Science and the Future of Mankind
Pontifical Academy of Sciences, *Scripta Varia* 99, Vatican City 2001
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THE FIGHT AGAINST DISEASES: COMMENTS RELATED TO "SCIENCE FOR MAN AND MAN FOR SCIENCE"

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While the main topic of my presentation is science in search of solutions against diseases, therefore a topic definitely concerned with the contribution of "science for men", I want to express my concern about the topic "man for science". We cannot have only science applied to the betterment of mankind, or improvement of technologies: *There will be no applied science if there is no science to apply*.

We have to make science more attractive to young men and women at the start of their careers. We must fight more vigorously against the discrimination of women scientists – and I do not mean "affirmative action". We do not have to lean backwards, just give them the chance they deserve. And we must include in our responsibility as scientists towards society at large the special responsibility towards younger scientists.

Responsibility towards younger scientists

It has been fashionable in recent years for scientists to dwell, both publicly and privately, on the complexity and ambiguity of their relationship with, and obligations towards, society as a whole. In the face of the extreme sensitivity we have all developed as a result, will it be seen as undue temerity on my part to suggest that perhaps there is yet another sphere of responsibility that has been overlooked: that is, the responsibility of scientists towards other scientists? Accountable to the world we certainly are, but what of our bounden duty to the young scientists in our midst, to those men and women whom we have undertaken – as their seniors – to guide, shape, teach and counsel? The fact, I believe, is that, trapped in the maze of scientific administration, puffing and blowing our way over the hurdles we confront in the increasing-

ly competitive race for funding, preoccupied by the need to find solutions for problems such as space and equipment, submerged in the flood of printed and electronic information that inundates our desks, we are no longer as vigilant as we should be about guarding the beacon we have been charged to pass on to those who will follow us in the scientific hierarchy.

Perhaps, therefore, the time has come for us to return to more substantive attitudes towards our own profession. To remind ourselves – for our own sake as well as for that of those who model themselves on us – that science is more than merely one way of earning a living, and with it status. Let us face it: at its best, scientific research is not just another system locked into a larger set of systems. It is a calling. What is more, a calling whose success rests, in the final analysis, on the finest and the rarest attributes of civilized man: on intellectual courage, on hazardous hypotheses, and on the wisest uses of intuition. The responsibility of scientists to the society of which they are a part, and to which they contribute so significantly, is indeed an awesome matter, but should not overshadow other considerations. What has fallen by the wayside, I suspect, may be the responsibility of scientists towards their own tradition, towards the younger generation, and towards the flame itself.

Challenges in diseases

But let me now move to the main topic of my presentation – the fight against diseases. We have desperate situations in which present day science cannot even define the reason for a disease, as is the case for ALS – amyotrophic lateral sclerosis, also called in the States, Lou Gehrig's disease. And, on the other hand, the amazing finding that ulcer is a bacterial disease, caused by Helicobacter, and can be treated with antibiotics.

In neurological diseases there may be hope for nerve regeneration, and there are biochemical and genetic approaches to schizophrenia and paranoia. These will be the developments of the next century, but today the great challenges are Alzheimer and Parkinson, multiple sclerosis and myasthenia gravis. I cannot discuss here for lack of time vascular diseases, but I would like to devote the rest of my presentation to infectious diseases, autoimmune diseases and cancer.

Genetic and immunological diseases

The two important approaches are genetic and immunological. There are 30,000 rare genetic diseases such as cystic fibrosis, muscular distrophy

or phenylketonuria. These are usually due to the defect in one gene, and there is a good chance of being able to correct it. But these 30,000 diseases form less than 1% of diseases, whereas 30 major diseases account for the other 99%. In the case of these diseases, both environment and genetics contribute, and the genetic moiety is multigenic and complicated. Nevertheless, a substantial effort is being devoted to elucidate the nature of such genes.

