Resorption of intraarticular diffusible and microcolloid tracers

Rabbit studies of normal and synovitic knees

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The resorption of two radiotracers (^{99m}technetium-labeled microcolloid particles to study lymphatic transport and ^{51}chromium-EDTA to study diffusion) from the knee joint and the subcutaneous tissue of rabbits was investigated simultaneously. In 12 rabbits, synovitis was induced in the right knee 6 weeks or 3 months before the investigation; 6 rabbits served as controls. The final number of Tc-particles in the normal knees and in the subcutaneous tissue in the three groups did not differ; but removal from the synovitic knees was increased. The final number of Cr-EDTA particles did not differ within or between groups. The initial decrease was highest in the knees with acute synovitis ($P < 0.05$). The results indicate (1) that in synovial tissue lymphatic transport is of little importance, (2) that leakage through the synovial membrane increases in synovitis, and (3) that a subcutaneous depot can be used as a reference instead of injections into a normal knee.

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Submitted 90-08-25. Accepted 91-02-01

The resorption by either blood or lymph of synovial fluid through the synovial membrane of normal and inflammatory joints has been studied by several authors using inert or radioactive tracers (Dick et al. 1971, Wdowiak et al. 1980, Christensen et al. 1982). We found earlier that ^{99m}technetium-labeled albumin colloid is suitable for following particle absorption from knee joints (Reimann et al. 1987, Vittas et al. 1987). ^{51}Cr-EDTA has been found useful as a diffusible tracer (Bill 1979).

The present study was designed to investigate resorptive patterns in and around knee joints in the rabbit using an experimental model well known in our laboratory (Reimann et al. 1989).

Material and methods

Eighteen female Danish country-breed rabbits weighing 3.0 to 3.4 kg were used. In 12 rabbits, synovitis was induced in the right knee by making it unstable (Hulth et al. 1979) 6 weeks or 3 months before the investigation, and 6 rabbits served as controls. In this model, maximum effusion and synovitis are expected to be present after 4–6 weeks (Svalastoga and Reimann 1985). The rabbits were anesthetized during the operation and investigations, and they were killed with potassium chloride intracardially.

The radiotracers ^{51}Cr-EDTA (Solco) and ^{99m}Tc-nanocoll (Hoechst), dissolved in 0.2 mL saline, were injected using a 25-gauge needle placed in the retropatellar space of the right knee, where the position was secured by aspiration; also, the same dose was injected subcutaneously in the contralateral hind limb distal to the joint. The two tracers have separable gamma energies of 365 and 140 KeV, and were injected in doses of 7.4 and 40 MBq. The rabbits were placed on their back under a Siemens ZLC gamma camera coupled to a scintiview computer. We used our routine scintigraphic procedure (Reimann et al. 1987). Counting was performed at time zero and 20–180 minutes after the injection. The regions of interest were placed over the injected knee and the contralateral subcutaneous depot and over the regional lymphatic vessels and lymph nodes. Count rates were corrected for background activity, cross over, and ^{99m}Tc-radioactive decay. The corrected count rates were expressed as a percentage of the initial values. The results of the investigations were based on direct visualization on the gamma-camera screen, and were estimated from the count rates using parametric statistics.

Table 1. Retained ^{99m}Tc-nanocoll in rabbit knees in normal, acute and chronic synovitis, and in subcutaneous tissue expressed as a percentage of the initial value. Mean *SD*

Time min	Knee normal		Subcutis		Knee acute		Subcutis		Knee chronic		Subcutis	
0	100		100		100		100		100		100	
20	100	*1*	97	*3*	99	*0*	95	*4*	97	*5*	101	*0*
40	100	*1*	99	*4*	97	*0*	95	*4*	97	*4*	100	*0*
60	99	*1*	100	*2*	95	*0*	96	*3*	97	*4*	98	*0*
90	98	*4*	98	*2*	94	*0*	96	*4*	95	*3*	98	*0*
120	98	*3*	96	*3*	93	*3*	95	*4*	92	*3*	99	*9*
180	95	*5*	95	*3*	87	*2*	95	*6*	86	*3*	97	*7*

