Nigerian Veterinary Journal Vol. 23 (1) 27-32

POTENTIAL APPLICATIONS OF RECENT ADVANCES IN VACCINE RESEARCH AND DEVELOPMENT IN OVERCOMING CONSTRAINTS TO ANIMAL DISEASES' VACCINATION PROGRAMMES IN DEVELOPING COUNTRIES – A REVIEW

IHEDIOHA, J. I.

Department of Veterinary Pathology and Microbiology
University of Nigeria, Nsukka
P. O. Box 3236, Nsukka
Enugu State, Nigeria

SUMMARY

Immunization remains the most cost-effective and sustainable health intervention in developing countries. Vaccination programmes for animals had faced the major constraints of inadequacy in the quantity and quality of vaccines obtainable, difficulties in maintaining a cold chain in storage/delivery of vaccines and shortages of qualified veterinary manpower/personnel. Recent advances in vaccine research and development offer ample opportunities for overcoming these constraints. These include "sugar-glass" drying of vaccines to enhance their thermostability, the discovery of more effective adjuvants called immune-stimulating complexes (ISCOMs), and the application of the principle of micro-encapsulation in vaccine production to overcome the difficulties associated with multiple visits by a veterinary personnel as required in routine vaccination schedules. Also nucleic acid vaccines now offer opportunities to vaccinate animals without using the infectious agent/its parts, and to produce one single vaccine for all major diseases. Further, the possibilities of producing plant/edible vaccines, combination vaccines, and the recognition of the great value of the use of mucosal route for vaccination stand out as great promises for more viable animal health and husbandry worldwide.

KEY WORDS: Vaccine research & development, Animal diseases prevention/control.

INTRODUCTION

Vaccines are the most cost effective invention of scientific medicine and immunization holds the greatest promise of sustainability among health interventions because of its cost benefit (Cowley and Jamison, 1993). It should be accorded the highest priority when finite resources are being allocated, as is the case in most developing and poor countries of the world. Its gains in the area of human health is so evident with the expanded programme on immunization, which had led to the vaccination of approximately 80 per cent of the world's children under the age of one in 1990, with a total of about 3.2 million deaths being averted annually (WHO and UNICEF, 1991).

Recent spectacular advances in molecular

biology, immunology and genetic engineering, plus the increased total funding world-wide for vaccine research and development had led to the development of a "new generation" of vaccines, which could revolutionize both animal and human health. These "new generation" vaccines are more easily and efficiently administered, and are effective for longer periods and in less frequent doses. They are also produced more efficiently to equal or greater standards of quality at the lowest possible cost, and are more stable in a range of environmental conditions (Hunter, 1996; Maurice, 1999). These vaccines are able to confer strong immunity against all major diseases with only one or two doses and can be stored for reasonable periods without refrigeration. They therefore overcome the major constraints to effective immunization programmes in developing countries especially the difficulties in maintaining a cold chain in storage/transport of vaccines, and sustaining multiple visits by a veterinary personnel for primary and booster vaccinations (Ozawa, 1988). These new developments include the application of the principle of micro-encapsulation in vaccine production, the use of enhanced adjuvants called immune-stimulating complexes; "sugar-glass" drying of vaccines to enhance their thermostability; production of nucleic acid vaccines; and increased recognition of the value of the mucosal route of vaccine administration.

Application of the principle of micro-encapsulation in vaccine production

Vaccine micro-encapsulation entails coating the vaccine with a protective biodegradable micro-sphere that can release its active products at a rate determined by its size and chemical composition. A single injection of microencapsulated vaccine can provide a vaccine delivery system ensuring pulsed antigen system release mimicking an immunization of primary and booster dose administration. It is also possible to administer different vaccines in a single injection because different micro-spheres do not interact with each other and each vaccine can be microencapsulated in such a way as to ensure its own specific pulsed schedule independent of other vaccines (Eldridge, 1992). These attributes of a microencapsulated vaccine can for instance make it possible to completely administer all the vaccines on an immunization schedule at only one injection such that a broiler could receive a single injection on the first week of life which will ensure the release of Newcastle disease vaccine-intra-ocular and Infectious bursal disease vaccine on the first week, Newcastle disease vaccine-Lasota on the fourth week, and Infectious bursal disease booster on the fifth week to fulfil the basic immunization needs of such birds. This eliminates the multiplicity of visits by veterinary personnel, which is needed to fully vaccinate such birds through their life span. Microencapsulated vaccines are unaffected by any specific antibodies (e.g. maternal) that contraindicate the pre-natal use of many current vaccines. They are also protected from the acidic and enzymatic environment of the gastrointestinal tract which limits the use

need heat stabilizers nor a cold chain (Bloom, 1990).

