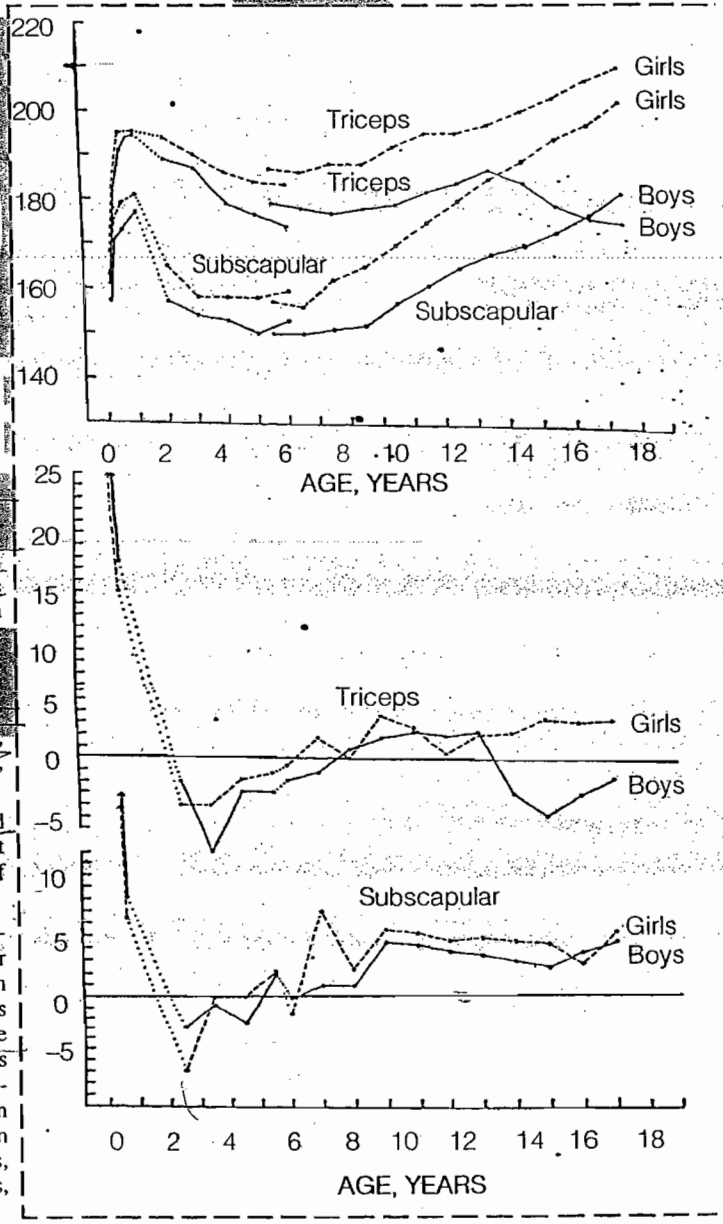
THE lymphoid tissue, of tonsils, adenoids, appendix, intestine, and spleen, has quite another growth curve. It reaches its maximum amount before adolescence, and then, probably under the direct influence of the sex hormones, declines to its adult value.

THE subcutaneous fat layer has also a curve of its own, and a somewhat complicated one. Its width can be measured either by X-rays or by specially designed calipers applied to a fold of fat pinched up from the underlying muscle. The distance and velocity curves of skinfolds taken on the back of the arm over the triceps muscle, and under the angle of the scapula, are shown in graphs on next page. Subcutaneous fat begins to be laid down in the foetus at about 34 weeks and increases from then until birth, and from birth until about 9 months (in the average child: the peak may be reached as early as 6 months in some and as late as a year or 15 months in others). From 9 months, when the velocity is thus zero, the subcutaneous fat decreases, that is, has a negative velocity, until age 6 years to 8 years, when it begins to increase once again.

IT MUST be noted that we have discussed the width of the fat layer; a decrease in this width does not necessarily imply a decrease in the cross-sectional area of fat. The fat is a ring around a musculo-skeletal centre which is itself increasing at all ages; if the cross-sectional fat area stayed constant the width of the ring would be reduced simply by enlargement of the musculo-skeletal core. However, calculations from measurements of fat on X-rays show that the cross-sectional area does in fact decrease during these early childhood years. The decrease is less in girls than boys, so that after age 1 year girls come to have more fat than boys.

THE increase from age 7 years or so occurs in both sexes, in measurements of both limb-and body-fat. At adolescence, however, the limb-fat in boys decreases and is not gained back until the age of about 20 years. In boys' trunk-fat a much smaller loss, if any at all, occurs; there is only a temporary half to the gradual increase. In girls there is a slight halting of the limb-fat increase, but no loss and the trunk-fat shows a steady rise until the age of discretion is reached.

BECAUSE body-weight represents a mixture of these various tissues its curve of growth is often less informative than those of its component parts. In general, however, individual velocity curves of weight follow a similar course to the height curve. Though to some extent useful in



following the health of a child, weight has the severe limitation that an increase may signify growth in bone and muscle, or merely an increase in fat. Similarly, failure to gain weight in the older child may signify little except a better attention to diet and exercise, whereas failure to gain height or muscle would call for immediate investigation.

POST-ADOLESCENT GROWTH

GROWTH of the skeleton does not entirely cease at the end of the adolescent period. In man, unlike some other mammals such as the rat, the epiphyses of the long bones close completely and cannot afterwards be stimulated to grow again. However, the vertebral column continues to grow from age 20 to 30 years by apposition of bone to the tops and bottoms of the vertebral bodies. Thus, height increases by a small amount, on average 3-5 mm, during these years. From the age of 30 to 45 or 50 years it remains stationary, and then begins to decline. The timing suggests that androgenic hormones may be of importance in maintaining this growth, as they are in stimulating the vertebral column growth at adolescence.

FOR practical purposes, however, it is useful to have an age at which one may say that growth in stature has virtually ceased, that is, after which only some 2 percent is added. Longitudinal records indicate that an average figure for this is currently about 17.5 years for boys and 16.0 years for girls, which a normal variation for different individuals of about 2 years either side of these averages.

MOST head and face measurements continue to increase after adolescence steadily, though very slowly, to at least age 60 years. The increase from 20 to 60 years amounts to between 2 percent and 4 cent of the 20-year-old value.

SENESCENCE

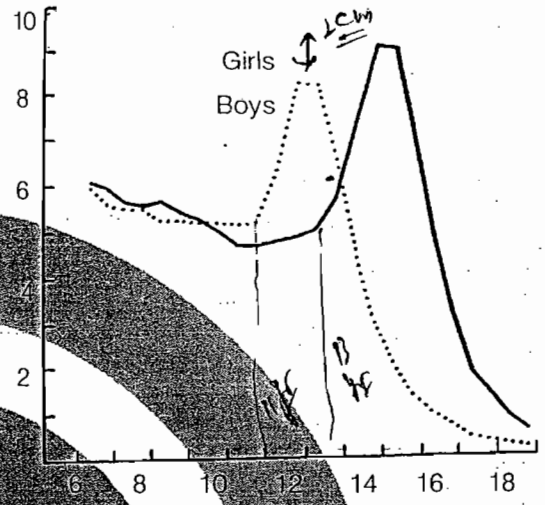
OLD AGE and senescence follow the prime years of adulthood. The aging period is one of gradual, or sometimes rapid, decline in the ability to adapt to environmental stress. The pattern of decline varies greatly between individuals. Though specific molecular, cellular, and organismic changes can be measured and described, not all of these occur in all people and rarely do they follow a well-established sequence. Loss in terms of elasticity of skin, vision memory, heart functioning, lung functioning etc. have been attributed to senescence in many studies. But studies with contrary and contradictory observations are alos available. This suggests that, unlike the biological self-regulation of growth prior to adulthood, there is no biological or genetic plan for the aging process. There are many theories about the aging process and about why we must age all. One theory with empirical experimental support links aging with the limited mitotic (Cell duplication) ability of hyperplastics cells Hayflick (1980) found that when raised in tissue cultures human embryo hyperplastic cell lines double in number by mitotic division only 50 (+ 10) times and then die. Tissue cultures of cells from adult humans have an even more limited mitotic potential, doubling only 14 to 29 times before dying. This doubling limit of hyperplastics cells provides a theoretical limit to life in practice, few people ever reach this limit. Rather, the inability of all cell types, including nerve, muscle and other non-replicating cells, to use nutrients and repair damage begins before the cells die. Undoubtedly, aging is a multi-causal process. The reason why there is no biological plan or developmental sequence for aging may be because there is no biological reason to age in any particular way it is only recemt;u, in the evolutionary history of our species, that human populations have come to live past the prime adult years. Throughout prehistory, death by predation, disease and traume caused by violence and accidents was probably more common than death due to old age. Death is inevitable, but nature did not have the time or the selection pressures to mold our manner of death into a predictable pattern.

RECENT researches have demonstrated that brain cells keep replicating even in the old age and damaged *is'ets of Langernans* can regenerate themselves. White the gene for aging has been identified only recently further information is still awarded.

GROWTH AT ADOLESCENCE

THE adolescent growth spurt is a constant phenomenon and occurs in all children, though it varies in intensity and duration from one child to another. The peak velocity of growth in height averages about 10 cm a year in boys, and slightly less in girls. In boys the spurt takes place on the average between 12 and 15 years of age, and in girls some 2 years earlier.

THE sex difference can be seen in figure on next page which shows the velocity curves for a group of boys who have their peak velocity



between 14 and 15, and a group of girls with their peak between 12 and 13. The difference in size between men and women is to a large degree due to differences in timing and intensity of the adolescent spurt; before it boys and girls differ only by some 2 percent in height, but after it by an average of about 8 percent.

