Salvador E. Moncada - Self-Presentation

Sir Salvador Moncada

Thank you, Mr. Chairman. It is a great honor to be here this morning and I would like to give you a sketch of my life and my scientific work. I was born on 3 December 1944 in Tegucigalpa, Honduras, from a Honduran father of Spanish descent and from a Jewish mother born in Romania, in Cernovich, now known as Chernivtsi, located in the Ukraine. Her immediate family escaped from Europe in 1938-39 and, following a series of unexpected events, they settled in Honduras. A number of her relatives were persecuted and disappeared during the Second World War. My mother was a housewife and my father, although trained as a medical doctor, never practiced medicine. My family moved from Honduras to El Salvador in 1948, where I lived for the next 22 years. Neither of my parents was religious, but they possessed well-defined cultural stereotypes. This created a rich environment and provided me with a wide perspective on things. I developed an early interest in biology and medicine, and by the age of 11 I was determined to study medicine and to do research as the only career option in my life. I also developed from very early on an awareness of the social injustice that existed in El Salvador and a desire to work to change the situation. From 1951 to 1961 I attended the primary and secondary schools in El Salvador and from 1962 to 1970 I studied medicine at the Faculty of Medicine of the University of El Salvador. At that time, that medical school was one of the best medical schools in Central and South America, since it had been updated and restructured along the lines of modern medical schools in the United States. This was carried out by a group of distinguished Salvadoran doctors who had trained in the United States. Chief among them was María Isabel Rodríguez, a Salvadoran cardiologist who became my mentor. In medical school I also met Augusto Campos, a Peruvian pharmacologist working on the pharmacology of the sympathetic system. He provided my introduction into pharmacology and medical research.

When I started my medical school, my interest was in science and I intended to combine research with medical practice. During my clinical years, however, I was confronted by the poverty of the majority of the population in El Salvador and realized that their medical needs could only be addressed through structural changes in society, leading to improvements in public health. As a result of this, I became politicized. Politics in my country at that time was of a militant nature and by June 1970, immediately after I graduated, I was captured by the secret police in El Salvador, beaten up and expelled from El Salvador back to Honduras. All this happened shortly after the border war between El Salvador and Honduras, which created a great deal of animosity between the people of the two countries. In Honduras I started to work in the Department of Physiology of the University. My wife and child were not allowed to join me as they were Salvadoran, so we were forced to meet occasionally in Guatemala.

In order to keep my family together, the only option was to go abroad. A Guatemalan doctor, Fernando Molina, had spent some time in the UK at the Royal College of Surgeons, where he had met John Vane. Molina suggested that we write to him to see if he could give some advice about postgraduate education in the UK. John replied inviting me to come to work in his laboratory, based on the recommendation of Molina. I arrived in London in 1971. John Vane was Professor in the Department of Pharmacology at the Institute of Basic Medical Sciences at the Royal College of Surgeons. The environment in the department was highly interactive and intellectually stimulating, with many distinguished British and foreign scientists working there. I was lucky because at the time of my arrival the hypothesis about the potential mechanism of action of aspirin and other non-steroidal, anti-inflammatory drugs was being discussed. I was invited to join the project and set out to work on a series of successful experiments that a few months later formed part of a tree of publications in the journal *Nature*. Those papers explain, for the first time after 70 years of usage, the mechanism of action of aspirin and similar compounds and also the reasons for the main side effect, gastric damage. The result was that I found the work in the laboratory so exciting that I never went back to medical practice and that is something that I don't regret.

Between 1974 and 1975 I tried to go back to Honduras, where I tried to set up a laboratory, but the conditions in the country were not conducive to research and I returned to the UK as an employee of the Wellcome Research Laboratories in Beckenham, Kent, to lead a research group working on inflammation. By then, however, I had become interested in platelets and their role in vascular diseases. This was a significant and productive change of direction since, within a year, we had discovered an enzyme in the platelets that generates Thromboxane a2, a powerful vasoconstrictor and proaggregating agent, and shortly afterwards we discovered in the vascular

wall prostacyclin, a vasodilator with potent antiplatelet aggregating properties. The fact that the platelets and the vessel wall generated substances with opposing biological activities led me to suggest that probably a balance between the generation of these two substances was important for the homeostatic regulation of the cardiovascular system.

The later finding that Thromboxane a2 is inhibited by very small concentrations of aspirin, without affecting the generation of prostacyclin in the vessel wall, has led to the widespread use of small doses of aspirin for the prevention and treatment of cardiovascular disease. It is calculated that between three and four hundred million people these days in the world take a small dose of aspirin and benefit from taking this medicine in relation to their cardiovascular disease. I stayed in Wellcome for the next 20 years, occupying different positions until, in 1987, I became Director of Research. In 1984 I became interested in Endothelium-derived relaxing factor discovered by Furchgott a few years later, and began a project that led to the identification of nitric oxide. At that time, the idea that the biological system could generate nitric oxide as a mediator was not accepted in biology and it was highly controversial. Nitric oxide, until that point, was considered to be just a pollutant in the atmosphere. However, work in my laboratory elucidated within a year the biochemical mechanism leading to the synthesis of nitric oxide in biological systems and our findings led me to propose that the L-Arginine-Nitric Oxide pathway, as we called it, is a widespread transduction mechanism for the regulation of cell function and cell communication. This turned out to be the case following the discovery of nitric oxide in the peripheral and the central nervous system, where it plays an important role in the generation of memories and also in the immunological system. The implications of the discovery of this noble mediator continue being explored but is clear that it has represented a significant advance to our biological knowledge and that it has provided clues for the prevention and treatment of disease. I worked at the Welcome Research Laboratories until 1995. In my ten years as a research director I oversaw the making of a number of useful medicines, including medicines for cancer, for malaria, for epilepsy and for migraine.

Following the takeover of Wellcome by Glaxo, I moved to University College in London to establish and to direct the Wolfson Institute for Biomedical Research. My main objective was to set up a center of excellence of research that would be an interface between fundamental research and applied research, a center of translational research. My research during the years of the Wolfson were characterized by exploring new areas, including that of mitochondrial biology, and later the metabolic basis for cell proliferation. Since 2013 I have been working at the University of Manchester, where I have directed the Institute of Cancer Sciences. As a result, I have become interested in the epidemiology and management of this disease, both from a scientific, medical and from a social point of view. Besides experimental science, I have been interested in higher education and in society issues related to the plight of developed countries. I have, as a result, worked as a consultant for WHO in Latin America, and I feel committed to finding ways to aid the scientific and technical development of the Third World. I was a founder member of an organization which we call *Honduras Global*, which is a network of successful Hondurans living abroad and interested in helping the country in different areas of development.

I am especially honored to be here today to join this Academy and to join you. In the last two days I have been exposed to your wide discussions and to your deep thinking. I have learned a great deal. Your deep concern about the world around us has also impressed me very much. As I join, besides thanking you, I would like to say that my main desire is to contribute to the work for a better future for all mankind.

Thank you very much.