Vaccines & Adjuvants

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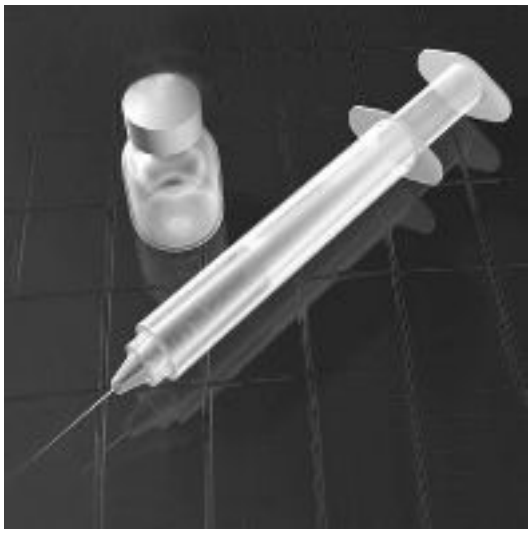
Vaccine Overview

Vaccines save millions of lives every year and has improved quality of life in developed and developing countries [1]. Vaccines are most effective and cost efficient method for preventing diseases caused by infectious pathogens [2]. The goal of vaccines is to make a pathogen-specific immune response providing long-lasting protection against infection. Canadian children get vaccinated against 6 viruses (polio, measles, mumps, hepatitis and varicella) and 6 types of bacteria (tetanus, diphtheria, pertussis, type b *Haemophilus influenzae*, 7 of the 90+ strains of pneumococcus and type C meningococcus) [3]. Development of safe and strong vaccines are still required due to the emergence of new pathogens, reemergence of old pathogens and the protection of past and existing vaccines [2]. Not all vaccines are the same. There are 3 types of vaccines. The most effective vaccine is the live-weakened vaccine which can replicate and trigger immune mediated immunity. Inactivated/ killed vaccine trigger only weak immunity and requires many doses in order to achieve full immunity. The third type of vaccine is the purified vaccine, it is non-living and provides the lowest level of immunity as it has only the core parts of the virus [2]. Purified vaccines have the lowest adverse reactions as it relies on the body to do most of the immunity work. Vaccine adjuvants make vaccines cost effective, beneficial in antibody production, making cytotoxic T cells (healthy cells that kill sick cells in blood), long lasting in immune response, and stronger (less dose is needed) [4]. Developing new vaccines requires finding and using immune responsive adjuvants to help improve vaccine strength, effectiveness and safety [2]. Due to safety and toxicity concerns, there is a limited number of adjuvants licensed for use in human vaccines [2].



Adjuvants in vaccines

An adjuvant is Latin for *adjuvare*, which means “to help” or “to aid”, as adjuvants are helpful agents in vaccines that increase immune response and immunity [2]. Adjuvants are needed to help proteins become stronger and last longer in fighting pathogens [2]. Most of the adjuvants being made in research labs fail due to stable, lack of effectiveness, and safety concerns, this is a concern for vaccine research due to pathogens having antigenic drift (they have genetic mutations) which impacts the number of adjuvants available for use in human vaccines [5].

Adjuvant types

Adjuvants containing aluminium (“alum”) have been used in human vaccines since 1926, because it strengthens the body’s immune response [1]. The two main aluminium salts (alum hydroxyphosphate and alum oxyhydroxide) used in human vaccines adjuvants are relatively weak and very small (nanoparticle size) and prevent vaccine clumping [6]. There are different types of insoluble aluminium salts used in human vaccines; alum potassium sulphate, alum hydroxide, alum phosphate, alum hydroxide, and alum magnesium hydroxide [7]. Aluminium salts do not have the ability to trigger cytotoxic T cells (cells that attack infected cells), and is why it has a long lasting stabile safety record [2]. Aside from aluminium salts for adjuvants, there are adjuvants MF59 and AS09 that are a oil-in-water kind, which recruit specific red and white blood cells for immunity and are very effective [2]. Virosomes are remade viruses but without genetic information is another adjuvant used, which improves cell mediated immunity. Virosomes are of high quality, long lasting, do not degrade over time and are very safe for people with weakened immune systems [2]. The last licensed vaccine adjuvant in use is the AS04, it improves cell immunity, mostly used for Human Papillomavirus (HPV) and Hep B vaccines [2].

Vaccine myths

There are some published articles that raised concerns over safety of vaccines, one regarding mercury and the other aluminium linked to Autism Spectrum Disorder. In 1999 concerns over mercury in thiomersal vaccine was believed to have exceeded the Environmental Protection Agency in the USA for methyl mercury [8]. The study that raised concerns over mercury levels was flawed in methodology and has not been proven in other studies. Public Health Service and the American Academy of Pediatrics called for the removal of thiomersal from infant vaccines as a precautionary measure, soon after fear spread over the possibility that exposure to thiomersal in vaccines may cause autism which has not been proven [9]. The fact is the thiomersal vaccine contains only ethyl mercury and based on pharmacokinetic data, ethyl mercury is excreted in

stools and does not accumulate over time in the blood [8]. It is important to know that mercury tests represent population averages and do not reflect individual toxicity level thresholds [10]. Thiomersal has a mercury containing compound that is commonly used in multi-dose vials of vaccines to preserve it (used since the 1930s), and no studies have found evidence of increased neurodevelopmental problems of it used in thiomersal vaccine [3,9]. Canadian vaccines use single vials and have trace amounts of thiomersal. There is no current evidence of a link between vaccines and cancer, multiple sclerosis, diabetes mellitus or autoimmune diseases [3].

Aluminium adjuvant concerns with Autism Spectrum Disorder came from a flawed study that made population comparisons and did not address individuals [8]. Comparing populations does not provide causal associations to be made because no link of exposure to outcome is established. Aside from population comparisons these studies had flaws in assumptions, accuracy and calculations regarding autism spectrum disorder diagnosis and vaccines schedules in other countries [8]. The US FDA analysis indicates that alum in vaccines never exceeds safety regulatory thresholds, including low birth-weight infants [8]. There are over 6 decades of experience with aluminium used as an adjuvant, there is no evidence to support a safety issue regarding its use in attenuated virus vaccines [11].

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