THE PROMISE AND PROBLEMS OF TODAY'S BIOLOGY AND BIOTECHNOLOGY AND THEIR APPLICATIONS

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I. INTRODUCTION

I feel deeply honoured to be invited to give this year's Durgabai Deshmukh Memorial Lecture. Though I saw the now legendary Durgabai Deshmukh several times, I did not have the privilege of knowing her. I have, however, known enough about her to recognise that she represented a select group whose values and commitments were precisely those that are needed today to make this fantastic country of ours a model of Utopia. To do so, we would also need to use our, if I may say so, unparalleled foundation of history and achievements, and values already laid down by people like Durgabai Deshmukh. It is, indeed, on this foundation built painstakingly over five thousand years, by her predecessors that we would need to make a new structure, using bricks of modernity, that would stand the vagaries of time and winds of change for a long, long time to come.

Against this background, I imagine, it would be relevant to ask today as to what these bricks of modernity would be or should be made of. I would imagine that everyone gathered in the audience - indeed, a very distinguished audience - would accept that one essential component of such bricks would be science and technology. And by science and technology I do not mean just the hard facts of science or material gains of technology. I also include in it the temper of science or the scientific temper, a term coined by Jawaharlal Nehru which defines the way that we look at the scientific method. The fact is that over the last one-hundred-and-fifty years, slowly but surely - perhaps at an exponentially increasing rate - the method of science has permeated every facet of human endeavour. So the sociologist, Malinowski, wrote his famous book, A Scientific Theory of Culture, more than half a century ago. Relationships have been established between music and DNA, in both of which the sequence of building blocks is important. And we ourselves in Hyderabad have talked about the scientific basis of aesthetic appreciation and relationship between science and beauty. The problem with our today's politicians has been that they have been increasingly throwing reason and rationality that are important corollaries of the scientific method, to the four winds as was evident from the summary rejection by politicians of all hue and colour of the recent Supreme Court judgement on electoral reforms in 2002, in spite of the Central Election Commission's endorsement of it.

One of the attributes of science is that it allows one to make testable predictions. If these predictions turn out to be wrong, we must modify or change the theory on the basis of which these predictions were made. An important prediction over the last 15 years or so made by scientists all over the world (and I have been just one of them) is that our lives - certainly for 200 years if not more - would be governed by advances in just about ten areas. Let me list them:

biotechnology and modern biology, information technology, space, energy, robotics and automation, microelectronics, computers, nanotechnology, new materials, and artificial intelligence. An amazing inference which only a few recognise, is that all these areas, diverse as they may seem to be, are related; and all of them without exception have many implications: social, ethical, moral, economic, political, and legal. Today, I wish to share with you my perception of one of these areas, that is, modern biology and biotechnology, with its various implications.

It might amuse you that when I finished my university education, which was more than five decades ago, only five percent of the scientific literature was in biology, including medicine and agriculture. Today, over 80 percent of the entire scientific and technological literature is represented by biological sciences. The emergence of today's biotechnology was predicted in the early 1970s. I had the privilege of coining the term, 'genetic engineering', in 1973; I was, in fact, one of the two who did so independently that year. What was the basis of this kind of prediction that something like biotechnology was coming to stay and govern our lives in ways one could never imagine? This happened as, around that time (the early 1970s), we began to recognise that all biological systems can be defined in terms of just four parameters. First, what they are made of that is, their chemistry. Secondly, what the mechanisms are that are responsible for synthesising, inter-converting and degrading the millions of chemical entities found in living systems, be it a bacterium or an elephant - that is, their biochemistry. (A lowly bacterium like *E.coli*, can make all its thousands of carbon-containing chemical constituents from just one carbon source - glucose; we humans need about twenty five preformed carbon-containing nutrients to make the millions of different chemicals that we have in our body.) Thirdly, the specific manner in which the chemical constituents of a life-form are organised in space - that is, its structure. Fourth and last, what the functions are that the life-form or the biological system can perform.

So, the chemistry, the biochemistry, the structure and the function of biological systems came to be defined fairly accurately - at least at the gross level - around the 1970's. In fact, by this time enough advances had been made in our understanding of the chemistry, biochemistry, structure and function of living organisms that the total picture of life began to emerge, with the crucial pieces of the jigsaw puzzle of life falling in place; we were able to perceive what the larger picture may look like. It was a great intellectual revolution unparalleled in history, counting in the atomic revolution as well.

The history of science has repeatedly demonstrated that once we begin to understand the basic rules that govern any area in science, we automatically gravitate towards applying this knowledge for the benefit of or gain to mankind. This is what happened in chemistry: when we began to understand the laws of chemical combination and so on, we had the industrial revolution. This is what happened in physics around the beginning of the last century that led to the physics-based revolutions, with radio, television, X-rays, lasers, optical fibers, and integrated circuits. And this is what happened around the 1970s in biology: that enough came to be known

about the fundamentals of life - the chemistry, the biochemistry, the structure and the function of living systems - to make the emergence of modern biotechnology become inevitable. Not only that, one could predict that the consequences of biology and the emerging biotechnology, and of their various implications, would be of a totally different nature, qualitatively, than the fall-outs of the chemistry and the physics-based revolutions mentioned above. For example, it became clear that the new knowledge in biology would bring about a revolution in regard to the way we think about our origins.

In this context let me mention three conclusions that have emerged following the post-World-War-Two revolution in biology, that are destined to have an enormous impact on the way that we think of life. First, we know that life evolved on our planet from non-living materials, somewhere between 3.5 and 4 billion years age. After the first living cell was formed from chemicals in the environment, Darwinian evolution probably worked on it at various levels to, slowly but surely, give rise to the large number of species that we have had on our planet and have today - the most evolved of them all being our own. Secondly, it now seems that we all - those who have lived before us and those who are living today - are the progeny of a single woman who lived in Africa some 200,000 years ago. Man has been on our planet for nearly two million years but, apparently, all other lineages died down. Thus, we all are related ten thousand generations apart. Thirdly, we can today say with a great deal of confidence that all phenomena that pertain to life, without any exception, have a scientific basis rooted in laws of physics, chemistry and mathematics. Miracles that defy scientific laws have never happened or would never happen, and that god men who would like you to believe that they have supernatural powers are no more than ordinary men who have acquired the art of deceiving people; the miracles they claim to perform are no more than a manifestation of common magic that has always had a scientific basis.

II. SCOPE OF TODAY'S BIOTECHNOLOGY

The age of biotechnology dawned a little over two decades ago. Today's biotechnology consists of at least twentyfive well-defined areas, some of 'which were predicted while others came about unexpectedly. I would now like to list the above-mentioned areas of biotechnology and say a few words about those which would not seem to be self-explanatory.

(1) ***Genetic engineering of microbes, plants and animals.*** The term, genetic engineering, is now a part of common vocabulary. What is genetic engineering? Before we try to understand what genetic engineering is, I would like to point out that whatever we are - or, for that matter, whatever any living system is - is the consequence of two types of factors, the genetic and the environmental. Genetics - that is, the DNA of the organism - determines its capabilities, while the environment determines the extent to which these capabilities would be converted into abilities. Let me explain with an analogy. I have no doubt that everyone in the audience can, if required, learn Spanish or Chinese, but the chances are that there would be few,

if any at all, in the audience who would be proficient in either of these languages as of now, the reason being that they never had the need to learn the language. Similarly, there are a large number of people in the country, for example in our villages, who do not know how to drive a motor vehicle but given an opportunity, most of them would have no problem in doing so. On the other hand, the mighty elephant or the powerful tiger or lion cannot learn any of the languages we can, nor can we teach them how to drive a truck or a car, for the simple reason that they do not have the genetic capabilities for doing so. In genetic engineering, all that we do is to identify a piece of DNA (our genetic material) that is responsible for a particular capability of the parent organism, scissor this DNA out and transfer it to an organism which does not have the above capability, in such a way that the foreign DNA now becomes an integral part of the genome (the total complement of DNA) of the recipient which has now acquired a new capability. The second challenge in genetic engineering is to convert this newly acquired capability into ability by providing the right environment in the recipient organism. Thus, the common bacterium, *E.coli*, or a yeast, does not have the capability of making human insulin, a widely used drug for patients of diabetes. We can, today, isolate the gene (a piece of DNA) for human insulin and transfer it into *E.coli* or into yeast; we can then make this gene express in *E.coli* or yeast so that it now produces human insulin. This is how human insulin is being made today. Till it was produced as above by genetic engineering less than a decade away, the insulin used was cattle or pig insulin to which a number of patients did not respond. Innumerable lives are now being saved because human insulin produced by genetically engineered micro-organisms is now available commercially. In India, too, our own human insulin made as above will be in the market later this year.

