

Lymphatic transport from normal and synovitic knees in rabbits

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The resorption pattern of synovial fluid through the lymphatic system from normal and synovitic knee joints in rabbits was studied with ^{99m}technetium-rhenium-sulfur colloid injected intraarticularly and monitored for 14 hours with a gamma camera.

On the normal side the regional lymph nodes were visualized after 1 hour and after 14 hours still 75 percent activity remained in the knee. In the synovitic knees no lymphatic transport could be detected; and the radiotracer was unstable with rapid liberation of technetium, which was excreted in the urine. This radiolysis was not found in vitro in synovitic joint fluid.

The lymphatic transport from normal rabbit knees is low. We found a clear difference in lymphatic transport between normal and synovitic knee joints.

The resorption pattern of synovial fluid through the lymphatic system has not been fully explained (Wdowiak et al. 1980, Williams and Warwick 1980). Lymphatic transport from inflammatory knees has been studied after colloid injection with radioactive isotopes applied for treatment (Strand and Persson 1979, Williams et al. 1976).

We have studied the lymph flow from the knee joints in rabbits to demonstrate the route and rate of the local synovial fluid drainage to the lymphatic system.

Material and methods

Twelve Danish country-breed rabbits weighing 3.0-3.4 kg were investigated. Six rabbits were used as controls; and in the other six, synovitis was induced in the right knee 5 weeks before the current investigations. To induce synovitis, articular instability was produced (Hulth et al. 1970) by cutting both cruciate ligaments, excising the medial collateral ligament, and

extirpating the medial meniscus. In this animal model, maximal joint effusion and synovitis were present after 4-6 weeks (Svalastoga and Reimann 1985). Therefore, the investigations were performed 5 weeks post-operatively. After the measurements, arthrotomy revealed in each operated on knee hypertrophic synovitis, which was confirmed with light microscopy.

The rabbits were lightly anesthetized with a mixture of Fentanyl[®] (0.2 mg/ml) and Fluanizone[®] (10 mg/ml) using 0.2 ml/kg body weight. ^{99m}Technetium-rhenium-sulfur colloid (CIS TCK 17) with 40 MBq in 0.2-ml saline was injected in each knee. In all but one knee, injections were performed without leakage through the needle canal.

Immediately after the injection and at the following 1, 2, 3, and 14 hours, scintigraphy was performed with a Siemens gamma camera (ZLC 370S) coupled to a Siemens Scintiview II system. We used our routine scintigraphy procedure (Reimann et al. 1987).

The stability of the tracer was tested in vitro before the intraarticular injection by thin-layer chromatography using a Merck RP-18 with acetone and isotonic saline as the eluent. The amount of free ^{99m}technetium was in all cases less than 3 percent. In vitro stability, particle size, and protein binding were also investigated in saline and in normal and synovitic joint fluids. Rhenium-sulfur colloid had a particle size of 40-80 nm, a binding of ^{99m}technetium of 90-95 percent, and a high protein binding in normal as well as synovitic joint fluid.

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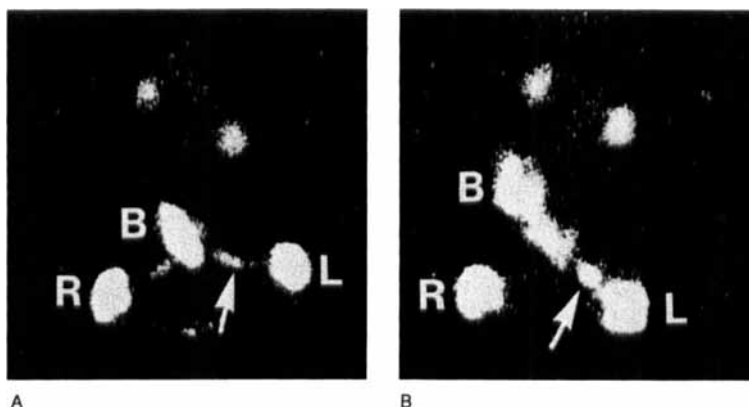


Figure 1. Scintigram over the lower part of a rabbit.

