

The Effect of Oxytetracycline on Leukocyte Migration into Inflammatory Exudate

The migration of leukocytes to sites of infection and tissue injury is a primary defence mechanism. When localized at the infection site polymorphonuclear leukocytes phagocytose bacteria and other foreign particles. The leukocyte is also of interest as a source of inflammation mediators e.g. metabolites of arachidonic acid (*Simmons et al.* 1983).

Functioning leukocytes are of vital importance for the successful outcome of antibacterial therapy. The ideal situation is achieved when the host's defence mechanisms and the antibacterial drug act synergistically. The relationship between the host and the invading bacteria is very complex and may be further complicated by the fact that certain antibacterial drugs may impair some of the non-specific defence mechanisms.

The literature on the effects of antibacterial drugs on leukocyte function has grown rapidly during the last decade. Several comprehensive reviews have been published on this topic (e.g. *Milatovic* 1983). Tetracyclines is a group of drugs which has often been reported to impair leukocyte migration *in vitro*.

As oxytetracycline (OTC) is widely used in veterinary medicine it was considered to be of interest to study its effect on leukocyte migration *in vivo*.

Several techniques have been used to study leukocyte migration *in vivo*. The most used method includes induction of an inflammatory process in the peritoneal or pleural cavities of small laboratory animals. Samples can easily be obtained from these cavities for

cell counting and the study of cell function (*Bird & Girod* 1985). Most of the basic knowledge about leukocyte migration *in vivo* is based on results from studies using these or similar methods.

Tissue cages were used for the study of leukocyte migration in the present experiments. The tissue cage is a partly perforated capsule of an inert material which can be implanted e.g. subcutaneously. After 2-3 weeks there is an ingrowth of granulation tissue through the perforations, leaving a fluid-filled cavity in the middle. The tissue cage technique was originally developed for sampling of interstitial fluid and has been widely used in pharmacokinetic studies, but also in studies of local inflammatory reactions. The technique is e.g. excellent for the study of local prostaglandin release (*Higgins et al.* 1984, *Luthman et al.* 1988).

In the present study 6 calves were used in a cross-over experiment. All animals carried 4 subcutaneously implanted tissue cages of the type described by *Bengtsson et al.* (1984). The cages had been *in situ* for 5 weeks and had been previously used in pharmacokinetic studies. An inflammatory reaction was induced within a cage by injection of 0.5 ml of a 1% carragenan solution. Three of the animals were given an intravenous injection of OTC (10 mg/kg) immediately before the carragenan injection. The OTC injection was repeated after 12 h. The remaining 3 animals served as controls. The experiment was repeated after 1 week in a way so that all animals had been treated with OTC and

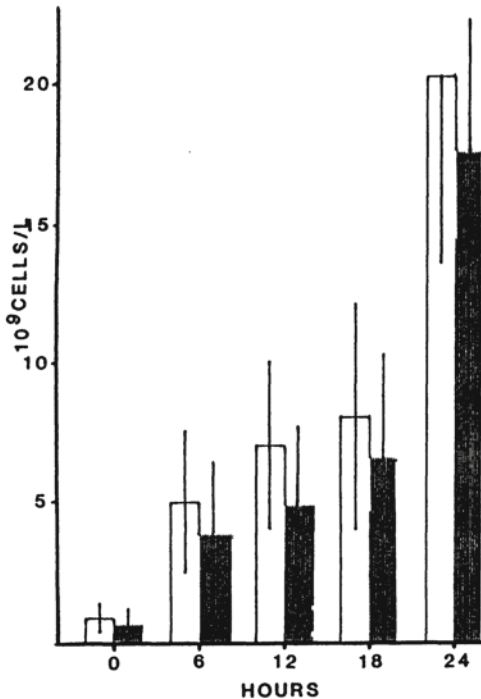


Figure 1. Changes in the number of leukocytes in tissue cage fluid after injection of carragenan into the cage, before (open bars) and after (shaded bars) oxytetracycline treatment. $n = 6$, $\bar{X} \pm \text{SEM}$.

served as controls at the end of the study. Different cages were used in each part of the experiment.

OTC was obtained from Sigma Biochemicals and was dissolved in saline immediately before use.

Tissue cage fluid (TCF) was sampled as described by *Bengtsson et al.* (1984) for counting of leukocytes. It was found necessary to dilute TCF in an equal volume of Hank's solution containing 0.5% trypsin to avoid aggregation of the cells.

All injected cages responded with a significant increase in the number of leukocytes in TCF. The highest number was recorded

after 24 h. As shown in Fig. 1 repeated OTC treatment did not significantly alter leukocyte migration into TCF.

The serum concentration-time profile of OTC was very similar to what was earlier reported in calves after the same treatment (*Bengtsson et al.* 1986).

The results showed that tissue cages can be used for the study of leukocyte migration in cattle. There was however a very wide variation in response to carragenan between individual cages. It is possible that this variation can be reduced by using a different cage model or a more concentrated carragenan solution.

The clinical implications of *in vitro* studies showing an inhibitory effect of antibacterial drugs on leukocyte function is difficult to evaluate. From a theoretical point of view it should be doubtful to use drugs which seriously impair the non-specific defence mechanisms when the antibiogram of the invading bacteria is unknown. The results presented in Fig. 1 do not support the findings from most *in vitro* studies.

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