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TECHNOLOGY OF GENETICS

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Many centuries ago man gave up his hunting and nomadic habits and settled down to grow plants and rear animals. He selected the seeds of the plants, and mated the animals, showing characters in them which he liked, to breed the next generation. In this way primitive man began very slowly to improve his crops and livestock in quality and in quantity so as to produce more food and clothing for himself. With the more settled way of life he could now enjoy, he was able also to leisurely think about his diseases and also perhaps to relate some of them to his own heredity.

This trend of affairs continued until long after modern civilization as we know it had begun. Although man could manipulate his plants and animals to obtain improved varieties he still did not know how this was brought about. The basic mechanisms of inheritance were still shrouded in mystery, myth and superstition. It was generally believed, even as late as the last century, that the characters of the mother and the father were mixed in equal proportions in the children, although everyday life would have surely demonstrated that this was not so. Any concepts of inheritance which they had, too were based purely on empirical observations and intuitive reasoning.

Then in 1866, a Roman Catholic monk in Austria, Gregor Mendel, published a paper, in German, in an obscure natural history journal of that country. This was to change the entire outlook of man. Using very simple but elegant and rigorously scientific methods, and mathematically analysing his results, which was unusual for a biologist at that time, he announced to the world the, hitherto, secret laws of inheritance! He was ahead of his times, however, as most trail-blazers are. No one at that time understood what he said; for 34 long years this treasure lay buried in the shiftless sands of ignorance.

After his death, three European botanists, de Vries, Correns and Tschermak, independently carrying out experiments similar to those of Mendel stumbled upon the same truths about inheritance, and they introduced Mendel in 1900 to the scientific world and explained the significance of his work. The Science of Genetics is therefore, actually a product of this century.

According to Mendel, characters are produced in animals and plants by the action in them of unseen factors or particles which are the ones that are transmitted from generation to generation in the reproductive cells. He further showed that to explain his experimental findings, these factors, which we now call genes, must act in pairs to produce each character in the plant or animal but that they separate into the individual factors in the germ cells. In the paired condition, one factor could suppress the effects of the other, or in other words, one factor could be dominant and the other recessive. This concept of the particulate nature of a hereditary material and their dominance and recessivity proved to be the essence of the new science of genetics. He further showed that such pairs of factors for different characters could combine at random in different ways in each generation.

With this methodological and conceptual breakthrough in the understanding of the processes of inheritance, new vistas of genetical knowledge opened up. Very soon it was shown by other geneticists that genes are linked to one another in groups, like strings of beads, and that beads from one string could exchange places with beads of its complementary string; that genes are actually carried on paired structures called chromosomes inside the nuclei of cells and seen only through a microscope, that the genes are made of a chemical substance called deoxyribonucleic acid, or more popularly as DNA; that DNA has a definite structure which beautifully accounts for all the known properties of a hereditary material; that this DNA stores all the information in code for producing proteins that go to form the organism, and that although DNA is very stable under normal conditions producing exact copies of itself, sometimes spontaneously, or under the effect of certain irradiations and chemicals, the codes get altered producing changes in the genes, these are termed mutations.

With the expanding mass of basic knowledge, genetics soon became a flourishing technology. This technology of inheritance has produced dramatic, important and practical results for the farmer and the animal breeder.

The application of the new technology to plants has produced by far the greatest economic benefits to man.

The cultivated plants which are of paramount importance to man as they serve as the basic source of energy-giving food for him and his livestock are the cereals, rice, wheat and maize. Selective breeding programmes on these plants to improve their yields, their protein content and to make them resistant to pests and diseases form the single largest research endeavour of geneticists in the whole world.

Selective breeding is where individuals showing the desired characters are selected to breed the next generation. This is very similar to what ancient man practised, but with a difference. It is more sophisticated, more efficient, and produces the desired results in a very short time. They are no longer trial and error methods. Certain characters have a high genetic component and only these characters can be manipulated by selective breeding. Other characters have very little genetic variability but can be influenced by environmental factors. Such characters usually cannot be improved by selective breeding methods but depend on cultural practices, namely the way they are grown, to show improvements. To distinguish between these two types of characters requires a great deal of careful experimentation.

In mutation, breeding seeds are treated with substances which induce changes in genes, and the new mutant genes are then subjected to selection. This is a very wasteful process as very often the changes produced in the seeds are harmful and may even kill them or produce unwanted characters in the plants that grow from such treated seeds. Few useful changes are effected by this method, but where large numbers of seeds or individuals are available for treatment as with cereals or micro-organisms, this technique does give quick and economical results. In the yeasts and other fungi this method has been exploited to increase the yields and improve the quality of their products such as alcohol and antibiotics.

