

Connective Tissue and Immobilization

Key Factors in Musculoskeletal Degeneration?

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Periarticular connective tissue is one important part of the musculoskeletal system. Its unique ability to adapt to the shortest distance between its origin and insertion, however, produces harmful effects during immobilization. All situations that lead to immobilization can cause some degree of degenerative change in the musculoskeletal system. When immobilization, whatever its cause, cannot be avoided, every attempt should be made to minimize it and to try to treat its harmful effects. There is some evidence that early mobilization, traction, and continuous passive motion overcome the harmful effects of immobilization, but more knowledge on this subject is needed. Animal experiments play an important role in the attainment of knowledge of immobilization and mobilization processes in health and disease.

One of the major sources of human functional limitation is osteoarthritis (arthrosis); however, the information available as to the cause or prevention of this condition is deficient. It has been claimed that osteoarthritis is not one disease, but an end condition of many diseases.⁸ More information is needed about (1) the etiologic factors involved (although sometimes injuries or inflammatory processes can be identified as causes), (2) the pathogenic chain of events (what changes in which tissue are important, what appears first, *etc.*), and (3) at the very least, relevant

methods to evaluate the degree of the condition. The status of the periarticular tissues must be important.

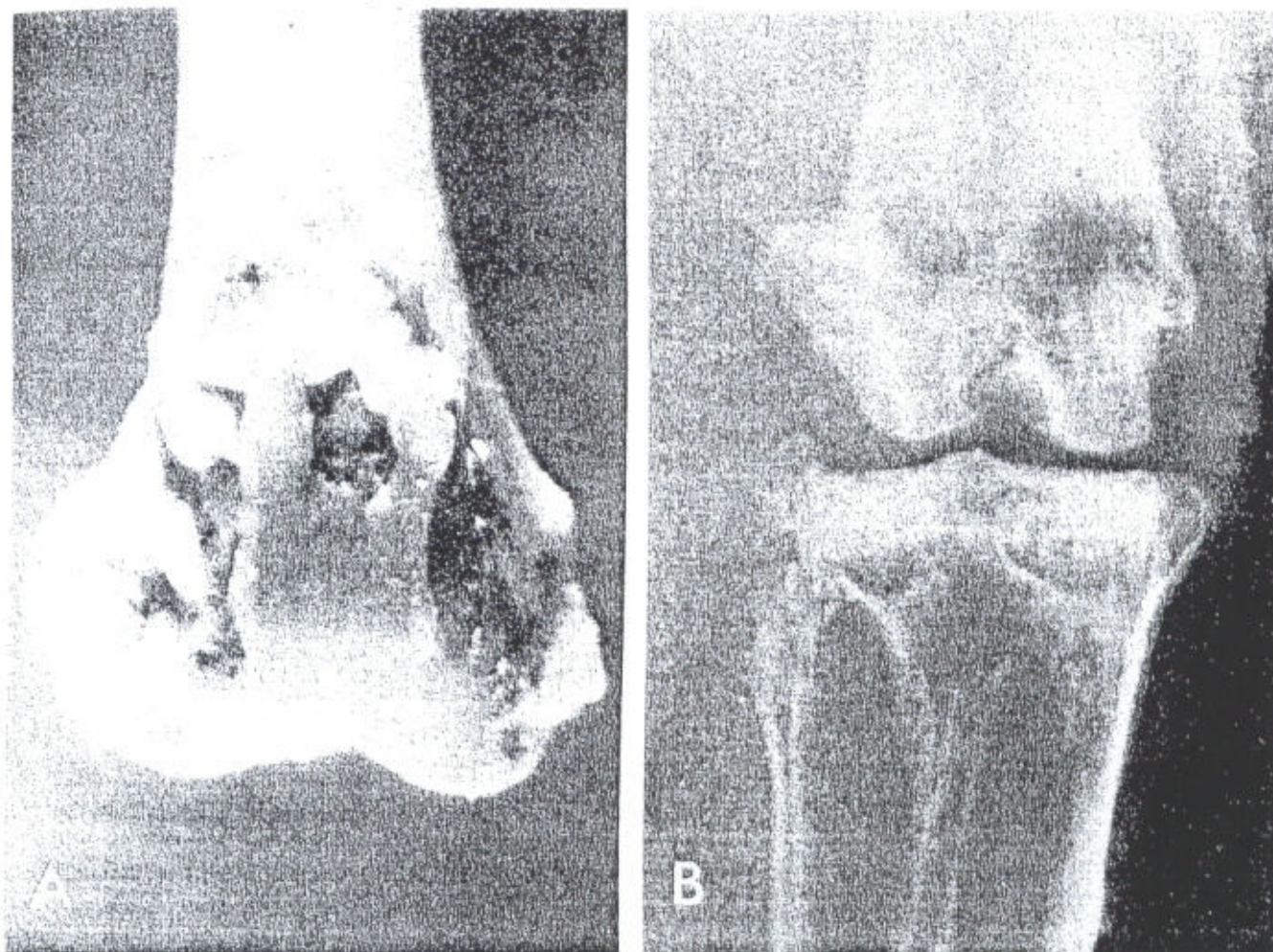
The shrinking of scar tissue is a common phenomenon that is not fully understood, but can be related to collagen fiber orientation and its interaction with altered glycosaminoglycans. The amount of shrinkage is determined by the shortest distance between the insertions of the structure in question. This phenomenon is important and is useful for ensuring the stability and proper function of the dynamic musculoskeletal system. During immobilization, connective tissue reacts principally in the same way. It adapts to the shortened functional distance between the capsular origin and insertion; *i.e.*, the capsule becomes tight.