Genetically engineered microbes are today widely used, in the above manner to produce and make available on a large scale and at a low cost, many drugs and vaccines of great importance besides human insulin, such as erythropoietin, interferon and Hepatitis B vaccine. Indian companies are already marketing genetically engineered erythropoietin and Hepatitis B vaccine at costs which are a fraction of the cost of the imported product before we started manufacturing it.

Genetically engineered plants - for example those that make their own pesticides or are resistant to weedicides - are already in the market. Thus, over 60 percent of the acreage under soyabean in the United States has now genetically engineered soyabean that is resistant to the weedicide, Roundup. In fact, the total acreage under genetically engineered crops (for good or for bad) around the world exceeds 100 million acres today.

Genetically engineered plants are also poised to produce vaccines. A few hundred acres of genetically engineered banana plantation can provide enough vaccine to immunize 120 million children every year that need to be protected against four common diseases. One of the future sources of cheap protein-drugs in the coming years, would be genetically engineered animals who would secrete these drugs in abundance (1-15 mg/ml) in their milk, thus making them available at a cost which could be three or more orders of magnitude lower than the current cost.

(2) Gene therapy- in a way, genetic engineering - of humans, which would allow a person suffering from a disabling genetic disorder to lead a normal life. The first case of gene therapy was two decades ago when a young girl suffering from adenosine deaminase deficiency (a genetic disorder) was treated in this manner. Her blood cells were taken out, genetically engineered to correct the deficiency, and then put back in her.

(3) ***Immunotechnologies,*** such as monoclonal antibodies (MABs) for diagnosis and therapy. Antibodies, a special set of **proteins**. are an important weapon in the armoury of higher animals such as humans, that enable them to fight incursion of their bodies by harmful chemicals or microorganisms. *Monoclonal* antibodies are single chemical species of antibodies, prepared in the laboratory by a special technique for which a Nobel Prize was awarded in the 1980s to Cesar Milstein and Georges Kohler. For diagnosis of human diseases, one can use, say, mouse MABs; for therapy, however, one would require human MABs. As human MABs are difficult to produce in the laboratory, genetically engineered plants are poised to find wide application in the production of human MABs. Technologies are also being developed to humanize animal MABs. The market for MABs for diagnosis alone, in just Hyderabad, may be about Rs.10 crores.

(4) Tissue culture, of both plant and animal cells, for micropropagation of elite or exotic materials (such as orchids), production of useful compounds such as taxol (the widely used anti-cancer drug) and vanillin, and preparation in the laboratory of "natural" tissues such as arteries for arterial graft or skin for burn victims. Modern tissue culture technologies allow the multiplication in the laboratory of cells isolated from plants and animals. In the case of plants, one can grow in the lab a whole plant from a single cell. This technology was developed more than five decades ago by Stewart in the UK. The second largest foreign exchange earner for Thailand is export of orchids grown through tissue culture which brings the country a revenue of some 700 crores of rupees every year. It is unfortunate that we the 600 and odd species of orchids in Arunachal Pradesh - specially when techniques for growing them in tissue culture have already been standardised by Arunachal Pradesh's scientists.

(5) Stem cell techniques which would involve purification and isolation of stem cells from various tissues, and their directed development into the desired tissue which could then be used for transplantation, remembering that, for example, we have only some 2000 kidneys available annually as of today for transplantation, when over 90,000 patients require such a transplantation every year. Stem cells can be either totipotent (as most plant cells are) - that is, they have the capability to produce any desired cell type or organ of the body under specific conditions - or they can be pluripotent, that is, they are able to develop into several though not all cell types or organs. As embryonic stem cells are more likely to have capabilities nearing totipotency than stem cells from adult tissues, the immediate emphasis in the area of stem cells is going to be first in the direction of establishing cell lines derived from early human embryos, from which stem cells could be isolated. The numerous infertility clinics of our country will be, perhaps, the best source of such embryos.

(6) Enzyme engineering and technology involving, for example, immobilized or stabilised enzymes, new or modified enzymes, new classes of enzymes such as ribozymes, or new enzymatic routes, to produce important organic compounds. Enzymes are biological catalysts (generally proteins) and are poised to replace inorganic catalysts that are today widely used in chemical industry. (Proteins are abundant biological entities made up of twenty aminoacids strung together like pearls in a necklace, by a special type of thread - a chemical bond called the peptide bond. One protein differs from another in the total number of aminoacids and their sequence in the chain.) The use of enzymes in todays chemical industry would offer many advantages: no by-products (so, lesser expenditure on purification of the primary product); no pollution; and much less expenditure on energy as enzyme-catalysed reactions take place at our ambient temperatures (30-37° C) and at ordinary pressure, unlike reactions catalysed by inorganic catalysts that require high temperature and pressure.

(7) Increasing photosynthetic efficiency to increase biomass production in the plant, using the same amount of light and other inputs.

(8) New DNA technologies, such as DNA fingerprinting (which allows unequivocal identification of an individual even from a single hair-root); sequencing of genomes; development and use of new molecular markers for plant identification and characterization; development of DNA-based probes for diagnosis of inherited disorders (some 5000 such disorders being already known); antisense technologies that are aimed at blockage of the function of a particular stretch of DNA (that is, a specific gene); and computing using DNA. For example, the DNA fingerprinting technology developed in the CCMB (Centre for Cellular and Molecular Biology) at Hyderabad by Lalji Singh has helped resolve innumerable paternity disputes and some hundreds of criminal cases such as Rajiv Gandhi assassination case and the Tandoor murder case. Genetic disorders can be diagnosed in three ways: by using DNA-based probes, chromosomal analysis, or enzyme analysis. Therefore, production of DNA-based probes for diagnosis of genetic disorders is bound to become a major business. And already DNA-based computers have been designed, for example, to solve the travelling salesman problem. As of today, DNA-based computing is slow but it is a matter of time for it to become competitive. Remember, how slow the computers at the beginning of the last half-century were when compared to today's machines.

(9) Plant-based drugs: Use of modern biological techniques for validation, standardization and manufacture of (where necessary, appropriately modified) indigenous plant-based drug formulations. This area is of special interest to our country and has the potential of making us the world-leader in medical care. We have some 40,000 unique traditional plant-based drug formulations that have come to us through the documented Ayurveda, Unani, Siddha and Tibetian systems of medicine and the undocumented tribal systems of medicine. They are based on, perhaps, 10,000 medicinal plants out of which at least 7,000 have been documented already. There are infalliable arguments supporting the view that while a proportion of these formulations is unlikely to work if tested impartially, using modern validation protocols, a fair number of them - in my estimate, at least 4,000 - are extremely likely to work and be shown to

be efficacious. Against this background, it is extremely sad that we have only one traditional formulation, Liv 52 marketed by Himalaya Drug Company, which is today a prescription drug in some parts of the world outside India. We ourselves have prepared a project according to which it should be possible to document these 40,000 formulations over a period of ten years and to market at least 100 standardized and validated traditional plant-based drug formulations during this period, which would bring in a net profit (after deduction of tax) of above rupees 6,000 crores at the end of the tenth year at today's prices

(10) Peptide synthesis to make new drugs or other materials of industrial and/or commercial importance, such as salmon GnRH analogue (Ovaprim) to induce ovulation in fish. Proteins are major constituents of living systems. As already mentioned, proteins are made of 20 naturally occurring building blocks called amino acids which, in a protein, are strung together in a chain, like pearls in a necklace. Proteins have generally more than 100 aminoacid moieties in each of their molecules. The sequence of the aminoacids and the number of each aminoacid in a protein molecule is what defines the particular protein. Peptides are just small proteins of, say, 2 to 50 aminoacids. One could thus have 400 possible dipeptides. Similarly, there would be 8,000 possible tripeptides and 160,000 possible tetrapeptides, this number would increase exponentially as the number of aminoacid residues in the peptides increases. As it turns out, over the last three decades, a very large number of peptides have been shown to have useful pharmacological activity. For example, when we discovered in the CCMB the 47 -aminoacid peptide, seminalplasmin, it was the second such peptide shown to have antimicrobial activity. Today, there are perhaps more than 1,000 such peptides known. Many peptides are already in the market to serve various purposes but that is clearly not even the tip of the iceberg. In fact, we can predict safely that, by the end of the next four decades, plant-based drug formulations derived from traditional medicine around the world (such as India; China and Latin America), will account for some 50 percent of the drugs in the market; 20 percent will be produced through genetic engineering, 5 percent will be monoclonal antibodies, 5 percent would come through rational drug design, and 20 percent would be peptides.

