Essay title: There is still considerable distrust about the use of vaccines, and in some countries and communities vaccine hesitancy is a significant issue. Discuss how vaccines work to produce an immune response and how we can reassure the public that they are safe.

Abstract

Vaccines are manmade formulas that contain a weakened or inactive form of an infection. There are many types of vaccines, and each depends on the specific infectious part utilized. They work to stimulate the immune response without causing an infection leading to the production of antibodies, highly selective immune cells that fight against the infection they were created for. This process leads to the formation of long-lived memory cells which remain dormant until a similar infection returns, in which an immune response would be stimulated much faster this time around. The recent increase in anti-vaxxers posed a major barrier for medical professionals to increase compliance and vaccinations. It becomes paramount that people receive their information from reputable sources and peer-reviewed medical journals since numerous statements derived from anti-vaxxers were supported by disproven and retracted studies. Vaccination education and encouragement is essential when considering the increased incidence of infections such as measles due to opting out of vaccines.

Over the course of a few decades, we have witnessed ground-breaking advancements in our healthcare, resulting in a major decrease in mortality from infectious diseases that were originally thought to be deadly and incurable. Arguably one of humanity's greatest medical discoveries was vaccines back in 1796 [1]. The use of vaccines has completely transformed how we tackled infectious diseases and viruses, as well as reinforced new techniques to protect the immune system. This was shown when the first vaccine in 1796 was created to inoculate cowpox, ultimately leading to its eradication in 1980 [1]. Vaccines have also shown to effectively contain and suppress a wide array of infections, such as measles, mumps and rubella (MMR). Despite these major advancements in our healthcare and the eradication of a virus that had been estimated to have killed over 300 million people since 1900, there exists a group of people that believe vaccines bring more harm than good and that the use of these vaccines should be removed as a form of resistance against these pathogens [2]. This group of "Anti-vaxxers" have been lurking since the initial discovery of vaccines however, they have been recently emerging and growing due to the plethora of Blogspot's and online forums where voicing opinions rather than facts for thousands to read becomes very problematic, often causing facts formulated from quality research to be misconstrued with baseless opinions [3]. As a result, it is vital for healthcare professionals to take the necessary time to educate and reassure these groups of people on the safety of vaccines, in order to minimise the occurrence of contracting a life-threatening disease that could have been avoided via vaccination. In light of this, this essay will be explaining what a vaccine is and the different types of vaccines. Furthermore, I will be discussing how a vaccine elicits an

immune response before going over why anti-vaxxers claim their stance and how we can reassure them as well as the general public that vaccines are safe.

Vaccines are “biological agents that elicit an immune response to a specific antigen derived from an infectious disease-causing pathogen” [1]. There are several types of vaccines, each designed to educate your immune system on how to fend off certain pathogens and the diseases they cause. When creating vaccines, scientists must factor in how your immune system reacts to the pathogen, who needs to be vaccinated and the best approach to creating it [4]. Based on these factors among a few others, scientists will decide which type of vaccine to produce. The options are visible on fig.1. where each type is corresponded to the specific section of the pathogen it is derived from. Whilst they differ in terms of what sections of the pathogen they contain, they all carry out the same role in stimulating the immune system [4]. It is important to note that altering the pathogen or using sections of it can lead to loss of immunogenicity [7]. This can be rectified with the use of adjuvants; compounds that would boost immunogenicity [7]. Inactivated vaccines use a killed or altered form of the pathogen so that it cannot replicate. Due to the inability to replicate, the vaccine only provides short term immunity, usually requiring several booster shots to receive ongoing protection [5]. In contrast, live attenuated vaccines contain genetically modified versions of the pathogen so that they elicit

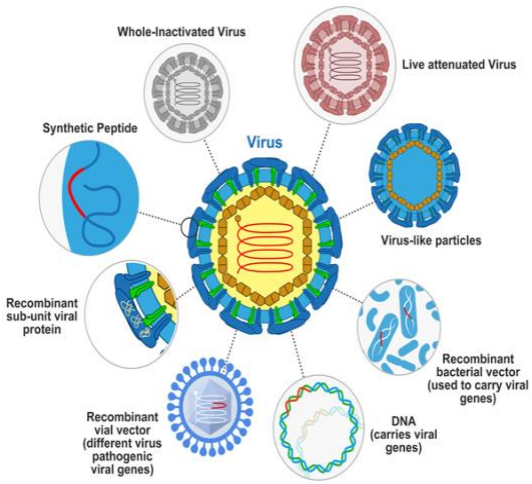

Figure 1 (fig.1): Diagram illustrating the different types of vaccines that can be made [6].

