Lubrication of synovial membrane

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Joint stiffness is a significant clinical manifestation of patients with arthritic disease. The articulating surface area of most joints is to a great extent synovial tissue. Cartilage-on-cartilage friction is extremely low and most of the resistance to joint motion is from the capsule, ligaments, tendons, and skin which 'ride' over the joint on synovium (Smith, 1956; Johns and Wright, 1962; Barnett and Cobbold, 1969). Although analyses have been made of the types and amounts of stiffness encountered with arthritis and age (Barnett and Cobbold, 1968; Wright, Dowson, and Longfield, 1969), there have been no studies of the lubrication mechanisms actually involved in synovium on synovium or synovium on cartilage motion.

Such studies might also be of great value in explaining the possible role of lubricant viscosity in joint function. Synovial fluid is characteristically viscous, but since this viscosity is not the primary

determining factor in cartilage-on-cartilage lubrication (McCutchen, 1962; Linn, 1968), it has been suggested that lubricant viscosity might well be playing a significant role in synovial tissue slipperiness (McCutchen, 1969). For these reasons an investigation of synovial membrane lubrication was undertaken and is reported here.

Method

Synovial tissue was obtained from the knee joints of healthy cows, aged 3 to 4 years. The knees were first inspected to insure freedom from arthritic change. Square pieces of synovium, about 3×3 cm., with their attached capsule, were cut, washed in isotonic buffer, placed synovial side down on a motor-driven polished glass slider, and attached to a force transducer (Statham Instruments, Inc., Los Angeles, California) by a thin silk thread (Figure). Cartilage rubbing on glass has frictional

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FIGURE Diagram of friction testing apparatus. The glass slider was driven under a weighted piece of synovium. Before each test, lubricant was spread along the glass plate. The frictional force was measured with a force transducer.

characteristics similar to those of cartilage rubbing on cartilage (McCutchen, 1962; Walker, Dowson, Longfield, and Wright, 1968). The use of a glass slider allowed the measurements of the frictional forces generated by synovial tissue to be made in the flat, rather than in a system confounded by an ever-changing geometry.

It is assumed that synovium is generally lightly loaded *in vivo*; therefore the synovial piece was, in these experiments, loaded with a 200 g. weight, 3 cm. in diameter. Isotonic veronate buffer, pH 7.2, was used as the standard lubricant to which all test lubricants were compared. Bovine synovial fluid obtained fresh and centrifuged to remove the cells was also friction-tested. A thin film of whatever lubricant was being tested was spread on the glass slider before each test run.

The drag between the synovial tissue and the glass slider, measured by the force transducer, was recorded on a paper chart recorder and expressed as a coefficient of friction by dividing the recorded frictional force by the load. The average of three repetitions of each test is reported. The experimental error was within ± 0.005 . Each of these sets of friction tests was preceded and followed with tests using standard buffer. The glass slider and synovium were thoroughly washed with buffer and then carefully patted dry with tissue before each change of lubricant.

We measured the normal bovine gait at about 30 steps per minute and approximated the cow's total knee flexion in gait at 60°. In an oscillating knee the tangential motion of a single point on a femoral condyle represents a sinusoidal oscillation with an amplitude of about 2.6 cm. Multiplying the amplitude by the oscillatory frequency gives a peak tangential velocity of about 4 cm./min. Friction tests were run at 2.5, 5, 7.5, and 10 cm./sec. at 37°C. The heat was supplied by heating lamps, controlled by a thermostat placed next to the slider.

A series of other fluids was also friction-tested and compared to synovial fluid and buffer. These were:

(1) Hyaluronate (M.W. 20 million) made from protein-free rooster coxcomb (Swann, 1969) diluted in veronate buffer to a concentration of 0.2 mg./ml.

(2) Hyaluronidase-digested synovial fluids and hyaluronate solutions [75 USP units/ml., 23°C. for 10 min. using HSEP Hyaluronidase, Worthington Biochemical Corp., Freehold, New Jersey], which because of this digestion have had their viscosities reduced to almost that of water.

(3) Bovine serum.

(4) A proprietary lightweight oil (22.5 centistokes) ['3-in-1 Oil', Boyle Midway Corp., New York, New York].

(5) Silicone fluid (200 centistokes) [Dow Corning Corp., Midland, Michigan].

In order to study the relationship between viscosity and lubricant effectiveness further, four synovial fluids of varying viscosities were friction-tested on the same piece of synovium.

Results

In the test system described, synovial fluid achieves coefficients of friction in the order of 0.04 to 0.05, about half those obtained with buffer. Hyaluronidase

digestion of these fluids destroys their lubricating advantage over buffer (Table I).

Table I Coefficients of friction with various lubricants (2.5 cm./sec., 37° C.)

Lubricant	Coefficient of friction		
	Experiment 1*	Experiment 2*	Experiment 3*
Synovial fluid	0.030	0.024	0.047
Hyaluronic acid	0.033	0.025	0.049
Hyaluronidase-treated synovial fluid	0.056	0.075	0.089
Hyaluronidase-treated hyaluronate	0.056	0.074	0.089
Veronate buffer	0.056	0.074	0.090
Lightweight oil	0.058	0.077	0.092
Serum	0.059	0.078	0.092

*A different piece of synovium and a different batch of serum and synovial fluid was used for each experiment. Values given represent an average of three measurements which were within ± 0.005 .