(11) ***Assisted Reproductive Technologies*** **(ART)** such as artificial insemination (using husband's or donor semen), in vitro fertilization, intracytoplasmic sperm injection, and techniques involving egg donation, embryo transfer, and surrogate motherhood to help couples that are infertile or to help women who does not wish to go through a pregnancy to have their own biological child. In fact infertility is the most highly prevalent 'disease' in the world, with some fifteen percent of couples being infertile. As of today, with the help of the assisted reproductive technologies I have mentioned above, it is possible to take care of 85 percent of the infertility cases and make them conceive. In vitro fertilization (IVF) was first used successfully by Robert Edwards and Patrick Steptoe to produce the first test-tube baby, Louise Brown, who was born in July 1978. Today the technology has advanced to a stage where one can just take a single sperm (say, from men that are infertile on account of low sperm count) and then inject it into a oocyte to effect in vitro fertilization; this technique is called introcytoplasmic sperm

injection. One can today freeze embryos and then bring them back to life at any given point later on and implant them into the uterus of a woman. Thus, a woman can give birth to a child from her husband even after the husband is dead. In surrogate motherhood, a couple who is otherwise normally fertile but the wife does not want to go through the nine-month pregnancy that would confine her for a substantial period, can have the egg of the wife fertilized by the sperm of her husband in the test tube and then have the fertilized egg. implanted, not in the uterus of the wife but of another woman who would then give birth to a child totally unrelated to her. The development of IVF technologies has made it possible for an infertile couple to have a child, using the egg or the sperm of a donor if necessary. In the last 10 years or so, our country has seen a mushrooming of infertility clinics claiming to do all the above, all over the country.

(12) New cloning technologies, especially cloning of genetically- engineered animals that would produce useful products such as those mentioned in Section (1) above. As you would recall, Dolly was the first cloned animal that was produced in the laboratory. That is what we do when we grow another plant from a cutting. Similarly, when we grow an entire plant from a single cell in tissue culture, we are essentially cloning the plant from which the cell used for tissue culture was derived. As it turns out, cloning of animals has been much more difficult. These difficulties have now been largely overcome and cloning of animals is now common place. The CCMB at Hyderabad has been trying to conserve endangered animal species through cloning.

(13) Organ transplantation, especially xenotransplantation- that is, transplantation into humans of organs from other animals. It appears that, for this purpose, pig may be the most suitable, biochemically, anatomically and immunologically. The major problem in xenotransplantation is the hyper-acute immunological rejection of the "foreign organ", which occurs in a matter of minutes, but which does not occur in homotransplantation - for example, in the case of a kidney transplant from one human donor to another human recipient. This problem has been recently overcome by identifying the molecular basis of the hyper- acute rejection and then genetically engineering a pig to avoid it.

(14) New drug-delivery systems such as lipsomes and electrical patches, and the use of circadian rhythms to optimise the effectiveness of the drug. It has been found that different people have different circadian rhythms. Thus, the level of drug-metabolizing enzymes may be minimal
at, let us say 12 o' clock midday and 12 o' clock midnight in one individual, while this may be so at 6 o' clock in the morning and 6 o' clock in the evening for another individual. If we give the drug to the patient at a time that it would be metabolized to a much lesser degree, one would need to give smaller amounts of the drug than otherwise. When we have ways and means of quickly assessing such circadian rhythms, we would be entering the age of individualized

medicine which would be less expensive and less toxic for the individual. An electrical patch on your skin (if you are diabetic) could take care of your insulin requirements for, say, a month. All that you would need to do is to carry a small pocket computer (like a cell phone) which has been programmed to direct the electrical patch to release a measured amount of drug at predefined intervals; the drug would then get electrophoresed through the skin on account of the generation of a voltage gradient and then get into the blood stream. This would replace the cumbersome injections of insulin that so many around the world have to take, often twice a day.

(15) Nutraceuticals that help recovery after surgery or after an episode of a major disease, or help protect one against certain medical and health problems. For example, a Swedish company, Probi, has isolated a strain of *Lactobacillus planetarum* which is apparently present in the digestive tract of Europeans and Americans. (Indians have not yet been tested for its presence.) The presence of this organism has been correlated with the ability of the person to recover after major surgery or after chemotherapy of cancer; this organism also seems to protect people against a vast range of stomach disorders including stomach ulcers, irritable bowel syndrome and constipation. If this organism is depleted from the digestic tract, one becomes far most susceptible to the after effects of surgery or cancer chemotherapy. Probi is, therefore, marketing this organism in various forms including a highly delicious soft drink!

(16) Rational drug design: Until a few decades ago, the only way to discover a new drug was to synthesise a very large number of compounds, mostly on an adhoc basis, in the hope that one of them would turn out to be effective against a particular disease. This led to a situation where it cost something between half a billion to a billion dollars for bringing a new drug in the market. Consequently, over the last many years, we have not added more than, say, ten new drugs per year to the repertoire of medicines already available. In rational drug design, we first identify the molecular target that we wish to attack. To do so, it becomes necessary to understand the mechanism of causation of the disease. Once we understand this mechanism and identify the molecular target, we have, today, highly effective computerised programmes to design a molecule which would hit the target. This is what rational drug design is about. It could cut the cost of discovery of a new drug by one order of magnitude and, in addition, reduce the time from concept to marketing (now 12 - 15 years) to 7 - 8 years.

(17) Production of useful materials - existing (for example, polyunsaturated fatty acids or beta-carotene, both of which are essential for normal vision) or new- from so far unutilized or underutilized but widely available resources such as marine organisms. India is already producing high quality beta-carotene (which gets converted to vitamin A in the body) from *Donaliela,* a marine algae, at a factory of Shantha Marine near Tiruchendur in Tamil Nadu. I have the pleasure of being the Chairman of Shanta Marine. We are able to produce betacarotene at a very low cost, as Tiruchendur coast has some 340 days of

uninterrupted sunshine and the right temperatures all through the year. All that we need to do is to pump the sea water from the coast in open raceways, and seed them with the organism that we have isolated. The sun does the rest. We have, therefore, an enormous saving in energy cost. We have, in fact, offered to take care of the entire Vitamin A requirement of our children as prescribed by the WHO, for Rs. 8/- per child per month if the Government is willing to put it in the midday meal programme and we are assured that what we supply would be used for this purpose.

18) Production of new materials using new ideas. observations or research findings, such as bacterial ropes or biodegradable polymers. For example, bacterial ropes that essentially consist of certain mutant bacteria which have the ability to grow into spagetti- like structures, when impregnated with certain metal ions, can be stronger than steel but much lighter and biodegradable.

19) DNA vaccines, which would be much cheaper than protein antigen- based vaccines that are generally used today.

20) *New medical diagnostic technologies,* such as combination of MRI and PET-SCAN for correlation of structure and function in normal and diseased individuals. The well-known technique of MRI gives information about the structure of a system, while the new technique of PET-SCAN gives information on the functioning of the system. Let us take the case of a person suffering from neurocystosarcosis on account of a parasitic infection of the brain. This infection can occur through uncooked pork or unwashed raw vegetables. The parasite can undergo three possible fates in the brain: remain active and alive, die, or remain dormant. If you look at the MRI of such a brain, you will be able to see the cysts caused by the parasite but not know which cyst is dead, alive or dormant. This becomes important as we have drugs which can be safely given only if the number of live cysts is small. PET-SCAN can distinguish between an active, a dormant, or a dead cyst. Unfortunately, we do not have any commercial full-fledged PET-SCAN machine in India as of today. The Department of Atomic Energy (DAE) , at a meeting held in Mumbai on 17th April 2003, has apparently decided to locate two medical cyclotrons - one in Kolkata and the other in Hyderabad - to produce the short-lived radioisotopes needed for a PET -SCAN. If the DAE does that, a consortium of hospitals in Hyderabad is ready to buy the PET- SCAN machine and run the whole establishment.

21) *Biosensors,* for example, optical sensors using special thin films for detection of bacteria.

(22) *Use of microbes (selected or genetically engineered} for effecting chemically difficult transformations,* for example in the field of steroids that are widely used as drugs.

(23) Bioremediation, for example of effluents or waste, using biological systems. A septic tank and an oxidation pond are simple examples of such bioremediation. Production of biogas

is value-added bioremediation!

(24) Processing of low-grade ores using microorganisms: Commercially viable bio-processes are available today for processing such ores of over a dozen metals.

