DISCURSO PRONUNCIADO POR EL NUEVO DOCTOR D. JAMES MICHAEL SHARP

Excmo. Sr. Rector Magnífico
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Miembros del Claustro Universitario
Señoras y señores

I HAVE been fortunate in receiving my education at establishments that have a long and distinguished history. As a boy, I attended a school that was established by King Edward VI in 1552, followed by my undergraduate and postgraduate studies at the University of Glasgow [established in 1451] and the University of Edinburgh [established in 1583]. The University of Zaragoza has an equally long and distinguished history and it, therefore, is a signal honour to be invited today to receive the title of *Doctor Honoris Causa*.

The University of Zaragoza was the seat of learning of one of its most distinguished graduates, Santiago Ramón y Cajal, who was born in a small village in the Aragon region. Cajal graduated from the University Zaragoza in 1873, only a few years after the creation of the School of Veterinary Medicine in Zaragoza by Royal Decree in 1847. Cajal was one of the founding fathers of the modern science of neuroanatomy, which developed from his detailed

anatomic drawings and descriptions of nerve cell organisation in several animal species that he published as «Textura del Sistema Nervioso del Hombre y los Vertebrados». I still recall the thrill of being shown some of Cajal's original descriptions during my first visit to Zaragoza in the early 1980s. Cajal's pioneering studies on neurology were duly recognised by the award of the Nobel Prize for Physiology or Medicine in 1906.

The Department of Pathology in the Veterinary Faculty at the University of Zaragoza has continued this proud tradition and expertise in anatomic pathology and histopathology, as well as maintaining close links with the agricultural communities, working with them to improve animal health. Indeed, it was these mutual interests that provided the basis for the early collaborations between my laboratory at the Moredun Research Institute in Edinburgh and the Department of Pathology in Zaragoza.

The Moredun Research Institute was established in the 1920s by sheep farmers who were concerned about a number of diseases that were causing heavy mortalities in their flocks. Within a few years, the veterinary scientists had developed a suite of vaccines that protected the sheep against these diseases and which continue to be used today, more than 70 years later, not just in Britain but worldwide. To this day, it is governed by a Management Board representing various sectors of the agricultural community, which ensures that the research retains a strong focus on strategic science as well as associated applied research to support the agricultural community. Throughout this period, Moredun has conducted research on a wide range of diseases of sheep and other ruminants and it was a mutual interest in one particular disease that stimulated a fruitful collaboration between my laboratory and that of my good friend, Professor Juan Badiola Díez. Paratuberculosis is an economically important infection of ruminants in both Britain and Spain, but we have no effective tools or strategies to help farmers to control or eradicate the disease. So, in the late 1980s, Professor Badiola and I developed a strong collaboration that widened to draw in other laboratories in Spain and Greece, assisted with funding from the European Union. The programme provided a springboard for the research careers of several young colleagues in each country, as well as making advances towards improved control of this disease. I will return to this topic later as interest in paratuberculosis has increased because of potential links with a similar human disease.

I started my research career as a veterinarian and virologist in a multidisciplinary team investigating respiratory diseases of sheep with a special responsibility for virus infections. This research culminated in the development of vaccines that are now the world leaders for prevention of bacterial pneumonias in sheep. During this period, by a rather serendipitous route, I became aware of an extremely intriguing group of three diseases affecting sheep and goats that continue to provide immense intellectual challenges across the whole spectrum of biological research. These diseases have unique features; they are contagious, they are low-grade tumours of specialised cells lining the respiratory airways and, as we now know, are caused by related but distinct viruses that are not recognised as foreign by the host. Such coincidences are extremely rare in nature and I felt that studies on these diseases would be very rewarding and reveal new aspects of host-pathogen interactions that would have broad biological and comparative medical relevance, as well as lead to direct benefits for the agricultural community.

In Britain, we have only one of the three diseases and, naturally, this was the focus in my laboratory. But if my belief was correct that these contagious tumours would reveal new general features of biology then I needed to establish contacts with other laboratories that had an interest in the other diseases. Fortunately, a young veterinary pathologist from Zaragoza, whom I had met at a scientific meeting in Britain, recalled my interests and he later contacted me for assistance with his studies into the two other forms of contagious respiratory tumour that do not occur in Britain. This young pathologist became my very good friend, Dr Marcelo de las Heras, who is one of my padrinos today. Again, I recall vividly welcoming Marcelo at my laboratory after he had driven more than 2 500 kilometres from Zaragoza to Edinburgh with samples that he had collected from goats with nasal tumour. Within three months, we had enough new data to write and submit a manuscript that was accepted for publication in one of the top virology journals. This publication was the first of several that confirmed my belief that these contagious tumours would reveal new general features of biology.

