Type of vaccines available and results that can be expected from each

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Highlights

The current vaccines against the PRRSV are the live attenuated and the inactivated vaccines. The development of new generation vaccines has been limited, up to now, by the relative lack of knowledge of the virus components involved in its protection and its poor immunogenicity.

The live attenuated vaccines give rise to a humoral and cellular immunity characterised by the appearance of antibodies measurable with the ELISA technique, neutralising antibodies and IFN-γ producing cells.

When administered to negative animals, the inactivated vaccines give rise to a poorer immune response than the live modified vaccines. After the first vaccination, sometimes seroconversion is not seen, just like neutralising antibodies or a significant number of IFN-γ producing cells which are rarely produced. Nevertheless, the repeated doses of vaccines could lead to an increase in the frequency of IFN-γ producing cells.

The stronger immune response induced by the live vaccines in negative animals generates a better protection when the vaccinated animals are exposed to field strains.

The inactivated vaccines are capable of priming the immune system, and the response toward a later challenge is quicker than in non-vaccinated animals.

The vaccination (with live attenuated vaccines or with inactivated vaccines) of animals previously exposed to the virus, due to their vaccination or infection, causes a measurable humoral and cellular immune response.

The vaccines that we can currently find on the market for controlling the PRRS virus can be divided in two great groups: live attenuated vaccines and inactivated vaccines. These vaccines are developed in a classical way. The absence of vaccines developed by means of genetic engineering is a result of the difficulties encountered in obtaining an appropriate protection in pigs exposed to the antigens found in different experimental studies that throughout time, have been considered important for the control of the infection. This fact is an indirect evidence of the relative lack of knowledge concerning the mechanisms related to the immunogenicity of the virus and the protection already existing, as well as an indicator of the difficulties for achieving a good immune response in animals.

The live attenuated vaccines are based on the use of live viruses with a decreased virulence through the serial passage of the parental strain of each vaccine through cell cultures. This mechanism improves the adjustment of the virus to the culture and it decreases its adjustment with respect to the host, so with the passages, their ability to cause the disease falls progressively. Nevertheless, this kind of vaccines replicates in the body of the vaccinated animal, although to a lower extent than the field strains. This fact is crucial in the case of the negative animals that have never been exposed to the virus, because, according to all the evidences, it is necessary that the vaccinal virus replicates in the organism of the vaccinated animal so the primary immune response obtained is enough to confer an appropriate protection. In practice, this means that, for the immunisation of negative animals the use of live attenuated vaccines is recommended, because the results obtained with inactivated vaccines are not as expected.

Although the reasons behind this phenomenon have not been clarified, it is thought that it could be due to the antigenic stimulus produced by two types of the vaccine. In the case of the live vaccines it is thought that the *in vivo* replication could produce a higher antigenic stimulus, since the final antigenic mass to which the animals are exposed is higher than in the case of the inactivated vaccines that lack the replication ability and only have the antigenic mass contained in the dose administered to each animal. Also, the processing of the antigen and the type of antigenic presentation are different in the inactivated vaccines (in which the antigen is absorbed in the inoculation site) and in the live attenuated vaccines (that contain a virus that replicates in the organism of the vaccinated animal and that spreads through it in a way similar to that of the field strains).

This spreading causes the vaccinal viruses to replicate at least in some of the target cells for the virus, causing an antigenic stimulus that is closer to that caused by a field strain. As a consequence, the immune response acquired shares many of the characteristics of the immune response obtained against the field viruses, this is, a detectable cellular and a humoral immune response is observed, although generally less intense than the one obtained with other viral infections, and it shows certain differences that depend on the traits of the vaccine strain, also happening with the field viruses. In that way, the vaccination causes an easily detectable seroconversion with the ELISA techniques. Some of the generated antibodies also have a neutralising activity, since these antibodies can be found, at least against the vaccinal strain, after the vaccination. Likewise, the vaccination induces a cellular immune response, as seen with the appearance of virus-specific gamma interferon (IFN-γ) producing cells.

The immune response obtained after the vaccination is enough to induce a variable protection that depends on the challenge strain, which is partial after the exposure of vaccinated animals to field viruses. This produces: a decrease in the duration of the viraemia, a lower transplacental infection rate, a lesser spreading through the organism and an inferior excretion of viruses in the vaccinated animals in comparison with the non-vaccinated pigs. These effects are the same that appear when an infected animal becomes reinfected with another strain, although, in general, they are somehow more moderate.