THE difference partly comes about because of the later occurrence of the male spurt, allowing an extra period for growth, even at the slow prepubertal velocity, and partly because of the greater intensity of the spurt itself. In absolute terms the adult sex difference is around 13 cm, of which 2 cm are due to prepubertal growth, 7 cm to the later occurrence of the male spurt, and 4 cm to the greater intensity of the spurt.

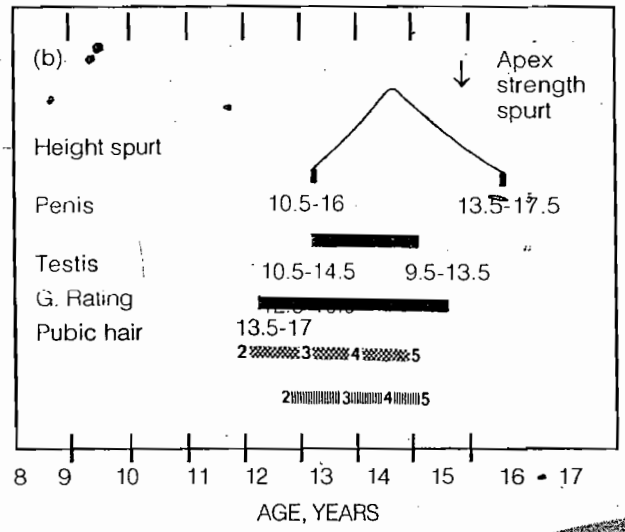
PRACTICALLY all skeletal and muscular dimensions take part in the spurt, though not to an equal degree. Most of the spurt in height is due to trunk growth rather than growth of the legs. The muscles appear to have their spurt about 3 months after the height peak; and the weight peak velocity occurs about 6 months after the height peak.

THE heart has a spurt in size no less than the other muscles, and other organs accelerate their growth also. Probably even the eye, the most advanced of any organ in maturity and thus the one with least growth still to undergo, has a light spurt, to judge from the particularly rapid change towards myopia (short-sightedness) which occurs around this age. The degree of myopia increases continuously from age 6 or earlier till maturity, but this accelerated rate of change at puberty would be most simply accounted for by a fractionally greater spurt in axial than in vertical diameters.

SEX DIFFERENCES

MANY of the sex differences of body size and shape seen in adults are the result of differential growth patterns at adolescence. The greater general size of the male has already been discussed. The greater relative widths of shoulders in the male and hips in the female are largely due to specific stimulation of cartilage cells, by androgens in the first instance and oestrogens in the second. The greater growth of the male muscles also results from androgen stimulation, as do some other physiological differences mentioned below.

NOT all sex differences develop in this way. The greater length of the male legs relative to the trunk comes about as a consequence of the longer pre-pubescent period of male growth, since the legs are growing faster than the trunk during this particular time. Other sex differences



begin still earlier. The male forearm is longer, relative to the upper arm or the height, than the female forearm; and this difference is already established at birth, and increases gradually throughout the whole growing period. It is probably caused by the laying down in early foetal life of slightly more tissue in this area in the male, or of slightly more active tissue. It occurs in some other primates, as well as in man.

A SIMILAR mechanism may be responsible for the sex difference in relative lengths of second and fourth fingers. The second finger is longer than the fourth more frequently in females than in males, and this difference is also established before birth. The most striking of all the prepuberty sex differences, however, is the earlier maturation of the female.

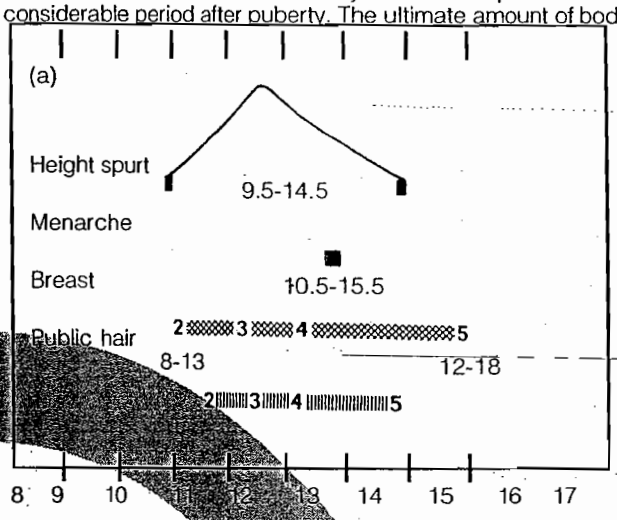
DEVELOPMENT OF THE REPRODUCTIVE SYSTEM

THE adolescent spurt in skeletal and muscular dimensions is closely related to the rapid development of the reproductive system which takes place at this time. The events of adolescence in the male are outlined below diagrammatically.

The solid areas marked 'penis and testis' represent the period of accelerated growth of these organs, and the horizontal lines and rating numbers marked 'public hair' stand for its advent and development. The sequences and timings represent in each case the average value. To give an idea of the individual departures from this, figures for the range of ages at which the spurts for height, penis, and testis growth begin and end are inserted under the first and last points of the curves or bars. The acceleration of penis growth, for example, begins on average at about age 12½ years, but sometimes occurs as early as 10½ years, and sometimes as late as 14½ years. There are thus a few boys who do not begin their spurts in height or penis development until the earliest maturers have entirely completed theirs. At age 13 and 14 there is an enormous variability in development amongst any group of boys, who range practically all the way from complete maturity to absolute pre-adolescence. The fact raises difficult social and educational problems and is itself a contributory factor to the psychological maladjustment sometimes seen in adolescence.

THE *sequence* of events is much less variable than the age at which they take place. The first sign of puberty in boys is an accelerated growth in testes and scrotum. Slight growth of public hair may start at about the same time, but proceeds slowly until about the time the height and penis simultaneously accelerate, when it also grows faster. This is usually about a year after the first testicular acceleration. The testicular growth is mainly due to increase in size of the seminal tubules; the androgen-producing Leydig cells appear to develop more or less simultaneously.

AXILLARY hair usually first appears about 2 years after the beginning of pubic hair growth, though there is sufficient individual variability so that in a very few children axillary hair actually precedes public hair in appearance. In boys facial hair begins at about the same time as axillary hair. An increase in length and pigmentation occurs first in the hair at the corners of the upper lip, then spreads medially. Hair next appears on the upper part of the cheeks and in the midline just below the lower lip, and finally along the sides and lower border of the chin. The remainder of the body-hair appears from about the time of first axillary hair development until a considerable period after puberty. The ultimate amount of body-



hair an individual develops seems to depend largely on heredity, though whether because of the kinds and amounts of hormones secreted or because of the reactivity of the end-organs is not known.

THE enlargement of the larynx in boys occurs at about the time the penis growth is nearing completion. The voice change is a gradual one and is often not complete until adolescence is practically over. In boys at adolescence there are frequently some changes seen in the breast: the areola enlarges in diameter and darkens. In some boys—about a third of most groups studied—there is a distinct enlargement with projection of the areola and the presence of firm subareolar mammary tissue. This occurs about midway through adolescence and lasts from a year to 18 months, after which in the majority of boys the mound and tissue disappear spontaneously.

SPERM begin to appear in early morning urine samples on average a few months after peak height velocity; but in some boys sperm appear somewhat earlier than this. Whether they are fully functional during the first year or two after their appearance is doubtful.

AS IN BOYS, there is a large variation in the time at which the spurt begins in females (shown above) though the sequence of events is fairly constant. The appearance of the breast-bud is as a rule the first sign of puberty, though the appearance of pubic hair may sometimes precede it. The uterus and vagina develop simultaneously with the breast. Menarche (the first menstrual period) occurs almost invariably after the peak of the height spurt has been passed.

MENARCHE marks a definitive and probably mature stage of uterine development, but it does not usually signify the attainment of full reproductive function. The early menstrual cycles frequently occur without an ovum being shed; during the first year or two after menarche there is a period of relative infertility, characteristic of apes and monkeys as well as the human. In one study, 75 percent of cycles during the first 2 years after menarche were anovulatory, and during the subsequent 2 years still 50 percent. Two years later the figure was down to 25 percent.

FACTORS CONTROLLING GROWTH

PRENATAL PERIOD

GENES on the Y-chromosome cause the previously undifferentiated

divided b/w hereditary / Environmental factor.

gonad to become a recognizable testis at the ninth week of foetal age, reckoned post-menstrually (or seventh week post-fertilization). Whether this is the result of hormonal action is at present uncertain. At the eleventh post menstrual week *Leydig cells appear in the testis and by the twelfth week they secrete testosterone or an allied substance, probably under the influence of chorionic gonadotrophin, which reaches a peak in the mother's urine at this time (where its presence is used as the standard test for pregnancy).* The testicular hormone causes the previously undifferentiated external genitalia to form a penis and scrotum. In the female, it seems that differentiation of the ovary and external genitalia proceeds more passively. In the absence of the Y-chromosome, nothing happens at the ninth week and at *about the tenth post-menstrual week the gonad turns into an ovary. The external genitalia become female at around the fourteenth week, apparently without hormonal intervention.*

THE prenatal role of other endocrine glands is somewhat uncertain. *Maternal oestrogen passes across the placenta and causes the uterus of newborn girls to be temporarily enlarged at birth.* Thyroid hormone is necessary for the normal development of the brain, and is secreted by the foetal gland. The adrenal gland has a special zone which is well developed at birth and regresses soon afterwards; its significance and its cause, however, are still matters of debate.

POSTNATAL PERIOD

THE most important hormone controlling growth from birth up to adolescence is *somatotrophin or growth hormone.* This is a polypeptide secreted by the pituitary and showing a greater degree of species (or rather order) specificity than other pituitary hormones. Thus, only human or monkey hormone has a growth-stimulating effect in man.

