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**THE DISPOSITION OF GENTAMICIN IN
EQUINE PLASMA, SYNOVIAL FLUID
AND LYMPH**

**A THESIS
PRESENTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
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ABSTRACT

Although it is easy to monitor blood concentrations of antimicrobials most bacterial infections occur in extravascular sites, more specifically within the interstitial fluid. It is very difficult to sample interstitial fluid and many different methods have been used. Reports of the relationship between blood and interstitial concentrations of antibiotics have varied depending on the tissue/tissue fluid sampling technique used. The sampling of tissue fluid for antimicrobial studies in horses has been limited. Most studies have measured antibiotic concentrations in readily accessible body fluids such as urine, peritoneal fluid and synovial fluid. The relationship between these fluids and interstitial fluid in the horse is not known.

The disposition of gentamicin in equine plasma, synovial fluid and in peripheral lymph was studied. A lymph vessel (dorsal digital lymph trunk) on the medial aspect of the distal hindlimb was selected for the disposition study. To better define the relationship between synovial fluid and tissue concentrations of an antimicrobial it was shown that this vessel had a contribution to its lymph derived from the synovium of the fetlock joint. Very high concentrations of gentamicin were retrieved in the lymph collected from the cannulated vessel after intra-articular injection (150mg dose). The mean maximum lymph gentamicin concentration was approximately 50 $\mu\text{g/ml}$ and the time to reach this, approximately 1.7 h after joint injection. The mean synovial fluid concentration 0.25 h following injection was $7244 \pm 660 \mu\text{g/ml}$ and disappearance from the synovial fluid was consistent with first order kinetics with a mean disappearance half-life (harmonic mean) of 0.99 (0.83-1.22) h.

A technique for chronic cannulation of the dorsal digital lymph trunk was developed. Two Trials were conducted and in the first (Trial A) the disposition of gentamicin in plasma and lymph was studied after intravenous injection (2.2 mg/kg). In Trial B the disposition of gentamicin in plasma, synovial fluid and lymph was studied. Kinetic parameters were similar to other reported studies. There was no significant difference in kinetic parameters

between trials. The disposition curves for all three fluids were similar. Mean maximum lymph concentrations were approximately $4.6 \mu\text{g/ml}$ and were 40% of the plasma concentrations 15 minutes after injection. These were achieved approximately 1.35 h after injection. The maximum concentration of gentamicin in synovial fluid ($2.86 \pm 0.45 \mu\text{g/ml}$) was significantly less than in lymph. Three hours after injection plasma, synovial fluid and lymph concentrations were very similar and it was concluded that a sample of any one would be a good index of the others at this time. The relationship between synovial fluid and tissue fluid 3-8 h after injection was less clear with marked divergence of the disposition curves. Gentamicin was more slowly eliminated from lymph than plasma but a parallel relationship between the two fluids was observed 3-8 h after injection, with a mean lymph:plasma ratio of approximately 1.6. It was concluded that plasma concentrations were a good index of tissue fluid concentrations.

Maximum lymph concentrations of gentamicin after intravenous injection were 10 times less than after intra-articular injection. The presence of very high concentrations in lymph derived from the synovium of a joint after intra-articular injection suggest that subsynovial interstitial fluid concentrations are also this high and therefore that intra-articular injection may have some therapeutic advantage over systemic injection.

Lymph cannulation in the horse appears to be a viable technique for antimicrobial disposition studies.

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