



## **Microbes and Mankind – how bacteria and viruses shape humanity**

### **APC Public Forum 12 November 2009**

#### **Summaries of talks**

#### **How microbes have shaped our history**

**Professor Colin Hill, Chair of Microbial Food Safety, Alimentary Pharmabiotic Centre and University College Cork, Ireland**

Microbes (including bacteria, viruses, moulds and parasites) are invisible to the human eye, but are indispensable to all life on Earth. The vast majority of microbes are either harmless or actually beneficial to human existence, but there is a price to be paid for this largely benign co-existence in the form of pathogenic microbes (often referred to as germs or bugs) which can infect humans with outcomes ranging from mild disease to death. These infectious microbes have extracted a terrible toll on humanity over the centuries, in terms of cutting short the lives of extraordinary individuals such as Alexander the Great (died of typhoid at 33 years of age while preparing to invade Arabia) to global pandemics which have threatened the very survival of our species and have had devastating effects on whole civilisations. These diseases have caused hundreds of millions of deaths, in a world where the global population was only a fraction of what it is today. Pathogens causing diseases such as smallpox, plague, tuberculosis and typhus have brought ruin to vast civilisations, including the Roman Empire, the Incas and Aztecs of South America, the native Indian population in North America, to name but a few. Who can know how modern society would look today if the indigenous populations of the Americas were not essentially eliminated by infectious disease, or if feudal society in Europe had not been ended by plague, or if Alexander had continued conquering until a ripe old age?

In the 14<sup>th</sup> century the Black Death led to the Dark ages in Europe, having first caused the death of almost 50% of the population, but also had similar effects in China and in the Middle East. The impact on society is still felt to this day, not least in arresting population growth for at least a couple of centuries. In Ireland we had our own disaster, the Great Hunger, when blight as a result of a potato pathogen (*Phytophthora infestans*) led to a severely weakened community which fell prey to a series of human pathogens and over a million deaths due to typhoid, typhus and cholera. Of course the Irish diaspora can be traced back to this cataclysmic event, a phenomenon which it could be argued benefited other societies, including the USA.

In these battles between pathogens and humans modern society has a weapon which was not available to those who lived and died in earlier times, and that weapon is science. This means that we can combat, or even overcome pathogenic microbes which once killed millions. Take smallpox for example, once a devastating killer (over 300 million died in the 20<sup>th</sup> century alone, and perhaps a billion people over the last few millennia) it was the very first pathogen to be completely eliminated, with the last case occurring in 1979. It would be complacent to imagine that we will always prevail in these 'battles' between man and pathogens, but science offers us hope that we will never again have to experience the prospect of complete annihilation.

Despite scientific advances, global pandemics are not a thing of the past; we are currently undergoing a resurgence of plague in China, of AIDS in Africa and of tuberculosis, again primarily in Africa. The World Health organisation estimate that up to 17 million people still die every year as a result of infections. The ability of modern society to exploit collaborative scientific research to help to detect and treat disease is our best defence against the resurgence of an old enemy, or the emergence of a 'new' enemy which could once again decimate human populations.

## **Disorders of a modern lifestyle**

**Professor Fergus Shanahan, Consultant Gastroenterologist Cork University Hospital, Head of Dept of Medicine, University College Cork and Director APC**

