

## Vaccine

### Introduction

Prevention of disease through vaccination is an important approach to maintain fish health. Exposure of a fish to a pathogen stimulates the immune response and the fish will develop the memory to these pathogens so that it can combat the pathogen very quickly during future encounter. This adaptive immunity is specific against the pathogen and persists for a relatively long period. This persistence is because of an adaptive change in the population of lymphocyte which results from the exposure of the fish to the pathogen that consist the antigen.

Vaccines exploit the two key elements of adaptive immunity and those are specificity and memory. This is because after vaccination the adaptive immune system responds specifically to the invading pathogen and the response become stronger and stronger on the second and subsequent exposure to the pathogen.

Vaccines are preparations of antigens derived from pathogenic organisms, rendered non-pathogenic by various means, which will stimulate the immune system in such a way as to increase the resistance to disease from subsequent infection by a pathogen.

Inducing a protective immune response to a pathogenic organism before the individual becomes naturally exposed to it seems at first sight a highly sensible way of preventing an infectious disease. Unfortunately, achieving this goal not an easy task. vaccines must be safe (no side effects) and potent (induce a high level of protection) and although occasionally it has been possible to achieve these characteristics using simple procedures (usually heat or chemical inactivation of cultures of pathogenic microorganisms) in most cases some degree of antigen purification or enrichment is necessary and the problem lies in identifying the relevant antigens, out of many hundreds present, which are important in stimulating a protective immune response.

Vaccines are generally of two types: Dead vaccines, which are composed of inactivated pathogens or extracts, and Live vaccines, which are attenuated pathogens with no or low virulence."

#### Dead vaccines

- Inactivated virus or bacterial antigens
- Sub-unit vaccines
- Recombinant vaccines
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#### Live vaccines

- Attenuated live vaccine
- Gene deleted live vaccine

The Ideal Fish Vaccine should have:

- Sustained immunity and protection
- Early mass application
- Efficacious for a broad number of species
- Safe to use
- Cheaply available
- Easily produced

- Should have stable antigen
- Can be stored for long time.
- Will not interfere with diagnosis
- Easily licensed

### **Types of vaccine**

#### **1. Killed whole cell vaccines**

Killed whole cell vaccine is a suspension of heat or chemical-killed pathogens that are able to induce specific protective immune response against those pathogens when administered into the host. Killed whole cell vaccine are administrated when it is unsafe to use live microorganisms. These vaccines are prepared from normal wild type bacteria that are made nonpathogenic usually by treating with heat, formaldehyde or gamma irradiation.

Killed whole cell vaccine can be used in controlling some of the important fish bacterial pathogens like *V. anguillarum*, *V. salmonicida*, *V. ordalli*, *Y. ruckeri*, *E. tarda* and *A. salmonicida*. Among carp virus killed vaccine of spring viremia of carp virus (SVCV) was commercially available for some years.

#### Advantages:

- Safe to use
- Cheaper than live attenuated vaccine
- Storage is easier than live vaccine

#### Disadvantages:

- Large number of microorganisms is required to stimulate immunity.
- High cost of their production in cell culture,
- Difficulty in the purification and delivery.
- In general killed vaccines alone trigger only the humoral immune response
- Needs to be given booster doses
- Presence of some un-inactivated microbes can lead to vaccine-associated disease.
- Inactivation, by formaldehyde may alter antigenicity.

#### **2. Live-attenuated vaccines**

Live-attenuated vaccine is a suspension of attenuated live pathogens that are able to replicate inside the host and induce protective immune response but unable to cause disease. To make an attenuated vaccine, the pathogen is grown in foreign host such as animals, embryonated eggs or in tissue culture under controlled conditions and altered to a non-pathogenic form to make it less virulent. They mimic the actual infection by pathogens and hence a small dose of vaccine is enough to induce long lasting protective immune response. Live attenuated vaccines can induce both humoral and cell-mediated immune responses.

#### Advantages

- Live-attenuated vaccine can stimulate cellular immune responses, memory cells as well as humoral immune responses.
- Administrating lesser quantities is sufficient to induce protection.
- Single administrating of vaccine is sufficient to produce high efficacy and long lived immunity.

- Administration of live attenuated vaccine has a possibility to stimulate immune response to all protective antigens.

#### Disadvantages

- Live-attenuated vaccine may rarely revert to its virulence form and cause disease.
- Live-attenuated vaccine cannot be given to immunosuppressed individuals.
- Since they are live they require proper storage.

### **3. Subunit Vaccines**

Subunit vaccines are the purified antigens of the whole organisms. These antigens are capable of stimulating antibody response. Subunit vaccines may contain toxoids, subcellular fragments, or surface antigens. The effect of subunit vaccine can be increased by administering these subunits with adjuvants.

