



CHARLES RIVER LABORATORIES REFERENCE PAPER

SPRING 1989

Revised Reporting on Simian Virus 5 (SV5) and Sendai Virus in Guinea Pigs

Charles River Laboratories has recently stopped reporting on the simian virus 5 (SV5) antibody status of its VAF/Plus[®] guinea pigs. We continue to report on Sendai virus, but customer health reports now indicate serology results from sentinel mice, not guinea pigs. The reasons for these two changes are as follows:

I. Sera from guinea pigs and Syrian hamsters, as well as humans and monkeys have frequently been found to contain SV5 antibodies (1, 2, 3). SV5 is part of a morphologically and antigenically related group of viruses termed parainflaviruses (family Paramyxoviridae; genus Paramyxovirus). These are large, enveloped RNA viruses occurring worldwide in animals and humans, which are associated with local, usually subclinical, infections of the respiratory tract (4). Four distinct serologic types exist, including Sendai virus, a type 1 parainflavivirus and common contaminant of laboratory rodent colonies (5).

SV5, a type 2 parainflavivirus, was initially isolated by Hull and co-workers (6) from monkey kidney cell cultures. Its isolation from guinea pigs or hamsters has not been reported, but as detection of antibodies suggests infection with SV5 or a related type 2 virus, it has been customary to monitor these animals for SV5 antibodies. Traditionally, the hemagglutination inhibition test (HAI) has been used (7, 8), though we recently switched to the indirect fluorescent antibody test (IFA) and the enzyme-linked immunosorbent assay (ELISA) upon finding them more sensitive and accurate than HAI.

Using these methods, we have sporadically detected SV5 antibodies in various VAF[®] guinea pig colonies. Following initial detection, we sometimes observe that the incidence of seropositive animals gradually decreases to low levels, with some positive colonies becoming SV5 antibody-negative. In any case, ANIMALS FROM SEROPOSITIVE COLONIES SHOW NO RESPIRATORY DISEASE SIGNS OR PATHOLOGY, NOR DO THEY THREATEN MICE, WHICH ARE RESISTANT TO PARAINFLAVIRUSES OTHER THAN SENDAI.

The origin of the viruses causing seroconversion has not yet been identified. Its occurrence in the absence of any potential animal source has led us to

consider a human source. Guinea pigs are susceptible to human strains of parainflavivirus, which is why they are often used to produce serotype-specific antisera to these human strains (4). WE STRONGLY SUSPECT THE VIRUS STRAIN CAUSING OUR GUINEA PIGS TO SEROCONVERT MAY NOT BE SV5 BUT, RATHER, AN ANTIGENICALLY RELATED HUMAN STRAIN OF PARAINFLUENZA 2, such as croup-associated (CA) virus. Exposure is likely despite our barrier production procedures, because parainflavivirus 2 is ubiquitous in people. In fact, as humans lose their local respiratory immunity to parainflavivirus 2, they can become reinfected and shed the virus repeatedly.

Detection of virus specific antibodies in any Charles River VAF[®] colony generates considerable concern and a specific course of action. To corroborate preliminary findings, we retest the positive serum specimens by an alternate serologic method and test additional serum specimens from the colony. We also examine animals for signs of infection and may attempt to isolate and characterize the etiological agent. If preliminary results are confirmed, the antibody-positive colony is usually recycled.

Recycling involves the destruction of all the animals in the room in which the colony is located, thorough cleaning and formaldehyde gas sterilization of the area, and eventual repopulation from isolator or VAF[®] barrier-sustained colonies. As part of the process, customers who received infected animals are alerted. Charles River can almost always resupply customers with rodents from an alternate VAF[®] colony.

In the present case, however, recycling seems inappropriate. As underlined above:

1. Animals seropositive for SV5 remain free of any clinical disease or pathological changes. (This lack of disease or changes is reportedly typical of parainflavivirus when there is no secondary infection.)
2. Natural infection of mice with type 2 parainflaviruses has not been reported. Thus, investigators can be assured that guinea pigs from SV5 antibody-positive colonies (which are otherwise pathogen-free) will not compromise the health status of their VAF[®] mice.

3. Even when maintained under the strict barrier conditions utilized at Charles River, it is virtually impossible to prevent exposure of guinea pigs to human parainfluenzaviruses, since human infection and reinfection is common. Even if animals are uninfected when shipped, they may become infected by personnel at customer facilities, despite the best barrier conditions and husbandry.

II. For the past couple of years, we have been detecting Sendai Virus ELISA positive reactions in some of our VAF[®] guinea pig areas. The positive ELISA results have sometimes been confirmed by HAI and IFA. In most areas the ELISA reactions are weak and sporadic. On the other hand, the incidence of Sendai seropositive animals in a colony can be high.

The cause of these positive results has not been definitively determined. As was suggested above for SV5, the guinea pigs may be seroconverting in response to an antigenically related human parainfluenzavirus. Alternatively, the positive results may simply be serologic artifacts. WE BELIEVE, HOWEVER, THEY ARE NOT DUE TO SENDAI VIRUS INFECTION. This opinion is based on the absence of any potential source of Sendai virus for guinea pig colonies in VAF[®] facilities. In addition, all sentinel mice tested so far from VAF[®] guinea pig colonies have been virus-antibody free. (As noted above, mice are resistant to infection with parainfluenzaviruses other than Sendai.)

As positive Sendai virus antibody test results in guinea pigs do not accurately predict Sendai virus infection, we will have to continue to test sentinel mice to determine the Sendai virus status of our guinea pig colonies. Our protocol is to maintain these sentinels on soiled bedding from representative locations in a guinea pig colony to ensure adequate exposure to Sendai and any other rodent viruses that may be present. Sentinels that have been exposed to soiled bedding for one month or more are tested every six weeks.

Now that this protocol has become routine at Charles River, we have changed our customer health reports to indicate that Sendai virus serology results are from sentinel mice, and not guinea pigs.

Should you require additional information on this matter, please contact our Technical Assistance Department.

References

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