Much is known about cartilage and joint structures, but that knowledge has not been useful in everyday medical practice. This state of affairs is understandable because structural changes are end results after metabolic and functional disturbances and the morphology does not reflect the acute situation. There is increasing interest, however, in developing sensitive methods for evaluating function. Such interest has been supported by many animal experiments and also reflects the importance of soft tissues (capsules, ligaments, fascias and muscles) in the pathogenesis of bone and joint diseases.^{5,10} The objective of this presentation is to review briefly the results of some basic experimental studies on this subject.

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FIGS. 1A AND 1B. (A) Macroscopic picture of the distal end of the femur; the soft periarticular tissues have been removed to show the unusual bone and cartilage formation after periodic immobilization. (B) Roentgenogram of rabbit knee that was immobilized for one week at four different times; moderate osteoarthritic changes can be seen.

EXPERIMENTAL EVIDENCE

Immobilization of the knee in extension has been used as an experimental method to produce irreversible, progressive osteoarthritic joint changes (Fig. 1). The compression between articular surfaces increases in the immobilized knee and reaches a level three times greater than the initial level after four weeks of immobilization. Thereafter it decreases to below the initial level (Fig. 2).⁹ The increase is accompanied by shrinkage of periarticular soft tissues and a marked increase in the synthesis rate of collagen² and glycosaminoglycans¹ (Figs. 3 and 4). The manifold increase in synthesis rates can also

be seen in the increased contents of fibrous tissue in the histologic pictures (Fig. 5). Increased fibrosis of periarticular tissues, cartilage proliferation at joint edges, atrophy in weight-bearing areas, and regional bony eburnation, sclerosis, and resorption can be found after two weeks of immobilization. In general, these changes are irreversible.³ Many of them have been labeled as diagnostic findings for specific joint diseases, even though they are actually the result of immobilization.

