Vision for the prevention of infections using Homoeopathy

The past few decades have seen a dramatic increase of epidemic diseases. With increasing loss of lives due to rapidly spreading devastating epidemics, there is a strong need of protective immunization and prevention. Dealing with epidemic diseases broadly involves understanding of its spread, transmission, interactions of infectious agents and host, and possibility of prevention at individual or community level. Understandably, vaccination has greatly reduced the burden of infectious diseases.[1] However, the concerns about the safety of certain vaccines have led to downturns in vaccination rates and outbreaks of disease.[2] A recent survey on what homoeopathic doctors think of vaccination shows that there is no contradiction between homoeopathy and primary prevention by means of vaccination.[3] In this article, I am broadly comparing the conventional vaccination and the steps involved in the development of homoeopathic medicine that can be used for the prevention of emerging diseases.

Conventional Immunization Methods

Vaccine development has a proud history as one of the most successful public health interventions to date. As vaccine development moves increasingly to draw on modern concepts of rational design, the number of candidate vaccines is increasing.[4] Many innovative concepts in immunization have emerged. Nanotechnology offers the opportunity to design nanoparticles varying in composition, size, shape, and surface properties, for application in the field of medicine. The use of nanotechnology in vaccinology, in particular, has been increasing exponentially in the past decade, leading to the birth of "nano-vaccinology." We can observe the interaction of nanoparticles with the antigen of interest, differentiating the role of the nanoparticle as either delivery system and/or immunostimulant adjuvant.[5] Nanotechnology offers new vistas for the engineering of vaccine formulations. Yet another Vaccine Research Group has defined the concept of vaccinomics, i.e., using a person's genetic information to design and choose vaccines specifically for that person.[6] Researchers are now discussing personalized vaccines to maximize the effectiveness and minimize the side effects for each person.

Dengue virus vaccine development has been an active area of research for years, but the virus has proven to be a complex candidate for vaccine development. A vaccine designed against serotype 2 could potentially enhance the symptoms associated with a subsequent infection with serotype 4. To circumvent this complication, millions of dollars and countless man-hours have gone into developing optimized antigen and vaccines to elicit protection against all four serotypes.[7] A recent publication has demonstrated that human dengue virus antibodies enhance *in vitro* infection with Zika virus, suggesting that antibody-dependent enhancement is not merely a theoretical concern.[8] Talking about chikungunya virus which caused large epidemics of arthritogenic disease around the world since 2005 and had created havoc in India this year with a substantial disease burden due to long-term, debilitating symptoms in many patients, more than twenty candidate vaccines are under development for it; some are in Phase I/II trials, however due to the unpredictable, focal, and periodic nature of chikungunya outbreaks, Phase II/III randomized controlled trials in humans to demonstrate vaccine efficacy are likely to be logistically challenging.[9]

Vaccine Development, Testing, and Regulation

Development of any vaccine for immunization is the end result of years of discovery and development. Only a tiny percentage of candidate vaccines progress to licensing, making the costs of vaccine research and development extremely high. The vaccine development and testing follow a standard set of steps beginning with exploratory stage which includes the basic laboratory research and often lasts for 2–4 years.[10] The academic and governmental scientists identify natural or synthetic antigens that might help prevent or treat a disease. These antigens could include virus-like particles, weakened viruses or bacteria, weakened bacterial toxins, or other substances derived from pathogens.

Types of vaccine

Scientists take many approaches to design vaccines against a microbe(s) based on fundamental information about the microbe, such as how it infects cells and how the immune system responds to it. Vaccines are made using several different processes. They may contain live viruses that have been attenuated (weakened or altered so as not to cause illness); inactivated or killed organisms or viruses; inactivated toxins (for bacterial diseases where toxins generated by the bacteria, and not the bacteria themselves, cause illness); or merely segments of the pathogen (this includes both subunit and conjugate vaccines).

Live, attenuated vaccines[11] are living microbes that have been weakened in the laboratory, so it cannot cause disease. They elicit strong cellular and antibody responses and often confer lifelong immunity with only one or two doses; there are some downsides and the nature of microbes can change or mutate. Not everyone can safely receive live, attenuated vaccines, rather they usually need to be refrigerated to stay potent. Vaccines against measles, mumps, and chickenpox are made by this method.

