SMGroup

SM Vaccines and Vaccination Journal

Letter to the Editor

The Challenges of Vaccine-Preventable Diseases in the 21st Century

Mohamud Sheek-Hussein*[1]

[1]*Institute of Public Health, UAE University, United Arab Emirates*

Article Information

Received date: Jul 05, 2015
Accepted date: Jul 10, 2015
Published date:Jul 30, 2015

***Corresponding author**

Mohamud Sheek-Hussein, Institute of Public Health, UAE University, United Arab Emirates, Tel: +971 3 713 7456; Fax: +971 3 767 2022; Email: msheekhussein@uaeu.ac.ae

Recently, I attended the Modern Vaccines Adjuvants and Delivery Systems conference held in Leiden, The Netherlands (May 18-20, 2015); which highlighted some of the major challenges in the development of efficacious vaccines and their effective delivery for both (re) emerging infectious diseases and endemic Neglected Tropical Diseases (NTDs). These infections include not only the "big three" of Malaria, HIV/AIDS and Tuberculosis, but also Leishmaniasis, Ebola, MERS-COV, helminths and others. Notably, for the "big three" attempts to develop such vaccines have been largely disappointing. Some of the challenges lie with the extreme genetic variability of the pathogens. Most successful vaccines have been against slowly evolving pathogens with a limited number of antigenically different strains that induce immune responses dependent on neutralizing antibodies; a mechanism that is well understood. Also, for most vaccine preventable diseases, natural infections with their pathogens leave the host (temporarily, partially) immune to reinfection or disease with the same (strain of) pathogen. The danger of these pathogens is that they often win the race between their own rapid rate of multiplication and the host response which depends on immune recognition and activation and proliferation of immune cells, specifically-B cells. Once the host mounted an immune response and survived the fight he has won the race. Most of the infections above, however, do not conform to that pattern. In TB, cellular mechanisms are essential for controlling the infection, but do not eliminate it. The pathogens, *Mycobacterium tuberculosis (Mtb),* reproduce very slowly and disease occurs, if at all (in a minority of infections), months or years after infection. Disease, once cured, does not offer protection against reinfection or disease from reinfection. Speed of immune recognition seems to play no role, as most individuals who develop TB have detectable (by IGRA or TST) immune responses to the pathogens. Rather, it seems, a failure of the cellular effector mechanisms is at fault, and if so the prospects for an effective vaccine that protect against disease are slim. As neutralizing antibodies play no role in protection, also the prospects of conferring protection against (re) infection seem equally poor. Immune mechanisms against malaria and HIV are also complex and poorly understood, and attempts to develop an HIV vaccine have been graphically called "shots in the dark" [1]. The more I learn about vaccines and vaccination, the more I become perplexed, less optimistic, but also fascinated. Despite the stunning recent advances in immunology and medical research why do we still fail, and what are the missing scientific links? Are vaccines for some infections simply impossible, or are we simply not aiming our efforts correctly? Progress seems increasingly difficult, but the rewards of success, therefore so huge. The English physician Edward Jenner developed (or rather discovered) that cowpox offered a relatively safe alternative to the risky practice of variation in 1796 and in 1977 smallpox was eradicated worldwide. On May 8, 1980, the World Health Assembly announced that the world was free of smallpox and recommended that all countries cease vaccination: "The world and all its people have won freedom from smallpox, which was the most devastating disease sweeping in epidemic form through many countries since earliest times, leaving death, blindness and disfigurement in its wake" [2]. Jenner just observed, but knew nothing about viruses, let alone immunology.

Other successes followed. Newer vaccines were developed against the rotavirus, meningococcal and pneumococcal disease, herpes zoster, and human papillomavirus vaccines, as well as tetanus, diphtheria and pertussis [3]. In the 1950's Jonas Salk and Albert Sabin developed two polio vaccines, which have now eliminated polio from most countries and have reduced the worldwide incidence of polio to just 1300 cases in 2007 [4,5]. Equally groundbreaking was the discovery of the infectious origin of several cancers and other chronic disorders: at least 13 of 39 recently described infectious agents induce chronic syndromes. This has made these diseases vaccines preventable. For example, Hepatitis B Virus (HBV) infection may progress to Chronic Liver Disease (CLD) and Hepato Cellular Carcinoma (HCC) [6]. A vaccine against hepatitis B has been available since 1982. This vaccine is 95% effective in preventing infection and the development of chronic disease and thus liver cancer due to hepatitis B. Cervical cancer, which is the second most common cancer in women living in less developed regions with an estimated 445 000 new cases in 2012 (84% of the new cases worldwide) today can be prevented by vaccines against HPV which have been approved for use in many countries. Not all attempts were equally successful. In 1882 Robert Koch discovered and identified the causative agent of Tuberculosis, (*Mtb*) and subsequently in 1900 *Albert Calmette* and

