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would presumably have shown greater differences in the seroprevalence of MV virus infection.

To explain the relevant role of this transmissible tumour, the coexistence of maedi and SPA in individual sheep has to be a rather frequent happening. Our results indicate that the concurrence of lesions of both diseases is an unusual finding that can not justify the epidemiologic results.

Nevertheless, we found a high proportion of SPA affected animals to be also infected by MV virus. As the affinity of this virus for the alveolar macrophages has already been demonstrated (Narayan and others, 1982), it is likely that these animals harbour MVV in those target cells, which are abundant and characteristic in SPA lungs. This possibility, which is also taken into account by other authors (Dawson and others, 1985), would explain the epidemiologic role of SPA in the lateral transmission of MV.

We conclude that the favourable conditions for the respiratory transmission of maedi/visna in sheep flocks depend upon the presence of animals that, being MVV infected, show lesions and clinical signs of SPA. In those animals there would be no need of development of lesions and symptoms of maedi, a fact that seems to be important for the lateral spread of MV, when it occurs as single infection (Palsson, 1976).

In maedi affected animals, a correlation between the rate of replication of MVV in pulmonary macrophages and the presence of characteristic lesions has been described, so that the expression of viral antigens in the surface of these cells starts the inflammatory response (Lairmore and others, 1988). According to our results, this does not seem to happen when the infected macrophages are those of SPA. There, MVV appears to replicate without eliciting any clear or constant lymphocytic response, but the mechanisms to explain this are still obscure.

References

1. Dawson M. et. al. (1985): Vet. Rec. *116*, 588–589. — *2. Houwers D. J., Terpstra C.* (1984): Vet. Rec. *114*, 23. — *3. Lairmore M. D.* et al. (1988): J. Imm. *140*, 779–785. — *4. Markson L. M.* et al. (1983): Vet. Rec. *112*, 267–271. — *5. Narayan O.* et al. (1982): J. Gen. Vir. *59*, 345–356. — *6. Palsson P. A.* (1976): Slow virus diseases of animals and man: 17–43. Ed. R. H. Kimberlin. North-Holland Publ. Comp. Amsterdam. — *7. Snyder S. P.* et al. (1983): A. J. Vet. Res. *44*, 1334–1338. — *8. Winward L. D.* et al. (1979): A. J. Vet. Res. *40*, 564–566.

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TOXIC EFFECT OF REACTIVE OXYGEN SPECIES ON OLIGODENDROCYTES

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The mechanism underlying demyelination in the CNS of dogs suffering from canine distemper (CD), an animal model for multiple sclerosis, is still unclear. Macrophages and their secretory products have been suggested to be partly responsible for the severe necrosis observed in the white matter of animals with CD that develop chronic inflammatory lesions. We have shown that anti-CD virus antibodies binding to CD virus-infected glial cells are capable to stimulate brain macrophages *in vitro* leading to the release of reactive oxygen species (ROS), potentially harmful products (*Bürge* et al., 1989, *Griot* et al., 1989). It is likely that these events also occur *in vivo* since CD virus-infected glial cells, macrophages and antiviral antibodies are present in close proximity in chronic inflammatory lesions in CD. Activated macrophages generate superoxide (O_2^-) and hydrogen peroxide (H_2O_2) as primary reduction products. In the presence of transition metals such as Fe^{++}, O_2^- and H_2O_2 can give rise to highly toxic hydroxyl radicals (°OH) which are known to cause considerable tissue damage through reaction with DNA, protein and membrane lipids (*Halliwell* and *Gutteridge,* 1989). Since the above described tissue destruction is predominantly seen in the white matter, we examined whether myelin, or oligodendtrocytes (the myelin producting cells in the CNS) are particularly susceptible to ROS.

Therefore, we exposed primary cell cultures prepared from neonatal dog cerebella to xanthine/xanthine oxidase (X/XO), a well known O_2^- producing system (*Griot* et al. in press). Oligodendrocytes, astrocytes and brain macrophages (the main celltypes present in these cultures) were visualized using immunocytochemical methods and examined using a light microscope.

This treatment resulted in a specific time-dependent degeneration and loss of oligodendrocytes whereas the morphological appearance of astrocytes and macrophages was unchanged (Figure). Further, an

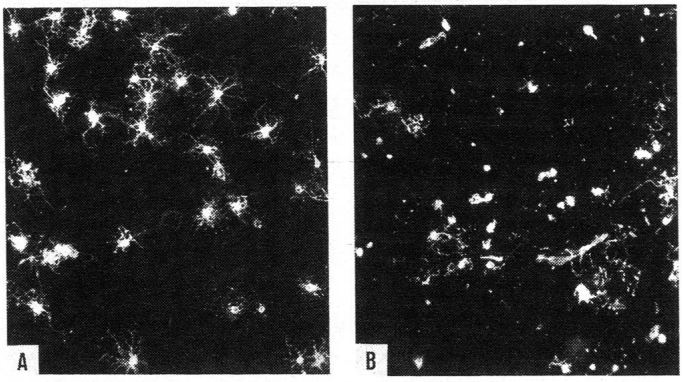

Fig. 1: Morphological appearance of FITC-immunostained oligodendrocytes in normal (A) and X/XO-treated glial cell cultures (B) in which most of the oligodendrocytes show severe signs of degeneration. x100.

evaluation of the effect of several ROS scavengers and transition metal chelators suggests that a metal-dependent formation of °OH could be responsible for the observed damage (Table).

