



his book attempts to highlight the fact that microorganisms are generally beneficial and essential for life as we know it. It cannot be denied, however, that some microbes are far from beneficial, and, rather like a small number of hooligans in a full stadium of respectable fans, tend to attract the most attention. This section turns the spotlight on the troublemakers. Not so long ago, pathogenic microorganisms such as the smallpox virus were a major cause of death, and epidemics devastated human communities, worldwide. This changed radically in the nineteenth and twentieth centuries, with the discoveries and innovations that led to the development of vaccines and antibiotics. Common childhood diseases were successfully targeted and their impact on people was greatly reduced. However, the original optimism that accompanied these spectacular achievements has waned completely. We now realize that in vaccine development, the low hanging fruit has been picked. The remaining dangerous pathogens are adept at avoiding attempts to control them.

In this section, tuberculosis, malaria, HIV and flu are highlighted as examples of diseases caused by resistant and well-adapted pathogens which are notoriously difficult to handle. They can evade the human immune system and hide within the host. They have learned that, from an evolutionary perspective, rapidly killing their host is not a good survival strategy as this would result in their own rapid extinction. However, our increasing understanding of the lifestyles of these pathogens, together with the rapidly expanding development of molecular biology tools, offers promise for future vaccines against these exceptionally difficult pathogens.

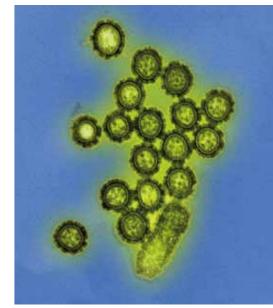
The challenges are not just technical. The development of a novel vaccine takes at least ten years, and the cost from research and discovery to product registration can reach US \$500 million! This can only be achieved when pharmaceutical companies, governments and charity funds collaborate on the necessary long term commitment. Once an approved vaccine is finally available, how can global distribution and access in underdeveloped countries be ensured? How can we respond to "alternative facts" about the side effects of vaccines and make the public aware that in the long run, as Erasmus pointed out about 500 years ago, prevention is better than cure?

Another problem is that the easily-produced antibiotics which are relatively simple to produce have been identified and explored. We are now having to dig deep to find novel antibiotics that are not normally produced under laboratory conditions, again relying on molecular and structural biology tools and unconventional culture methods.

A growing threat to human health is the rise of antibiotic resistance in pathogenic bacteria. Although resistance to antibiotics occurs naturally, its misuse in humans and livestock has contributed substantially to the increasing spread of resistance over the last decades. For some multi-resistant bacteria, known in the public media as "superbugs", there are no effective antibiotics any more, not even in the antibiotic development pipeline, and quarantine may be the only remaining option. We urgently need new antibiotics, preferably antibiotics that will not induce resistance so quickly. Obviously, we must also focus on novel strategies to prevent resistance development in the first place, and reconsider alternative strategies such as bacteriophage therapy and the use of predatory bacteria. There is a lot to be done, but we are now aware of it and, since "necessity is the mother of invention", hopefully new antimicrobials are on their way!



A sputum sample from a tuberculosis patient containing *Mycobacterium* tuberculosis.



Colourized transmission electron micrograph showing H1N1 influenza virus particles.