That early contact, more, than twenty years ago has developed into an extremely active and productive collaboration, a functioning virtual laboratory, to use the current terminology, that I consider to be a model for others to follow. It is very appropriate that my collaboration on these diseases deve-

loped with Zaragoza because some or the earliest and best descriptions of the pathology were produced by Dr Diego Dualde Pérez during his doctoral studies in the Department of Pathology in the Veterinary Faculty. In fact, the pathology of these diseases has a strong Hispanic flavour with major contributions from Drs Cuba Caparo and Raúl Rosadio in Perú and more recently, Dr Lorenzo González Angulo, another graduate of the University of Zaragoza, who now works in Britain.

One of the earliest publications on these contagious tumours opens with the words «The higher we climb the hill of knowledge, the steeper the ascent becomes» [Dykes and M'Fadyean, 1888]. The research on these diseases is particularly difficult because, even today, we cannot grow the viruses that cause these diseases and standard virological approaches cannot be applied. There have been many times during my research that these words have seemed prophetic but, fortunately, crucial breakthroughs followed the application of molecular virological techniques in conjunction with an understanding of the pathogenesis of infectious diseases that is a feature of a veterinary training. The close relationship between Dr de las Heras's laboratory and mine facilitated an efficient and effective *modus operandi*, involving not only exchange of reagents and information but also post-graduate students and post-doctoral scientists. Since we started working together in 1991, we have published over 20 scientific papers together and currently are preparing several others.

The reagents, techniques and advances that we have made have opened this field to the wider research community and, in particular, attracted collaborations with other research groups in Europe and the USA. This wider network has extended the scope of the research, which ranges from basic studies, such as mechanisms of tumour formation, immune tolerance and immune evasion, gene therapy and the role of viruses in human lung tumours to applied research to develop strategies to control these diseases on affected farms. Nevertheless, the Edinburgh-Zaragoza collaboration retains a crucial role in all of the current research and future initiatives.

If I look back at what have been the important elements or ingredients that have contributed to the success of the link between Edinburgh and Zaragoza, I would identify four major features:

— The very natural synergy between the two teams and complementarity of skills and techniques

— The energy and work ethic of each member of the teams that have contributed to their impressive scientific output.

— The flexibility of the teams that has enabled Dr de las Heras and I to maintain a clear focus and redirect efforts as required.

— A mutual vision of the full implications of the research, which is relevant not only to veterinary medicine but also has important comparative medical and general biological relevance.

On a more general note, as a veterinarian, I am a strong advocate of veterinary research and the need to maintain a strong infrastructure and cadre of qualified scientists to do this. In our fight against infectious diseases, we rarely conquer them but we must be better equipped to deal with them when they arise. Veterinary research impacts not only on animal health but also public health and provides valuable unique insights into biology that cannot be provided by studies on model systems or laboratory animals. A recent report from the House of Lords in Britain noted that many emerging human infectious diseases are zoonotic. This point has been well illustrated in recent years by the emergence of AIDS. This disease is caused by a retrovirus that probably originated from an African primate and is causing such terrific mortality in sub-Saharan Africa that it is changing the demography of some countries. Closer to home, bovine spongiform encephaopathy [BSE] has not only imposed an enormous economic cost on the cattle industry but, tragically, led to the deaths of a small, but now declining, number of human patients who developed the human form of the disease after consuming infected food. There undoubtedly will be other zoonoses or potential zoonoses that will demand a strong veterinary response. I mentioned earlier that the bacterium that causes paratuberculosis in cattle has been associated with a similar human disease. Veterinarians and veterinary scientists need to consider the implications of this potential zoonosis and anticipate what is required to ensure that public health is ensured.

It is not only new diseases that deserve our attention, as recent events in several Member States of the European Union have demonstrated. The devastating outbreaks of Foot and Mouth disease in Britain and Avian Influenza

in the Netherlands have highlighted the need to develop new methods to control such outbreaks. Fortunately, this is an exciting time to be involved with biological research, and especially veterinary research, as major technical advances are announced that will accelerate the development of new vaccines for both emergency use and long-term protection, as well as other strategies.

I believe that the scientists at Zaragoza and Edinburgh are well placed to take advantage of these advances and continue to deliver the high quality science that we have come to expect from them. It should be noted that in global terms they have rather small teams. But this need not be a disadvantage and I would direct them to the words of the Dalai Lama: «If you think that you are too small to make a difference, try going to bed with a mosquito».

Finally, I would repeat and emphasise that it is a great honour for me to be awarded the title *Doctor Honoris Causa* by this historic University. I have been very fortunate to work in stimulating environments and I am very grateful to all of my teachers, mentors and co-workers who have contributed to my research. I hope that, over the years, I have been able to return some of their efforts and that this honour today is, in part, a recognition of their contributions. I am most grateful to you, Excelentísimo Señor Rector Magnífico, to the Claustro Universitario and to all of my colleagues in the Faculty who were involved in supporting my nomination. Thank you also to my two two padrinos, Dr Marcelo de las Heras and Dr Mercedes Jaime, for their friendship and support over many years and their generous comments in the laudatio.

Gracias

James Michael Sharp