(25) Bioinformatics, including genomics and proteomics. It is amazing how quickly bioinformatics has, like biotechnology, become a part of the common vocabulary of man around the world. Bioinformatics involves analysis of data pertaining to biological systems and converting this analysis into commercially exploitable knowledge. This could be data on the sequence of the building blocks in DNA or in protein. For example, one could look at the sequence of the genome (DNA) of a pathogenic microorganism and discover new drug targets - an exercise in which, as of today, amongst others, the bioinformatics group of Sat yam Computers at Hyderabad is actively engaged. Remember, there are several million species known. The sequence of the building blocks of DNA of just one human being alone will fill nearly 700 books (typed single space) of 500 pages each. So there is an immense amount of information pertaining to biological systems that is waiting to be analysed!

(26) Nanobiotechnology, in which the operating or useful unit is of the scale of, say, a nanometre (millionth of a millimetre). It is today possible to entrap molecules in nanostructures and carry out reactions in such structures, which offer many advantages. However, as of today, this is only an emerging and exciting field to pursue.

(27) ***Biological warfare:*** Recall the anthrax attack in the U.S. in 2001. Today, it is possible to design even ethnic weapons that would target only a particular group.

III. ADVANTAGES OF BIOTECHNOLOGIES

Biotechnologies are always non-polluting and, often, labour intensive. They make use of replenishable natural resources and help their conservation. They help, directly or indirectly, in saving energy. The cost of products produced through a biotechnological process is almost always less than that of the same product produced, say, through a chemical synthetic route.

Biotechnologies are less accident-prone. In spite of their high level of intellectual sophistication, it is easier to train people to handle biotechnologies than other technologies. Above all, they are interesting and exciting for all those involved with them.

IV. THE INDIAN ADVANTAGE

No other country in the world today has the unique set of advantages that India offers for large-scale practice of biotechnology. We have one of the largest bio-diversities - including human biodiversity - in the world. We also have one of the largest coast lines anywhere. We have at least seven distinct climatic zones, and one of the largest and most varied set of marine organisms anywhere. The ambient temperature in most parts of the country - often all the year round - is just what living organisms need for their activities that result in a biotechnological product; this curtails immensely the cost of cooling or heating which becomes obligatory for the practice of biotechnology in most parts of the Western world. There are places on the Indian

coast (like Tiruchendur already mentioned), where there is uninterrupted sunshine for some 340 days in the year so that one can grow marine organisms in open raceways.

We have an enviable infrastructure and a large pool of trained manpower, with experience in most of the areas of biotechnology. Our labour and infrastructural costs are, perhaps, lower than anywhere else where biotechnology can be done and is being done, with the possible exception of China. We have large tracts of land available for growing the desired plants required for agriculture-based biotechnologies. We have experience of building world-class institutions in virtually every sector of human endeavour - from outstanding basic research to efficient industrial production. We have, of course, many problems but we also know how to overcome them; in a nutshell, the advantages, far outweigh the disadvantages.

It is a pity that we started much later in biotechnology than we should and could have but, even now, the prospects for the future are bright, provided we have an appropriate biotechnology policy, adequate investment both in the private and the public sector, and adequate cooperation between the research institutions and the industry.

V. SOCIAL, MORAL, ETHICAL, LEGAL, ECONOMIC AND POLITICAL IMPLICATIONS OF MODERN BIOTECHNOLOGY

Never before in history have newly emerging areas of knowledge had so many diverse implications and import as modem biology and biotechnology have. The primary reason for this has been that biology touches our lives as no other science does.

The areas in biotechnology with significant socio-politico-economic, ethical, moral and legal implications, are genetic engineering, gene therapy, tissue culture, stem cell culture, DNA technologies (including DNA fingerprinting, DNA-based diagnosis and sequencing of genomes), plant-based drugs, assisted reproductive technologies (ART), cloning technologies, organ transplantation, bioinformatics, and biological weapons. I will deal with the implications of ART and genetic engineering in some detail, but before I do that I would like to give a few examples from other areas.

Not long ago, a case of immigration was referred to the CCMB at Hyderabad by the British immigration authorities. In this case, an Indian couple living in England with two children, had a third child in India while they were visiting the country. When they wished to take the third child back to England, the immigration authorities asked them to establish that they were the biological parents of the child to rule out the possibility that they were bringing an abandoned child for sale in the U.K. The case was referred to the CCMB for DNA fingerprinting. When Lalji Singh, Director of the CCMB, did the DNA fingerprinting of the entire family, he found that while the child born in India was the child of the husband and wife who were taking it to the U. K, one of the two children living with them in England wasn't their child. The wife had committed adultery without the husband being aware of it. The question that Lalji Singh faced was, what to say to the immigration authorities. If the truth was told to them and later became known to the parents, the family may break up. On the other hand, would hiding the truth be ethical ? What Lalji Singh finally decided was to answer only the question that he was asked by the immigration authorities, and keep to himself the other relevant (and valuable) information

that he had. Did Lalji Singh do the right thing?

Genetic disorders can be classified broadly into two categories. In the case of one category, if you carry the particular defective gene(s), you are bound to suffer from the disorder sooner or later in your life. This is the case with sickle cell anaemia, thallasemia, cystic fibrosis, haemophilia, or albinism. There are, however, a much large number of genes, called susceptibility genes, the presence of which only makes one susceptible to the disease sometime in the person's life. As of today, we do not know what environmental or life style factors are responsible for converting the susceptibility status in such cases, to the diseased status later in the life of an individual. All that we can say today in this regard is based entirely on statistical data; so we can only say what the chances are of a person having a particular susceptibility gene, becoming diseased later in life. For example, if a woman carries a BrC 1 or BrC 2 gene, it makes her more likely to have breast cancer later in her life than those who don't have such a gene. Thus, the incidence of the presence of one of these genes amongst the Parsis is the highest in the country; so is the incidence of breast cancer in Parsi women. However, having these genes does not mean that one is bound to have breast cancer.

Now put yourself in the position of a doctor, say 20 years from now when we should have cheap technologies available for screening a new-born child for the presence of a large number of such susceptibility genes. You take your child to the doctor and he finds out that the child is carrying a gene such that there is a 20 percent chance of his suffering from a particular disease after he crosses 40. Should he or should he not share this information with you? If he did, and the child turned out to be amongst the 80 percent who did not suffer from the disease after crossing 40, you could sue the doctor for keeping you and the child under suspense for 40 years for nothing. If, on the other hand, the doctor did not share the above information with you, and the child happened to be amongst the 20 percent who suffered from the disease after crossing 40, you could again sue the doctor for withholding information from you which information would have made you better prepared to meet the challenge of the disease.

Suppose you have obtained a traditional plant-based drug formulation from a tribe which the tribe has been using for a thousand years. You then commercialise and make money out of it, without sharing it with the tribe. Would it be ethical? And even if you wished to share the profits, how much should go to the tribe?

There is a plant called *Phyllanthus amarus* which has been used widely in virtually all parts of the country in several indigenous medical systems of ours, as well as in many other parts of the world, to cure certain liver disorders. Since the use of our traditional drugs is based on symptoms, what is implied is that the above plant-based drug formulation could take care of certain symptoms, without the disease as we know of it today having been identified. What the Nobel prize-winning scientist, Barry Blumberg who discovered the Hepatitis B virus, did was to show that extracts of *Phyllanthus amarus* inhibited two key enzymes of the Hepatitis B virus, and eliminated the virus from the system in an animal model, thus indicating that the extract could be

a cure for human Hepatitis Band might even clear off the Hepatitis B virus from the nearly 300 million carriers of the virus around the world. He obtained two patents [P S Venkateswaran, I Millman and B S Blumberg, US Patent numbers 4673575 (16th June 1987) and 4937074 (26th June 1990)] on this work, giving due credit to ancient Indian tradition for use of the plant for curing symptoms which correspond, amongst other diseases, to Hepatitis B. Legally, these patents could not be challenged as none of the ancient medical systems in our country ever claimed to have cured Hepatitis B using extracts of *Phyllanthus amarus.* However, were these patents morally or ethically justified?

Is therapeutic cloning ethical? By therapeutic cloning I mean cloning an individual and allowing the foetus to grow to a stage where organogenesis has begun so that one could harvest the organs which could then be further grown in the laboratory and used for transplantation on the individual who has been cloned; in such cases, there will be no immunological rejection of any kind and one would not need to be on expensive immunosuppressive agents like cyclosporin as is the case with organ transplantation (from another individual) today, for no two individuals (except identical twins, who are like clones of each other) are immunologically identical; without an immunosuppressive drug, the transplanted organ will be rejected.