The exact biochemical mechanism of oligodendroglial degeneration mediated by ROS needs still further investigation which may ultima-

Table 1: After treatment of dog glial cell cultures with X/XO and ROS scavengers or metal chelators, oligodendrocytes were classified in three groups according to their morphological appearance: (+). Cells that have lost their peripheral fine branching of processes, (++) cells with major loss of processes and cytoplasmic protrusions, (+++) cell-fragments without processes.

Scavenged Species	Scavenger	Concentration	Damage
O_2^-	SOD	100 U/ml	++
H_2O_2	Catalase	100 U/ml	++
$H_2O_2+O_2^-$	SOD/Catalase	100 U/ml	+
$^{\circ}OH$	Mannitol	50 mM	+
Fe^{++}	Desferal^R	50 µM	+
None			+++

tely provide data for therapeutic intervention of brain damage in encephalitis caused by ROS.

References

1. Bürge T. et al. (1989): J. Virol. *63*, 2790–2797. — *2. Griot C.* et al. (1989): Acta Neuropathol. (Berlin), *78*, 396–403. — *3. Griot, C.* et al. (1990): Free Rad. Res. Communs. (in press). — *4. Halliwell B., Gutteridge J. M. C.* (1989): Free radicals in biology and medicine. Clarendon Press, Oxford.

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PATHOLOGICAL FINDINGS IN DIETARY PRODUCED OXIDATIVE STRESS IN GROWING PIGS

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The classical mulberry heart disease (MHD) with microangiopathy (MAP) of pigs, according to Grant (1961), is characterized by vascular lesions principally in the myocardium whilst degenerative changes occur inconstantly. Van Vleet et al. (1977) described an atypical mulberry heart disease involving mainly degenerative changes.

The aetiology of MHD is not yet clearly understood although the present knowledge presume a multifactorial genesis with dietary involvement. According to Korpela (1988), an increased myocardial and hepatic iron concentration in pigs with microangiopathy acts as a risk factor of oxidative damage.

We produced an experimental myodegeneration of skeletal muscles in all 8 pigs with a diet deprived selenium and vitamin E. In order to produce MAP we had provoked the oxidative stress by injecting 3 ml irondextran IM in four pigs.

Macroscopically the condition of nutritional myodegeneration, also known as white muscle disease, was characterized by an overall pale, yellowish colour and a translucence of the skeletal muscles. Further gross pathological changes included ascites (100%), hydrothorax (37%), pericarditis (62%) as well as edema of lymph nodes (50%) and lungs (50%).

The microscopical examination of the skeletal muscle (M. longissimus dorsi) revealed varying degrees of degeneration including swelling of muscle fibers and loosening of the fibrillar pattern. Also the longitudinal and cross striations were no longer visible. The local arrangement of nuclei in chains was considered being a reparative process. The histopathology showed further hepatosis diaetetica and myocardial degeneration as described by Grant (1961) and Van Vleet et al. (1977).

As previous studies show, selenium deficiency is associated with hepatosis diaetetica and nutritional myodegeneration but not with MAP (Lindberg et al., 1972; Moir and Masters, 1979). In our study none of the pigs showed vascular lesions in the myocardium. Further experiments are necessary to study the role of iron supplementation in dietary produced oxidative stress in growing pigs.

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PATHOLOGY OF AGING IN THE CHICKEN

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Although the process of aging in man and laboratory animals has been studied quite extensively during the last couple of decades (Andrew, 1971), not very many data concerning food producing animals are available. This is mainly due to the fact that for economic reasons the life of these animals is considerably shorter than it would be under natural circumstances.

In order to make a contribution to the knowledge of the pathological processes which take place in senescent animals, we carried out a statistical and morphological study on the pathology of aging in the chicken with the belief that these observations could be of some relevance both to veterinary and comparative pathology.

Sixty-seven chickens, 61 females and 6 males, obtained from small farms at different ages were housed in our facilities until natural death occurred. The animals, aged 3 to 11 years, were necropsied immediately after death and the gross lesions were recorded.

The cause of death could be established in 51 animals and the related results are summarized in Table 1.

The data concerning the occurrence of the gross lesions involving the different organ systems are reported in Table 2. The alimentary tract was affected by pathological changes in 93% of the chickens; these mainly consisted of inflammatory, degenerative, necrotic and neoplastic (Fig. 1, 2) lesions affecting the liver parenchyma. Very often ascites and peritonitis could also be observed. 84% of the