Enhanced adjuvants-immune stimulating complexes (ISCOMs)

Vaccine adjuvants stimulate the immune system by enhancing the immune response to an antigen with which they are mixed. They direct the mechanisms whereby antigen structures are processed and presented to the immune system, induce the release of cellular mediators that modulate immune response, expose the epitopes of the antigen capable of stimulating a specific immune response, and prolong the delivery of the vaccine antigen (Sadoff, 1993). The effectiveness of a variety of adjuvants had currently been investigated and one had been found to hold great promise for the future: immune stimulating complexes (ISCOMs). ISCOM is a novel antigen delivery system that consists principally of a glycoside -Quil A derived from the bark of a South American tree. ISCOMs had been extensively studied as an adjuvant system for vaccines against viral, bacterial and parasitic infections and had been found to induce protective immunity in virtually all systems even where other adjuvants had failed. ISCOMs had also been shown to be potent enhancers of long-lasting specific antibody responses even in the presence of passively transferred antibodies because of their ability to rouse all the three arms of the immune system - the helper T-cells, the cytotoxic T-cells and the B-cells (Osterhaus, 1993). They can also be successfully administered through the mucosal surfaces, a route which avoids the obstacle of maternal circulating antibodies in the young - an attribute that raises the possibility of the use of ISCOMs for vaccines against respiratory infections and even for oral delivery of some vaccines currently administered by injection (Grabowski and Vernon, 1997).

Sugar-glass drying of vaccines to enhance their thermostability

Vaccines in current use are protected from damage by heat and other environmental threats by transporting them as freeze-dried powders or through a cold chain of refrigerators and ice packs. The cost and logistic constraints of maintaining a cold chain and the risk of contamination of freeze dried powders at points of reconstitution are the major problems of current vaccination programmes in most developing countries of the world. A newly discovered disaccharide sugar - trehalose, which is widely found in biological tissues, has offered a solution. Trehalose is particularly good at restoring dried biological tissue to its original structural and physiological integrity because of its ability when cooling in a saturated solution to slide smoothly from a liquid to a viscous and ultimately to a solid glass-like state. The glass commonly called "sugar-glass" immobilizes, preserves and protects proteins and other molecules that were in the solution and readily dissolves on contact with water and releases its contents which quickly recover their original form and function (Maurice, 1999). Vaccines dried in the presence of trehalose could be produced in a variety of formulations and they had been found to suffer no detectable loss of

potency after long periods of exposure to heat and freezing e.g. the diphtheria and tetanus (toxoid) vaccine keep their original activity after a year of storage at 60^0C (Grabowski and Vernon, 1997).

Nucleic acid vaccines

Nucleic acid vaccination is a new method that entails taking a gene from a pathogen, injecting it into an animal so that the animal's cells produce the vaccinating molecule (antigen) and so provoke a protective immune response against future infection by the pathogen. The gene thus gives the body instructions on how to produce its own protective molecule against a disease. In contrast to other types of vaccines that give the body a ready-made antigen (a controlled infection), nucleic acid vaccines give the body the genetic information to make its own antigen (Robinson, 1997). This technique had been carried out successfully in all domestic animals where it had been shown to offer protection not only against viruses, bacteria, mycobacteria, fungi and parasites but also against cancer, autoimmune diseases and allergies (Maurice, 1994b). Nucleic acid vaccines has the potential of carrying a large number of foreign genes and to have the recipient cells produce many antigens of many different disease agents thus providing the opportunity of a single vaccine for all major diseases (Eldridge, 1992; Maurice, 1994b). They further eliminate the risk of side effects associated with whole-organism vaccine or vaccine vectors, and had been found to produce a strong protective immune response. They are also cheaper and quicker to make with no observed side effects.

Plant/Edible vaccines

Edible vaccines are those contained in edible plants, which had been genetically engineered to carry genes from disease causing microbes. Within the microbe, the genes control the production of molecules or antigens known to provoke an immune response in animals infected with such microbes. Such genes force the plant's genetic machinery to produce the vaccinating antigens that are needed - thus the plant acts as both the factory and vehicle (Arntzen, 1996). Plant vaccines had been found to be capable of stimulating not only the more general antibody and cellular immunity needed for protection against disease - causing microbes but also local immune system of the gut which is the first line of defence against diarrhoea-causing microbes (Levine, 1997). The most suitable plants for vaccination had been found to be those that are eaten raw since heat would inactivate protein antigens (Mason and Arntzen, 1995). Plant vaccines offer a multiplicity of advantages to animal health and husbandry because growing fields of plants for vaccination will always be a cheaper source of vaccine than the microbial fermenters used in today's vaccine production facilities. Plant vaccines would not need costly refrigeration as many of today's vaccines do, and plants can be grown anywhere cheaply in the developing world where the new, complex and sophisticated technologies required for modern vaccine production are often lacking (Schartzmayr, 1993).