Inactivated vaccines are made by killing the disease-causing microbes with chemicals, heat, or radiation, and they are more stable and safer than live vaccines. Most inactivated vaccines, however, stimulate a weaker immune system

response than do live vaccines, so it likely takes several additional doses, or booster shots, to maintain a person's immunity.[12]

Toxoid vaccines are for bacteria that secrete toxins or harmful chemicals. The "detoxified" toxins, called toxoids, are safe for use in vaccines. Vaccines against diphtheria and tetanus are examples of toxoid vaccines.[11-12]

If a bacterium possesses an outer coating of sugar molecules called polysaccharides, as many harmful bacteria do, researchers may try making a conjugate vaccine for it. Polysaccharide coatings disguise a bacterium's antigens so that the immature immune systems of infants and younger children cannot recognize or respond to them.[11]

Once the genes from a microbe have been analyzed, scientists could attempt to create a DNA vaccine against it. Still in the experimental stages, these vaccines show a great promise, and several types are being tested in humans. DNA vaccines take immunization to a new technological level. The body's own cells become vaccine-making factories, creating the antigens necessary to stimulate the immune system.[11]

The preclinical stage uses the tissue culture or cell culture systems and animal testing to assess the safety of the candidate vaccine and its immunogenicity or ability to provoke an immune response on animals. They may also do challenge studies with the animals, meaning that they vaccinate the animals and then try to infect them with the target pathogen. This also depends on the available animal models for specific testing. Many candidate vaccines never progress beyond this stage because they fail to produce the desired immune response. Followed by this, candidate vaccine goes through three clinical phases.[10]

Phase I vaccine trials include clinical studies with humans. The goals of Phase I testing are to assess the safety of the candidate vaccine and to determine the type and extent of immune response that the vaccine provokes. The researchers may use the challenge model, attempting to infect participants with the pathogen after the experimental group has been vaccinated. The attenuated, or modified, version of the pathogen is used for the challenge.

Phase II testing is to study the candidate vaccine's safety, immunogenicity, proposed doses, schedule of immunizations, and method of delivery. A larger group of several hundred individuals participate in Phase II testing. Some of the individuals may belong to groups at risk of acquiring the disease. These trials are randomized and well controlled and include a placebo group.

Phase III vaccine trials involve thousands to tens of thousands of people to assess vaccine efficacy and safety in a large group of people.

In the final phase after the vaccine has got approval and licensed, rare adverse effects as well as long-term efficacy are detected which is also called postmarketing surveillance.[13]

Adjuvants and novel delivery systems that boost immunogenicity are increasingly needed as we move toward an era of modern vaccines. Public health care is looking toward solutions that are easily replicable and less time consuming and provide immunity against rapidly spreading infectious diseases.

Homoeopathic Perspective

Homoeopathy as a modern scientific system of medicine has the potential to provide solution to this. Due to the rapid resistance of the influenza vaccines to presently available antiviral drugs and the emergence of various influenza strains as a consequence of reassortment, climatic changes, and rapid globalization, there is a significant need for the proper health-care system and the search of specific antiviral drugs. During the progress of vaccine knowledge, influenza viruses may come up with a new strain, which may bring new challenges. Hence, complementary and alternative medicine mode of treatment may provide a substitute approach as a potential preventive and therapeutic strategy.[14]

Homoeopathy has been reportedly used with variable degree of success in influenza, cholera, and other epidemics for 200 years. In recent years, homoeopathy is associated with a dramatic reduction in leptospirosis infection in the Cuban population. A homoeopathic medicine was prepared from the inactivated causative organism provided by the Cuban National Vaccine Institute. Cubans' experience with homoeoprophylaxis against leptospirosis remains a very positive one. It has given rise to further government-directed immunization against hepatitis A, swine flu, pneumococcal disease, and dengue fever using homoeoprophylaxis.[15] As opined,[16] "anything which appears to reduce infection rates in a potentially fatal infection, particularly when it can be prepared and delivered quickly, safely, and cost effectively, has to be taken seriously and studied further." "The study has huge data and we need more research into the effectiveness of homoeopathic preparations in preventing infectious diseases, complications, and the economic viability of a homoeopathic approach".