There may be religious objections to xenotransplantation using pigs, amongst certain sections of the world population. If so, how should one deal with it? Will such transplantation be considered ethical by Muslims ! There was recently a case in the United States in which a child born to an American couple was found to be suffering from a rare blood disorder. A remedy was suggested for the situation. If the couple would agree to produce another child (which the couple wanted in any case) who would be selected at the early embryonic stage, after in vitro fertilization but before transfer of the embryo into the woman, in such a way that a certain part of his immunological make up would be the same as that of the sick child, the latter could be cured by transplantation of cells from the new born without doing any harm to the new born (Verlinsky *et al.Reproductive BioMedicine Online,* 2000, Vol. 1, pp 31-32). This was precisely what was done by the couple. The second child was a son; cells from the umbilical cord of the second child were transplanted into the diseased child who was then cured. It was a win-win situation for everyone. Yet the question was raised: was it ethical to produce a pre-selected child? A similar procedure was recently approved for a British couple in the United Kingdom (Designer baby wins court go-ahead, *New Indian Express*, 10th April 2003)

In the latter part of the last half century, the Chinese had a female chimpanzee inseminated with human sperm. It is believed that the idea of the Chinese was to develop a race which would have the minimal intelligence of human beings and the strength of a chimpanzee - a kind of a slave race. In fact, the pregnancy was established. It was, however, terminated during the Cultural Revolution. Scientifically, the results of such an experiment would be extremely interesting, and such experiments are not difficult to do. Should we permit them or put a moratorium on them?

We are all familiar with the fragrance of vanillin (who hasn't had vanilla icecream?). Till recently, virtually the entire vanillin of the world came from Malagasy Republic where seventy thousand farmers have been involved in cultivation of vanillin. Now, vanillin is being produced more cheaply through tissue culture by American and Japanese companies. There is, therefore, no market for vanillin produced naturally, and the seventy thousand farmers may be facing unemployment? Has this all been fair?

There is a protein called thaumatin found in a particular plant endemic to parts of Africa such as Nigeria. Thaumatin is five thousand times sweeter than sugar and is completely non-toxic. Being a protein, it is degraded in the digestive tract after ingestion and, therefore, does not get into the blood stream. It has been also produced through genetic engineering. I believe it may not be difficult to make it fifty thousand times sweeter than sugar. Once we do that we can produce it at a cost which would be a fraction of the cost of the cheapest cane sugar or beet sugar around the world. If that happens, some seven million workers in the sugarcane industry in the third world alone may face unemployment. This would be a major socio-economic problem. How should we brace ourselves to face it?

Biological warfare is upon us. I have discussed its history and various ramifications in a series of articles in the *New Indian Express* (7th, 14th, Z i– and 28th November, and S- December, 2001).

As I have already mentioned, we can today design ethnic weapons that would affect only a particular segment of world's population. For example, Americans above 50 are known to have a depleted immune response. Therefore, certain pathogenic organisms released in the environment may affect only the elderly Americans but would leave us, the Indians, completely unaffected. The depleted immune response in the older Americans is likely to be a consequence of the fact that they have lived in a virtually semi-sterile environment so that their immune system has not been challenged enough and could have atrophied. On the other hand, we in India are being continuously challenged by low levels of infection in our environment and, therefore, our immune system is robust. We can thus exploit this advantage to produce an ethnic-specific weapon. Would that be ethical?

Recently, a group of Australian scientists inadvertently produced a virus which, like HIV (the virus which causes AIDS), affects the immune system. Imagine what would happen if such a virus is released in the environment. The Russians, not long ago, genetically engineered the legonnaire disease-causing organism, to make it more deadly.

The list of biological weapons on which considerable work has been done includes nearly 60 bacteria, viruses, other organisms, and toxins. (Examples would be: viruses that cause small pox, Ebola fever, Marburg fever, Lassa fever, and various haemorrhagic fevers; bacteria that cause anthrax, plague, glanders, and tularemia; and toxins such as botulin and ricin.) How ethical is it

to manufacture and store them as is being done by many countries? Great Britain, the US, the erstwhile USSR (now Russia), Canada, Germany, South Africa, Japan, Iraq, Iran, Syria and North Korea are known to have had extensive biological weapons development programme. Botulin is the most deadly poison known to us, its LD50 (the amount required to kill 50 percent of the exposed individuals) for human beings being 6 nanograms per kilogram weight, that is, approximately 400 nanograms per person. We may thus need less than one kilogram of botulin to kill the entire population of the world, and the delivery of it would be easy: just put it in the water supplies (botulin is an intestinal toxin). Then, there are pests that can be released to destroy our agriculture. There is indeed no doubt that biological weapons are the most dreaded ones today - far most dangerous than nuclear, chemical or conventional weapons. It is, therefore, not surprising that the Fifth Review Conference on the Biological Weapons Convention held in December 2001, was a disaster! The United States has refused to sign the proposed inspection and verification protocol for biological weapons. Has all this been ethical?

VI. THE ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)

I will discuss here some of the ethical dilemmas that we are currently facing in India in respect of ART. Some of these problems probably exist everywhere, but some are no doubt the consequence of the special social and economic conditions prevailing in India.

The Market for ART in India. With a population of over one billion, India will have at least 300 million individuals in the fertile group which will translate into 150 million couples. With the incidence of infertility in India being approximately 15 per cent - as, perhaps, elsewhere in the world - we would have approximately 22.5 million infertile couples in the country at any given time. If we assume that 10 percent of these couples would provide a market for infertility treatment every year, this would mean approximately 2.25 million couples per year who, if their resources permit and if adequate facilities exist in the country, may like to visit an infertility clinic for advice and treatment.

At an average of, say 50,000 Indian rupees per couple, this would tantamount to 112.5 billion rupees per year as the potential market for infertility in the country. As of today, perhaps only ten percent of those who have a infertility problem, have access to appropriate professional medical advice. This would mean 225,000 couples and a market of rupees 11.25 billion.

We have no registry of, or a licensing system for, infertility clinics in the country so far, therefore, we have no way of knowing as to how many such clinics exist in India as of today. However, several estimates give the figure somewhere between 200 and 300. Assuming the upper number to be close to reality, and an even distribution of patients across the clinics, it works out to 750 new cases of infertility reporting at each clinic every year, on an average. As everywhere else, some clinics would have a larger clientele, but the *average* gross income (turnover) of an infertility clinic in India, at present, could be approximately 37.5 million rupees.

The Infertility Clinics. While India has no doubt, several infertility clinics the facilities and quality of which would match with similar clinics anywhere else in the world, the unfortunate element in the story is that there are many which have extremely inadequate facilities and staff. It is also widely known that many clinics, including some of those that have excellent facilities and staff, engage in a number of unethical practices. Let us look at some examples.

Many instances are known where a patient has only been given intrauterine insemination (lUI) but charged for in vitro fertilization (lVF). Many other similar malpractices become possible in India because 70 percent of the country is rural and about half the women of the country (a much larger proportion in the villages) are illiterate. The average per capita income in the country may be about the lowest in the world, if one takes away the upper creamy layer of the society which, say, pays tax and represents a very small proportion (less than 5 percent) of the population. Therefore paying for IVF when only IUI has been done on an infertile couple, must cause an immense financial strain on the couple. As having a child in India is of paramount importance - both socially and economically - and a stigma is attached to a couple (specially the woman) if the couple does not have a child, the couple does everything possible to have a child. Often, people in the villages sell their land and/or other assets to come to an infertility clinic. It would, therefore, be not only unethical but even criminal from the social point of view for such a couple to be charged for IVF if only IUI has been done.

There was a case in 2002 in the State of Andhra Pradesh in India where a woman was declared pregnant by an infertility clinic, following an ART procedure on her. Later, it was found that the woman was never pregnant. There is no law in the country which would allow appropriate and expedient action to be taken against the erring ART clinic.

There have been advertisements in Indian newspapers by ART clinics saying that their success rate in IVF has been over 60 percent - that is, more than three times the average success rate around the world. Such clinics have been clearly misleading the people through such an advertisement to gain advantage over other infertility clinics.