Why me? Why did I get this disease? Why are these diseases becoming so common? These are questions that patients ask their doctors all the time when referring to common chronic inflammatory conditions such as Crohn's disease, colitis, asthma, eczema, multiple sclerosis or early onset diabetes. These seemingly disparate conditions have important features in common: they are immuno-allergic, i.e. they involve the immune system which in each case seems to misbehave in some way. In addition, they are uncommon in 'developing' regions of the globe but increase swiftly in frequency when modernisation occurs with the transition from 'developing' to 'developed' nation status. This abrupt increase in frequency occurs at a pace that is too fast to be accounted for by changes in genetic susceptibility within the population. Furthermore, we know from studies of identical twins that the concordance rate (risk of developing the disease in one if the other twin has the disease) suggests that there is a substantial environmental or lifestyle contribution to the risk of developing these immuno-allergic disorders. Whatever is responsible within the modern environment of industrialised countries, it clearly acts at an early stage in life. We know this from migration studies where the risk of disease relates to the age of migration. Those who migrate from a low-risk geographic region of the world to a high-risk region acquire the high risk of the new country only if they migrate in childhood. The earlier the age of migration the greater the risk; whereas, those who migrate in adulthood retain the low risk of the old country. What is so critical in childhood that can explain these observations? Increasing evidence suggests that a modern lifestyle influences the developing immune system by virtue of its influence on the microbes (bacteria, viruses and other microorganisms) that colonise the newborn baby. Although the immune system is intact at the time of birth, it requires input from the environment for full maturation. The immune system is essentially a sixth sense; it is the

sense of danger in the microbial environment, sensing the difference between harmless organism versus dangerous pathogens. To perform optimally in adult life, the immune system, like other senses, needs to be educated. It obtains this education by interacting with the normal microbes that colonise the skin and gut immediately after birth. Any disturbance of this microbial-mediated education of the immune system might predispose to misbehaviour of the immune system. Experimental studies have already shown some of the mechanisms by which the gut microbiota (flora) shape the developing immune system, and such research is ongoing at the SFI-funded *Alimentary Pharmabiotic Centre* in Cork, which is a research alliance between University College Cork and Teagasc. Thus, the composition of the microbial flora that colonise the body may be influenced by a modern lifestyle and by turn determine the outcome of the maturation of the immune system and subsequent risk of immuno-allergic disease. Finally, what elements of a modern lifestyle could be responsible for increasing risk of disease by virtue of an influence on the normal gut microbial flora? The most obvious influence is antibiotic usage but dietary or nutritional factors also play an important role. Other influences include sanitation and hygiene, refrigeration, life on concrete, urbanisation, smaller family size, and even a sedentary lifestyle and obesity have been associated with a shift in bacterial composition in the gut. It may come as a surprise to many that public health improvements such as water sanitation, the decline in endemic parasitism, delayed exposure to certain childhood infections and reduced frequency of infections such as hepatitis A, may have come at a certain cost, and may actually have contributed to a rise in immuno-allergic disorders in the modern world. Progress comes with a cost.

## **Microbes Benefitting Human Health**

**Professor Paul Ross, Head of Food Research, Teagasc & Principal Investigator, APC**

Prof. Ross's presentation focused on how bacteria which reside in our gut influence human health and in so doing he also addressed such concepts as probiotics, prebiotics and the scientific evidence which surrounds them. Man can be considered as a "superorganism" which is made of human cells and a beneficial bacterial flora which resides mainly in the gut. In particular the gut cells outnumber human cells in the body at least by a factor of ten. Indeed, each person has up to a 1,000 different species of bacteria in their gut – the composition of which varies with respect to age, genetics and diet. It is important to emphasize that these bacteria play important roles in maintaining human health through aiding digestion, modulating the immune system and protecting against infection. Indeed, recent evidence has suggested that the composition of these gut bacteria is altered in some disease states including infection, Crohn's disease and obesity. The APC researchers are particularly interested in how to improve the composition and functioning of these beneficial bacteria through the food we eat and in particular to develop new Functional Foods which positively impact on human health. In a number of studies we have shown that produced by gut bacteria can have an impact on other tissues in the body including adipose, liver and brain tissues – demonstrating the impact of these bacteria across the whole body. Prof Ross also highlighted the potential of mining these bacteria for health-promoting substances. Indeed, they have recently discovered an

antimicrobial protein called thuricin which can kill the dangerous human pathogen *Clostridium difficile* – which has been the cause of recent deaths due to gastrointestinal infection. Thuricin may represent a radical improvement over conventional antibiotic therapy in that it is extremely potent at targeting the pathogen but does not affect the good bacteria in the gut. Importantly, this technology has recently been patented by the UCC/Teagasc team and licensed to the Irish company Alimentary Health