Value of the mucosal route of vaccine administration

Mucosal vaccination is the administration of a vaccine that enters the body via the mucosal linings of body passages and cavities such as the gastrointestinal tract, respiratory, urogenital and nasal passages, the eye and the ear. The mucosa had been found to possess a huge immune system largely untapped for vaccination purposes and the mucosal surfaces of an adult is 200 times his skin surface (Hunter, 1996). Mucosal vaccines provoke an IgA response that show the mucosal immune system what the pathogen looks like, allows it to remember what it has seen and thus provides lasting protection against the pathogen. They can provoke response in many different sites because some of the mucosal IgA antibodies as well as the lymphocytes that produce them can travel to far-off places in the body (Maurice, 1994a). 80-90 per cent of infectious diseases caused by bacteria and viruses enter the body via the mucosal tissues and can thus be blocked and destroyed before they go further (Grabowski and Vernon, 1997). With the recognition of the great value of mucosal vaccination and utilization of the mucosal route for vaccination, most of today's common vaccines usually given by injection could be administered just by a drop into the mouth, nose, ear or eye, thereby overcoming the drawbacks of injectable vaccines. Mucosal vaccination also offers the opportunity of controlling and even possibly eradicating diarrhoeal, acute respiratory and sexually transmitted diseases since a mucosal vaccine can be given at or shortly after birth by just a drop into the mucosal membranes.

CONCLUSION

The recent advances in vaccine research, development and technology enumerated above hold great prospects for animal health and husbandry in developing countries if the different new inventions and discoveries are utilized to overcome the basic constraints facing vaccination programmes. They shall hopefully lead to a future "ideal" or "model" vaccine which will be more easily and efficiently produced and administered at low cost; and which will also be more effective and stable under a wide range of environmental conditions.

ACKNOWLEDGEMENTS

The author is grateful to the Children's Vaccine Initiative, World Health Organization, Geneva for freely supplying most of the information materials on which the article was based; and to the Foundation for Education and Research on Health, Nsukka through whose library/resource centre the information materials were accessed.

REFERENCES

ARNTZEN, C. C. (1996): Plant vaccines: edible but how credible? *CVI Forum* **12**: 10 –13.

BLOOM, B. R. (1990): Vaccines for the Third-World. *World Health*, June-July-August 1990: 13 –15.

COWLEY, P. and JAMISON, D. T. (1993): The cost effectiveness of immunization. *World Health*, March - April 1993, **2**: 7 – 9.

ELDRIDGE, J. (1992): Advances in vaccine research and technology. *CVI Forum* **6**: 2 – 3.

GRABOWSKI, H. G. and VERNON, J. M. (1997): The Search for New Vaccines. AEI Press Washington DC.

HUNTER, A. (1996): Animal Health - General Principles Vol. I, CTA and Macmillan Educ. Ltd London.

LEVINE, M. (1997): Oral vaccine production in edible tissues of transgenic plants. In: New Generation Vaccines, 2nd ed. Marcel Decker Inc. New York.

MASON, H. S. and ARNTZEN, C. J. (1995): Transgenic plants as vaccine production systems. *Trends in Biotechnology* **13**: 388 – 392.

MAURICE, J. (1994a): A Forum guide to mucosal immunization. *CVI Forum* **6**:2 – 3.

MAURICE, J. (1994b): A Forum brief on nucleic acid vaccines. *CVI Forum* **7**: 7 – 10.

MAURICE, J. (1999): A Plethora of hi-tech vaccines - genetic, edible, sugar glass and more.*CVI Forum* **18**: 5 – 23.

OSTERHAUS, A. D. M. E. (1993): Immune stimulating complexes (ISCOMs): antigen delivery with a bang. *CVI Forum* 3: 7.

OZAWA, Y. (1998): Improvement of veterinary vaccine production in Africa. In. Viral Diseases of Animals in Africa, A. O. Williams and W. N. Masiga Eds. OAU/STRC and CTA of ACP/EEC, Lagos Nigeria.

ROBINSON, H. L. (1997): The Scientific Future of DNA for immunization. American Academy of Microbiology, Washington DC.

SADOFF, J. C. (1993): Adjuvants for new or improved vaccines: some current research options. *CVI Forum* **3**: 6 – 9.

SCHATZMAYR, H. G. (1993): Third World vaccine production. *World Health,* March - April 1993 (2): 12 – 13.

WHO and UNICEF, (1991): Immunizing the world's children: A Global Update. WHO and UNICEF, Geneva & New York.