There have also been advertisements in the recent past in our newspapers by infertility clinics saying that they can give a couple a child of the desired sex by pre-natal sex selection - that is separation of the X and Y spermatozoa - when the fact is that no established technique yet exists which would separate X and Y sperm with one hundred percent efficiency. Techniques for enriching a sperm faction with X or Y cells are, of course, known but in that case the concerned doctor in the infertility clinic should state that all that he or she will be able to do is to merely increase the chances of the couple having a child of the desired sex, without guaranteeing the sex of the prospective child. Instead of doing this, such infertility clinics, bank on the fact that 50 percent of the time they are going to be right. For the failures, in view of the vast ignorance of an

average infertile couple, the concerned doctor of the infertility clinic can take umbrage by laying the blame on the couple for not strictly following the unwarranted instructions given to the couple at the time of insemination, in the full knowledge that if the number of such instructions is large and if they are complex (irrespective of their relevance to the desired objective), they can always lay the blame on the couple for not following one or more of these instructions, in case the child born is not of the desired sex.

In many infertility clinics in the country today, there is no professional counselling available. There is no codified system to decide as to when the couple must be asked to give up the treatment on ethical grounds, and advised to adopt a child; instead, the treatments are prolonged unnecessarily over a large number of cycles in spite of the fact that the gynaecologist knows that the expense that the couple would be incurring would be infructuous. There is no check in the country as of today to prevent such a malpractice. Some gynaecologists engage in artificial insemination by the husband's semen (AIH) or by donor semen (AID), when no adequate facilities exist with the gynaecologist for the processing of semen, or for doing appropriate checks if the semen that is being used is of the designated individual, or for documentation of what is being done.

In my estimate, unethical practices such as those mentioned above, today, perhaps, result in an infructuous expenditure of somewhere between three and four hundred million rupees by the people of the country, most of whom would have sacrificed a great deal to be able to pay the expenses of treatment at an infertility clinic.

The Ethical Issues.

(a) An important issue in the practice of ART in India is, who should be the donor of semen for AID? In this respect we ought to remember that a vast majority of the population in India today still live as a part of the larger joint family. Further, barring a small proportion of the emancipated, the mother-in-law still exercises substantial control over the daughter-in-law, specially in a joint family. Let us also remind ourselves of the widely prevalent deficiencies in the country in regard to the status of a woman. (I must add here that ours is a country full of diversities, even contradictions. In fact, the only statement that is true about India is that no statement about India is either true or false. Therefore, there are exceptions to everything that I have said or will say about the country in this article.) Against this background let me present a common Indian scenario.

Traditionally, if a couple is infertile in India, the family always lays the blame on the woman even though, in about half the diagnosable cases, a male factor is the cause of infertility. The mother-in-law would never acknowledge in public that her son, and not the daughter- in-law, is at fault. Therefore, even if she is convinced of the biological fact that the daughter-in-law is fine but her son has a problem, she would want to make sure that her son's infertile status is kept as

close a secret as possible. Therefore, she takes the daughter-in-law to an infertility clinic and, following the advise of the clinic that the daughter- in-law needs to be inseminated by donor semen, the mother-in-law asks the clinic to inseminate the daughter-in-law by the semen of the husband's brother or of a close family friend. The daughter-in-law would normally have no say in this regard, no matter how opposed she might be to the idea of being inseminated by the semen of someone whom she has been seeing and would continue to see all the time. The psychological stress that the daughter-in-law will go through for the rest of her life, including during pregnancy, on account of the knowledge that the biological father of the child she is carrying is someone whom she knows and has social intercourse with all the time, would not be a matter of concern to the rest of the family. We have to remember that in the current social milieu in the country, lack of concern for the daughter-in-law, and exploitation of her by the rest of the family in almost every conceivable way, is extremely common. It is for this reason that there are hundreds of what are called dowry deaths in the country every year, where a woman either kills herself or is killed by close relatives (such as the husband or his parents) because she has not brought enough dowry at the time of the wedding, or because she is unable to get more money from her parents after the wedding, to satisfy the greed of those who control her new home after marriage.

In such a scenario, quarrels between a mother-in-law and her daughter- in-law are not yet a thing of the past in India. Against this background, imagine the following scenario. At the instance of the mother-in-law, a woman is inseminated with the semen of her husband's brother or friend. A few years later, the mother-in-law and the daughter-in-law quarrel. The mother-in-law then says publicly that her daughter-in-law has committed adultery and names the person with whom the adultery has been committed. DNA fingerprinting - a technology which has been widely used in India since 1986 and in the development of which in the country I had a small role - will establish that the basis of mother-in-law's allegation that the child is not the daughter-in- law's husband's child but of another man, is correct. As the infertility clinics are, as of today not required to keep appropriate records, there will be no way that the daughter-in-law can establish that she never slept with the man who is the biological father of the child, and that she was artificially inseminated with that man's semen with the express approval - even suggestion - of the mother-in-law.

When we asked the National Commission for Women, a statutory organisation set up by the Government of India, as to their opinion in regard to the anonymity or otherwise of donors of semen in cases such as the ones mentioned above, the Commission was strongly of the opinion that all sperm and egg donation must be anonymous. The situation I have outlined above would clearly support this view. I hope the following incident that actually happened in Hyderabad, would clear any doubts anyone may still have on this score. A woman - more courageous and self-reliant than usual (as what I am going to say now, would establish) - was taken by her mother- in-law to an infertility clinic to be inseminated at an appropriate time later by the semen of a close friend of the husband, whom the woman knew well. An advance was paid to the clinic for the procedure of AID (artificial insemination using donor semen) to be performed on the

woman later on. A while later, the woman went back to the clinic, this time all by herself, and asked that the money that was paid to the clinic as advance on her behalf, be returned to the woman. When the clinic asked as to why this request was being made, the woman said that this was so because she was now pregnant. The doctors at the clinic were naturally puzzled and asked her as to how she became pregnant. She then answered that since she was going to be inseminated by the semen of her husband's friend, whom she knew very well, she saw no harm in sleeping with him at an appropriate time just for once. The pregnancy was a natural consequence of this act which she did not consider as unethical, for she had promised to herself that she will never sleep with that man again. She clearly did not perceive any difference between being inseminated by the semen of a person whom she knew very well, and sleeping with him just once for achieving the objective of AID without having the family spend any money. I leave it to the readers to judge whether, given the circumstances I have mentioned, what she did was ethical or unethical.

(b) The second major question that the ART clinics in India are facing today, pertains to donation of the oocyte. Who should be an oocyte donor? As of today, in India, it is almost always a close relative from the side of the man or the woman. The idea of having a close relative or friend of the family as donor of the sperm or the egg, is that the entire story is kept within the family-friend boundary. The other implications - including the genetic and the social implications - of such donation are not understood. For reasons mentioned in the preceding section in respect of sperm donation, I strongly believe that donation of sperm or eggs by a close relative or a close friend is unethical and that we should have a law requiring that both sperm and egg donation be anonymous. We need to have sperm banks that would also keep track (for example, through appropriate advertisement) of possible oocyte donors against monetary compensation. We also need to encourage the system of egg sharing in which an indigent infertile couple that needs financial resources for ART agrees to donate oocytes to an affluent infertile couple wherein the wife can carry the pregnancy through but cannot produce her own oocyte, for in vitro fertilization with the sperm of the male partner of the affluent couple, for a monetary compensation that would take care of the expenses of an ART procedure on the indigent couple.

(c) The third question being raised in our country in regard to the practice of ART pertains to surrogacy. Who may act as the surrogate mother? As of now it, again, is a close relative - for example, the mother of the male partner or the sister of the female partner. Thus, in many cases in the country, a woman has given birth to her own grandchild without incest. On the other hand, there are also regular advertisements, for example in the magazine, Woman's Era, for surrogate motherhood. I believe it is unethical to have a close relative act as a surrogate mother, especially in the Indian environment where family ties are very close. In a closely-knit family, the fact that the child was delivered by so-and-so will always be known to the members of the family and, eventually, to the child. Carrying a child in one's own womb is, in the Indian society, the epitome of a close relationship. Therefore such a relationship could come in the way of the child establishing the expected relationship with the biological mother, without confusion in the child's mind, especially if the child and the surrogate mother see each other frequently. Perhaps, the

ideal solution would be what is already being practiced by some in the country, that is, to advertise for a surrogate, and strike an appropriate financial arrangement that will adequately compensate the woman who agrees to act as a surrogate mother.

Another relevant issue that is exercising the minds of people in our country in regard to surrogacy is whether or not surrogacy in India should be considered ethical if the reason is only convenience of the couple. There is a view that surrogacy by assisted conception should be considered only for those for whom it would be physically or medically impossible or undesirable to carry a baby to term, and not for those who are perfectly capable of producing a child in the normal way but desire a surrogate mother because the woman does not want to go through pregnancy for the sake of convenience or for reasons such as a break in professional service or simply the risk of having one's vital statistics affected. I am personally in favour of allowing surrogacy for whatever reason the couple consider as important.

