

Acceptance Speech by Staffan Normark

[Check against delivery.]

The title of Robert Koch's Nobel lecture December 12, 1905 in Stockholm was "The Current State of the Struggle against Tuberculosis". That was more than 20 years after publishing his famous paper on "Die aetiology der tuberculose". It was in this classic paper, Koch formulated his four postulates - the stringent criteria, which an organism must fulfil before it, can be considered the cause of an infectious disease. Based on personal experience and a really good scientific evidence Robert Koch defined four steps in this basic principle. The four steps were; association of a microbe to disease, isolation of the microbe, inoculation and re-isolation of the same microbe. That was all. Some 100 years later another giant medical microbiologist on which shoulders I have been fortunate to stand, Stanley Falkow, formulated the molecular Koch postulates; the criteria required to conclude that a virulence trait of a microbe was required for disease. I have for the major part of my scientific life tried to fulfil molecular Koch's postulates for properties expressed by a number of pathogens associated with a range of infectious diseases. My focus has been to identify molecular mechanisms by which the surface of bacterial pathogens can interact with human cells, and to what extent these interactions promote and shape an infectious disease.

I have moved from pathogens of the urinary and genital tracts to those dwelling in the stomach and are currently focussing on respiratory pathogens. This move upwards in the body may seem small and insignificant, but not for a molecular geneticist like myself brought up with laboratory strains of *Escherichia coli* as the study object. This background and lack of clinical understanding of infectious diseases prevented me from exploring the potential of microbes in the aetiology of common diseases such as gastric and duodenal ulcers, even though a connection was suggested to me by observant clinicians long before the discovery of *Helicobacter pylori* by Marshall and Warren, a bacteriological discovery awarded the Nobel prize precisely 100 years after giving it to Robert Koch.

The molecular work I have been involved in, carried out over a period of fifty years, has involved many dedicated students, post-docs, and collaborators including clinicians with unique talents and expertise. I am proud that many of them, independent of me, have developed new aspects of microbe-host interactions that go beyond fulfilling the molecular Koch's postulates. I have learnt from them and come to appreciate that many infections are caused by organisms that are members of the normal human microbiota. However, to survive as a species these potential pathogens have evolved a wide range of baby step strategies that together may allow a tiny number of them to sometimes pass biological barriers, to enter a safe haven inside our cells or to resist our immune defence system. The likelihood for these

events to happen is very small in young healthy adults, but much higher in compromised individuals. The main risk factor for attracting a bacterial pneumonia for example is to be elderly, and this risk increases dramatically after an influenza-virus infection. Hundred years after the Spanish flu epidemics, I have promised my wife and close collaborator for the last 20 years, Birgitta Henriques-Normark to get that flu vaccine when returning back to Sweden.

Thank you for honouring me, and indirectly all those that have been working with me over the years, with the Robert Koch Gold medal for 2018.