In addition, periodic short-term immobilization has harmful joint effects that are cumulative.¹⁰ Periodic immobilization over more than 30 days leads to progressive os-

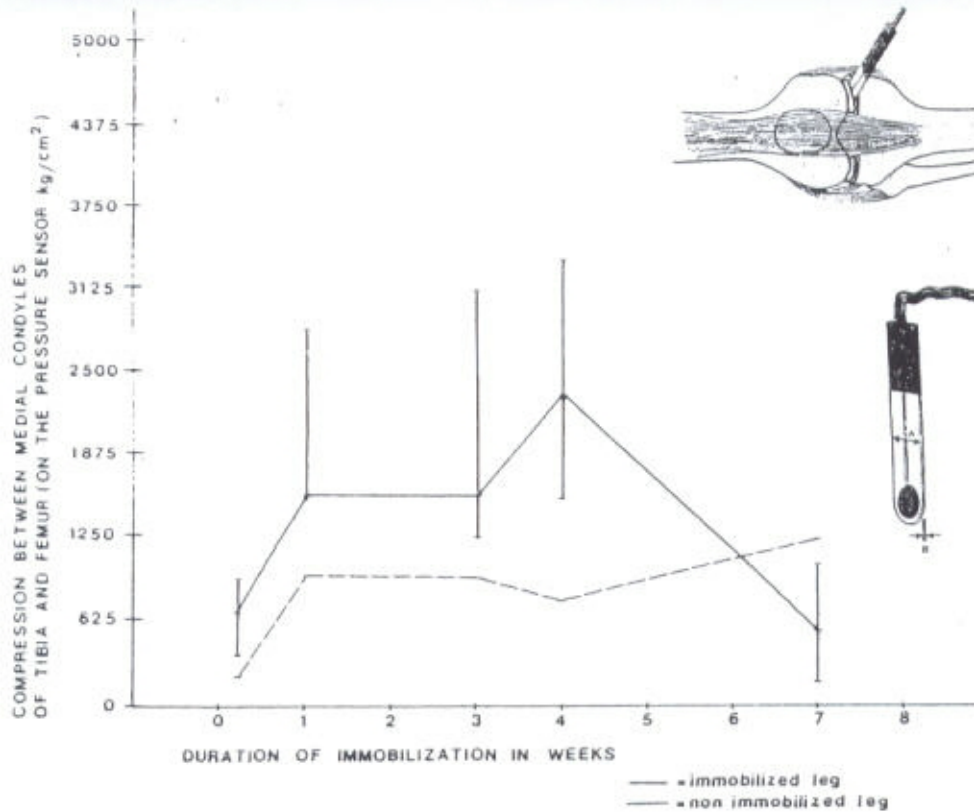


FIG. 2. Compression between the medial condyles of the tibia and femur during seven weeks of immobilization.⁹ The measured forces on the subminiature pressure sensor (technique shown in the right upper corner; $A = 7.3$ mm, $B = 0.6$ mm) had increased threefold in the immobilized knee after four weeks but had also increased slightly in the nonimmobilized knee. After seven weeks of immobilization, the compression was less in the immobilized knee than in the contralateral side (median \pm upper and lower quartiles).

