by

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The question of the ethical and social implications of recombinant DNA must be considered in the broader context of the function of Science in society. This in turn has always been determined by the attitute of society towards science and scientists. If I speak of science here I refer to the peculiar Western type of inquiry which arose pretty suddenly during the Renaissance and ever since has had a great impact on the world view , the activities and the life of Western Man.

Science has never been independent of society. Only the form in which society has taken control of science has changed over time. There have indeed been some rich or otherwise comfortably situated scientists who carried out their work without support from Society directly. Copernicus, Darwin and Mendel are the great examples from the past; but even in our own time some of the biological work of Caryl Haskins and William Loomis has not been supported by any gevernmental or private agency or foundation. But most scientific research, starting with the Remaissance, has been subsidized by governmental authorities, first individual princes, then, starting with the 16th and 17th century academies which had been chartered and endowed by kings and pronces. This is still the way how research is supported in the Soviet Union where the Academy of Science and the State Academies are the main research centers, and the same function was taken on by the State Academies in this country all through the 18th and 19th centuries. That at present most scientific research in the U.S. is supported either by the Government or by Industry or by private Foundations is well known. Less well known is the fact that the strong direct supprt of science by the Federal Governmant in the U.S. is relatively recent starting only with World War II. But in other countries such as Germany France and England the Government had supported scientific research actively since the 19th century.

If the authorities, governments and princes and their delegates have supported science for 400 years it may be concluded that threey expected science to bring benefits to themselves and to their subjects. This expectation is indeed very old. Already Leonardo da Vénci points to the prospective advantages which can be expected from scientific work and further claims the primacy of basic to applied research: " Science is the captain and practical applications are the soldiers". Francis Bacon's works, particularly the Nova Atlantis are filled with predictions of technical and medical advances through application of the scientific method. A similar optimistic approach to science can for examplée be seen in Descartes' Discours de la méthode which is fundamentally an application for a grant from the queen of Sweden to study the hearts of antmaks with the promise that he would find useful results which would reduce illness and promote health. I would like to give two somewhat later quotations which show the same optimistic attitude. André Chénier, at the end of the 18th century said: "La science vaincra la mort". The Board of Useful Affairs wrote in 1838 in a report to Sultan Mahmud:"Religious knowledge serves salvation in the world to come but science serves the perfection of Man in this world." All through the period covered by these quotations, from the 15th to the early 19th century science had indeed made progress and discoveries bubut the practical applications were quite modest. Some inventions, e.g. the clock, the telescope and the pressure cooker had indeed been achieved, but the industrial revolution had barely started. Particularly any claim for progress in the fight against disease and death was quite unjustified at the time. The control of bacterial diseases by means of epidemiology was developed in the last 25 years of the 19th century. Even when I was a boy in the early 20th century there was liftle that a doctor could do for a patient, except for aspirin, castor oil and salvarsan. The suffa

drugs appeared only in the 1930s and the antibiotics in the 1940s. Thus only since that time does the optimistic attitude of progress towards control of disease appear justified.

It is ironic that just at the time when remedies are available for some but not all diseases our attitude toward success in the control of disease has completely changed. We complain that there are many diseases which cannot be successfully treated and that some of the successful remedies have annoying and sometimes even dangerous side effects. Whence this change of attitude arose I do not know. But it is expressed most clearly in the literature, both popular and artistic. The evil or mad scientist who tries to achieve power by his expertise is a stock figure in the comics and in the pulp magazine stories and is apparently derived from the sorcerer of the Middle Ages. In serious literature, Aldous Huxley in his "Brave New World" described a totalitarian society in which social classes are determined by scientific means reprimarily cloning of a small number of different genotypes. This idea has been more widely popularized in George Orwell's "1984" . Thus, there has arisen in the last 50 years a suspicious attitude towrds science and scientists. They are not openly blamed for the inventions which make our present life style possible. Nobody wants to do without cars, airplanes and television. But there are loud complaints about some of the consequences of the production of these amenities, pollution of the environment with smoke, noise and radiation. An important factor in this change of attitude towards science was certainly the development of nuclear weapons during World War II with their extremely high destructive potential and the associated radiation dangers.