THOUGH growth hormone is present in the foetus it is not necessary for foetal growth. From birth onwards, however, it is essential if a normal rate of growth is to occur. By the age of 2½ children with isolated growth hormone deficiency are recognizably smaller than normal (though in fact they seldom are recognized till age 5 or later when they go to school, or when younger siblings come to surpass them in height).

GROWTH hormone does not itself cause the epiphyses to grow. It causes growth by stimulating an increase in cartilage-generating cells and by making them secrete another hormone called Somatomedin C or Insulin like Growth-Factor I. It stimulates the liver also to produce Somatomedin. C which is also a peptide but of smaller size than growth hormone. The administration of growth hormone to a person who lacks it causes growth of muscle with increased incorporation of amino acids into tissues to form protein. It also causes diminution of the amount of adipose tissue, shifting the metabolic balance from the laying down of fat to the laying down of protein. Thus, children who lack the hormone are fat as well as small.

THE secretion of growth hormone, like that of other pituitary hormones, is controlled by the hypothalamus. There are two hypothalamic hormones concerned, a stimulator called growth-hormone releasing factor (GRF) and an inhibitor called somatostatin. Both are relatively small peptides. The exact way in which they interact is not yet entirely clear.

GROWTH hormone is secreted in pulses throughout the 24 hours of the day, not continuously. Exercise, anxiety, and sleep regularly cause secretion, but other factors are uncertain. Under normal circumstances some six or eight pulses occur each 24 hours. The amplitude, and perhaps the frequency of pulses increases at puberty, contributing to the adolescent growth spurt. It is at present not clear whether shortness and tallness within the normal range are caused by differences in amounts of somatomedin but much more probably in amounts or characteristics of receptors in the cartilage cells.

THYROID hormone plays a vital role throughout the whole of growth. The activity of the thyroid, judged by the basal metabolic rate, decreases gradually from birth to adolescence, at which time it probably increases, or at least falls less rapidly, for a year or so. So far as rate of growth in size is concerned, the action of the thyroid is permissive and not controlling. In hypothyroidism growth is delayed; skeletal maturity, dental maturity, and growth of the brain are all affected.

THOUGH clearly the normal mechanism controlling the rate of skeletal maturation must be hormonal, the balance of hormones is not yet clear. Lack of thyroid hormone and lack of growth hormone both cause retardation; sex hormones and adrenal androgens cause advance. Small quantities of sex hormones and adrenal androgens circulate in the blood before adolescence, but what part variations in their amount play in controlling tempo of growth is quite unknown.

PUBERTY

AT ADOLESCENCE a relatively new phase of growth occurs in which hormones from the gonads combine with growth hormone to produce the adolescent spurt. It seems that a full spurt is dependent on both sets of hormones being present; boys with growth hormone deficiency have a spurt only reaching about half the normal peak velocity.

TWO out of the three major groups of hormones produced by the adrenal circulate in the blood at relatively unchanged levels from birth onwards; these are cortisol and aldosterone, the latter being the hormone which maintains within acceptable limits the concentrations of electrolytes in the tissue fluid.

THE third group of adrenal hormones, the androgens, appears in quantity only in mid-childhood, at the time of the mid-growth spurt. Androgens increase gradually from about age 7 until puberty begins, when their rate of increase about doubles. What part they play in the body's economy is uncertain; it seems likely to concern muscular function. However, testosterone is the major cause of the increase in size and strength of the male muscles at adolescence, and of the increase in number of red blood cells.

THE sequence of endocrine events at puberty is fairly clear, though rather complicated. The sequence is initiated by events in the hypothalamus. Before puberty the pituitary contains gonadotrophins, or can manufacture them, but does not release them to the general circulation because it is not stimulated by the hypothalamus to do so. Gonadotrophin release is caused by a releasing substance, luteinizing hormone releasing hormone (LHRH), an octapeptide which is synthesized in the cells of the arcuate nucleus of the hypothalamus and reaches the pituitary via the hypophysial-portal system of blood-vessels. It is the hypothalamus that carries the information as to maturity, not the pituitary. At the 'correct' stage of bodily maturity the hypothalamus matures in some way and LHRH is released.

THE way in which this happens has a general importance for the clarification of developmental mechanisms. In the neonatal period there is a feedback system already established and in operation whereby the levels of circulating testosterone (in boys) and oestrogen (in girls) inhibit the hypothalamic neurons which secrete LHRH and thus reduce the initially high gonadotrophin level. Thereafter, throughout childhood, this system seems to go into cold-storage; the arcuate nucleus goes to sleep, apart from a very occasional burst. Then, at puberty, something wakes up the arcuate, LHRH is secreted, gonadotrophins are released, at first only at night and subsequently in bursts throughout the 24 hours. The gonads respond by secreting sex steroids and these now re-establish the original feed-back system. Just what causes the awakening of the arcuate nucleus remains a mystery. Clearly, we are dealing with some sort of internal clock, but one dependent on the passage of numerous prior events in the organism and not simply dependent on chronological nor even wholly on developmental time.

THE reason for the increase of adrenal androgens at puberty is less clear. Since cortisol continues to be secreted at pre-adolescent rates it is unlikely that adrenocorticotrophic hormone secretion is increased at puberty. It seems likely that there is a specifically adrenal-androgen-stimulating pituitary hormone, not yet isolated.

MUCH else remains obscure. The cause of the pre-adolescent increase in fat is unknown, though its timing seems to

coincide with the fast increase of adrenal androgen. Though we are beginning to understand the delicate linkage of the hormonal events of adolescence, detailed knowledge will have to wait upon longitudinal studies conducted with the more sensitive chemical and biological methods that have recently become available.

The Interaction of Heredity and Environ-ment in Controlling Growth Rate

MANY factors that affect the rate of development are known. Some are hereditary in origin and act by hastening or retarding physiological maturation from an early age. Others, such as dietary restriction, season of the year, or severe psychological stress, originate in the environment and simply affect the rate of growth at the time they are acting. Others again, such as socio-economic class, reflect a complicated mixture of hereditary and environmental influences.

THE height, weight, or body-build of a child or an adult always represents the resultant of both the genetical and environmental forces, together with their interaction. It is a long way from the possession of certain genes to the acquisition of a height of 2 m. In modern genetics it is a truism that any particular gene depends for its expression firstly on the internal environment created by all the other genes and secondly on the external environment. Furthermore, the interaction of genes and environment may not be additive. That is to say, bettering the nutrition by a fixed amount may not produce a 10 percent increase in height in all persons irrespective of their genetical constitutions; instead a 12 percent rise may occur in the genetically tall and an 8 percent rise in the genetically short. This type of interaction is called 'multiplicative'. In general a particular environment may prove highly suitable for a child with certain genes and highly unsuitable for a child with others. Thus it is very difficult to specify quantitatively the relative importance of heredity and the environment in controlling growth and physique under any given circumstances; the particular circumstances must always be made clear. In general the nearer optimal the environment the more the genes have a chance to show their potential actions; but this is an overall statement only and undoubtedly many more subtle and specific interactions occur, specially in growth and differentiation.

GENETIC factors, however, are clearly of immense importance. The fundamental plan of growth is laid down very early in the comparative safety of the uterus. An immature limb-bone removed from a foetal or newborn mouse and implanted under the skin of the back of an adult mouse of the same inbreed strain (which therefore produces no antibodies to it) will continue to develop until it closely resembles a normal adult bone. Furthermore the cartilage scaffolding of the bone, removed at the stage preceding actual bone formation, will do the same. Thus, the structure of the adult bone in all its essentials is implicit in the cartilage model of months before. The later action of the bone's environment, represented by the muscles pulling on it and the joints connecting it to other bones, seems to be limited to the making of finishing touches.

GENETICS OF GROWTH

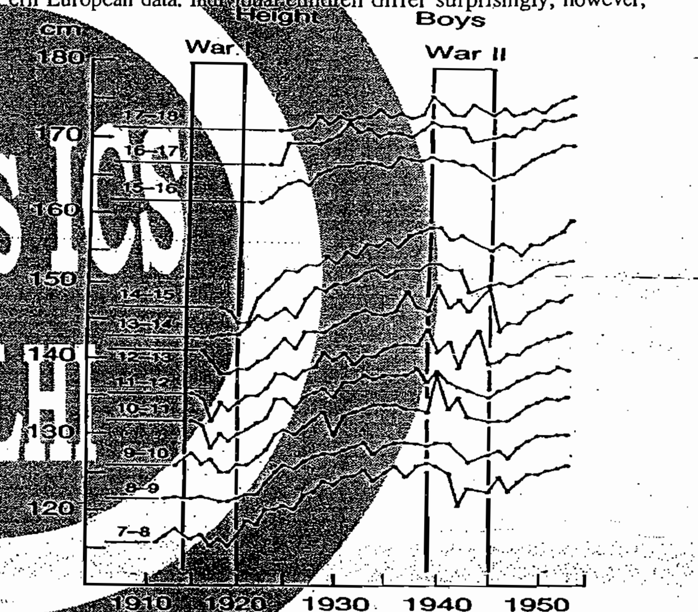
THE genetical control of tempo of growth is manifested most simply in the inheritance of age at menarche. Identical twin sisters reach menarche an average of 2 months apart; non-identical twin sisters an average of 10 months apart. The correlation coefficient between age at menarche of mother and daughter is about 0.4, only slightly lower than similar correlations for height. These are indications that a high proportion of the variability of age at menarche in populations living under European conditions is due to genetical causes. The inheritance of age at menarche is probably transmitted as much by the father as by the mother, and is due not to a single gene, but to many genes each of small effect. This is the same pattern of inheritance as that shown by height and other body measurements.