In return, the replication of the vaccinal viruses contained in the live vaccines makes possible that these viruses are shed through different routes and that they infect susceptible animals that come into contact with vaccinated animals or with their biological materials. They can even cross the placental barrier and cause the infection of some developing foetuses. This replication in the foetuses of vaccinated sows and in non-vaccinated animals that come into contact with the vaccinal viruses is not accompanied by the appearance of the symptoms typical of the disease. Nevertheless, we must underline that the seriated passages of the vaccinal strains in non-vaccinated animals can lead to changes in the characteristics of the vaccinal viruses which can increase their virulence. In fact, field strains have been described with a genomic similarity with vaccinal strains showing that they are derived from viruses from the vaccinal ones.

On the contrary, the best trait of the inactivated vaccines is their safety, because they can be used in any kind of animal with the certainty that they will not spread to non-vaccinated animals and that they are not going to cross the placental barrier. Nevertheless, the inactivated vaccines cause a weaker immune response than the live attenuated vaccines because, as mentioned earlier, they do not replicate in the body of the vaccinated animals. Therefore, after the vaccination of seronegative animals we do not always see a humoral immune response, because not all the vaccinated animals show antibodies measurable with the ELISA technique, and significant titres of neutralising antibodies are rarely seen after the vaccination. Likewise, the first vaccination induces

a poor cellular immune response that is frequently undetectable. However, we must underline that the repeated vaccine doses administered to seronegative animals could induce the appearance of significant levels of IFN-γ producing cells, although it has been speculated that this effect could be more related to the adjuvant used than with the antigen itself.

What is actually a fact is that the vaccination of negative animals with inactivated vaccines has the ability of priming the immune system and of producing a quicker specific response (humoral and cellular) right after the infection. Nevertheless, this trait is not enough to confer protection to the vaccinated animals, and frequently, the poor immunogenicity of the inactivated vaccines, when administered as the only component of the vaccinal programme, causes a poor protection of the vaccinated animals, which usually show lengthy viraemias and a high transplacental infection rate.

As a consequence of all that has been previously mentioned, the use of inactivated vaccines is not recommended for the immunisation of negative animals. Nevertheless, the vaccination of seropositive animals, (whether due to a natural infection or to the vaccination with live vaccines), with inactivated vaccines causes a marked humoral and cellular secondary immune response that allows their use in combined vaccination programmes.

Finally, we must underline that the use of adjuvants can modify the kind of induced immune response after the vaccination, because they can favour one kind or another immune response. In fact, it is thought that, at least, part of the cellular immune response induced by the inactivated vaccines can be due to the action of the adjuvant. Also, the use of adjuvants strengthens the immune response when alternative inoculation routes are used; for instance the intradermal route.

Table 1. Main characteristics of the different kinds of vaccines.

Kind of vaccine	Safety	Inducement of immune response after the first vaccination		Induction of secondary immune response		Protection expected after the first vaccination
		Humoral immune response	Cellular immune response	Humoral immune response	Cellular immune response	
Live attenuated	• They replicate in the body, they may cross the placental barrier and they are excreted by the vaccinated animals • They are attenuated viruses that do not cause the disease in the animals exposed to them, although there is the risk of reversion to virulence	• They cause seroconversion, measured with ELISA techniques, in almost all of the vaccinated animals • They can induce the apearance of neutralising antibodies, although generally with low titres	• Poor response in comparison with other viruses, but detectable in terms of IFN-γ producing cells	• Secondary response detectable in the antibodies measurable with ELISA techniques, but with a very short duration and not in all the animals • Increse in the titre of neutralising antibodies in most of the animals, although with a variable duration and intensity. This effect can disappear with time	• Moderate increase of the frequency of IFN-γ producing cells	• Decrease in the length of the viraemia • Lower spreading of the virus throughout the body • Lower transplacental infection • Lower shedding of the virus through different routes • Variable degree of clinical protection
Inactivated	• They do not have the ability to replicate, and therefore they are very safe in any kind of animal or production stage	• Not all the vaccinated animals developed antibodies measureable with the ELISA technique • Normally, no neutralising antibodies appear after the first vaccination	• Poor or indetectable response of IFN-γ producing cells	• Increase in the number of seropositive animals mesured with ELISA techniques, although not all of them seroconvert • Increase in the frequency of animals with neutralising antibodies, although not all of them get to develop this kind of antibodies	• Increase in the frequency of IFN-γ producing cells	• There is not a significant decrease of the viraemia, the spreading throughout the body nor the transplacental infection • Low protective value at a clinical level

In this case it is important to stimulate the immune system to generate an efficient response and to avoid the immunotolerance phenomena typical of the mucous membranes. Nevertheless, the administering of vaccines with adjuvant through this route seems to favour the early appearance of the immune response.

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