(d) Then there is the question of the right of the child born through donation of a germ cell, to know who his/her biological father or mother is, when the child attains adulthood assuming, of course, that the sperm or the egg donation has been anonymous. In the Indian environment it would, perhaps, be both impractical and unethical to give this right to the child. Given the closeness of relationships in India, this right would be psychologically unfair to the child, to the donor and to the couple who have brought up the child; the child, of course, must continue to have the right to know everything else (except the name and address) about the person who donated the oocyte or the sperm.

However, we have the technique of DNA fingerprinting available today which establishes biological parenthood without any doubt. If a need arises for DNA fingerprinting to be done on the child, it would become obvious that the couple who brought up the child does not comprise both the biological parents of the child. Such a discovery for the child, all of a sudden, could alienate him from his parents whom he could accuse of deliberately hiding the truth from him. Therefore, there may be no harm in the couple's telling the child at an appropriate time that he/she was born following anonymous sperm or egg donation.

Lack of transparency in surrogacy can lead to some hilarious situations. In 2001, a woman came to one of the best-known maternity hospitals in Hyderabad, to be admitted for delivery. She wanted to be registered in the name of her sister as she was acting as a surrogate mother for her sister's and brother-in-law's child. Not having handled such a case earlier, the doctor-in-charge of the hospital - an eminent and highly ethical person - agreed to this request, only to realise a little later that this was a mistake. What would she do in case the woman dies during childbirth? Whose death certificate would she sign - of the sister in whose name the woman had registered, or of the woman herself? This is an outstanding example of lack of transparency leading to extremely difficult situations.

(e) There are also several other issues that have still not been resolved in respect of the practice of ART in India. For example, we still have not yet finally decided on the age limits - upper and lower - for germ cell donation or surrogacy, and the number of times one can act as a surrogate mother.

The silver lining is that the Indian Council of Medical Research (ICMR) released, on 4th September 2002, a draft of national guidelines for accreditation, supervision and regulation of ART clinics in India following the recommendations of a high-power committee set up by the ICMR (Indian Council of Medical Research). These guidelines have been publicly debated in the country, and are being processed for having an appropriate Act passed by our Parliament.

VII. RELEASE OF GENETICALLY ENGINEERED (GENETICALLY MANIPULATED) ORGANISMS (GMOs)

There are two types of GMOs: one that are used in a factory to make a product such as Hepatitis B vaccine or human insulin, and the other that are released in the environment as such. The first kind pose no problems at all and, as has been already mentioned, have provided a number of extremely valuable drugs which have changed the face of medicine. In fact, at least three of the ten largest selling drugs in the world market today are made through GMOs. These GMOs are used under highly contained conditions; even if they happen to get released they would not survive in the environment on account of their special genetic make up. They, therefore, pose no problem. However, the release of GMOs in the environment is another cup of tea, as a living organism, once released, can never be recalled. It, therefore, becomes extremely important to ensure that before any GMO is released in the environment, all the risks that such a release poses are assessed in great detail. I have listed these risks and the manner of assessing them in great detail in two recent articles: (1) P M Bhargava, GMOs: Need for appropriate risk assessment systems, *Economic and Political Weekly,* 13th April 2002; and (2) The perils of mutant food, *Down* to *Earth,* 15th April 2002. I would, therefore, not repeat them here. What I would like to say is that even though we have over 100 million acres of agricultural land planted with GMOs (which include genetically engineered cotton, soyabean, canola and com) around the world today, the fact is that in no case have all the risks that should have been assessed and could have been assessed, have actually been appropriately assessed. The marketing of these organisms by multinational corporations (MNCs) around the world has had two purposes: first to make quick money, and second to obtain control of agriculture in the developing countries and erode the rights of their farmers. The argument has been very simple. If, today, someone wishes to control the destiny of a country like India or Nigeria where seventy percent of the population derives its total income from agriculture or agriculture-related activities, all that one has to do is to obtain control over seed and agrochemical businesses in the country. If this happens for India, we would no longer be a free nation. This is precisely what the MNCs have been wishing to do through a nexus between them, the concerned Governments and the bureaucracy. And new biotechnologies such as genetic engineering, while holding great promise for the benefit of mankind (as already mentioned earlier), also happen to be the tools that the above nexus would

use to lure unsuspecting farmers (specially of the Third World countries) into their net, to control world food production. In this context, we should take note of the fact that, as of today, the US is the biggest bribe giver in the world. And one of the purposes of such bribe is likely to be to obtain control over world's food resources through the nexus mentioned above.

The proponents of release of GMOs in the environment, especially the GM crops, say that there are no examples of any damage caused by GMOs. This is not true. Let me give a few examples.

In the last decade, Japan developed a GMO that produced large amounts of tryptophan, an essential aminoacid that is widely used as a nutritional supplement, specially in the affluent West. It turned out that over 30 persons in the United States fell sick, suffering from a rare disease, eosonophilia mylangia, after consuming the Japanese tryptophan-based preparations. It was fortunate that this happened in the vicinity of the famous Mayo Clinic in Rochester, Minnesota, which is one of the world's best-known centres for identifying rare diseases. If this would have happened in a country like ours, or Zambia, the people would have simply continued to die for long, without anyone knowing what the cause of the deaths was.

An American company put a gene from Brazil nut in soyabean to make up the deficiency of an essential aminoacid, methionine, in the soyabean protein. It turned out that a number of Americans were allergic to the genetically engineered soyabean which was, therefore, never marketed in the US (United States of America). However, the GM soyabean was sent, against all ethical principles and even the Cartagena protocol to which both the US and India have been a signatory, to Orissa by the US to be distributed to the Orissa famine victims a few years ago. (This happened even though we had 60 million tonnes of grain in our stock with the Food Corporation of India at that time.) In late 2002, in spite of widespread food shortage and starvation in Zambia and Zimbabwe, the Governments of these two countries refused to allow genetically engineered corn to be given as a gift by the US. The US refused the request of these two countries to send corn flour so that no one could plant the GM corn and thus contaminate the corn produced in these countries. In this context it is important to realize that Europe has totally banned the import of GM food; if the food in the African countries gets contaminated by foreign genes, Europe will stop importing any food from these countries, thus affecting these countries' long-term economic interests. This is, perhaps, what America has been wanting to do by, again, establishing a nexus between its own Government and the MNCs who have been virtually exclusively marketing GM seeds, and the Government and bureaucracy of the recipient developing country that would have no hesitation in selling their country for their own personal interest.

Even in the case of Bt cotton - one of the most widely used genetically engineered crops (in which a gene from a bacterium, *Bacillus thuringenesis*, which gene codes for a toxin protein that can kill certain pests, has been transferred through genetic engineering into cotton to make it pest resistant, thus not requiring the use of pesticides) - in the United States, after the fifth generation, as much as forty to fifty percent of the plantation has to be of non-Bt cotton as a refuge to which

the insects could go, sparing the Bt cotton as, over the years, the insects develop resistance to Bt cotton. Further, according to a recent study *(Nature*, 6th March 2003, Vo1.422, p.5), about 65% of the cotton farmersin the particular geographical area that is contiguous, must plant Bt cotton for it to be economically viable - a situation unlikely to occur in countries like India where the holdings are small. (The cost of Bt cotton seeds in India currently is at least 5 times the cost of good non-Bt seeds.) Then, there is the risk of the foreign gene put in a GMO, being transferred to non-GM crops, even across the species. Such horizontal transfer of genetic traits is now widely known and has also been established for GMOs that are in the market today; it seems possible even in the oral cavity (and rumen in the case of cattle) (P S Duggan et a*J. British Journal of Nutrition,* 2003, Vol. 89, pp.159-266). In fact, it is estimated that between 10 to 20 percent of all genes in today's living organisms have come about as a result of horizontal gene transfer. An outstanding example of such a transfer is the recent contamination of non-GM, wild type corn in a region in Mexico which has the world's largest corn biodiversity, by GM (genetically manipulated) corn grown nearby.

Both developing and developed countries are, in fact, already beginning to pay a price for the use of improperly assessed GMOs in agriculture. For example, in China where Monsanto's Bt cotton (which has been genetically engineered to be pest resistant) and their own Bt cotton have been used on a substantial scale, it has been found that, over the years, the proportion of insects which are not killed by the toxic gene put in the plant through genetic engineering, has increased, thus affecting the promised yield *(Daynan Xue*, 2002. A summary of research on the environmental impacts of Bt cotton in China, The State Environmental Protection Administration of China, P O 'Box 4202, Nanjung 210042). China has also decided recently - causing great annoyance to the United States - that it will not import any GM technology from abroad but develop its own as and when it considers it necessary to do so in the country's own interest.