Table 2. Retained ^{51}Cr-EDTA in rabbit knees in normal, acute and chronic synovitis, and in subcutaneous tissue expressed as a percentage of the initial value. Mean *SD*

Time min	Knee normal		Subcutis		Knee acute		Subcutis		Knee chronic		Subcutis	
0	100		100		100		100		100		100	
20	57	*14*	56	*15*	42	*12*	49	*17*	52	*12*	73	*4*
40	38	*9*	43	*13*	19	*8*	33	*15*	34	*11*	55	*4*
60	28	*6*	34	*10*	11	*6*	24	*12*	25	*9*	44	*6*
90	18	*3*	24	*6*	7	*2*	17	*9*	15	*5*	29	*5*
120	14	*4*	17	*4*	5	*1*	12	*7*	17	*3*	21	*5*
180	8	*5*	10	*2*	4	*2*	9	*4*	7	*1*	12	*3*

Results

The labeled colloid particles showed a decrease for 3 hours that was of the same magnitude in the subcutaneous tissue and normal knees (Table 1). A higher disappearance rate was found in acute and chronic synovitis. Because we could not determine whether or not the activity was within the joint cavity, we flushed some joints with isotonic saline. The count rates were about the same after this procedure, indicating that nearly all the activity in the joint was bound to the synovial membrane (Figure 1).

Figure 1. Autoradiograph of ^{99m}Tc-nanocoll distribution in a rabbit knee with acute synovitis. Observe that almost all the activity is located in the synovial membrane.

The diffusible tracer declined to about 10 percent in all the cases for 3 hours, but the initial decline was more rapid in acute synovitis (Table 2). A multiexponential analysis of the disappearance curves showed that the mean transit time in acute synovitis was reduced when compared with all the other groups.

Discussion

The present study supports our earlier findings that lymphatic transport from the knee is of little importance in the normal knee (Reimann et al. 1987, 1989). Within 3 hours, in both acute and chronic synovitis, 10–15 percent of intraarticularly injected radioactivity disappeared from the joint. Because we demonstrated earlier that less than 5 percent of the radioactivity will be retrieved in the regional lymph nodes, we assumed that the tracers were partly unstable in the joint. However, we found that after we flushed the joint cavity nearly all the radioactivity was located in the synovial membrane after 3 hours.

Because the albumin colloid has been shown to be stable in joint fluid (Reimann et al. 1989, Nielsen et al. 1990), it seems likely that the albumin colloid

is taken up in the lining cells by phagocytosis, and after being partially metabolized the colloid releases ^{99m}Tc either as an ion or in a low molecular diffusible form. In favor of the possibility that visualization of the regional lymphatic vessels and lymph nodes is due to leakage through the synovial membrane is that both acute and chronic synovitis have a higher rate of removal than normal knees. It has not been possible to investigate this phenomenon in chronic synovitis in humans, but use of subcutaneous tissue in the contralateral leg as a reference or control could possibly elucidate this aspect.

Removal of the diffusible tracer from the knee was increased in acute synovitis with hyperemia, and this has been previously demonstrated by using radioactive inert gases or radioactive microspheres (Dick et al. 1971, Christensen et al. 1982, Piepsz et al. 1982). Chronic synovitis showed the same disappearance curve for the diffusible tracer as the normal knee and subcutaneous tissue. The excess removal of colloid-bound radioactivity in the joint that was equal in both acute and chronic synovitis was most likely due to an increased surface area of the synovial membrane in synovitic knees, although an increased phagocytotic activity of the lining cells may be of some importance.

Acknowledgement

This investigation was supported by grants from The Danish Agricultural and Veterinary Research Council. Dr. Steen Bach Christensen kindly performed the autoradiographs of some rabbit knee joints.

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