Serum and lightweight oil have effects equivalent to that of buffer. It is difficult but not impossible to wash hyaluronate and synovial fluid off the synovium. Lightweight oil and silicone fluid could not be washed off at all. For these reasons, lightweight oil was tested last in the lubricant series and silicone fluid was tested separately on three different pieces of synovium. Under these circumstances silicone fluid consistently gave coefficients of friction about three times higher than buffer.

Representative values of the relative viscosities and coefficients of friction obtained with the various lubricants tested on single pieces of synovium are listed in Table II. This was repeated with three different pieces of synovium with similar results. Relative viscosity in and of itself was not shown to be a significant factor in determining the coefficients of friction, since some fluids of varying viscosities lubricated well, whereas some fluids of similar viscosities did not.

Table II Effect of viscosity on soft-tissue lubrication (2.5 cm./sec., 37° C.)

Lubricant	Relative viscosity	Coefficient of friction*
Veronate buffer	1.0	0.056
Synovial fluid ¹	4.4	0.030
Synovial fluid ²	6.0	0.031
Synovial fluid ³	2.4	0.028
Synovial fluid ⁴	10.7	0.029
Hyaluronate	19.0	0.030

*Values given represent an average of three measurements which were within ± 0.005 .

The velocity of the glass slider had no effect on the friction values obtained. All data is reported for slider velocities of 2.5 cm./sec., a representative speed.

Discussion

The differences in coefficients of friction obtained with different pieces of synovium could be ascribed to unavoidable differences in the manner in which the thread attaching the synovium to the force transducer passed through the capsule attached to the synovium. For this reason all friction values should be considered relative rather than absolute.

The coefficients of friction obtained are, in general, one order of magnitude greater than those previously obtained in cartilage-on-glass (McCutchen, 1962) or cartilage-on-cartilage (Linn, 1968; Radin, Paul, and Pollock, 1970) systems. The reason for these higher friction values is in all probability related to the absence of the lubricating mechanisms which depend on the elasticity and 'weeping' characteristics of articular cartilage (McCutchen, 1959; Walker, Dowson, Longfield, and Wright, 1968). The other basic lubrication mechanism functioning in joints is a boundary one (Jones, 1934; Charnley, 1959) dependent on molecules in the lubricant binding to the articular surfaces. The moving surfaces are made to slip easily one over the other because they are kept separated by a bound molecular layer or layers. This would appear to be the phenomenon functioning in the synovium-on-glass system. Presumably the bound molecule in this system is hyaluronate. Hyaluronidase treatment of synovial fluid destroys this mechanism, and of the lubricant tests reported here only hyaluronate-containing solutions lubricated as efficiently as synovial fluid.

Potentiating the spread of lubricant would seem to be the primary contribution of synovial fluid's viscosity to the role of synovium as a soft-tissue lubricant. Relative viscosity is obviously important to soft-tissue lubrication in so far as it is a direct characteristic of the molecular weight and concentration of the lubricant's constituents. It is the boundary activity of hyaluronate that seems to be synovial fluid's primary lubricating contribution in synovial tissue lubrication. Viscous fluids lacking hyaluronate did not function efficiently, and the varying relative viscosity of the various hyaluronate-containing solutions tested (2.4 to 19.0) had no effect on their lubricating abilities. It may be, however, that under certain special circumstances truly viscosity-dependent (hydrodynamic) lubrication of synovium does occur, but with what is now known about physiological loads on synovium and joint velocities this is doubtful. Thus it would seem fruitless to attempt to mimic synovial fluid's lubricat-

ing effectiveness in soft-tissues merely by approximating the viscous characteristics of synovial fluid.

The extremely high coefficient of friction obtained with silicone oil, three times that obtained with buffer, may well be related to silicone fluid's very high viscosity (200 centistokes), which in and of itself probably increased the frictional force. This weight silicone fluid was chosen because it is the type being used in clinical trials of artificial lubricants (Helal and Karadi, 1968). Lightweight oil, of a much lower viscosity, was equivalent in effectiveness to buffer.

What then of joint stiffness? Is it possible that the soft-tissue lubricating mechanism is at fault? Changes have been reported in the molecular configuration of the hyaluronate polymers in pathological joint fluids (Sundblad, 1953; Bollet, 1956; Hamerman and Sandson, 1963; Barker, Bayyuk, Brimacombe, Hawkins, and Stacey, 1963; Stafford, Neidermeier, Holley, and Pigman, 1964; Balazs, Watson, Duff, and Roseman, 1967; Davies and Palfrey, 1968; Caygill and West, 1969; Ferguson, Boyle, and Nuki, 1969; and Vos and Theyse, 1969). However, it is difficult to explain the amelioration of the stiffness upon resumption of joint motion on lubrication mechanisms and the concept that it is due to synovial fluid 'gelling' is unlikely (Wright and others, 1970). We rather tend to support the view that the joint stiffness is due to oedema of the periarticular soft-tissues, which is 'milked' out of these structures with motion. This is supported by the observation that the hand volume of rheumatoid patients, who are most plagued by 'morning stiffness', is circadian (Wright and others, 1969). Further studies are in process.

Summary

The coefficient of friction of bovine synovial tissue on a motor-driven glass slider was measured. Synovial fluid and high molecular weight protein-free rooster cox comb hyaluronate were found to lubricate about twice as well as buffer, but with coefficients of friction one order of magnitude higher than obtained in cartilage systems. Hyaluronidase digestion completely obliterated the lubricating advantages of these fluids. Hyaluronate appeared to be lubricating synovium as a boundary lubricant. The possible relationship of these findings to the joint stiffness associated with arthritic conditions is discussed.

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