We must also remember that the developed countries may be able to absorb any long-term damage through the use of GM crops. This, however, would not be so in the case of most developing countries.

Having said all this, I do not wish to argue for one moment that we should not engage in genetic engineering of plant and microorganisms with the eventual objective of releasing them in the environment. However, our objective should not be to exploit and/or only to make money. There should be the larger objective of national or international good - an objective in which the requirements for sustainable development are met. For example, there should be no objection to putting in new genes that would delay ripening of fruits that are otherwise fragile - such as custard apple. As of today, this delicious fruit cannot be transported over a long distance. Similarly, it would be worth looking at the possibility of putting in new genes that would allow plants of economic importance which cannot normally tolerate high salinity, to grow in semi-arid or arid areas. In this context, what is most important is that nations like ours, China or Nigeria must make sure that seed business is our own national business. If we need to develop a genetically engineered crop for a valid reason that is in our interest, we should do it ourselves.

The fact is that such capabilities exist in certainly the three countries I have named above.

What is equally important is that before we release any GM crop, we must have in place an appropriate risk assessment procedure which we do not have anywhere in the world today - least of all in our country. In addition the entire risk assessment data must be put in public domain, which has not happened in our country so far. Before commercial or public release, any GM material (be it a drug or a crop) has to go through two committees in India the RCGM (Review Committee on Genetic Manipulation) of the Department of Biotechnology (DBT), and the GEAC (Genetic Engineering Approval Committee) of the Department of Environment and Forests. The first applicant for such release of a GM crop through these committees has been Monsanto which sought approval for release of its Bt cotton that would be resistant to the common cotton pest, the bollworm.

As it turns out, both these committees are unknowledgeable, self-centered, unprofessional, socially and politically insensitive, (probably) corruptible, and without any commitment to the country. Fortunately, on account of many protests from responsible quarters, no permission was granted by the GEAC for the release of Monsanto's Bt cotton through their Indian associate, Mahyco in which Monsanto has 26 percent stake, till June 2001, in spite of DBT's unwarranted pressure on GEAC for permitting such release. Yet it was found that in Gujarat, in the latter half of 2001, Bt cotton seeds were sold by a company called Navbharat, and planted in some ten thousand acres; a similar plantation was also made in a much smaller area in Andhra Pradesh. (I would not be surprised if Monsanto had a direct or an indirect stake and/or role in these plantings.) What is amazing is that even though these plantations were totally illegal and the GEAC did issue a (weak) directive that the crops should be burnt and the seeds confiscated, nothing of that sort happened, and the farmers who used the seed, as well as those who sold the seeds, are living happily since then, in spite of their contravening one of the important laws of the country. This incident substantiates what I have said above: that a nexus between the multinationals, the Government and the bureaucracy is very much alive and kicking in our country.

In March 2002 - Mahyco was finally granted permission by the GEAC to market their (that is, Monsanto's) Bt cotton under a set of absurd stipulated conditions. Reports from Andhra Pradesh, Maharashtra, Madhya Pradesh and Gujarat where Bt cotton was planted in the last season after the permission from GEAC in March 2002, have established unequivocally that the Bt cotton in these States has been largely a failure [e. g., Bt cotton leads to losses: farmers say there was no increase in yield, *Deccan Chronicle,* 4th March 2003; Cotton ryots a confused lot, *The Hindu,* 5th March 2003; Government promises compensation to Bt cotton farmers, *The Hindu,* 11th March 2003; What ails Bt cotton (by D Banerji), *The Hindu,* 18th March 2003; Government to move cautiously on Bt cotton, *New Indian Express,* 24th April 2003; In Gujarat, Bt cotton seed loses out to illegal Navbharat, *New Indian Express,* 25th April 2003]. The reasons for the success of the illegally planted Bt cotton in Gujarat in 2001 are not clear as the powers that be did not

wish to investigate the matter. It is quite possible that this success was manipulated (perhaps with the knowledge of the authorities concerned), for example, by putting in several Bt genes (instead of just one that has been approved so far) in the cotton plant; such an unauthorized and unlicensed procedure, although providing possible initial advantage to the farmer, could be a disaster subsequently. The purpose of such an exercise could have been to pressurize the professionally incompetent GEAC to grant the permission it did a few months later (in March 2002) to Mahyco (indirectly, Monsanto) to market their Bt cotton in India. No risk assessment of any kind - even rudimentary - has been done for cotton having more than one Bt gene.

The unfortunate fact is that in spite of our asking the Indian Council of Agricultural Research and the Council of Scientific & Industrial Research that they jointly set up an agency where the seeds could be tested using modern DNA fingerprinting techniques, no trustworthy organisation exists in the country which could even determine routinely whether a particular seed has a Bt gene in it or not. Nor have our Governments - State or Central - encouraged and popularized Integrated Pest Management developed in the country (first for cotton) and shown to be effective, again indicating collusion with the multinational corporations (like Monsanto) that are marketing GM seeds and pesticides in the country.

Contrast the situation in India with that in China that has already been mentioned, and in Nigeria - the seventh largest country in the world in terms of population. I had a meeting with the President of Nigeria, Mr O. Obasanjo, on 9th September 2002 and, at his instance, subsequently with the senior officers of the Nigerian National Seeds Service, in Abuja on 12th September 2002. Nigeria has been convinced that it is not in their interest to permit any MNC to have any control of any kind on their seed business. If they wish to use a GM crop, they have the ability to make it themselves. Further, they have realized the need for putting in an appropriate and fair risk assessment system, before release of any GM crop, either their own or an imported one, keeping in mind the long-term interests of the country. And China - if we need the example of a scientifically advanced developing country - is exercising immense caution in regard to GM crops; it is not permitting the growing of GM food crops, and ensuring that if any GM crop has now to be introduced in China it would be their own and not that of a MNC.

CONCLUSION

I hope I have underscored the tremendous promise that modem biotechnology holds for us, as well as immense and wide-ranging implications of the progress in modem biology and biotechnology. The challenge, therefore, before us- informed and responsible world citizens - is to ensure that we use the new biotechnologies in such a way that their use is ethically defensible, and in the largest interests of mankind in our country and around the world. In the present context, this will not happen unless responsible and socially sensitive citizens understand what modem biotechnology is about and what its various implications are, and then build pressure to break the existing nexus between the MNCs, the politicians and the bureaucrats.

I must, to be fair to all of science and technology, reiterate what I said in the beginning - that it would be not only modem biology and biotechnology that would bring about dramatic changes in our life-styles and the way we think and deal with problems, but also several other areas. For example, in course of time, the world store of fossil fuels such as coal and petroleum, would be exhausted. We would, by then, have to learn how to exploit the virtually inexhaustible sources of energy such as biomass, solar energy, nuclear energy and wind energy. Sooner or later, the mineral wealth of the planet would also be depleted. The only inexhaustible source of materials would be carbon-containing (organic) compounds. We would, therefore, have to learn to replace minerals with suitably designed organic compounds. The increased dependence of man for survival on the use of his brain rather than brawn has already led to a situation where, unlike the warriors of yesterday, men of today may find it practically impossible to fight with the kind of armour used by our ancestors. We have other evidences of continuing evolution of man. What we do not know is what direction it would take. What, however, is clear is that the nature of skills for which human beings of tomorrow would be adapted through evolution, would be very different from such skills of a thousand years ago.

With increase in automation, there would be more time available for leisure and for activities that would satisfy the creative urge in man that has been one of the most important of the attributes that have aided the survival of the human species. One would like to believe that, as man becomes more knowledgeable, it would become increasingly difficult for him to be exploited. This belief, however, may be erroneous, for one is likely to see an increase in sophistication in the techniques of exploitation, with the increase in knowledge on the part of an average human being. The techniques of exploitation of man by man and of nation by nation, have undergone a dramatic change in the last one hundred years. On the other hand, it would be unwise to underestimate the ingenuity of man to fight - even prevent+ such exploitation. The emerging biotechnologies would surely provide a tool to prevent such exploitation, just as they would also provide means of exploitation by identifying gaps in the knowledge of people at the given time.

Perhaps, the only insurance against exploitation in the world of rapidly advancing knowledge (specially in science and technology), would be to work towards reducing the gaps in people's knowledge around the world, to as insignificant a level as is possible, in real time.

That is a major social challenge we all face today. It is in this context that discussion of topics such as the one to which this talk is devoted, becomes relevant.