#### Advantages

- They can be safely administered to the immunosuppressed animal.
- The side effects caused by sub unit vaccines are very rare.

#### Disadvantages

- Since the vaccines are purified the purification process may affect antigen in retaining its native form, so the organism may not recognize the antigen on pathogen.
- These proteins may not stimulate the immune response.

### **4. DNA vaccine**

This vaccine is still in experimental form. Here the gene of the pathogen is clone into vector and the vector is inserted into the animal by using gene gun. Once the vector is introduced the protein that act as antigen is produced inside the host and stimulate the immune response. DNA vaccine can induce both humoral and cellular immunity.

#### Advantages

- DNA is stable, hence can be easily stored and transported.
- DNA sequence can be changed easily in the laboratory.
- DNA does not replicate and encodes only the proteins of interest.

#### Disadvantages:

- Insertional mutation may be possible
- Anti DNA antibodies may be produced against the inserted vector
- Since the antigen is expressed in the host immunologic tolerance may develop.
- Ethical issues.

#### **Mode of vaccine administration**

Vaccines may be delivered to fish by:

- Intraperitoneal or intramuscular injection method

- Oral vaccine method
- Direct immersion method

(Vaccination is done to the healthy fish because it is a preventive measure and not a cure.)

## 1. Oral Vaccination

During the oral vaccination, the vaccine is given orally and it may be either through feed, where it is either mixed along with feed or coated on top of the feed or bio-encapsulated. During oral vaccination proper care must be taken to ensure that the antigen is successfully absorbed into the body. It is because the antigens incorporated in feed may be the heat sensitivity or the digestive system may digest the antigen. So when the vaccine is coated on the feed usually a coating agent is applied to prevent leaching of vaccine or to prevent the digestion of an antigen in the acidic environment of the fish stomach. Bio encapsulations are used usually when the fish fry are to be vaccinated, Bio encapsulation include the live feed such as Artemia nauplii, copepods or rotifers which are fed after incubation in a vaccine suspension. During incubation they accumulate the antigen in their digestive tract and as such, transform themselves into living microcapsules.

### Advantages

- Vaccine mixed with feed
- Easiest method for mass vaccination of all sizes of fish
- Saves labour
- Avoids stress to fish

### Disadvantages

- Large quantities of vaccines are required
- Some fish may not consume the feed.
- Protection generally weak and of short duration

## 2. Immersion vaccination

Fish being aquatic in nature it is constantly surrounded by the microorganisms of which some may be pathogenic ones. These fish have a mechanism to recognize these pathogens and elicit an immune response. So when the fish comes in contact with vaccine during immersion these vaccine is absorbed by the skin and gills, the specialized cells such as antibody-secreting cells are activated and will protect the fish during the later stage of exposure to the pathogen.

Immersion vaccine can be applied in two ways:-

### i. Dip method

In dip vaccination method fish are immersed in a highly concentrated vaccine solution for very short time say usually few minutes.

### ii. Bath method

In bath vaccination method fish are immersed in a lower concentration of vaccine solution for a longer period, usually one to several hours.

### Advantages

- Suitable for mass vaccination of all sizes of fish

- Reduced stress for fish
- Lower labour costs
- Less risk to vaccination team

#### Disadvantages

- Major disadvantages are the large amount of vaccine required
- Lower level of protection and
- Low duration of immunity

### **3. Injection vaccination**

Vaccination by injection works well with fish that are 5–10 g or larger and the injection vaccination is very popular in salmon industry. Light anaesthesia is given to the fish before injection to prevent mechanical injuries and also to overcome handling stress. Vaccine can be administered through intramuscular or intraperitoneal with intraperitoneal vaccination is being very common. The immune response development depends on the needle and method of injection. Short needles might deliver the vaccine in the muscle and cause inflammation and a bad immune response, while long needles may damage the internal organ. The right thickness of needle is also important because the viscous vaccine has to pass through the needle and if the needle is too large the vaccine may fall back and may lead to infection. Once vaccination is administered it will take weeks to develop immune response, so it is important maintain the fish in ambient temperature and not to stress fish because temperature variation and stress may suppress the immune system.

#### Advantages

- Provide protection for long duration
- multiple antigens can be administered in single injection
- every fish in farm can be vaccinated
- every fish in farm receives the correct dose
- Highly efficient in generating both humoral (antibody) and cellular cytotoxic response

#### Disadvantages

- Needs sophisticated machinery or large skilled workforce
- Significant handling stress and risk of post vaccination fungal infections
- Local reactions
- Unsuitable for small fish