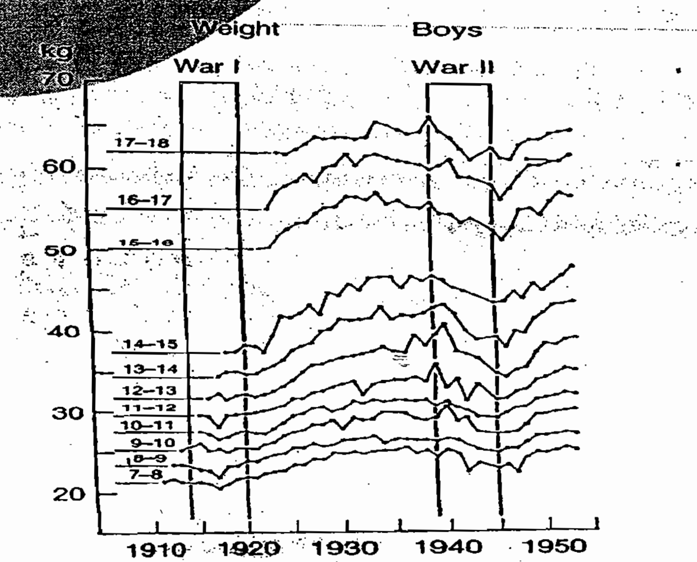
THE genetical control operates throughout the whole period of growth; skeletal maturity shows a close correspondence at all ages in identical twins. The time of eruption of the teeth, both deciduous and permanent, and also the sequence in which teeth calcify and erupt, is largely determined by heredity. Genes controlling growth range all the way from those affecting rate of growth of the whole body, probably through endocrine mechanisms, to those bringing about a highly localized growth gradient causing one tooth to erupt before another, or one ossification centre in the wrist to appear before another.

NOT all genes are active at birth. Some express themselves only in the physiological surroundings provided by the later years of growth; their effect is said to be 'age-limited'. This is the probable explanation of the curve described by the correlations between measurements of a child at successive ages and his or her measurements as an adult, which have been obtained by long-term longitudinal studies. The correlation of length at birth with adult height is very low, since birth length reflects uterine conditions and not the child's genotype. The child's genes increasingly make themselves felt and the correlation rises steeply during the first 2 years; but after this only a small rise occurs until adolescence. It seems likely that the magnitude as well as the time of the spurt is genetically controlled, perhaps by genes causing the secretion of large or small amount so of androgenic hormones. Such genes may produce no effect until the moment when androgen secretion begins. Certainly, there is a considerable degree of independence between growth before and growth at adolescence.

SEASON OF YEAR

IN MOST data from industrialized countries in temperate areas a well-marked seasonal effect on growth velocity can be seen. Growth in height is on average fastest in spring and growth in weight fastest in the autumn. The average velocity of height from March to May is about twice that from September to October in most of the older western European data. Individual children differ surprisingly, however,





both in the time when their seasonal trend reaches its peak, and in the degree to which they show a seasonal trend at all; in a considerable number little evidence of any seasonal effect is seen. These differences may reflect individual variation in endocrine reactivity.

NUTRITION

MALNUTRITION delays growth, as is shown from the effects of famine associated with war. In the graph given here, the heights and weights of school children in Stuttgart are plotted at each year of age from 1911 to 1953. There is a uniform increase at all ages in both measurements from 1920 to 1940, but in the latter years of the Second World War this trend is sharply reversed.

CHILDREN have great recuperative powers, provided the adverse conditions are not carried too far or continued too long. During a short period of malnutrition the organism slows up its growth and waits for better times. When they arrive growth takes place unusually fast until the genetically determined growth curve is reached or approached once more, and subsequently followed. During this 'catch-up' phase, weight and height and skeletal development seem to catch up at approximately the same rate.

GIRLS appear to be better buffered than boys against the effects of malnutrition or illness. They are less easily thrown off their growth curves, perhaps because the two X-chromosomes provide better regulatory forces than one X- and the small Y-chromosome.

PSYCHOLOGICAL DISTURBANCE

THAT adverse psychological conditions might cause a degree of retardation in growth is a thought that comes readily to mind. In recent years it has been clearly established that in certain children under emotional stress the growth hormone secretion is inhibited and they come closely to resemble cases of idiopathic growth hormone deficiency. However, when taken out of the stressful conditions they begin to secrete growth hormone again and have the usual rapid catch-up growth.

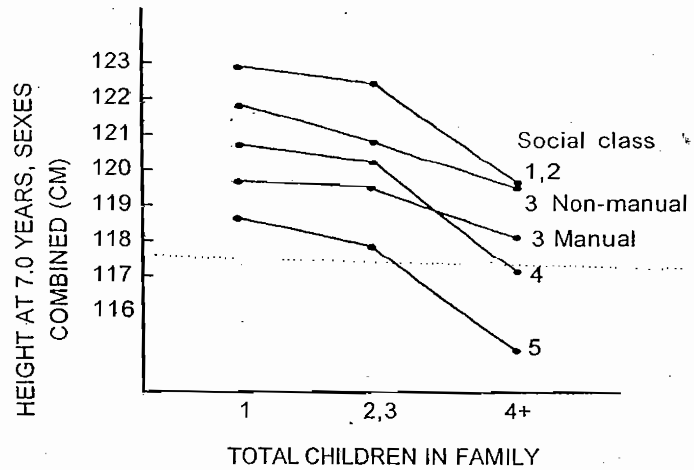
A SIMILAR thing may happen under less extreme circumstances and account for smaller variations in individuals' growth, though good evidence on this is naturally hard to come by. However, one experimental investigation by Widdowson is clearly (one might almost say providentially) controlled.

IN STUDYING the effect of increased rations on orphanage children living on the poor diet available in Germany in 1948 Widdowson had the rare opportunity of observing the change brought about by replacement of one sister-in-charge by another. The design of the experiment was to give orphanage B a food supplement after a 6 months' control period and to compare the growth of the children there with those in orphanage A, which was not to be supplemented. However, the result was just the reverse of that expected: though the B children actually gained more weight than the A children during the first, unsupplemented, 6 months, they gained less during the second 6 months, despite actually taking in a measured 20 percent more calories. The reason appeared to be that at precisely the 6-month mark a certain sister had been transferred from A to become head of B. She ruled the children of B with a rod of iron and frequently chose mealtimes to administer to individual children public and often unjustified rebukes, which upset all present. An exception was the group of eight favourites whom she brought with her from orphanage A. These eight always gained more weight than the others, and on being supplemented in B gained still faster. The effect on height was less than that on weight, but of the same nature.

SOCIO-ECONOMIC CLASS : SIZE OF FAMILY

CHILDREN from different socio-economic levels differ in average body-size at all ages, the upper groups always being larger. In most studies socio-economic status has been defined according to the father's occupation, though in recent years it is becoming clear that in many countries this does not distinguish people's living standards or life-style as well as formerly; an index reflecting housing conditions is becoming a necessary adjunct, as is some measure of the child-centredness of the family budget.

THE difference in height between children of the professional and managerial classes and those of unskilled labourers is currently about 2 cm at 3 years, rising to 5 cm at adolescence. In weight the difference is



relatively less since the lower socio-economic class children have a greater weight for height.

IN FIG. below the heights of a national sample of 7-year-old children from all over Great Britain (those born in one week of 1958) are plotted in relation to socio-economic class and numbers of children in the family. The tendency of the better-off children to be taller is visible in families of all sizes.

SOME of the height difference is due to earlier maturation of the well-off classes, but most persists into adulthood, where the social class difference I/II to V is currently (1990s) about 3 cm in men and 2 cm in women. There is a difference in age at menarche of 2-3 months between daughters of the managerial class and those of unskilled workmen; permanent tooth eruption occurs earlier in the more favoured groups by about the same margin, when all the teeth are averaged.

THE causes of this socio-economic differential are probably multiple. Nutrition is almost certainly one, and with it all the habits of regular meals, sleep, exercise, and general organization that distinguish, from this point of view, a good home from a bad one. Home conditions are more related to the growth differences than are the economic conditions of the families, and home conditions reflect to a considerable degree the intelligence and personality of the parents. Minor illnesses such as measles, influenza, and even antibiotic-treated middle-ear infection or pneumonia cause no discernible retardation of growth in the great majority of well-nourished children, but they may have some effect on relatively ill-cared-for ones. Possibly the greater incidence of such illnesses in the worse-off and more social disorganized families contributes to their reduction in growth rate, though this has not yet been certainly established. Smoking may also play a part. Babies whose mothers smoked during pregnancy average some 100 g and 1 cm smaller than others at birth, and the height deficit, though small, is apparently persistent throughout the whole of childhood. The socio-economic size differential has been getting somewhat less during the last 50 years, as social conditions have improved. In Sweden and Norway it has not disappeared. In all other countries investigated however, including the United States and the United Kingdom, it still persists, being seemingly dependent now more upon home conditions and parents' education than upon simple income.

EVOLUTION, ECOLOGY AND HUMAN GROWTH

THE pattern of human growth is characterized by a prolonged period of infant dependency, an extended childhood and a rapid and large acceleration in growth velocity a adolescence leading to physical and sexual maturation. These traits are considered to be a advantageous for out species since they provide :

1. an extended period for brain development.
2. time for the acquisition of technical skills, e.g. tool making and food processing and
3. time for socialization, play and the development of complex social roles and cultural behaviour.

These statements are standard textbook rationalizations for the value of the pattern of human growth, but they do not explain how that pattern of growth evolved, that is they do not provide a causal mechanism for the evolution of human growth. Rather, these are tautological statements, arguing for the benefits of the simultaneous possession of brains that are large relative to body size, complex technology, and cultural behavious. First causes may not be deduced from this type of circular reasoning, but the big brain-technology-culture argument is uncritically accepted by many students of human evolution.