an immune response but do not cause disease in the person [5]. Subunit vaccines as shown in fig.1. utilises one or more antigens from the pathogen, as opposed to using the entire pathogen. Similar to inactivated vaccines, repeated booster shots may be required as this vaccine does not always create a strong or long-lasting immune response as compared to live vaccines [5]. Recombinant vector vaccines take advantage of bacteria or viruses as a vector to manufacture a vaccine. This is done by taking a piece of DNA from the pathogen which we want to protect against and inserting it into the host cell [5]. This leads to the production of one of the surface proteins from the pathogen which gets recognised as a foreign material by the immune system, triggering an immune response [5]. Virus-like particles (VLP) closely resemble its parent virus but are non-infectious due to the absence of viral genetic material [5]. VLP can be naturally or synthetically synthesised, and if required can present numerous antigens from multiple pathogens simultaneously. Due to the presence of multiple copies of antigens, a more effective immune response is stimulated making this vaccination option a very effective one [5]. DNA vaccines carry the viral gene and is translated to mRNA within the cell nucleus so that antigens are translated, causing an immune response [5]. Finally synthetic peptide vaccines identify the specific peptide sequence that would trigger a protective response [8]. Once found, the sequence is synthetically made, which increases its stability and eliminates the risk of mutation or reversion whilst providing an increased number of antigens for a stronger immune response [8]. Ensuring that the public understand the different forms of vaccines will ease their concerns regarding what exactly is entering their body. To build upon that understanding, it is important to consider the mechanism of action for these vaccines.

Whenever a pathogen or foreign object enters the body the innate immune response acts as the first line of defence in alerting the adaptive immune system and engulfs or attaches to anything it has considered to be non self [9]. This initial detection is achieved through the recognition of epitopes on the pathogen's antigens. Numerous cell types in the innate immune system will activate and move towards the pathogens, such as the complement system which works to opsonize pathogens and aid its engulfment by antigen-presenting cells (APC) such as macrophages and dendritic cells [9]. This along with many other cell types work in unison to aid the adaptive immune system in destroying the pathogen. APC will process the required antigens along with the MHC protein and insert them onto their surface for recognition by the suitable T-cells [9]. If the vaccination contained viral antigens, then they would be bound by MHC I protein and presented to CD8 cells, triggering cell-mediated immunity [9]. If the vaccination contained bacterial or parasitic antigens then they would be bound by MHC II protein and presented to CD4 cells, triggering antibody-mediated immunity [9]. As shown on fig.2. antibodies have numerous methods in disposing of pathogens. Some of the listed functions are agglutination to prevent pathogens from spreading into other areas and directly attaching onto pathogens and killing them [7]. Antibodies also have the ability to attach onto pathogens and mark them, making them easier to find by other immune cells such as macrophages, resulting in their destruction [7]. The purpose of this exposure is the generation of long-lived plasma cells differentiated from B-cells which can secrete a large number of antibodies for the specific infection when

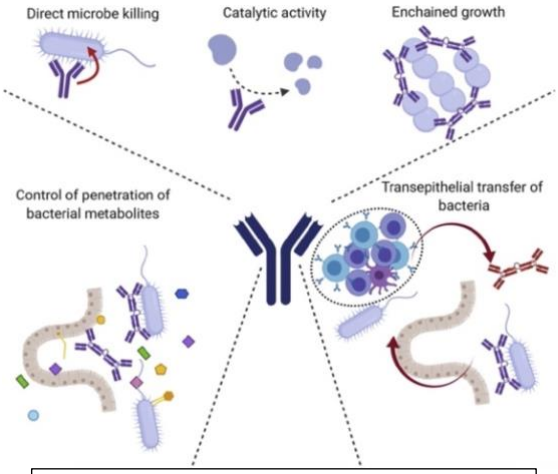

Figure 2 (fig.2): Diagram portraying the different ways that antibodies act in an immune response [10].

