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**Title** Penetration of a **topically** applied nonsteroidal **anti-inflammatory** drug into local tissues and synovial fluid of dogs.  
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**Abstract** **OBJECTIVE:** To investigate penetration of a topically applied nonsteroidal anti-inflammatory drug (NSAID) into tissues and synovial fluid. **ANIMALS:** 5 Greyhounds. **PROCEDURE:** Dogs were anesthetized and microdialysis probes placed in the dermis and gluteal muscle over each coxofemoral (hip) joint. Methylsalicylate (MeSA) was applied topically over the left hip joint. Dialysate and plasma (blood samples from the cephalic and femoral veins) were obtained during the subsequent 5 hours. Dogs were euthanized, and tissue samples and synovial fluid were collected and analyzed for salicylic acid (SA) and MeSA by use of high-pressure liquid chromatography. **RESULTS:** SA and MeSA concentrations increased rapidly (< 30 minutes after application) in dialysate obtained from treated dermis. Salicylic acid also appeared in plasma within 30 minutes and reached a plateau concentration after 2 hours, although combined drug concentrations (SA plus MeSA) in plasma obtained from femoral vein samples were twice those measured in plasma obtained from the cephalic vein (SA only). Treated muscle had a progressive decrease in NSAID concentration with increasing depth (SA and MeSA), but it was significantly higher than the concentration in untreated muscle. Substantial amounts of SA and MeSA were also measured in synovial fluid of treated joints. **CONCLUSIONS AND CLINICAL RELEVANCE:** Topically applied NSAIDs can penetrate deeply into tissues and synovial fluid. Local concentrations higher than circulating systemic concentrations are suggestive that direct diffusion and local blood redistribution are contributing to this effect. Systemic blood concentrations may be inadequate to describe regional kinetics of topically applied drugs.