Commentary: Liam Tremble

Climate change is transforming infectious disease

The recent COP27 climate conference in Egypt was a reminder that the challenges posed by global warming affect nearly all aspects of human life. Extreme weather events have uprooted communities and disrupted the production of food. They have also contributed to the transmission of infectious diseases from remote habitats to many locations around the world.

The emergence of the SARS-CoV-2 virus, the cause of Covid-19, is a case in point. While there is still uncertainty about the precise origin of the virus, scientists now believe the most likely source is bats. The virus may also have involved an intermediate host before infecting humans. In an article in *Frontiers in Medicine*, Saloni Gupta and colleagues argue that climate change has led to changes in the migratory habits of bats, making it possible for novel viruses such as SARS-CoV-2 to emerge.[1]

But viruses are not the only pathogens to cause infectious diseases. Fungi, worms, protozoa and bacteria can also trigger these illnesses. In the case of bacteria, the diseases include strep throat, urinary tract infections and tuberculosis. They also include a less well-known condition called melioidosis. Melioidosis, also known as Whitmore's disease, is caused by the environmental Gram-negative bacterium *Burkholderia pseudomallei* which is found in contaminated soil and groundwater. It is spread to humans and animals through contact with the contaminated source.

Until recently, the incidence of the disease was largely confined to South-East Asia, Australia and India. But climate change is having a substantial impact on its spread to new areas such as Brazil. Concerns are also growing about a further spread to non-tropical areas as global temperatures rise. Recently the bacterium was found in the environment along the Gulf Coast in the US state of Mississippi. The Centers for Disease Control and Prevention (CDC) and its state partners are conducting investigations to see how far the bacteria has spread within the continental US.

The number of cases of melioidosis per year is currently put at 165,000, of which some 89,000 are estimated to be fatal. The majority of people with acute melioidosis present with sepsis, a life-threatening disease. According to the CDC, the bacteria are naturally resistant to many widely-used antibiotics which makes the disease difficult to treat.

What is to be done? Surveillance is the first step. This is already underway at the CDC which routinely studies biological agents that might pose a risk to national security because of their ease of transmission and impact on public health. Melioidosis has been classified as a category B bioterrorism agent which is moderately easy to disseminate and would require enhanced disease surveillance. There are 11 other agents in category B including bacteria that pose a threat to human health such as the *Salmonella* species.

Treatment options for melioidosis include the antibiotics beta-lactams, carbapenems and doxycycline depending on the stage of the disease. However the bacterium is reportedly resistant to penicillin, ampicillin and first and second generation cephalosporins. New therapeutic approaches are therefore needed, as well as vaccines. There are currently no approved vaccines but several are in development.

At Poolbeg we are working on a candidate vaccine for melioidosis which is based on research carried out at University College Dublin (UCD) in Ireland by Siobhán McClean and her team. Dr McClean is associate professor at the UCD School of Biomolecular and Biomedical Science. The vaccine was invented following years of research some of which received funding from the Wellcome Trust. We took an option on the product in December 2021 and formally in-licensed it in September of this year.

The vaccine, POLB003, is based on a homologue of the bacterial antigen *OmpW* which is specific to the *Burkholderia pseudomallei* bacteria strain. It is currently in preclinical development. Experiments in immunised mice have demonstrated a 75% survival rate over 81 days. A separate toxicity study did not generate any safety signals. Subsequent characterisation of the immune responses from the mice confirmed the activation of CD25 and CD44 T cells and B cell responses which would be required for an effective vaccine.

As diabetes is a significant risk factor for the disease and is prevalent in many countries with the highest incidence of melioidosis infections, the vaccine was also tested in a standalone insulin resistant mouse model. This showed activation markers and cytokine production associated with an effective immune response, giving confidence that the vaccine would work in this patient sub-population.

Given the environmental challenges that we face, it is reassuring that many public bodies are offering financial incentives to companies researching and developing products for infectious diseases. The US Department of Defence commonly provides upwards of $50 million for these projects. It typically focuses on biothreats for which there are poor countermeasures or on diseases that can affect the performance of the US armed forces. On 18 October, the Biden Administration updated the government's biodefense and pandemic preparedness strategy. This includes a request to the US Congress to provide $88 billion in funding over the next five years to support the monitoring of infectious diseases and develop new diagnostics and vaccines.

This can only help generate opportunities for developers of vaccines and therapies designed to protect against infectious diseases caused by climate change.

Source: Gupta, Saloni et al, *Frontiers in Medicine*, 8 December, 2021.

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