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# Health Surveillance of immunodeficient animals

by *Ricardo Feinstein*
The National Veterinary Institute, Dept. of Pathology, P.O. Box 7073, S-750 07 Uppsala, Sweden

A range of factors should be considered when checking the health of immuno-compromised animals. These are different in many respects from the features of disease in their immunocompetent conspecifics.

Many infectious agents cause more severe lesions in immunodeficient animals than they do in their normal counterparts, and even opportunistic organisms can produce diseases that decimate stocks of immunodeficient animals.

The location of agents in the tissues of the infected immunocompromised host, and the duration of the infection also may differ. The same organism that causes short-lived infections in immunocompetent animals commonly produces chronic infections in immunodeficient animals (*Reed & O'Donoghue* 1982, *Richter et al* 1988, *National Research Council* 1989, *Walzer et al* 1989, *Feinstein et al* 1993).

In order to detect infections in immunocompromised animals a comprehensive health monitoring program should be combined with

a) - environmental checks, and
b) - diagnostic support based on complete necropsies.

Furthermore, the animals should be inspected constantly, so that sick individuals will be detected as soon as possible.

Sick animals should be removed and necropsied immediately in order to determine the cause of the disease (*National Research Council*, 1989)! Preventive measures, to avoid spreading of infections, should be taken without delay even before the diagnosis is confirmed. Ideally, one should progress from the need to detect what has happened to the reasonable assurance that nothing has happened (*Lang*, 1993).

Recommended schemes for the health monitoring of laboratory animal colonies are based on comprehensive etiological and serological tests (*FELASA*, 1994). The etiological tests, such as bacterial cultures and parasitological examination, are aimed at uncovering agents, whereas serological checks will demonstrate the presence of antibodies.

In general, viruses are more difficult to detect than other microbes. The epizootiology, clinical history, signs and lesions are important, but for most viral infections a presumptive diagnosis should be confirmed by laboratory tests, such as virus isolation. Since these tests are expensive, time consuming, and only performed by a few laboratories, serology has become the method of choice for screening for viral and mycoplasmal infections. Some bacterial and parasitic organisms also can be examined serologically.

Unfortunately, serology is not applicable in animals that cannot produce antibodies, such as many immunodeficient animals. One way to circumvent this problem is by checking immunocompetent animals that have been housed with the immunodeficient animals. Heterozygous littermates that cohabit with the immunodeficient stock can be used as contact sentinels. It has been recommended also to house the sentinels on dirty bedding (*Nomura & Kagiyama* 1982, *National Research Council* 1989, *Homberger & Thomann* 1994). However, the effectivity of these methods has been questioned by recent studies.

For example, the sentinel system seems to be inadequate for detecting Sendai virus infection in mice, as the seroconversion in the sentinels is erratic and occurs when the clinical signs are already evident in the infected mice (*Artwohl et al* 1994). Furthermore, these results suggest that the use of sentinels may be ineffective also for detecting other microorganisms.

Another alternative to detect infections is by means of pathology when serology is unapplicable. Histopathology may reveal unexpected infections and also micoorganisms that escaped detection by other etiological tests (*Feinstein* 1993). Previously unidentified microorganisms are frequently detected by histological checks (*Donovan et al* 1993).

Routine histology also is useful to diagnose infec-

*Table 1.* Examples of detection of microorganisms by means of immunohistochemical and molecular techniques.

| Agent | Technique | Reference |
|---|---|---|
| Rodent coronaviruses | I-histochemistry* | Jacoby et al 1985, Brownstein & Barthold 1982 |
| Mouse Pox virus | PCR** / I-histochemistry* | Homberger et al 1991, Christensen et al 1966 |
| Hantavirus | I-histochemistry* | Morita et al 1985 |
| LCM virus | I-histochemistry*<br>I-histochemistry*<br>in situ hybridization | Hotchin & Sikora 1975, Löhler et al 1994 |
| Mouse adenovirus – 2 | I-histochemistry* | Takeuchi & Hashimoto 1976 |
| MVM | I-histochemistry*<br>in situ hybridization | Brownstein et al 1991 |
| Polyomavirus | I-histochemistry*<br>in sity hybridization, PCR | Gerber et al 1980, Berke & Dalianis 1993 |
| PVM | I-histochemistry* | Richter et al 1988 |
| Rabbit haemorrhagic disease virus | I-histochemistry* | Stoercklé-Berger et al 1992 |
| Rabbit pox virus | I-histochemistry* | Christensen et al 1966 |
| Rat virus (parvovirus) | I-histochemistry* | Jacoby et al 1987 |
| Sendai virus | I-histochemistry* | Iwai et al 1979, Brownstein et al 1981 |
| Theiler's murine encephalomyelitis virus | I-histochemistry* | Wada & Fujinami 1993 |
| Bordetella bronchiseptica | I-histochemistry* | Uzal et al 1990 |
| Mycoplasma pulmonis | I-histochemistry*, PCR | Kohn & Chindokosowong 1989, Kunita et al 1990<br>van Kuppeveld et al 1993 |
| Encephalitozoon cuniculi | I-histochemistry*,<br>immunoblotting | Walzer et al 1989 |
| Pneumonycstis carinii | I-histochemistry*<br>I-histochemistry*<br>Immunoblotting | Sundberg et al 1989, Walzer et al 1989 |

* I-histochemistry: Immunohistochemistry ** PCR: Polymerase chain reaction

tions by agents that cause characteristic changes, such as MHV or ectromelia virus. Special stains, in addition, may be used to uncover agents like Bacillus piliformis, the CAR Bacillus and Pneumocystis carinii (*Tsuchitami et al* 1983, *Ganaway* 1986, *Walzer et al* 1989). Electromicroscopy is usually employed for diagnostic purposes. In addition, it has been used successfully for screening faecal samples for virus particles (*Eaton* 1984, *Peeters et al,* 1984). Immunohistochemical and molecular technologies offer both specificity and sensitivity. These techniques have been used for detecting viruses, mycoplasmas, bacteria, and parasites of laboratory animals (Selected examples are listed in Table 1). At the present time there are many diagnostic laboratories performing immunohistochemical tests, but the use of molecular methods is still limited, being mainly restricted to diagnostic laboratories dealing with human samples, and experimental studies. However, etiological tests based on molecular techniques have been developed for a few rodent pathogens such as rat and mouse coronavirus, parvovirus, and Mycoplasma pulmonis (*Sanchez* 1993), and the use of these technologies will certainly increase in the near future.

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