In an influenza review,[17] seven studies were included, of which three were prevention trials. Only two studies reported sufficient information to complete data extraction fully. Trials do not show that *Oscillococcinum* can prevent influenza; however, it can shorten the illness and thereby reduces morbidity, but more research is needed.

The large-scale opportunistic cohort study using a nosodal preparation in the context of a potential Leptospirosis epidemic in Cuba appeared to be associated with reduced infection rates although there were multiple confounders and the study has yet to be replicated.[18] A Cochrane review of an avian nosodal preparation for influenza concluded that there is low-quality evidence to support its efficacy.[19] There is little research in

the scientific literature to support the effectiveness of nosodes in the prevention of any infectious disease.[20] Majority of the studies are underpowered and are based on the traditional concepts of constitutional remedy, genus epidemicus, usage of nosodes made from infectious tissue, etc. The preventive programs for epidemics also need a synergistic association: formal approvals from government heads, tie-ups with health service centers, and adequate awareness about Homoeopathy of those who are involved in conducting or facilitating such a program.[21] An experimental laboratory test conducted on mice concludes partial protection from a nosode of tularemia in dilutions below those expected to have protective effects, but not as great as those produced by standard vaccination. If homoeopathic nosodes can induce protection from infectious agents for which vaccination is currently unavailable, they may provide an interim method of reducing morbidity or mortality from such agents.[22] Homoeopathic treatment of *Trypanosoma cruzi* infection should be further investigated as studies suggest that pretreatment with biotherapy modulates host immune response to *T. cruzi*, mainly during the acute phase of the infection. There is much evidence that these homoeopathic "ultramolecular" dilutions exert biological effects in living systems that cannot be explained with our current knowledge. There are numerous speculative hypotheses as to how such information might be captured and stored at ultra-diluted preparations, if this indeed occurs.[23] In addition, there are only a few attempts to investigate the potential of homoeopathic preparations in diseased plants, i.e., in phyto-pathological models. Further investigations are needed to reveal the potential of homoeopathic approaches for plant protection in agriculture since a homoeopathic treatment can be hypothesized to have fewer ecological side effects on nontarget organisms than some standard treatments because of the absence of harmful substantial doses of various chemicals.[24] The main problem in this research field, however, seems to be the reproducibility of the results obtained.[25]

The Council supported the preclinical study on the efficacy of *Belladonna* on Japanese encephalitis that reported positive outcomes.[26,27] The Council has also attempted few studies during epidemics, one of which was to assess the usefulness of homoeopathic genus epidemicus (*Bryonia alba* 30C) for the prevention of chikungunya during its epidemic outbreak in the state of Kerala, India.[28] The result reflects a 19.76% relative risk reduction by *B. alba* 30C as compared to placebo. Another exploratory observational comparative study on the evaluation of homoeopathic medicines as add-on to institutional management protocol in acute encephalitis syndrome suggests the reduction of mortality and morbidity with add-on homoeopathic medicine.[29] With these concepts and studies so far, we cannot bring Homoeopathy to that position where conventional immunization has reached. We need to identify the steps essential for the development of homoeopathic medicine for the prevention. There is an opportunity for testing such medicine clinically till a fully proven vaccine is made available. The Council is exploring all options of undertaking safety, preclinical, and field studies for the development and identification of homoeopathic medicines both single as well as complex for the prevention of existing as well as emerging infectious diseases.

In this issue, we are publishing one such preclinical study supported by the Council where the direct effect of homoeopathic medicine *Rhus toxicodendron* 6C (ultra-dilution of $10-12$) on primary cell culture from *Aedes albopictus* mosquito midgut was observed for any possible role of homoeopathic medicines, in preventing or reducing dengue virus type 2 invasiveness in these midgut cells. The result is favorable and will open a new avenue of future studies with this new primary cell culture.

The current issue of journal also features results of clinical verification of three drugs, namely, *Cynodon dactylon*, *Ocimum canum,* and *Formic acid*. The large amount of data of clinically verified symptoms have been evaluated, analyzed, and presented as prevalence in the population responding to the medicine and in the population not-responding to the medicine. The third and latest volume of series of books on Clinical Verification by the Council has also been reviewed for the users.

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