

Vaccines – *the Art of War*

In our struggle against infectious diseases, battles have been won but the war is far from over.

Two hundred years of work has transformed Edward Jenner's first vaccination experiments into a legacy that has eradicated smallpox, reduced polio infection by 99% and measles by 74%. Millions of people, and their descendants, now exist because of this.

However, these victories exist in the shadow of those threats which remain. Pathogens such as HIV, influenza virus and Hepatitis C virus represent more complicated foes, able to evolve beyond our existing techniques.

Fresh innovation is required – a battle-plan is needed.

Gathering Intelligence

Without information, the war is already lost. Understanding each pathogen's journey, through one host and into the next, can reveal its most vulnerable moments – our windows of opportunity.

Achieving this requires a strong foundation of research – particularly the existence models for studying pathogens at the lab bench, rather than in patients. Some diseases, such as Hepatitis C have proven challenging to grow in the lab, slowing efforts to study them.

Progress is being made in this area, but each discovery reveals new questions. By improving our tools we inch closer to spotting that chink in the armour, and exploiting it.

Selecting a Target

The right target makes all the difference. Vaccines are typically designed around a marker, called an epitope, selected from the outside of an invading pathogen. This trains the immune system to rapidly recognise and neutralise the invader, a vital head-start in battle.

Picking the right epitope is essential – it will be the calling card of the invader that the immune system remembers. However, successful pathogens often have a high rate of change in their DNA as they replicate – creating populations with a huge range of slightly different epitopes even within a single infected individual.

Pathogens such as HIV use this ability to create a constantly shifting battlefield – altering their epitopes to reset their recognisability. This constant guerrilla warfare keeps the pathogen hidden, and the immune system guessing.

Current research is overcoming this problem using shrewd selection, rather than brute force. Avoiding the obvious epitopes which can easily be changed, researchers are selecting areas which the pathogen needs to keep fixed in order to maintain its infectivity. This puts the pathogen in a lose-lose situation – either get recognised, or become less infectious.

With the target selected, an appropriate weapon is required.

In the Armoury

Vaccines are not all alike. We know the body creates different types of immune response according to the pathogen

encountered, and a successful vaccine needs to support the correct reaction.

Early vaccines have taught us many lessons – early HIV vaccines failed due to ineffective immune responses being made. The latest vaccines aim to create subtly-tuned and overlapping immune responses, best designed to repel the target.

We also need to think about how to deliver the vaccine – existing techniques using dead pathogens, or extracted epitopes are not sufficient. New ideas include using raw DNA to immunise people, or exposing immune cells outside the body before reintroducing them.

Counter-Insurgency

Despite best intentions, our immune systems can sometimes be misdirected by invading pathogens.

Research has shown that during HIV infection, one of our own immune sentinel cells unwittingly carries HIV from the entry site all the way to its target, deep inside the body. Such hijacking allows HIV to bypass the dangers of making this journey alone, protecting it from the immune system.

When planning our intervention, we need to allow for the failings in our own natural response and fill these gaps with carefully designed support. Once incorporating these features, a vaccine can be readied for deployment in the field.

Campaign strategy

A powerful vaccine is only a tool, and one that still needs to be applied correctly.

To maximise the life-saving potential of vaccine, we must prioritise those groups of people who are most at risk, catching the pathogen at a bottleneck and reducing its dispersal. The spread of disease, influenced by factors such as urbanisation and global travel, is studied by the branch of science called epidemiology which can guide the use of a new vaccine.

Epidemiologists can advise on how previous vaccination strategies have worked, and how local conditions such as lifestyles, diets and even other existing diseases can change the way a vaccine will work. Without this planning, even a good vaccine can fail to have the desired effect.

A Winnable War?

Advances are coming, but the remaining challenges are the hardest.

When fighting these constantly evolving pathogens, we must evolve our own tactics in parallel. Success lies in unifying the advances in all the fields mentioned, creating effective vaccines built upon a strong foundation of knowledge. Our intervention will take place in an already chaotic natural battlefield between a pathogen and our immune system, so understanding both belligerents is critical to lending useful support.

The challenge of understanding this chaos should not deter us, but give us hope for success –

“In the midst of chaos, there is also opportunity”

General Sun Tzu, *The Art of War*.