4. Slow childhood growth and delayed maturation may have originally evolved as feeding adaptations. The addition of fibrous, 'tough-to-chew' foods in the diets of our ancestors may have selected for a delay in molar tooth eruption which allowed for efficient processing of these foods throughout the life cycle. Delay in dental eruption produced, as an indirect by product delays in growth and maturation in other system of the body.
5. Small body size prior to adolescence, coupled with delayed maturation, tends to reduce intra family and intra group hostility. Small body size of juvenile young reduces competition with adults for food resources, because slow growing, small juveniles require less total food than bigger adults. Delayed maturation is also advantageious since it eliminated some social and sexual competition between adults and young during the years when technological, social and cultural learning occur.
6. Small body size of juvenile young also reduces competition for food resources with infants and young children. Since adult are compelled to feed infants and young dependent children, feeding competition with these younger offspring is minimise so as not to bring the interest of juvenile in to conflict with the interest of adults.
7. The human growth pattern of relatively early neurological maturity versus late sexual maturity allows juveniles to provide much of their own care and also provide care for young children. This frees adult for subsistence activity, adult social behavious and further child-bearing the economic, social and reproductive value of juveniles as baby sitters gives delayed sexual maturation added selective advantage.

The justification for adding these four reasons for the evolution of the human pattern of growth requires a review of some of the fossil and paleoecological evidence for human evolution. The review of these fossils, and their ecological setting, focuses on the evidence for the evolution of the human growth pattern.

PHYSIQUE & BODY COMPOSITION

PERFORMANCE in any sports event depends upon numerous associated factors like, body size, body proportions, physique, training exercise, and adequate nutrition to combat the energy expenditure during physical activity and general physical fitness. Lack of any one of these would result in relatively poor performance by athletes at national and international levels. If we wish to gain proper recognition in the sports world we must adapt certain basic steps that the advanced countries are taking to promote the sports with the help of available scientific technology. The quality physical performance is directly related to various traits of boys and girls pertaining to their body size, shape, proportion, maturation, composition and physique. Most of these traits are acquired through heredity but are affected by environmental influence. It is also true that the performance of a sportsman in any event is also dependent on his skill training; motivation, and psychological nature. Children differ significantly on these traits. Though the participation in physical activity will not appreciably change their maturity, body size and physique, these individual differences will greatly influence their physical performance. Thus, these factors must be kept in mind while judging individuals' potentialities for participation in physical activity.

IT HAS been observed that training and other extragenetic influences can change one's morphological status only within the narrow limits set by his genotype (Tanner, 1964). It is difficult to change the capacity of the genotype in order to maintain altered levels of different biochemical determinants. Thus it is imperative to lay more emphasis on the genetically determined morpho-physiological status of the individual.

IN 1978 ROSS *et al.* described the importance of a new scientific specilization-Kinanthropometry, and its application in Sports. Kinanthropometry is defined as the study of human size, shape, proportion, composition, maturation and gross function in order to help understand growth, exercise, performance and nutrition (Ross *et al.* 1980). It pertains to the measurement of man in a variety of morphological perspective, its application to movement and those factors which influence movement including various components of body build, body dimensions, proportions, constitution, shape and maturation, motor abilities, cardio-respiratory capacities, physical activities including sports performance. Kinan-thropometry a comprehensive approach to assess an individuals' physique.

PHYSIQUE AND SPORTS

PHYSIQUE, according to Eiben (1972), is the morphological institution of an adult which is formed by the manifestation of genetical endowment, and as a result of adaptation processes to environmental efforts, while according to Sodhi and Sidhu (1984) it pertains to the shape, size and form of an individual, as these are a manifestations of the internal structure and tissue components which are influenced by the environmental and genetical factors. The physique, visible phenotype of an individual is the outcome of the interaction of environmental modifications on his invisible genotype. With the progression of growth the characteristics of human physique undergo a marked transformation, while during adulthood these changes become extremely slow and gradual. Kretschmer, a German Psychiatrist categorised human beings into three constitutional types as the PYKNIC (fatty), the LEPTOSOME (thin and lean) and ATHLETIC (muscular) on the basis of anthroposcopic observations on human beings.

VIOLA, an Italian Physician, used body dimensions to classify human physique. He provided following categories of physique.

1. Longitype: having relatively long limbs compared to the trunk, massive thorax compared to the abdomen, and greater transverse diameters relative to the anteroposterior ones.
2. Brachitype (broad type): having the characteristics opposite to those of the longitype.
3. Normotype: This type constitutes of those individuals who fall in between the Longitype and Brachitype categories.
4. Mixed type: This category includes those individuals who exhibit characteristics of different types in different parts of the body, i.e. they may be brachitype in one part, longitype in the other and normotype in yet another part of the body.

SHELDON *et al* (1940) successfully devised a method to analyse and quantify human body form and called it as *Somatotyping.* According to them "somatotypes are morphophenotypic ranges along constantly recognizable characteristics and are the functional end products of the whole genetic and developmental complex." The somatotype is aimed at providing a sort of identification tag to an individual and may be regarded as an attempt towards general human taxonomy or classification. Sheldon recognised three basic components of physique, viz. *endomorphy, mesomorphy* and *ectomorphy.* Each individual has varying degrees of development of these three components. The somatotype is always written in three numerals; the first indicating the development of endomorphy, the second the mesomorphy, and the third representing the ectomorphy.

SHELDON'S observations were based upon 4000 undergradu

ate male students in the age range of 16 to 20 years. Photographs of front, back and side views of the nude subjects were taken at a standard distance, using a long focus lens (9½ inches) by rotating the subject on a revolving pedestal constructed to move between stops placed at intervals of 90 degrees. For the purpose of morphological observations Sheldon divided the body components into five areas :

1. Head, face and neck,
2. Thoracic trunk
3. Arms, shoulders and hands
4. Abdominal trunk, and
5. Legs and feet.

HE FURTHER arranged the photographs of 4000 subjects in fifteen ascending series in order to ascertain the range of variation of each component in each of the five body areas. Each series was based upon a continuous gradation of the estimated value of one component in one bodily region, through picture-to-picture comparison. A seven point scale for each component in each region was used by approximating the mid-point of each range and subdividing it into three equal intervals on either side of the mid-point. Thus each component in every series was scored from 1 to 7 and the somatotype of the subject was determined from the average score of each of the three components in the five regions combined. Each somatotype was thus represented by a three digit combination, i.e. 711 as Extreme Endomorph, 171 as Extreme Mesomorph and 117 as Extreme Ectomorph.

BRIEF description of the components of physique follows as under:

Endomorphy : It reflects general softness and roundedness of the body and its various parts. Proximal parts of the limbs are relatively massive than the distal ones, tapering of the extremities, abdomen predominating over thorax, soft body contours, hands and feet relatively small.

Mesomorphy : It reflects general massiveness and sturdiness of the musculo-skeletal system of the body, highly developed limb muscles with distal segments of the extremities relatively more prominent. Strong and highly muscular thorax which predominates over abdomen with small antero-posterior diameter of trunk than the transverse one.

Ectomorphy : It reflects thin and lean body with week muscles and thin skeletal diameters, pointed and sharp body projections, long and slender extremities with little muscles over them.

CRITICAL EVALUATION OF SHELDON'S METHOD OF SOMATOTYPING

1. This is a subjective method. An evaluator may give different somatotypes to the same photograph if asked to rate at two different time intervals.
2. This method has been developed on white males of a limited age-range, i.e. 16 to 20 years, and hence it does not include complete variations in human physique.
3. This method is applicable only on males as somato types of females as well as of other ethnic groups are not known.
4. This system is based on the concept that the phy sique of an individual does not change from birth to death and is unaltered by environmental factors. But with in crease in age certain changes in the body build do take place.
5. The overall body size and weight of the subject is not involved in the assignment of the somatotype.

DESPITE these shortcomings, Sheldon's method of somatotyping is a useful technique.

HEATH-CARTER METHOD OF SOMATOTYPING

AFTER Sheldon's method of somatotyping many attempts were made to further simplify the technique using anthropometic measurements (Cureton, 1951; Parnell, 1954, Damon et. al., 1962) but they could not gain much importance. Heath (1963) critically examined the shortcomings of Sheldon's method and came out with certain modifications and later, in collaboration with Carter, gave her own method of somatotyping in 1967. Heath and Carter Method of Somatotyping. This method differs from Sheldon's method in the sense that it evaluates the physique at the given time compared to the unchanging somatotype of Sheldon. The ratings of the three primary components of physique are assigned as the basis of following anthropometric measurements :

1. Height, (2) Body weight, (3) Triceps skinfold, (4) Sub-scapular skinfold, (5) Supraspinale skinfold, (6) Calf skinfold, (7) Humerus biepicondylar diameter, (8) Femur biepicondylar diameter, (9) mid-upperarm circumference, and (10) Calf circumference.

ACCORDING to Heath and Carter (1967), and Carter (1975) a somatotype is a description of the present morphological conformation. It is expressed in three numeral rating (consisting of three sequential numerals). Each numeral represents the evaluation of three primary components of physique which describe individual variations in human morphology and composition.

First Component (Endomorphy) : REFERS to relative fatness in individual physiques, as well as to relative leanness. That is, the first component ratings are evaluations of degrees of fatness which lie on a continuum from the lowest recorded values to the highest recorded values.

Second Component (Mesomar-phy) : REFERS to relative musculo-skeletal development per unit of height. The second component ratings are evaluations of musculo-skeletal development which lie on a continuum from lowest to highest degrees recorded. The second component can be thought of as *Lean Body Mass* relative to height. The Lean Body Mass pertains to the body without fat component.

