

## **1.4 Sometimes it is necessary to infect animals to grow viruses**

Welcome to a new class on viral Diagnostics. As you know, and we have repeated it several times, viruses need living cells to replicate. We have seen previously that the growth of virus in cell culture is a convenient system which has many advantages. But frequently you have to resort to live animals, such as mice, rabbits, Guinea pigs, hamsters, ferrets or zebrafish, for example, to cultivate viruses or to study the viral pathogenesis. Mice are the animals most commonly employed in Virology, while monkeys are used less and less. In this sense, lactating mice (less than 48 hours old) are the most widely used.

These mice have to meet certain requirements, such as being healthy and free of communicable diseases. On many occasions it is required that animals are SPF, i.e., free of specific pathogens or specific pathogen free. This ensures that they will not have certain microorganisms that interfere with what we want to study. For these reasons, it is recommended to obtain the animals for experimentation from centres or companies that grow them under very controlled conditions and analyze them frequently to confirm that they meet all the requirements.

The routes of inoculation in mice are subcutaneous, intracerebral, intraperitoneal and intranasal. After inoculating the animal with the suspension of viruses, we must observe it daily to determine if there are any signs of disease, visible lesions or even if it dies. After the death or at the end of the experiment, we must examine the infected tissues and the histopathological lesions in search of the virus or its consequences.

### **Disadvantages**

There are a number of disadvantages inherent to using experimental animals. Some of them are as follows:

Experimental animals are expensive and difficult to maintain. They need plenty of space and specialized caregivers, in addition to a specific diet and to eliminate waste by following strict protocols so there are no pathogens left in the environment.

Ideally and as I said before, they must be free from specific pathogens (SPF) and also isolated from each other.

There is individual variability (except in congenital mice).

It is difficult to choose the specific animal for a particular virus. Some human viruses, for example, do not infect animals, or, although they can infect them, they do not cause disease.

Some animals are susceptible to a particular virus only during a brief age window (i.e., when they are newborns, or infants, etc.).

Mice are not a good model for the development of vaccines. For that, we have to resort to larger animals.

And finally, there is also the issue of ethics and animal welfare systems.

### **Advantages and uses**

But despite the drawbacks, there are occasions in which it is inevitable to use experimental animals. Some of the uses are the following:

For example, to study the mechanisms of pathogenesis, i.e., how viruses produce disease and how the body reacts to control it, as well as the relationship virus-host.

They are suitable for the study of immune responses, oncogenesis, and to analyze the development of clinical signs.

Many viruses can infect mice experimentally. These animals represent a good model for the study of viral replication. So that results are more reliable, strains of transgenic mice have been achieved. Also, crossing mice of known ancestry, we can get the so called "congenital mice". These mice share the same genetic make-up, and all of them develop the same response.

Experimental animals are used to obtain virus-specific antibodies. Many of the serological tests, as we will see, use antibodies against the antigen or even against other antibodies (this is what is called secondary antibody). To date, the only way that is known to produce these antibodies is inoculating animals.

They can be used for the primary isolation of viruses or to isolate tedious viruses or difficult to grow in other systems.

And finally, they are also used for studies of antiviral drugs and vaccines. Although the initial tests are carried out in vitro (i.e., artificially grown cells), at some point of the process it is necessary to prove the effectiveness of antivirals and vaccines in experimental animals.

In this video we have seen what are experimental animals, how they are inoculated, what requirements they must meet, what are their advantages and disadvantages, and what are their uses. Thank you very much for your attention.