The third method of breeding – hybridization – makes use of the fact that when different strains of plants of the same species, such as maize, are crossed, the resultant seeds give rise to plants which are very vigorous in growth and extremely hardy towards pests and diseases. This phenomenon, called hybrid vigour or heterosis, has produced such bumper harvests, especially of maize in the United States, that the profits from the increased yields are said to have paid for all research activities in genetics up to the present time.

Using similar methods of breeding other plants such as vegetables, pulses, tea, rubber, coconut, cotton, tobacco, ornamental flowers and even forest trees have been improved to give higher yields of their products which are of better quality.

In certain plants like tea, for instance, once good strains have been bred they are propagated vegetatively as clones. Clones are genetically uniform cultures that are easy to cultivate on a large commercial scale.

With the help of the new technology of applied genetics, improvements in the quality and quantity of animals, and the control and elimination of pests and diseases have been achieved.

The greatest amount of research on animals goes into improving the production of food in terms of meat, eggs and milk by means of selective breeding. Breeding of horses, sheep, fish, dogs, cats, pigeons and various other pets to obtain useful and fanciful strains are carried out in the same way. Mutation breeding methods are used in the case of silkworms, bees and other useful insects where large numbers of eggs are easily obtainable and the generation time is short.

In the breeding programmes of large animals special use is made of two techniques. One, is the progeny testing of individual animals. In these tests, the genetic constitution of individual animals which are mainly males, are assessed by mating them to a number of different females and examining their progeny. Once a good male is detected having the genes for desirable characters then it is used as a stud for obtaining large numbers of progeny with those desirable characters for commercial purposes. A further improvement is in the use of the second of the techniques, namely, artificial insemination or AI. The sperms of the selected male is extracted and frozen and stored. Whenever the need arises they are thawed and used to inseminate a large number of females. In fact, the sperms of donor animals can be used in this fashion long after the animals are dead and gone. In advanced countries sperm banks, in fact, are maintained to cater to the needs of animal breeders. This has recently been extended to the sperms of humans as well.

With the use of AI, a further refinement in animal breeding has been introduced. Normally equal numbers of males and females are born to animals. But in certain instances as in dairy farming it is advantageous to have more female offspring than males. This is achieved with a reasonable degree of success by making use of our knowledge of how sex is detemined. In cattle, as in other mammals including human beings, as also in insects, sex is determined at fertilization by a chromosomal mechanism. In the nuclei of all cells there are pairs of identical chromosomes, but in male cells the two members of one pair is not identical in size and appearance. These are called the sex chromosomes and are designated X and Y, of which the X is the larger one. In the female cells there are two X chromosomes. When these chromosomes separate into the germ cells, each ovum or egg cell in the female would have an X chromosome and all the egg cells would be identical. But the sperm in the male are of two types, the X chromosome bearing sperm and the Y chromosome bearing sperm. Because the X chromosome is larger than the Y, the X sperm is heavier than the Y sperm. Centrifuging the seminal fluid separates to a certain extent the two types of sperm. Now when the fraction of fluid containing more of the heavier X sperm and less of the lighter Y sperm is used to inseminate a cow, the chance of getting a female calf is considerably increased. If males are required, as in the meat industry, then the lighter fraction of the fluid could be used to get more males. Electrophoresis as well as pH can also be used to separate quantitatively these X and Y sperms.

In the case of poultry, as in all birds, fish and moths, the mechanism of sex determination is just the opposite, two X chromosomes producing a male and an X and Y a female (actually called Z and W chromosomes). In poultry the sex of chicks is not distinguishable even two weeks after hatching and commercially it is definitely economical to know the sex of the chicks at least as they hatch out. The use of suitable genetic markers to give differently coloured males and females have been tried and proved successful in differentiating sex, but the majority of poultry farmers have not taken to the idea.

With regard to pest control, various genetic methods are used, particularly for controlling insect pests. The most successful and popular method is the sterile male technique. Irradiations or chemical mutagens are used to induce sterility in the male insect pests. This sterility is caused by the damage of the chromosomes in their sperm due to the treatment, without in any way affecting the viability of the sperm itself. When eggs of normal females are fertilized by these sperm they fail to hatch. In this way repeated releases of sterile males into pest infested regions will completely eliminate them from those areas. The success of this method was dramatically demonstrated in the USA when the screw-worm fly whose grubs eat into the flesh of cattle, was completely eliminated from the infested areas of that country.

Treatment of insects with mutagens can also induce, what are called translocations. These are exchanges of parts of dissimilar chromosomes and they produce semi-sterility in the individuals which have them. That is, half their germ cells are sterile. In this way the population of pests could be reduced. The important advantage in this method is that the translocation is carried into the next generation in increased numbers and help to depress the population size still further. There are many other genetic mechanisms which can be exploited for the control of pests. Out of all the methods of pest control the genetic methods are the safest to use, but they are very sophisticated and involve a great deal of effort and money for their successful exploitation. Still with the serious threat of global pollution with chemical pesticides and the hazards of other biological methods of control, very serious attention should be paid by entomologists to these genetic methods of control.

