Editorial

Canine Lessons for Human Lupus

Systemic lupus erythematosus (SLE) occurs spontaneously in humans, dogs\(^1,2\) and cats\(^3\), and SLE-like disorders have been reported in poikilothermic species such as snakes and iguanas\(^4\). Canine SLE has received considerable attention since the initial description in 1965, when seven dogs with unequivocal SLE were described\(^5\). The notable features included malaise, weakness, alopecia, Coombs' positive haemolytic anaemia, thrombocytopenia, membranous glomerulonephritis and serological abnormalities such as LE cells. Subsequently it has been recognized that canine SLE closely mirrors the clinical and immunopathological features of human SLE\(^6\). As such, naturally occurring canine SLE may be a useful research model for human lupus, in certain respects superior to the various experimental murine models of lupus.

Although the clinical and pathological aspects of canine SLE are now reasonably well described, some veterinary practitioners still fail to recognize the disorder\(^5\), while some authorities feel that veterinarians are identifying a condition that is distinct from the human disease\(^7\). Costa et al.\(^7\) found that, of 580 dogs with a clinical diagnosis of SLE, only 61 dogs fulfilled the revised American Rheumatism Association (ARA) criteria for the classification of human SLE\(^8\). However, it would be surprising if we did not need criteria specific to canines, which would need to encompass dogs and possibly wolves.

The authors of the paper on antinuclear antibodies (ANA) in canine SLE that appears later in this issue of Lupus are therefore to be commended on finding 100 dogs fulfilling the revised ARA criteria. These workers have characterized in detail the molecular targets of the ANA from these ARA criteria-fulfilling SLE dogs and have noted certain specificities that are distinct from the human SLE pattern. They confirmed some of their earlier findings, particularly a low incidence of anti-double-stranded DNA antibodies, but added to this by demonstrating that anti-SSA and anti-SSB antibodies are rare in canine SLE. Some clinical details of this large cohort of dogs would have been interesting, as this would have allowed a search for correlations between clinical and serological features.

Both genetic and environmental factors appear to be of paramount importance in the development of SLE. Breeding experiments, using dogs with both clinical and serological evidence of SLE, have demonstrated that as in the human condition genetic mechanisms alone cannot fully explain the aetiology of the disorder\(^9\).

The concept that a transmissible factor may be involved in the aetiology of SLE is not new and is supported by experiments in which splenic cell-free filtrates from an affected member of an SLE dog colony were inoculated intraperitoneally into four normal new-born beagles. This resulted in the development of ANA in all recipients within 12 months, and these antibodies persisted until the animals were sacrificed at 18 months of age\(^10\). Mice who received similar dog spleen inoculates all developed ANA. Additionally, some produced specific anti-double-stranded DNA antibodies while others developed malignant lymphomas containing murine leukaemia virus. Subsequently, puppies inoculated with cells obtained from these murine lymphomas developed ANA within 4 months\(^10\).

An infective aetiology for dog and human SLE therefore remains an attractive hypothesis and it is conceivable that a transmissible agent could be passed between members of a household. Several viral infections are known to be transmitted reciprocally between man and dog, including reoviruses and adenoviruses\(^11\). The intimate position of the family pet dog may render him/her an ideal subject on which to target research for putative environmental factors. In 1977 the possibility of a transmissible factor that may cross the species barrier was highlighted in a small study of dogs in households containing human SLE patients\(^12\). These authors recorded anti-DNA antibodies in two dogs of two households containing several SLE patients. In contrast, epidemiological studies on individuals exposed to dogs with SLE did not demonstrate an increase in (human) SLE as a consequence of such contact\(^13,14\). However, the debate was reopened when Zambinski et al.\(^15\) reported that hospital laboratory staff handling blood samples from (human) SLE patients were more likely to have anti-double-stranded DNA antibodies than those from other laboratory situations.

That factors common to dogs and their owners might be implicated in the aetiology of SLE therefore seems to be a possibility. A pilot study detecting autoantibodies in the serum of 15 household pet dogs, which had been
owned by SLE patients for many years, has recently been reported. Assay techniques were adapted from those used in the routine immunopathology laboratory to investigate human SLE, to facilitate the testing of canine sera. DNA-binding \( \beta \)-globulins, normally present in canine serum, can interfere in such assays, but their effect was eliminated by standard techniques. These dogs owned by patients with SLE had no apparent clinical signs of lupus but had significantly elevated levels of anti-double-stranded DNA antibodies, which were comparable to an autoimmune cohort of dogs. These dogs also had more serum protein electrophoresis abnormalities (polyclonal and monoclonal) when compared to a control population of dogs. However, the control dogs were not age and sex matched, nor were they household pets. These preliminary data need extending with community-matched dog controls, and it must be emphasized that, in the absence of supporting clinical signs, positive serology does not make a diagnosis of SLE. However, the ability of certain environmental factors to lead to the generation of autoantibodies seems likely.

Reports in the international press that 'Millie', the pet dog of George Bush, currently President of the United States of America, has SLE raise even wider issues when one recalls that both the President and his wife have autoimmune thyroid disease! Studies of the interplay between man and beast should enable us to explore the role of environment in the development of autoimmune diseases.

References


R.J. Powell
Department of Immunology
Queen's Medical Centre
Nottingham NG7 2UH, UK