Third Component (Ectomo-rphy) : REFERS to relative linearity of individual physiques. The third component ratings are largely but not entirely based on height/cube root of weight ratios. Height/cube root of weight ratios and third component ratings are closely related so that the low ends of their distributions both connote relative shortness of the several body segments, and the high ends connote elongation or linearity of several body segments. Ectomorphy ratings evaluate the form and degree of longitudinal distribution of the first and the second components.

THE observed ratings for endomorphy, mesomorphy and ectomorphy vary from 1 to 15, 1 to 12 and from 0.5 to 9, units respectively. These somatotype ratings are phenotypicaly, i.e. it is the somatotype as at the particular time of assessment and thus it may change.

EVALUATION OF HEATH-CARTER ANTHROPOMETRIC SOMATOTYPE METHOD

1. The most important aspect of this method is its objectivity. The results are dependent on the accuracy of measurements taken. Different raters would arrive at the same somatotype of any individual.
2. It is an excellent tool to explore spatial-temporal variations in human body form.
3. It is an easy, accurate and efficient method of somatotyping.
4. This method is workable both in the field as well as laboratory.
5. Females can also be subjected to this method, and somatotyped.

* * * * *

HUMAN ECOLOGY

CONCEPT & SCOPE

LIVING beings, in general, have the in-built capacity to adapt themselves to the environment and it is well demonstrated through the concepts of variation and natural selection. However, many species are capable of amending their micro-environment suitable to their survival. Birds, for example, make nests and many mammals make burrows. But, human beings are the only ones who can significantly change their micro as well as macro-environment through the capacity for, what we call, culture.

ECOLOGY

ECOLOGY refers to the study of interaction between living beings and their natural environment. In **Human Ecology,** Man is that living being. The capacity of a species to change itself to suit to the natural environment is known as adaptability. The term, *human adaptability* is also applied to the biological responses which improve any function of an individual or group in a specific environment.

THERE is no standard definition of the term *Human Ecology* and, being an *interdisciplinary* concern, there is no unanimity on the scope of the topic. For the sake of convenience, we can divide human ecology into cultural and biological.

CULTURAL ECOLOGY

SOCIAL ecology found its first adherent in A. Hawley, a sociologist who coined the term cultural ecology in 1950s. From the studies on animal ecology and behaviour in vogue even in that period, he inferred that such studies could yield much insight into the study of human behaviour.

JULIAN Steward, in early 1950s became fully convinced that natural environment had a strong bearing on social and cultural institutions of all human societies. Subsequently, through the amalgamation of his and other anthropologists' ideas developed Cultural Ecology where, according to Baker, the emphasis is on *the regularities of human behaviour, social structures and values which develop or evolve in response to particular natural environmental niches or situations.*

WHILE majority of cultural ecological studies are concerned with pre-literate and traditional societies, the recent trend is of studying the effects of variations in *environmental resources, population sizes and external intrusions of other societies* on cultural evolution.

IN EVOLUTIONARY Ecology, an approach initiated in 1970s, it is the individual who is the unit of study and not a population. Here, the models previously validated on other animal species are applied to individual humans. *Proponents of evolutionary ecology including Adam Smith believe that it can help to clarify human behaviour including (i) why people use specific behaviours for obtaining food; (ii) why they develop various mating practices; (iii) why they distribute themselves over space in different manners, and (iv) why they differ in such interrelated characteristics as population dynamics and community structure.*

A NUMBER of hypotheses have been formulated by Winterhalder and other evolutionary ecologists for testing various models, However, the major emphasis has been on the behaviour related to acquisition of food.

BIOLOGICAL HUMAN ECOLOGY

UNLIKE the behavioural interests of evolutionary ecologists, Biological human Ecology stresses on the effects of environments — man made or natural — on the biological traits of human populations. As biological anthro-pologists are derived from various scientific streams, there has not developed any standard set of assumptions or approaches. However, one assumption accepted by one and all is that during the course of evolution, selection resulted in survival and spread of certain traits which proved essential for the evolution to our own species.

BEFORE the advent of biological human ecology scientists (including physiologists and epidemiologists) assumed causal relationships for various happenings considering them applicable universally — totally ignoring the impact of diversities in cultures. Though theoretical postulates and traditional definitions of physiology have still to contribute much to such studies, many other physical and natural sciences have added to the scope of the subject in recent years.

AS A CONSEQUENCE, *a more compre-hensive approach to examining how people have adapted to their particular environments has developed. This paradigm emphasizes that a population's adaptive response to an environmental stress is likely to involve several mechanisms, including learned responses, species-wide physiological adjustment capabilities (acclimatisa-tion), and population-specific genetic characteristics which are the result of natural selection* (Baker 1990).

ECOLOGY

Baker is considered the father of Biological Ecology and on the basis of project in Andes wrote a volume : *"Man in the Andes* (1976)".

Thereafter, he took up an international project (International Biological Programme or IBP) through which he conducted the studies of the effects of various natural stresses on human populations the world over. IBP published several volumes; the most notable being *"The Biology of Human Adaptability"* (popularly known as *IBP-9)* by *Weiner & Lourie.* This volume enlists the ideal conditions for conducting studies on human adaptability. To study the effect of environment, heredity must be kept constant. Therefore, the effect of a natural stress must be studied on a genetically homogeneous population.

For example : To study the impact of altitude we should have a homogenous population with two components, one permanently living at high altitude (HAN) and one permanently living at low latitude (LAN). Again in recent times, a part of HAN might have migrated down (HAM) & similarly a part of LAN might have migrated up (LAM).

HAN	LAM
↓	↑
HAM	LAN

Comparative study of these four sections of population should ideally help in the understanding of impact of altitude. In practice, we see people moving down quite frequently, but people migrate up very rarely. Therefore, these are only ideal conditions which are rarely met and hence the conclusions drawn from adaptability studies though convincing are only tentative.

HUMAN ADAPTABILITY

AS SAID earlier, the diversity in the background, goals and approaches of researchers has been a major impediment in evolving a common focus and set of theories in human ecology. It is, however, commonly felt that ultimately the effects of natural and cultural environment (ignoring chance and supernatural effects) should be the key to the explanation for our

functioning and behaviour. With common perspective and increasing research data, human ecology may, in the long run, evolve into a unified sub-discipline of Anthropology.

REALISING that natural and cultural environment does affect biological traits individually (e.g. effect of radiation on skin and body) and specifically (e.g. resistance to cold), as also that changes in culture with following stress and strain do affect human body whereby humans — individually and collectively — keep adapting to the changing environments, the field of human ecology is now more often known as Human Adaptability.

FORMULATING Research Designs in the study of human adaptability is not an easy task because we need at least two individuals or groups of a society who vary only in one trait under study. To understand the effects of high attitude hypoxia, for example, we need two groups with identical cultural attributes and social preferences, but differing only in the altitude of their habitations. As getting such ideal setting is almost impossible (and we can not subject humans to deliberate experimental situations), the conclusions drawn from such studies can, at the best, be taken as tentative. The evolving sub-discipline of human Adaptability, therefore has to create means to identify the quantum of variations in inferences caused by the inherent difficulties in approaching the near-ideal situations.

TOLERANCE TO NATURAL STRESSES

TODAY science has developed certain methods and resources through which living beings can live almost anywhere for varying time durations. But all living beings comprise of living cells and the survival of these cells (and hence of living beings) depends on their potential to cope with stress. Nature exerts stress in a number of ways — through temperature, pressure, radiation, nutrition etc. — and majority of the living species have adapted themselves for living in certain specific *econiches*.

MANY mammals today have evolved in such a way that they can adapt themselves in various terrestrial environments but early primates developed no specific ecological niches and primates have not developed adaptations to live in all types of environments. It was probably the *Homo erectus* who, because of his knowledge of the uses of fire, could enter the erstwhile hostile extremely cold climates of the world. Otherwise, it is generally believed that most of the human evolution took place in the areas which were hot during the day but with comparative cooler nights, high solar radiation, comparatively low humidity and relatively high atmospheric pressure.

ADAPTATION TO HEAT

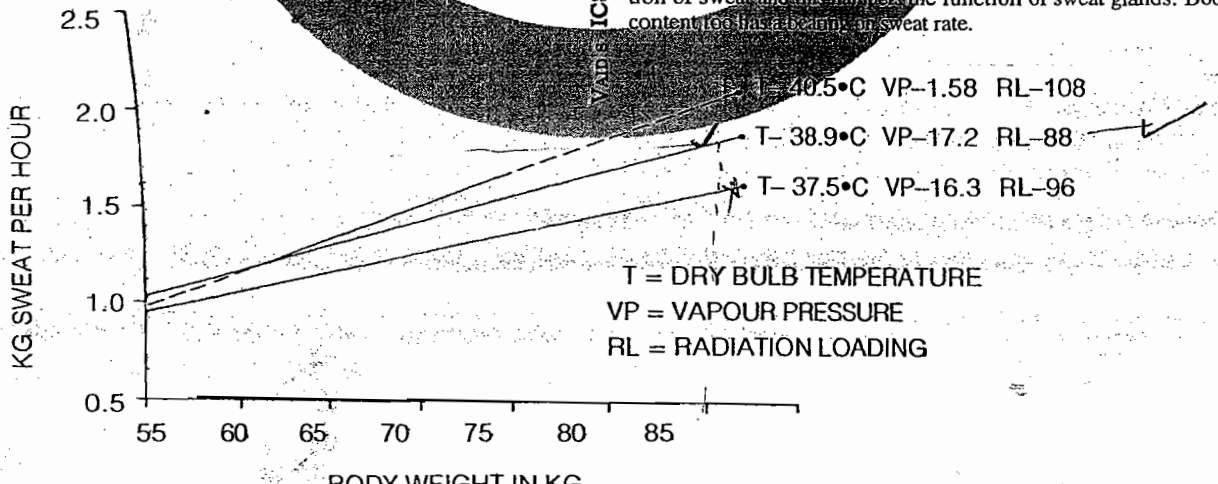
A HOMEOSTATIC system is the one that tries to maintain almost constant temperature. Human body tends to maintain its temperature at about 37°C and at this (normal) temperature it works quite efficiently. However, because of a number of factors including age, sex, nature of physical activity, weather, time of the day etc., this normal temperature keeps fluctuating. Young adults in resting period, for example (with only basic metabolic activities being performed) may have about 30°C as the normal temperature provided there is not much heat loss to the surroundings (due to cold weather).