required, resulting in its early elimination before symptoms can arise [7]. It is important to consider that each specific antibody produced for the infection has a unique half-life corresponding to that pathogen and if the half-life is 10 years for example, then protection must be maintained via booster shots to ensure antibody levels do not drop below the required level [7]. By building an understanding of what exactly occurs within the body during this immune response, confusion and doubt surrounding this field can be diminished which would further our cause in improving vaccination rates amongst the anti-vaxxers. In order to reach that hope we must factor in their reasoning in maintaining this stance to generate sensible solutions for added reassurance.

The increase in doubt of vaccine's benefits amongst the anti-vaxxers and the general public continue to act as a thorn in the medical community. The main argument presented by these group of people is the questionable link between vaccine administration and autism, which was the conclusion drawn in the infamous Wakefield study [3]. To provide perspective, this study utilised a small sample size of self-reported cases, whereas the plethora of studies that have debunked Wakefield's findings used sample sizes of over a million children to draw these conclusions [3]. The retraction of Wakefield's article should further emphasise the decreased credibility of his findings but unfortunately this is not the case amongst some parents desperate for answers. A possible rationale behind this could be the association of autism often being diagnosed around the same age where many vaccinations are administered, leading some parents linking these two uncorrelated instances together for the purpose of having something to blame [3]. It is important to note that people who are misinformed may be reading literature fabricated by a journalist's

opinion rather than peer-reviewed articles that have undergone a rigorous review process, which actively reinforces the quality and credibility of their findings and their drawn conclusion [3]. A further important aspect that many of the general public may be missing is the attention towards finding references to validate the quality of the articles they are reading [3]. It can be inferred that a large number of people reading these online forums and questionable journals may not be actively looking for references to determine credibility, which can be viewed as its own epidemic playing a leading role in swaying the misinformed towards the anti-vaccination movement [3]. It is these reasons among a few others that must be looked into further in order to improve vaccination usage amongst the public, thereby providing indirect protection via herd immunity for those who may be immunocompromised or simply allergic to vaccines [3].

Several past instances have suggested that decreased vaccination usage has major implications with an increased epidemic of a specific disease [3]. The increase of measles' cases to some of the highest numbers reported in decades is a testament of the true dangers behind opting out of vaccines [3]. This greatly raises the importance of developing strategies for increasing vaccine usage as this careless attitude can lead to detrimental consequences for the society as a whole. Attempting to sway the misinformed and confused with statistics and concrete evidence has proven not to be effective, so one must consider alternate methods to convince them of the benefits of vaccinations [3]. With the increase in self-published journals and Blogspot's as previously mentioned, the importance of educating the public to search for references becomes apparent. Being able to properly teach the public how to fact check the information they are reading and assess its validity

would greatly reduce instances of confusion and controversy, especially over something that is reinforced with a myriad of high-quality longitudinal research [3]. Knowing how to assess an article's credibility is an essential skill that should be taught at all age groups and educational backgrounds with the hope of initiating the rise of a new generation that is able to critically analyse the information displayed as well as build sensible conclusions based on recognised methods of literature [3]. Instilling this skill along with the education of a vaccine's composition and its mechanism of action would be the best course of action to suppress the outbreak of anti-vaccination campaigns. Utilising these methods would generate a driving force towards removing this thorn from the medical community, allowing them to focus their efforts onto more important matters, such as developing new methods of providing artificial active immunity for more potentially deadly diseases.

It is crucial to note that even the most intricate and creative methods for educating the public being available, there will always remain a small portion of the public that will choose to ignore this information presented to them. While this may be an unfortunate reality, it is essential for the medical community to divert their efforts onto those who can be influenced if the necessary measures are taken. The aim of this is to drastically reduce instances of vaccine refusal through reassurance, in order to create a community that is far less capable of contracting that disease, leading to its suppression and containment. Even though we still have a long way to go, by continuing to address this further the medical community can get closer to reaching this favourable reality.

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