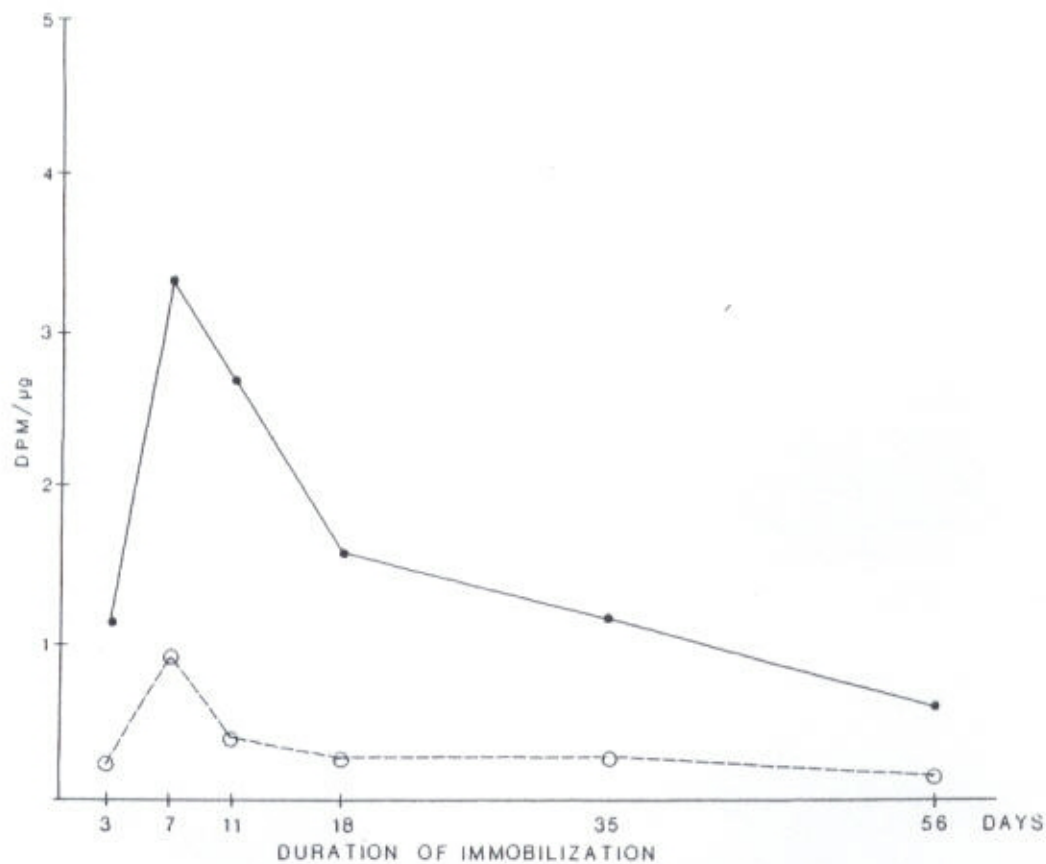
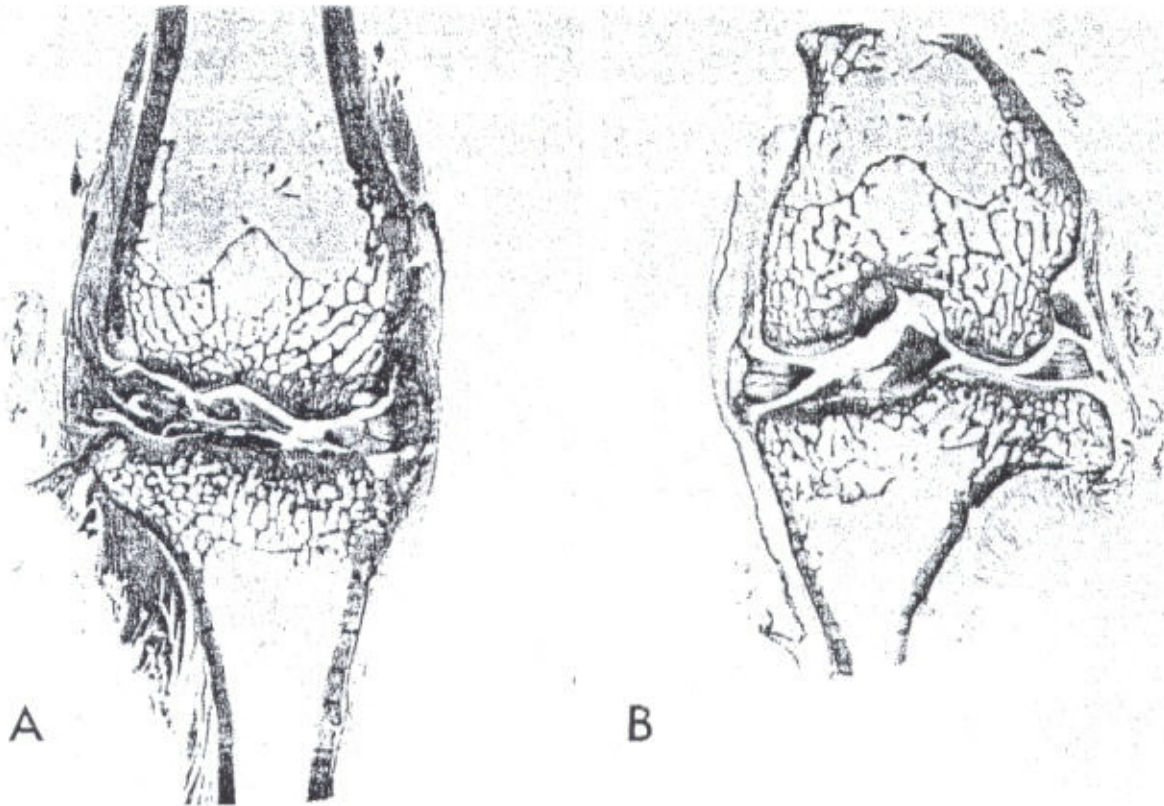