Concept of specificity

As far as immunology is concerned, I want to talk now about the notion of specificity in immune reactions, and their good use for therapeutic and prophylactic purposes. Vaccines are the method of choice to fight infectious diseases, and they are characteristically highly specific. This is due to the fact that substances used for vaccination are close molecular "cousins" of the virus or bacterial toxin that is the "troublemaker". Nobody expects one vaccine to be efficient for all infectious diseases. While the rate of success is great, we are still faced with those diseases which we are not yet able to prevent by vaccination, and I refer not only to AIDS, but to such old calamities as malaria and bilharzia. Actually, a new danger is tuberculosis: not only that classical tuberculosis is today the killer No. 1 of humanity, because the patients are not treated, but there is more and more of tuberculosis resistant to drugs and antibiotics, and the vaccination approach may be again cogent.

One new approach, possibly of great importance in the future, is DNA vaccination. Instead of immunizing with a protein – or with a mixture including the antigen of importance for vaccination – one isolates the natural DNA and uses it for immunization, with very encouraging results.

Autoimmune diseases

Now, a word about the concept of specificity and its extension to autoimmune diseases and to cancer. We are now extending this concept to autoimmune diseases and to cancer. Whenever it is possible to identify the putative cause of the disease, it should be possible to find a close molecular analog which will combat the disease. In one case of an autoimmune disease, that of multiple sclerosis, we have succeeded in developing a drug/vaccine which has by now been approved by the F.D.A. in the United States, as well as seventeen other countries.

This drug – or vaccine – as I prefer to call it – is a polymer composed of four kinds of amino acids, and prepared so as to resemble and cross-react immunologically with the main troublemaker of the myelin sheath of the brain, the myelin basic protein. This myelin basic protein can provoke an experimental disease – allergic encephalomyelitis, and our substance, denoted by us Copolymer 1, or Cop-1, can suppress the onset of the disease, and in rhesus monkeys and baboons, we showed that it can heal the actual disease. As this is an experimental model disease for multiple sclerosis, we moved to clinical trials. The phase 2 clinical trial was most successful. This was followed by several more big trials, before the FDA approved the drug/vaccine for daily injections for the exacerbating-remitting type of multiple sclerosis. We have proved recently that it can be given efficiently by oral route, and a trial involving 1400 participants is starting now in 9 countries. Copolymer 1 does not seem to have any effect on any other autoimmune disease.

In the same spirit we have approached another autoimmune neurological disease, myasthenia gravis, in which the disease is caused by an immunological attack on the acetylcholine receptor of our nerve cells. We are already successful in preparing a specific drug/vaccine against myasthenia gravis by limited amino acid substitution in two myasthenogenic peptides from the a-subunit of acetylcholine receptor. The analogs formed can heal the experimental myasthenia gravis in mice and rats, and we hope to start clinical trials next year. In principle, in every autoimmune disease in which you can put your finger on a potential candidate causing the disease, it should be possible to produce a close chemical relative that will suppress the disease.

Cancer

In the field of cancer there is an increasing number of tumor-specific or tumor-selective antigens, and therapeutic vaccination may soon become another weapon in the anti-cancer armamentarium, alongside surgery, radiotherapy, chemotherapy and non-specific immunotherapy. From recent reports it appears that even immunization against Alzheimer's disease is becoming a cogent possibility.

One hallmark of Alzheimer's is amyloid plaque, a protein deposit that builds up in the brains of those with the disease. In mice genetically engineered to develop an Alzheimer's-like condition, immunization with b-amyloid (Ab, the protein fragment that forms the plaque) reversed or prevented

plaque formation and neural damage. The finding “raises the possibility that immunization with Ab may eventually be used as a treatment, or prophylactically, for Alzheimer's disease”.

Globalization

For all these approaches to diseases, we must work together, as one world, globally. Globalization describes trends dramatically and relentlessly, increasing connections and communications among people, regardless of nationality and geography. But globalization without integration leads to a Babel tower. So to improve the health, and I mean first of all the developing world, we need both globalization and the integration of our efforts. And this must be done with great speed, as standing still is the fastest way of moving backwards in a world that is changing at an ever more rapid pace.