THE rise in body temperature in ordinary circumstances impairs activity and a rise of 4-5°C from the normal can cause permanent damage to any body system or even death. The temperature can be brought back to normal through continuous heat loss to the surroundings. This can be possible only if surroundings' temperature is less than body temperature. The mechanism for heat loss following Baker (1990) is as follows :

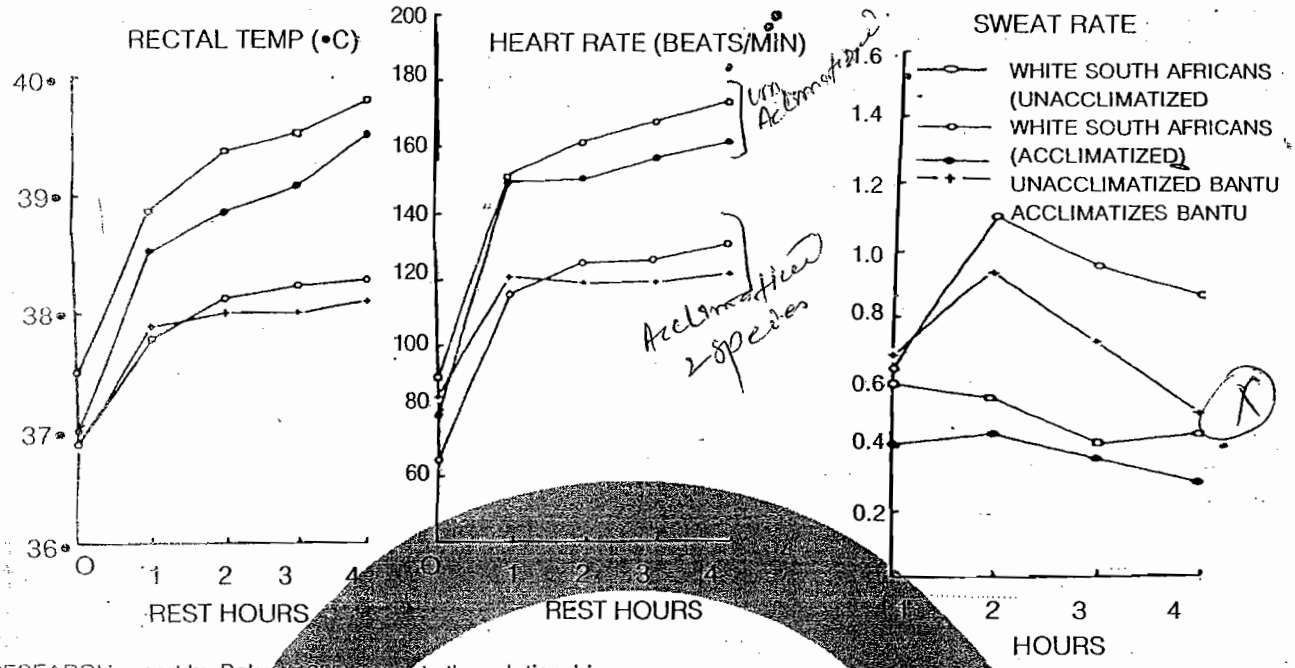
SWEAT glands in humans number over a million with minor variations among different populations, Researches have suggested that sweat glands are activated during childhood. If a child has faced acute heat stress, most of his sweat glands get activated that results in better heat tolerance for him throughout his life. Thus, heat tolerance developed among adults is a function of heat stress faced during childhood.

As the heat load on the individual rises there is first a peripheral vasodilation and a rise in heart rate which increases blood flow to the surfaces. The consequent rise in skin temperatures increases the rate of heat loss to surrounding air so long as the air temperature remains below skin temperature. With a further increase in heat load, sweating by means of eccrine glands begins. Rises in core temperature through its effect on the hypothalamus is the primary mechanism for stimulating total body sweating. Localized setting can also be stimulated by an areal application of heat.

THE capacity to sweat varies with acclimati-zation. In extreme hot desert a young male staying for a short while may excrete upto 4 lts/hour. Gradually it comes down to a stable 2 lts/hour. In such conditions an individual living for a considerable period excretes, on an average 8 lts of sweat per day. Sweating, however, depends not only on body temperature vis-a-vis external temperature, but also on radiation load and relative humidity. Hot desert and savanna conditions result in quick evaporation of sweat but extreme hot but humid conditions as in coal mines or some sea-shores, don't promote the evaporation of sweat and thus hamper the function of sweat glands. Body fat content too has a bearing on sweat rate.



MAXIMUM effect of sweating can be had only after heat acclimatization. Regular exposure to heat stabilizes sweating at rate compared to a freshly exposed one. Strain on heart activity is also reduced considerably. Baker & Weiner (19' shown the relation between heat acclimati-zation and physiological responses through the following graphs.



A RESEARCH report by Baker(1955) presents the relationship between radiation load, temperature and relative humidity as follows (see fig.) :

THERE exists a considerable variation in heat tolerance depending on the age, sex, shape, size & composition of the body. In most of the new borns, there is not much development of sweat glands and neurological apparatus, and therefore, they do not have much heat tolerance. They have a larger surface area compared to body mass. Therefore, higher air temperature increases body temperature quickly. Same is the case with increasing radiation load. Consequently, Little (1973) concludes that higher air temperatures as also high radiation load may be important factors in hot infant mortality.

CHILDREN in general have high surface area (SA) per unit of body mass (BM). This ratio (SA/BM) is about 0.6 (cm²/gm) among infants while it is hardly about 0.03 in adults. Taller people have this ratio further low. Besides, longer limbs increase the per unit surface area and hence, among such individuals, this ratio may be slightly higher.

ADULTS, therefore, have low surface area in proportion of body mass and hence, they exhibit much higher heat tolerance in the situation mentioned above. Fat in the subcutaneous region too may have important bearings for heat tolerance. A study conducted on American soldiers during Second World War shows that "men 10 percent above average weight for height had death rates nine times those of men 10 percent below average weight for height.

IN THE areas with high relative humidity (hot humid areas) sweat evaporation takes place very slowly and this affects the heat tolerance.

POPULATION differences keeping above cited factors, do exist and broad generalizations can be made depending on peoples' natural environments and their working conditions. However, with increasing acclimatization to a particular environment, these population and individual differences tend to merge.

ADAPTATION TO COLD

IN GENERAL, human beings possess a large body mass compared to the surface area. But probably our tropical origins and latter adaptation to colder environments has still remained a legacy. Humans' adaptation to hostile cold conditions is much less than that of the arctic animals. One reason may be that such animals have a thick coat of fur or hair while human body lacks all such insulating mechanisms except for the layer of subcutaneous fat.

AS A CONSEQUENCE, with a dip in atmospheric temperature below 28°C there starts persistent loss of body heat to the surroundings. To undo this process human body responds in a way explained by Baker (1960):

WHEN air temperatures fall below 28°C the arterials below your subcutaneous fat vasoconstrict. The warmed blood from the core of the body is then shunted away from the skin and, as the skin temperature declines, the loss of heat from the core of the body is reduced. In totally inactive individuals with very heavy subcutaneous fat deposits, the vasoconstrictive response will keep the core body temperature in the neutral range in air temperatures as low as 15°C. But for thin individuals further homeostatic responses in the form of shivering may be triggered by 25°C. Given freedom of response most people will also react to lower skin temperature by huddling, which reduces the surface area for heat loss, or by voluntary muscular activity which increases heat production.

IF THE individual remains inactive, involuntary muscle contraction, which eventually results in visible shivering, begins as core temperature begin to fall. Shivering can increase metabolic level 100 per cent above basal. Voluntary activity, such as running, can increase heat production much more, but the length of time over which voluntary activity at higher metabolic output can be maintained to prevent further declines in core temperature is limited.

SUBCUTANEOUS fat plays quite a significant role in cold tolerance. Ordinarily a dip of 3–4°C in temperature from the normal core temperature can result in loss of mental alertness and another further dip of 3–4°C may result in unconsciousness; but the individuals can recover without any permanent damage to the tissues. Individuals with significant amounts of subcutaneous fat may not be affected much under conditions mentioned above. Normal fit young adults can survive at low temperatures with low wind speed for several hours because they, can generate enough heat through physical exercise.

COMPARED to heat tolerance, tolerance to cold is much less and much varied among human populations. Early man, as also present day hunter-gatherers, have defied the effects of cold by the use of fire because of which humans can survive even without clothing. Clothing, however, has done a great favour to humans and now humans, through highly evolved scientific apparatus and clothing, can bear temperatures quite below the freezing point.

HANNA (1976) has shown that age and sex do have a bearing on susceptibility to and tolerance of cold. Through his study of highland Quechua Indians of Peru (see graph below), she has demonstrated that children have the least tolerance to cold probably because of the early-age disability in terms of skin-fold thickness and less neurological development among infants that continues in childhood too.

AS A CONSEQUENCE, their core body temperature falls very quickly in the early phase of sleep and remains fairly constant under the conditions of basal metabolism.

