AUTHOR:
Chenjerayi Kashangura[1]

AFFILIATION:
[1]Biological Sciences Department, University of Zimbabwe, Harare, Zimbabwe

CORRESPONDENCE TO:
Chenjerayi Kashangura

EMAIL:
ckashangura@kutsaga.co.zw

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Enhanced education on vaccines can reduce the scourge of vaccine rejection and hesitation

Development and improvement of vaccines are benefitting from advances in life sciences fields such as synthetic biology. However, amidst this technological revolution, the field of vaccinology faces challenges in keeping up with evolving viral pathogens and adverse vaccine response outcomes due to human genetic diversity. Moreover, anti-vaccination attitudes create a higher incidence of vaccine hesitation and rejection.

Global health is facing challenges from evolving existing pathogens that are becoming multidrug resistant and thus reducing the available therapeutic interventions that can be employed. Moreover, novel pathogens are emerging, such as the current pandemic of SARS-Coronavirus 2 (SARS–Cov-2). Some of the hot topics in vaccination – namely efficacy, impact and attitudes – were highlighted in an Elsevier Vaccine Special Article Collection[1] that also identified some of the challenges in vaccinology. These challenges include anti-vaccine thinking that leads to increased levels of vaccine rejection and the need to work fast to produce a vaccine such as the annual flu vaccine which must match new strains.[1] Developing vaccines is usually a race against time as the viral particles mutate and recombine and thus require annual development *ab initio*. Successful vaccinology depends partly on the vaccines interacting with the immune system and producing an immune response similar to that produced by the natural infection, but usually not creating clinical disease symptoms and potential complications.[2] Vaccines can be in the form of live attenuated pathogen, virus-like particles, killed sub-unit, killed virus and viral components such as polysaccharide and protein[3] that result in long-term protection that requires the persistence of vaccine antibodies and/or the generation of immune memory cells that are capable of rapid and effective reactivation upon subsequent exposure to the pathogen.[3]

Genetic diversity in populations is essential as high levels of diversity usually correspond to fitness or adaptability to environments. Thus, any change in the environment will most likely have a corresponding adaptive genome already present in the population. A population that is highly genetically uniform would need mutations to occur to adapt to a new environment and, in the absence of mutations, fitness is lowered, and the population tends towards extinction. However, for vaccinology, high genetic diversity is not ideal as the interaction of genetic factors, such as polymorphisms in genes encoding immune response proteins – HLA molecules, cytokines and cytokine receptors – and environmental factors such as the dose, route of administration and quality of antigen can result in non-uniform or unexpected outcomes.[4,5] These may include adverse side effects or complications after the vaccine is administered. This genetic variation in both humans and the pathogen causes antigenic variation in the infectious agent and a high inter-individual variability in the human response to the vaccine[6] which prevents the attainment of a universally effective vaccine. On the other hand, a genetically uniform population would potentially have uniform outcomes after administering a vaccine. Africa has rich human genetic diversity[7] which needs to be taken into account in developing and evaluating vaccines.

Enhanced vaccine development in the form of multidisciplinary synergistic approaches may enable novel ways to develop vaccines that utilise the rapidly growing field of artificial intelligence (AI) *in silico* deep learning, deep reasoning, reading and vision capabilities. Novel algorithms can reduce genetic diversity to uniform demes, predict[8], model and select the strain to use. In addition, the algorithms can be developed to: consider human genetic variants that determine disease susceptibility[9], identify potential vaccine-adverse outcomes, genetic signatures, suggest improvements to a candidate therapeutic agent and take into consideration the existing genetic diversity of the human species races, local demes and that within the pathogen. This would assist in producing a situation of high human genetic diversity within the population separated *in silico* into genetically uniform demes and the prediction of potential vaccine-adverse outcomes signatures. Vaccines for genetically uniform populations would be likely to reduce adverse side effects. Building on the experience and outcomes of the first phase of algorithm development and testing, AI algorithms that predict the ability of potential vaccine candidates to 'inhibit pathogen multiplication' or 'cell receptor binding' might be developed. Testing algorithms using available molecular databases of protein and nucleic acid sequences of components of pathogen particles, pathogen therapeutic agents, and available literature may enable rapid discovery or suggest the form of a candidate therapeutic agent. Employing AI in vaccine development has potential in determining *in silico* whether one or several different vaccines are required against a pathogen. The efficacy of the candidate therapeutic agent can then be improved through bioengineering, for example, synthetically derived nucleic acid or protein domains that are tailor-made for the identified different genetic groups that elicit an immune response in a safe way that does not produce clinical symptoms.

However, the fast production of an effective vaccine does not ensure vaccine success, as anti-vaccine beliefs are becoming widespread.[1] Thus, educating the public about vaccines, both novel and in use, needs to move from disseminating vaccine facts to 'enhanced vaccine education'.

Social media is one route through which polarised attitudes towards vaccination are popularised.[10] Enhanced vaccine education may take a multidisciplinary approach that includes traditionally non-allied activities such as virtual reality games, smartphone apps and cartoons, to conceptualise vaccinology processes and their attendant challenges. Teams can develop games and apps that present vaccine development, evaluation and vaccine facts in 'fun' ways to the public; these can be made available on online app stores, on social media platforms, in children's gaming arcades and even as part of the school curriculum. The educational media can cater for different age groups. This approach can potentially counter the 'infodemic' on vaccine science and reduce incidences of vaccine hesitation and rejection.

Vaccine development and education can also benefit from a further paradigm shift towards development specific to localised genetic diversity and other ways to develop antivirals and thus partly address the current challenges that lead to vaccine hesitation and rejection.

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