Distribution and Homing of Stem Cells After Intra-Articular Injection to Normal and Arthritic Joints

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If mesenchymal stem cells by intra-articular injection are effective, it may be through modulation of synovial fluid constituents, inflammation, or cytokine profile. Authors’ address: Comparative Orthopaedics Laboratory, Department of Clinical Sciences, Cornell University, Ithaca, NY 14853; e-mail: aew44@cornell.edu. *Corresponding author. © 2011 AAEP.

1. Introduction
Clinical evidence suggests that intra-articular injection of mesenchymal stem (stromal) cells (MSCs) is effective. We hypothesized that autologous bone marrow–derived MSCs would engraft to cartilage in osteoarthritic (OA) joints but not in normal joints after injection.

2. Materials and Methods
Twenty-nine joints from 10 horses were characterized as normal or OA through lameness and radiographic examination. Second-passage autologous MSCs (3 × 10^6 for fetlocks and 5 × 10^6 for femoropatellar joints) were labeled with fluorescent nanoparticles or remained unlabeled (7 joints). Seventeen normal and 12 OA joints were injected and examined after 1 week by necropsy, microscopy, and synovial fluid (SF) cytology. Twelve joints in 6 horses were injected with Modified Eagles Media (MEM) only.

3. Results
Clinical findings included lameness (n = 2) and severe effusion (n = 11), moderate effusion (n = 3), or slight effusion (n = 4). SF abnormalities included elevated nucleated cell counts (median, 2800/μL; interquartile range, 1750–4450/μL), consisting of large mononuclear cells and small lymphocytes. SF from MEM-only injections had a nucleated cell count of 850/μL (300–1700/μL). There were no statistically significant differences in synovial parameters between nanoparticles-labeled and unlabeled MSC injected joints. Nanoparticles-labeled MSCs were found predominantly in the synovial membrane compared with cartilage (p < 0.0001). Adherence of labeled MSCs to cartilage was minimal and found in 17 of 97 cartilage sections. The proportion of positive sections from synovium and cartilage was not different between OA and normal joints (p = 0.79).

4. Discussion
Although mild, joint flares were common after intra-articular MSC injection. SF was indicative of nonseptic inflammation and antigenic stimulation. MSCs did not reliably home to cartilage injury in OA joints.

Footnote
aQuantum®, dots; Qdot®, Invitrogen, Carlsbad, CA 92008.