A. Normal position of a lymph node is marked (arrow). R right, L left knee, B bladder.

B. Right-sided knee synovitis. Note that no regional lymph nodes are seen on the right side. Lymph node on the left side is marked (arrow). R right synovitic knee, L left normal knee, B bladder.

Results

All 12 control knees showed identical scintigrams. After 1-3 hours, most of the activity remained in the knee joints distributed over the joint surface. The regional lymph nodes were visualized after 1 hour (Figure 1).

In the 6 rabbits with synovitis in the right knee, a rapid decrease in activity was observed over the operated knee after 1 hour. The regional inguinal and iliac lymph nodes were only visualized on the side of the unoperated knee, and no regional lymph nodes were seen on the side of the synovitic knees (Figure 1). In all the operated rabbits, scintigraphic activity was observed in the urinary bladder, but never in the liver.

Within the first hour, scintimetry showed a dramatic fall of radioactivity in the synovitic knees, and then it remained stable for the next 13 hours. In the unoperated knees, a gradual fall identical to the normal material was observed, and about half of the removed activity from the knees could be found in regional lymph nodes (Figure 2).

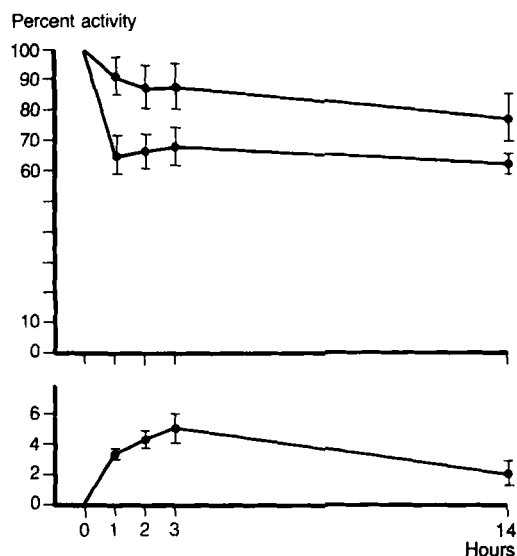


Figure 2. Percent of 40 MBq ^{99m}Tc -sulfur colloid remaining in the normal knees (top), synovitic knees (middle), and regional lymph nodes (bottom) after intrarticular injection.

Table 1. Retention of rhenium-sulfur colloid in the knee joints of 6 rabbits and an estimate of the uptake in the regional lymph nodes. Mean *SD*

Hours after injection	Percent remaining activity			
	Knees		Nodes	
0	100		0	
1	93	5.6	3.6	0.5
2	94	4.6	4.4	1.3
3	91	5.7	5.2	2.4
14	72	5.7	2.1	2.0

Discussion

Our results suggest that radiolabeled rhenium-sulfur colloid would probably be useful for studies of lymphatic accumulation in regional lymph nodes draining the knee (Reimann et al. 1987; Table 1). The radiographic activity remaining in the synovitic knee was completely different from the unoperated on knee (Table 2). The dramatic fall within the first hour is unlikely to represent lymphatic transport, and the regional lymph nodes were not visualized at that stage.

Table 2. Percent activity remaining in the knee joints of 6 rabbits after intrarticular injection of rhenium-sulfur colloid. The right knee had experimental synovitis, the left was normal. Mean *SD*

Hours after injection	Percent remaining activity			
	Synovitis		Normal	
0	100		0	
1	65	16	91	16
2	67	15	88	19
3	69	15	88	19
14	63	8	78	20

The radioactive tracer compound was unstable in the operated on knee. However, because protein binding, stability, and particle size in vitro were unchanged in

saline and in normal and synovitic joint fluids, it is unlikely that changes in the synovial fluid can explain the fall in activity within the first hour. Technetium (non-colloidal form) was absorbed from the knee and excreted into the urinary bladder. If colloid was evacuated via capillaries in the synovial membrane, activity should be observed in the liver; but this was never seen.

The radiolabeled colloid remained in the synovitic knee for the next 13 hours, indicating that lymphatic transport from the inflammatory knee was very limited. The lymphatic absorption process in a synovitic knee might be regulated in several ways. An increased phagocytic activity of the synovial membrane and an increased intraarticular pressure causing decreased vascular drainage or a decreased permeability of the synovial membrane may be of importance.

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