Finally we shall consider the important part genetical knowledge plays in relieving man from the sufferings caused by disease.

Cancers are due to some cells in the body becoming wayward and dividing too soon and too often, and in this uncontrolled fashion producing malignant growths. Irradiations and chemical mutagens disrupt the chromosomes of these fast dividing cells and as in the sterile male method cause cell death. In this way the growth of cancers is arrested. The origins and the causes of cancers are not yet fully understood, although it is known that some are due to viruses. Active research in molecular genetics is being pursued in the advanced countries to understand this cancer problem.

There are various diseases of man caused directly by genes. Some may be relatively harmless abnormalities like colour blindness and polydactyly, which is the presence of extra digits in hands and feet. Others are very serious and deadly, like haemophilia, the bleeding disease; phenylketonuria, a biochemical disease where certain substances accumulate in the body with lethal effects on the nervous systems of babies, muscular dystrophy, which results in the withering of muscles of the body; sickle-cell anaemia, a disease affecting the red blood cells and causing death in infancy, and so on. There are two ways in which these diseases could be prevented. The easiest way is to avoid marriage of two persons whose families are known to have had the same disease. Here we run into a practical difficulty. If two persons are in love with each other it would be difficult to prevent their marriage even if they know that they harbour dangerous genes in them. The other method is to recognise the genetic causes early and to prevent the expression of those bad genes. For example, in the case of haemophilia, bleeding can be stemmed by giving the patient a chemical called antihaemophiliac factor of AHF for short, which is the substance they are deficient in. In the case of phenylketonuria which is the inability to break down further the amino acid, phenylalanine, if this condition is recognised in early infancy, then the infant can be maintained on special diets which are deficient in that particular amino acid. In this way a horrible, convulsive death can be prevented, and the individual could grow into a normal adult. Not all genetic diseases can be controlled in this fashion.

Certain abnormalities arise in individuals due to chromosomal aberrations. Bisexual individuals or hermaphrodites, mongol idiots, are some of these abnormal beings. Generally such abnormalities arise when slightly older women give birth to children, and the only way to prevent such births is for older women not to conceive.

If we now turn to another aspect of the genetics of man we see that human populations belong to differnt blood groups that are determined by genes. Apart from the complications which arise in giving blood transfusions where these types have to be matched before use, the blood group systems cause secondary complications. The rhesus system particularly is the most dangerous of these groups. If a rhesus negative woman conceives a rhesus positive baby then the blood cells of the foetus could migrate through the placenta into the blood system of the mother and the antigens in these foreign blood would induce the mother to secrete antibodies. These antibodies could get back into the foetus or a subsequent foetus and attack and destroy its red blood cells. This causes the condition known as erythroblastosis foetalis giving rise to a still-birth.If this condition is recognised in the first month of pregnancy then, only a blood transfusion of the foetus through the mother's body can save it. The action of the rhesus group on pregnancies is not quite so straightforward in that their action is minimised by the other blood group system, the ABO group. Apart from these complicatoins, the blood groups genes have effects on other organs of the body. For instance in the ABO system persons belonging to certain groups are also known to be predisposed to certain types of diseases like cancers and peptic ulcers. The blood group genes can be put to good use. They can be used to exonerate a man from the accusation of being the father of illegitimate children in a paternity suit. If the child's blood group does not tally with that of the man then he definitely could not be the child's father.

In Sri Lanka much work has been done with this new technology. Improved varieties of rice, tea, rubber and coconut and of many other crops have been produced. Improvements in quality and in quantity have been achieved in cattle and poultry breeding for improvements in the production of milk and eggs. A great deal of unnecesary human suffering and pain has been reduced by application of genetics in medicine. I hope that such application would increase considerably in the future so that we could make Sri Lanka completely self sufficient in our basic requirements of food. We may not be able to rid ourselves of hereditary diseases, but we could at least relieve human suffering to a large extent through the knowledge of genetics in genetic counselling.

As for the future technology of genetics, our present knowledge of basic genetics may make it possible to manipulate genes in such a way as to alter individual genes of animals, plants and ourselves, to our liking. Lasers could perhaps be used to cauterize harmful genes without disturbing adjacent ones in their molecular environment; genes made to order in test tubes could, perhaps, be inserted into the genomes of individual organisms, or we could have chemicals on our benches which would alter specific genes the way we want to change them. This type of genetic engineering and directed mutagenesis, like many of the great discoveries in science, is rapidly passing from the realm of science fiction and fantasy to become a wonderful new technique for the benefit of man.