BODY weight as a function of total body mass (where subcutaneous tissue is the most important factor) too has a significant bearing on cold tolerance. For individuals with same height, heavier ones can tolerate much colder environment by maintaining better core temperature through the insulation provided by subcutaneous fat.

SEX differences are also discernible for cold tolerance. Women in general are shorter than their men and they also have shorter limbs, and consequently, less surface area per unit body mass. But thickness of subcutaneous fat is significantly more among them, and therefore, they are expected to have high core temperature. However, under experimental conditions of physical exercise in cold environment, sex differences do not appear significant.

A NUMBER of comparative studies involving genetically different populations have been undertaken to know about the variations in tolerance to cold. While Iampietro *et al* (1959, US Blacks v/s US Whites) and Elsner *et al* (1960, Canadian Indians v/s Whites) did not find any population difference in their studies; Scholander *et al* (1958, Native Australians v/s Whites) Hart *et al* (1962, Inuit v/s White), Anderson *et al* (1960, Lapps v/s Whites) and Baker *et al* (1966, Quechua v/s Whites) have found significant differences in the mean skin temperatures between the populations studied—with Whites in general exhibiting lower skin temperatures. From these studies (and including his own on Australians, Hammel (1964) suggests that (as the human evolution must have taken place in tropical areas), populations living in tropical savannas might have a genetic adaptation to cold sleeping conditions which might have been lost in populations native of other environments.

ADAPTATION TO ALTITUDE

THERE exists an inverse relationship between density of air and atmospheric pressure on the one hand, and altitude on the other. This can well be understood while travelling in a plane. The flight captain keeps announcing the height at which the plane is flying as also the atmospheric conditions outside.

IN THE high altitude (2500 mts or 8000 ft and above the sea level), the most important stress factor is *hypoxia*, a condition whereby partial pressure of oxygen gets reduced significantly. As a consequence, the amount of oxygen available per unit of air, to run the vital body systems is highly reduced resulting in great physiological stress.

LITTLE & Morren (1979) have demonstrated that the hypoxic conditions start affecting at about 2000 mts above sea level and at 4000 mts the amount of oxygen available to blood is significantly low. Low altitude people visiting high altitude areas, therefore, on reaching high altitude areas immediately experience increase in the rate of breathing as also faster heart rate. This, to an extent, helps in seeking more oxygen from the environment. However, after a few days, they get acclimatized and the body starts functioning in a normal manner.

A NUMBER of studies on the effects of high altitude hypoxia have been undertaken particularly under the International Biological Programme. The noteworthy finding of these studies is that the low altitude natives migrating to high altitude adapt themselves to the stress by less consumption of oxygen—Baker (1969) has observed a decrease of 24.4% and 9.7% respectively among US Whites and Quechua Indians. Peruvian sailors (Velasquez, 1964—19.5%), English mountain-climbers (Pugh, 1958—20.6%) and US White athletes (Reeves *et al*, 1967—25.1% & Buskirk *et al* 1967—27.2%) too experience significant reduction in the total oxygen consumption. This decrease in oxygen consumption capacity has a bearing on the work capacity of the individuals. Studies have shown that even a stay upto 1 year does not bring any significant improvement in the work capacity but a much longer stay of over 5 years does make a noteworthy change. Contrarily, when these migrants come back to their original low-altitude level their total oxygen consumption capacity rises.

HOWEVER, high altitude natives do not experience any such increase. A number of studies have been carried out on high altitude natives but inferences derived and conclusion drawn from these studies are not consistent.

IN THE project study titled "*Man in the Andes*", high altitude South American Andean children have been known to have low rate of physical growth particularly during infancy and adolescence. In Asia, while the results of studies in the Tien Shan mountains of CIS are in line with those of the Andes, high land Sherpas of Nepal (Pawson, 1974) do not differ much in physical growth vis-a-vis their low-altitude counterparts. Ethiopian highlanders, on the other hand exhibit a faster growth rate than the lowlanders. In the studies on highland populations and their comparison with their lowland counterparts, none of the investigators has specified the reasons for such variations. Probably, we are overestimating the effects of high altitude at the cost of other environmental and genetic factors.

IN CONCLUSION, we can add what Baker (1990) has already recorded:

> The high-altitude populations of the world appear well adapted to their environment in spite of the fact that temporary sojourners suffers a variety of symptoms and perhaps a permanent reduction in work capacity. While a short-term acclimatizational process contributes to native abilities, it appears that either developmental change or genetic adaptation is necessary for people to become fully functional at the higher elevations. As the graph developed by Buskirk (1978) suggests, most of the people reaching the top of Mount Everest (*Sagarmatha*) are likely in the near future to be native residents of higher altitude regions of the world.

ADAPTATION TO NUTRITIONAL STRESS

DEPENDING on their diet, animal species in general can be classified as herbivores (including fructivores), carnivores and omnivores. As animals can not convert radiant energy into useful forms (while plants can and do), herbivores are at an advantage in terms of available mass of convertible energy. The highly specific carnivores, on the other hand, have much less such energy available to them. Yet, general carnivores are at an advantage compared to herbivores surviving on specific plants and/or living in particular *econiches* because biomass available to them is much larger as they can tap more energy for survival.

WITH above mentioned facts it may be easy to conclude that omnivores (e.g. human beings) should be at a considerable advantage because they can benefit from both herbivores and carnivores, but this may not necessarily be the case. This is so because human beings can utilize only a part of the energy available and that too in the forms of convertible human types of nutrients viz. proteins, lipids, carbohydrates etc.

THE concept of basal metabolism is vital in understanding human energy needs. It is the amount of energy required by someone in complete rest and that is essential for smooth functioning of vital body organs. This amount of energy varies with the physiological conditions and is significantly higher during growth period as also for pregnant women and lactating mothers. This amount varies from about 36 kcal/hr in young children to about 78 kcal/hr in average sized adult male to about 95 kcal/hr in lactating mothers. In other words, the range of basal energy requirement per day varies from about 80(

kcal/day to about 2,300 kcal/day. These requirements also vary because of hot or cold stress because in either case there is a loss of energy from the body to the surroundings.

THE energy needs vary more dramatically during activity period. The total energy requirements of an individual for a day are much more than the basal requirements because spending of energy depends on the type of activity undertaken. Leslie *et al* have calculated the energy requirements for various types of activities as follows :

	Level	Cost above BMR	Example of activity (kcal/kg/hr)*
1.	Resting	0.00	Lying still
2.	Sitting 1	0.25	Sitting quietly
3.	Standing 1	0.50	Standing 'at ease'
4.	Sitting 2	1.00	Sewing, weaving
5.	Standing 2	1.50	Sweeping
6.	Walking 1	2.50	4.8 km/hr no load
7.	Walking 2	3.50	4.8 km/hr, 15 kg load
8.	Heavy	4.50	Hoeing, ploughing
9.	Very heavy	7.00	Tree felling
10.	Extreme	10.00	Near maximum exertion

FROM the table it is clear that total energy requirements/day of an individual may vary from the basal level to 100% more than the basal level.

Nutrient	Energy/gm
Protein	4.06 kcal (effective)
Carbohydrates	4.06 kcal
Lipids	9.08 kcal

AS DIFFERENT populations of the world live in varied environments and they also differ in the demographic structure, adult body size etc., it is imperative to conclude that there must exist considerable population differences with respect to the daily energy requirements. UN/FAO have attempted estimates of energy requirements of humans (see table below) but as their surveys were carried out in US and Britain, i.e. countries peopled by large body sized populations, these surveys overestimated the requirements of populations living in other areas of the world. Accordingly, Leslie *et al* have revised these estimates which are more representative.

PRIOR *et al* (1981) have shown that different populations have adapted to varied requirements of various nutrients. Inuit Eskimo derive their high energy content from animal fats but Polynesians do the same from vegetable fats of coconuts. Vegetarians in general consume much less protein while meat-eaters consume diet rich in proteins. Some populations of New Guinea survive on a diet with merely 4% protein content.

Standard Recommended intake by Oxford Nutrition Survey

Nutrient	Daily Requirement
Total Energy Intake	3,010 kcal
Total Protein	72 gms
Animal Protein	36 gms
Carbohydrates	432 gms
Fats	102 gms
Iron	10 mg
Calcium	750 mg
Phosphorus	1,000 mg
Vit. A	833 i.u.
Carotenoids	3,000 ug
Vit. D	200 i.u.
Thiamine	1.2 mg
Nicotinic Acid	12 mg
Riboflavin	1.8 mg
Ascorbic acid	30 mg

HUNTERS and food-gatherers are known to have fairly nutritious diet. Lee (1979) has reported quite diversified foods among the !Kung with meat contributing about one-third of the total food; rest of it comprised by mongongo nuts (over 25%) and other vegetables (over 40%). It is quite a balanced diet (2350 Kcal/day) and was recorded in July-August 1964 i.e. at a time when Westerners had not influenced their culture.

ENERGY NEEDS IN KCAL FOR FOUR POPULATION ESTIMATED BY TWO MODELS AND BY FOOD INTAKE SURVEYS

(Value in kcal/person/day)

Population	Age and Sex	Intake estimates	Leslie Model	FAO
Nunoa	All male	1632	1512	2211
(Thomas 1973)	All female	1420	1435	1834
Kaul (Norgan	Adult male	2347	2603	2970
et al. 1974)	Adult female	1830	2146	2350
Lufa (Norgan	Adult male	2570	2576	2970
et al. 1974)	Adult female	2245	2070	2350
!Kung (Lee	Juvenile male	2000	1218	1953
1979)	Juvenile female	2000	1178	1795
	Adult male	2250	2135	2477
	Adult female	1750	1818	1926

UN standard

2400) ICMR
2100)