It was in this context that the question of the responsibility of the scientist for the consequences of his discoveries was first raised. As stated earlier, the responsibility of scientists to work for the benefit of their, people and of mankind was generally acknowledged by scientists and the public as early as the Renaissance and through the succeeding centuries. It was enforced by the fact that society in the form of kings and princes and Government agencies supported scientific activities and had thus the power to direct the creative energies of scientists into channels they considered useful and appropriate. Scientists always have been aware of the fact that they have to account for their work to their colleagues, to the Government and to the public at large. The difference for the responsibility of scientists arises where their discoveries have consequences which at the time are unforeseen or unforseeable. When Faraday was asked about the applications and purposes of his studies in electricity he is said to have answered: "Madam, what are the application and purposes of a new-born baby?" In other words, the establishment of the laws governing electric and magnetic currents and fields was not sufficient to predict the possibility of using them to light rooms, speak through telephones , toast bread and many other applications.

The same questions apply to biological discoveries. Biologists have always thought of themselves to be engaged only in activities which will benefit mankind, through medicine and agriculture or at least be innocuous knowledge such as natural history or systematics. Many have seen themselves as involved in a continuous fight against three of the great worries of man, symbolized by the horsemen of the Revelation, famine ,plague and death. During the last century they have been conspicuously successful: epidemics have ceased to be a real danger to any community whose public health services are intact; however, the old fear of epidemics has not disappeared and small outbreaks of infectious diseases whose agent is not immediately identified cause great public apprehension. The application of scientific methods to the raising of domestic animals and plants has led to the development of a more efficient agriculture which in the more developed countries has banished the specter of famines which in previous times up to the early 19th century occured at regular intervals. These benefits are now taken for granted.

But they have been achieved at a cost. To give just one example, the reductic of the death rate has not been an unqualified boon but has led in many countries to SIXTH ICUS * San Francisco * 1977

a population explosion. The consequences have not been catastrophic in Western Europe, partly because of opportunities for emigration which arose at the same time, and partly because, as modern research in historical demography has shown, the idea of birth control had taken hold in parts of Western Europe quite early, at least in the 15th Century. In other parts of the world where a high reproductive rate has been esteemed as a social value the change in social customs necessitated by reduced mortality is not so easy. Furthermore, even interested the consequent increase in the proportion of the old and very old in the population poses at present serious social problems. If Schence should really defeat Death, as André Chénier predictedand I see no reason why it could not be achieved the social consequences would be unimaginable.

What does all that have to do with recombinant DNA? Recombinant DNA is an ingenious technique developed in the last four years from several independent discoveries which holds both theoretical and practical promise, It consists in isolating individual genes from higher organisms and inserting them into plasmids. Plasmids are small assemblies of genetic material which occur spontaneously in bacteria and contain genes independently of the chromosome of the bacterium. They multiply inside the host bacterium. The theoretical hope from this technique is that we can learn in this which much about the structure activity and function of the genes of higher organisms than we can by direct investigation in the organisms themselves. The practical promise is above all that it permits us to produce cheaply, in large amounts and without admixture of harmful byproducts the products of single genes such as insulin, which are used in the treatment of human diseases. The use of these gene-carrying plasmids directly in the treatment of hereditary diseases has been suggested but is actually an uncertain possibility. The danger perceived in this procedure is that the bacteria carrying plasmids with new genes may invade humans and thud pose the threat of an epidemic bytan essentially new pathogen. Workers in the field were the first to call attention to this possibility and have done considerable work to reduce this danger. At present, particularly through the work of Curtiss who developed a bacterial strain to be used as carrier for the plasmids which can live only under very elaborate laboratory conditions and which specifically is unable to invade humans, the danger of an epidemic caused by bacteria carrying recombinant DNA has been eliminated.

