

Personalised medicine for everyone? Developments in genetics and infection and what it means for global health

Melanie Newport inaugural lecture

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The Human Genome Project which deciphered the human DNA sequence, has revolutionised medicine by enhancing our understanding of the molecular basis of disease and facilitating the development of new diagnostic tools and treatments. The genomes of several microbes that cause infectious diseases have also been sequenced.

Professor Newport will give an overview of how advances in this fast moving field have influenced clinical practice in Western societies where future treatments can be tailored to the individual according to their personal DNA sequence. However, these advances have not filtered through to those who stand to benefit most – those living in developing countries which bear the main burden of illness and death due to infectious diseases. The existing gap in healthcare between the haves and have-nots will only widen unless we ensure that ‘tomorrow’s medicine and technology’ work for everyone.

About Melanie Newport

Melanie Newport is the Professor in Infectious Diseases and Global Health. She gained her MBBS at St Mary’s Hospital Medical School, University of London, where she later gained her PhD in 1996. Between 1996 and 1999, she was a clinician scientist for the Tuberculosis (TB) Group and Head of the Human Genetics Laboratory at the Medical Research Council Laboratories, The Gambia. From 1999 to 2004, she worked at the University of Cambridge School of Clinical Medicine, first as an MRC-Gambia linked Fellow and then as a Wellcome Trust Advanced Clinical Fellow and Honorary Consultant in Infectious Diseases. She joined BSMS in 2004 as a Senior Lecturer, then Reader, in Infectious Diseases and Global Health.

What inspired you to go into medicine?

I wanted to be a doctor since I was young. I liked science and nature and wanted to do something that could be useful and worthwhile.

Why did you choose genetics and infectious diseases as a speciality?

The genetics goes right back to studying biology at school. I always found it fascinating that when you look at genetics, DNA and chromosomes and how they work, it is all so simple. DNA is made from only four building blocks, but the order of these blocks, and how DNA unwinds and copies itself, can determine so many complicated things in the human body, both in terms of day- to-day function and disease when it goes wrong. What I like about working in infectious diseases is that it isn’t restricted to one part of the body or one organ. It’s varied and is clinically and scientifically challenging – you are always kept on your toes. I’ve managed to merge my two interests in my research. Infectious diseases are caused by microbes, but actually whether you get ill or not is determined partly by your genetic makeup. When you look at the impact of infection globally, diseases that were a problem in Britain and Europe 100 years ago are still a problem in the developing world, where the resources to control infection are lacking. This inequity has driven my strong interest in global health.

What research areas are you currently focusing on?

I have three areas of research. My PhD investigated a Maltese family in which four children had been affected by severe disseminated atypical mycobacterial infection. These bacteria are related to tuberculosis but are not normally harmful, unless there is weakness of the immune system. The children had been extensively investigated for immunodeficiency yet nothing had been found to explain their infection. Given that they were all related, it was likely to be a new genetic disease. My PhD identified the genetic abnormality in this family by mapping the disease gene to a specific chromosome and then identifying the mutated gene. We discovered that these children were completely deficient in the interferon-gamma receptor. This work it opened up a whole new field of immunology, as a lot of people were looking after children with similar undiagnosed clinical syndromes. My work identified the pathways required to control these infections and led to the discovery of mutations in other genes in other families.

I then got the opportunity to work in the Gambia on a TB project, moving from small families to large populations, and taking that knowledge to use on a grander scale. In sub-Saharan Africa there is a high prevalence of TB, so babies get immunised at birth with BCG. We have been studying immune responses to the BCG vaccine in twins as a simpler model for TB infection as there is a lot of overlap. Comparing identical and non-identical twins has enabled us to estimate how much our genetic makeup contributes to variation in immune responses to vaccines. Having shown that genes are important controllers of these responses, we are now identifying the specific genes involved. This work has been funded by the Wellcome Trust and the British Lung Foundation.

The other project I am working on is the podoconiosis project in Ethiopia. This is a disease in which exposure to a particular volcanic soil causes painful swelling of the legs. Not everyone who is exposed to the soil gets the disease and we think this is because affected individuals have inherited a mutated gene that predisposes them to react to the soil in this way. If you don't inherit the mutated gene you don't get the disease and wearing shoes prevents disease in those who have inherited the mutated gene. Theoretically, it is easily prevented, but the disease occurs in desperately poor areas where shoes are a luxury. I supervise an Ethiopian PhD student who is trying to identify the gene involved and we have also investigated the social and economic impact of this neglected disease.

What is the impact of your research?

Understanding the exact genetic basis of podoconiosis could lead to testing of individuals with higher propensity. The community could then target precious resources to affected families who could also benefit from genetic counselling. Just doing the research has raised the profile of podoconiosis within Ethiopia and internationally, and improved the clinical care for patients with this debilitating disease. With the TB/BCG project, the aim is to discover which genes determine why some people get ill and others don't. For example, if we find that people are protected because they are good at making a specific protein, we could potentially give this protein to cure others of TB. A major problem with TB is increasing drug resistance which means people can no longer be cured with the drugs that are currently available. We need new drugs and our work is directed towards improving the patient's immune response to kill the infection, rather than trying to kill the infection with new antibiotics where the concern is that resistance may also develop.

Why did you choose BSMS?

I like the idea of being part of a new medical school and being somewhere where you can develop your own interests. I get the opportunity to do things that I would not get in other places, and have been able to make the most of these. There is a dynamic research atmosphere here that is great to be a part of.

What does BSMS offer researchers?

It is a vibrant community, and the researchers are very committed. As a medical school we are still young but there is scope to develop our research more and more. Much of my research work is collaborative – and being at BSMS gives me a base. Links with departments from both universities, and organisations like the Institute of Development Studies, are beneficial for my research development. Also, I have been able to collaborate with other research teams at BSMS. You have to work hard and you have to make connections, but you do have the opportunity to be innovative.