Camille Guérin (BCG), began their research at the Pasteur Institute in Lille for an anti-tuberculosis vaccine, no doubt inspired by Jenner's cowpox story on the basis of *M. bovis*, the tubercle bacillus that affects cows (and sometimes humans, too). Their vaccine, *Bacille Calmette-Guérin* is currently the only TB vaccine available today and has been used for more than 90 years [7]. Unlike smallpox vaccine, its efficacy is still highly controversial, and may well be limited to infantile, non-infectious, manifestations of the disease. In spite of the complexity of (*Mtb*) and its pathogenesis within the human host, sixteen different TB vaccine candidates are currently in clinical trials. Some of the reasons why it took so long have been given as: the lack of an immunological correlate of protection; the reality that protection in preclinical challenge models does not reflect field efficacy data, and, in this context, the need for a human challenge model to help rationalize selection of candidates to proceed to efficacy studies [8]. However, all candidates TB vaccines may fail for the more fundamental reasons outlined above. A similar, fundamental, pessimism has been expressed by the Nobel laureate Zinkernagel who said that: While antibodies transferred from mother to offspring are a prerequisite for the survival of otherwise unprotected immuno-incompetent off springs, activated memory T-cells cannot be transmitted. Thus, attenuation of infections in newborns and babies by maternal antibodies is the physiological correlate of man-made vaccines T cells not only play an essential role in maintaining T-helper-dependent memory antibody titers, but also in controlling the many infections that persist in a host at rather low levels (such as tuberculosis, measles and HIV). (On Immunity Against Infections and Vaccines: Credo. 2004. R. M. Zinkernagel. Scandinavian Journal of Immunology Volume 60, Issue 1-2, Article first published online: 5 JUL 2004)

In developed countries, life-threatening childhood disease is now rare, largely due to large-scale vaccination, however lately sporadic outbreaks of measles and pertussis have occurred in North America and The United Kingdom. Adequate coverage is constantly under threat by neglect, as well as the disinformation spread by the anti-vaccine movement. In some developing countries vaccination programs and participation are inconsistent. As diseases such as mumps, measles and rubella may cause illness, disability and death [9], and the infections, in the absence of vaccinations widespread, the mortality rate from these diseases is high.

Also, not all vaccinations induce sufficient protection. Vaccination response can be measured by antibody titers. Most patients produce high titers. However, a small group of vaccines produce no or low levels of protective antibodies due to genetic predisposition, the immuno suppression, or other disorders, known as non-responders and low-responders. In our study (Sheek-Hussein et al) about 50% of the studied population were susceptible to HBV and measles virus and approximately 10% QuantiFERON-TB test was positive despite a proof of immunization.

Our major hurdle, however, seems to be the development of vaccines against "complex" infections. While our knowledge of biotechnology, immunology, genetics and virology is infinitely larger than at the time of Salk and Sabin, we seem to make increasingly slow progress against some of the major scourges of mankind.

Petra Oyston and Karen Robinson stated that "most of our current vaccines were developed by determining the components that consistently stimulated antibody responses in infected patients, and often without having a very detailed knowledge of the immune mechanisms required for protection, furthermore the financial commitment to license new vaccines is significant, and the more lucrative markets are often not those with the greatest need yet the scientific and financial challenges are substantial; hence there is broad agreement that the development of new and the effective vaccine products cannot proceed without a detailed understanding of the immune correlates of protection [10]. Whether it can with such understanding remain to be seen?

Acknowledgement

I would like to gratefully acknowledge Professor Nico Nagelkerke for his contribution of this editorial letter; we met in Leiden during Modern Vaccines Adjuvants & Delivery Systems MVADS 2015, I have discussed my impression of what I have learned in this conference.

References

1. http://www.amazon.com/Shots-Dark-Wayward-Search-Vaccine/dp/0393322254
2. Riedel S. Edward Jenner and the history of smallpox and vaccination. Proceedings (Baylor University. Medical Center). 2005; 18: 21-25.
3. CDC. MMWR. Ten Great Public Health Achievements - United States, 2001-2010 Weekly. 2011; 60: 619-623.
4. John TJ. The golden jubilee of vaccination against poliomyelitis. Indian J Med Res. 2004; 119: 1-17.
5. Willyard C. Polio eradication campaign copes with unusual outbreak. Nat Med. 2007; 13: 1394.
6. O'Connor SM, Taylor CE, Hughes JM. Emerging Infectious Determinants of Chronic Diseases. Emerging Infectious Diseases. 2006; 12: 1051-1057.
7. MANOLESCU BN. Paraoxonases as Protective Agents against N-Acyl Homoserine Lactone – Producing Pathogenic Microorganisms. Maedica. 2013; 8: 49-52.
8. http://www.who.int/immunization/research/development/tuberculosis/en/
9. Demicheli V, Jefferson T, Rivetti A, Price D. Vaccines for measles, mumps and rubella in children. Cochrane Database of Systematic Reviews. 2005.
10. Oyston P, Robinson K. The current challenges for vaccine development. Journal of Medical Microbiology. 2012; 61: 889-894.