But this danger, though the professed concern of people opposed to the study of recombinant DNA is not their only objection. There exists widespread fear that dangerous consequences might arise from tampering with the genetic material of any species, and particularlly that of human beings. This fear is often expressed in the form that recombinant DNA constitutes a completely new technique which permits us to achieve things which were impossible before and are fundamentally unnatural . This is actually not correct. Transfer of genes from one species to another has been shown to occur naturally in plants - this is called introgression - and there is some evidence that it occurs among bacteria in nature. In agriculture, introduction of genes from one species to another has been performed in the past by the use of sexual processes without recombinant DNA. The classical example is the transfer of a gene causing resistance against tobacco mosaic virus from the species Nicotiana glutinosa to tobacco. Also, the doubling of chromosomes in the infertile hybrids resulting from species crosses has been shown to occur in nature and has been used to produce new plant species. It is certain that better agricultural plants can be produced in this way, and have been produced before the advent of science; all our agricultural wheats are such fertile species hybrids, and maize contains a certain amount of genetic material which has been derived from the related genus Tripsacum. These methods have not been applied to animals. But the examples show that transfer of genes from one species to another has been an agricultural practice in the past which has indeed practical promise and is not a completely new and unpredictable innovation,

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Generally, strong objections exist to the application of genetic techniques to Man. Arguments that mankind could be improved by the application of genetic knowledge have been raised sporadically throughout the history of Genetics and have constituted an embarrassment and a certain difficulty for the progress of Genetics. Actually, few geneticists hold such opinions though some have always done so and probably still due. Genetics has often been misused to support claims of superiority of one group of humans over another. Also some people, geneticists and others, have recommended eugenic measures such as enforcement of selective breeding and sperm banks, which were expected to result in the production of superior human beings. It has been pointed out over and ober again that such proposals are unsound from the point of view of genetic theory and will not produce the predicted result. It is agreed amongst most geneticists that the breeding arrangements in force at present are highly appropriate and successful for the continued well being and success of the human species.

The potentiality for introducing a breeding program for human beings has always existed, but it has always been strongly resisted. Our ethical value system does not permit it even though sometimes the desire to institute such breeding programs has existed. They are usually called Eugenics and you know that there are some advocates of such programs. The important fact, in my opinion is the strong opposition against this type of program and the lack of success of Gevernments and social institutions which tried to enforce it. The use of recombinant DNA in humans for purposes of controlling the genetic constitution of humans, a threat envisaged in a somewhat different form in Orwell's "1984" would actually be less efficient than a breeding program. The bacterial plasmids could contain only small amounts of genetic material, one gene or a little bit more while behavioral characters in which a tyrant would be interested involve a large number of genes. Therefore, any one gene transmitted by a plastid would have neglgible effect on such a character.

If, thus, I cannot foresee any danger from the recombinant DNA experiments carried out at present, and cannot agree that scientists should be held accountable for unforeseeable consequeces of their discoveries, there still remains a very difficult question: to which degree should scientific research be controlled by Society, that means in practice by Government. We have stated earlier that scientific research has by governments by the way it allocates funds to different always been influenced fields of research. For instance, if government puts particular stress on cancer research and does not increase the total amount of funds available for medical research, it is clear that work on some other diseases must be curtailed. But this is in principle a very different matter from a government decision on the types of research which may or may not be carried out. This is not a question involving ethical considerations but rather a question of prudence. Certainly Government has the power to stop and forbid research in any field where it finds it desirable. And where experiments involve danger for the population it should indeed do so. But this should not be done arbitrarily particularly since it can be used to suppress the acquisition of knowledge about some facts of nature. The attituted that in some aspects of Nature ignorance is bliss and that added knowledge can only be harmful to Man is indeed implicit in some of the attitudes trying to curtail research in some areas. The only historical example, the attempt of the Russian Government to suppress, under the influence of Lysenko, all work in Mendelian Genetics has had the effect of inhibiting the acquisition of useful knowledge in the field of agriculture.

I think, thus, that the ethical questions raised in connection with recombinant DNA are not unique but apply to all forms of scientific research. They are actually quite simple: scientists should be careful not to carry out experiments which have consequences dangerous to their fellowmen, or which involve foreseeable dangers in the future. Government has the duty to protect the citizens against such dangers but it would be highly imprudent to make such decisions lightly since it can delay or inhibit the development of useful and necessary knowledge.