1. INTRODUCTION

Heterologous antilymphocyte serum (ALS) refers to antiserum that was raised in one species against lymphoid cell antigens of other species. Although the preparation of ALS was already reported by Metchnikoff in 1899 the use of this antisera for modulation of the immune response had to wait until the role of lymphoid tissue in the immune reaction was recognized. In the late fifties the experiments of Inderbitzen (1956) were the first to demonstrate that heterologous antiserum directed against lymphoid cells could inhibit delayed hypersensitivity reaction. Several years later Woodruff and Anderson (1963) showed clearly that ALS used either alone or as an adjunct to thoracic duct drainage could prolong the survival of skin allograft in rats.

Since 1967 ALS has been the subject of increasing numbers of publications and reviews. Its main use is in the field of immunosuppression. It has the ability to markedly diminish cellular immune responses particularly skin allograft and heterograft rejection in experimental animals. It also can abolish the immunity evoked by a previous allograft. The graft versus host reaction in irradiated animals such as mice or monkeys caused by the injection of allogenic spleen or bone marrow cells can be neutralized by ALS injection. ALS was one of the first tools used to study thymus dependent T cell functions and antibody mediated bone marrow dependent
B cell functions in the immune response. As an experimental tool it is still used to inhibit preferentially cellular immune response, while leaving humoral antibody mechanism generally intact. With regard to clinical immunosuppression ALS represents the first agent whose actions were limited to cells of the lymphoid system and which would specifically interact with lymphocytes in both resting and proliferative stages. The immunosuppressive effects of ALS can be increased by prior thymectomy, whole body irradiation, administration of corticosteroid and lymphocyte depletion by thoracic duct fistula.

ALS has been raised in horses, rabbits, pigs and ruminants against lymphocytes of the dog, mouse, rat, monkey and human. The sera usually possess optimal immunosuppressive activity when injected into the lymphocyte donor species. Anti-rat and anti-mouse antisera have also been raised in chickens and ducks, but their spectra of activity are somewhat narrower than mammalian antisera, because of their poor interaction with mammalian complement. Many different immunization techniques have been tried, yielding antisera of different potency.

Non-lymphoid tissues have been used to produce ALS with effective immunosuppressive action including mouse cell cultures (L cells), epidermal cells or plasma cells. Lymphoid cell and thymocyte cell fractions have also been used to produce potent, more highly specific and less toxic sera.
The 7S IgG fractions of ALS contain virtually all immunosuppressive potency, but the intact antibody molecule is required for optimal immunosuppressive activity. The pure 19S fraction of ALS separated by immuno electrophoresis has little or no immunosuppressive activity. The F(ab)2 portion of the antibody molecule, obtained by digestion with pepsin from horse-anti-rat lymphocyt IgG failed to prolong the survival of skin allograft in rats as reported by Woodruff et al. (1967).

Since the report of Starzl et al. (1967) ALS has been used clinically in humans. Although ALS remains the most powerful single agent for prolongation of skin grafts in mice, its effects in humans have been far less dramatic. It has become clear that ALS alone cannot be used to obtain a continuous immunosuppression, but rather must be applied in combination with conventional immunosuppressive agents used in clinical transplantations. The major clinical use of ALS at present is as an adjunct to usual immunosuppressive drugs such as azathioprine and prednisone in the management of patients with kidney or liver allograft, where the ALS acts on the cellular immunity and azathioprine on the humoral immunity. In cardiac transplantation ALS is now routinely added to the usual combination of azathioprine, prednisone and radiation. An important and rational indication of ALS and azathioprine is producing temporary immunosuppression to facilitate the take of allograft skin on patients with massive second and third degree burns until healing by second intention can take place.
Another important use of antilymphocyte globulin (ALG) is in patients with lymphoblastic anemia to allow the take of HLA nonidentical bone marrow. ALG has also been added to the list of agents which may be of value in the autoimmune disorders or other diseases with immune features. In the past ALG has also been used in the treatment or lymphoproliferative disorders like lymphatic leukemia.

In Veterinary Medicine the use of ALS is mostly for experimental purposes. The effects of ALS in mice, rats, dogs and primates have been studied intensively. It is known that the chimpanzee shares organ antigens with humans. Many human leucocyte antigens are present on the leucocytes of chimpanzees. Several primate species (chimpanzees) and rhesus monkeys have been used for the quality and safety control of anti-human lymphocyte serum. Anti-dog lymphocyte serum has been used in transplantation studies. However, the clinical application of animal ALS is very limited.

So far the effects of anti lymphocyt serum in cattle has not been published.

Originally the purpose of the production of horse anti-bovine lymphocyt serum (ABLS) was for the transmission of juvenile bovine leukose, which is a disease especially affecting calves.

The characters of the horse ABLS, however, is not yet known. Therefore its effects on some of the humoral and cellular immune functions in calves should be determined.