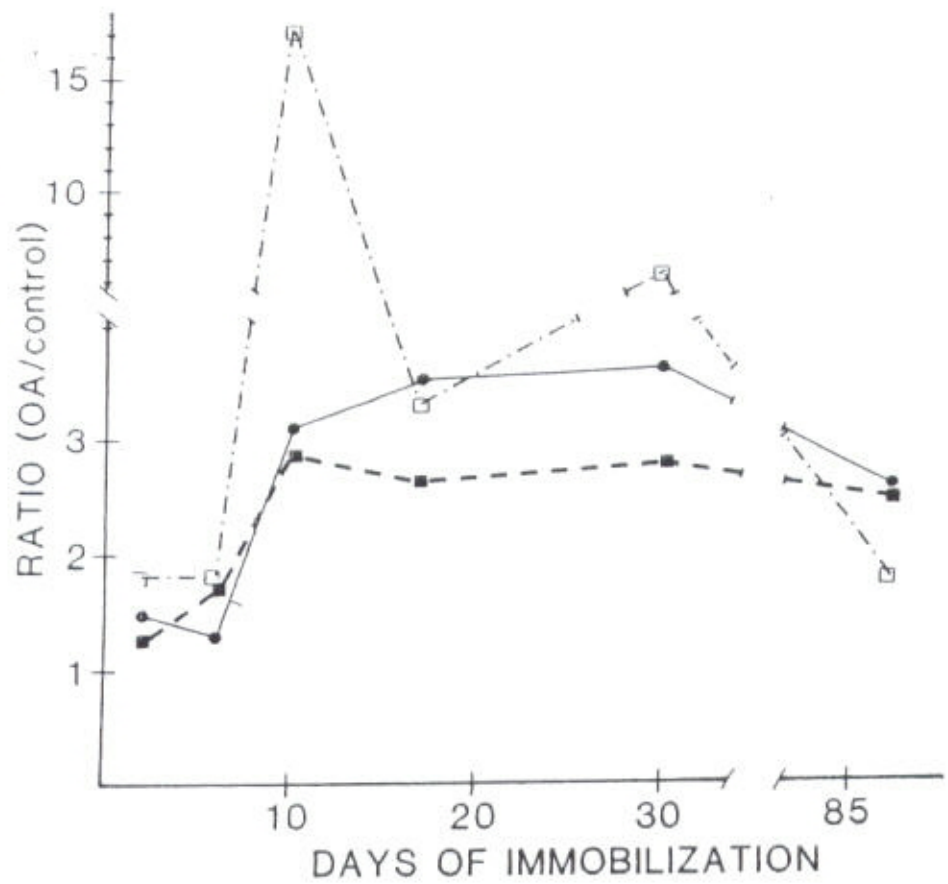
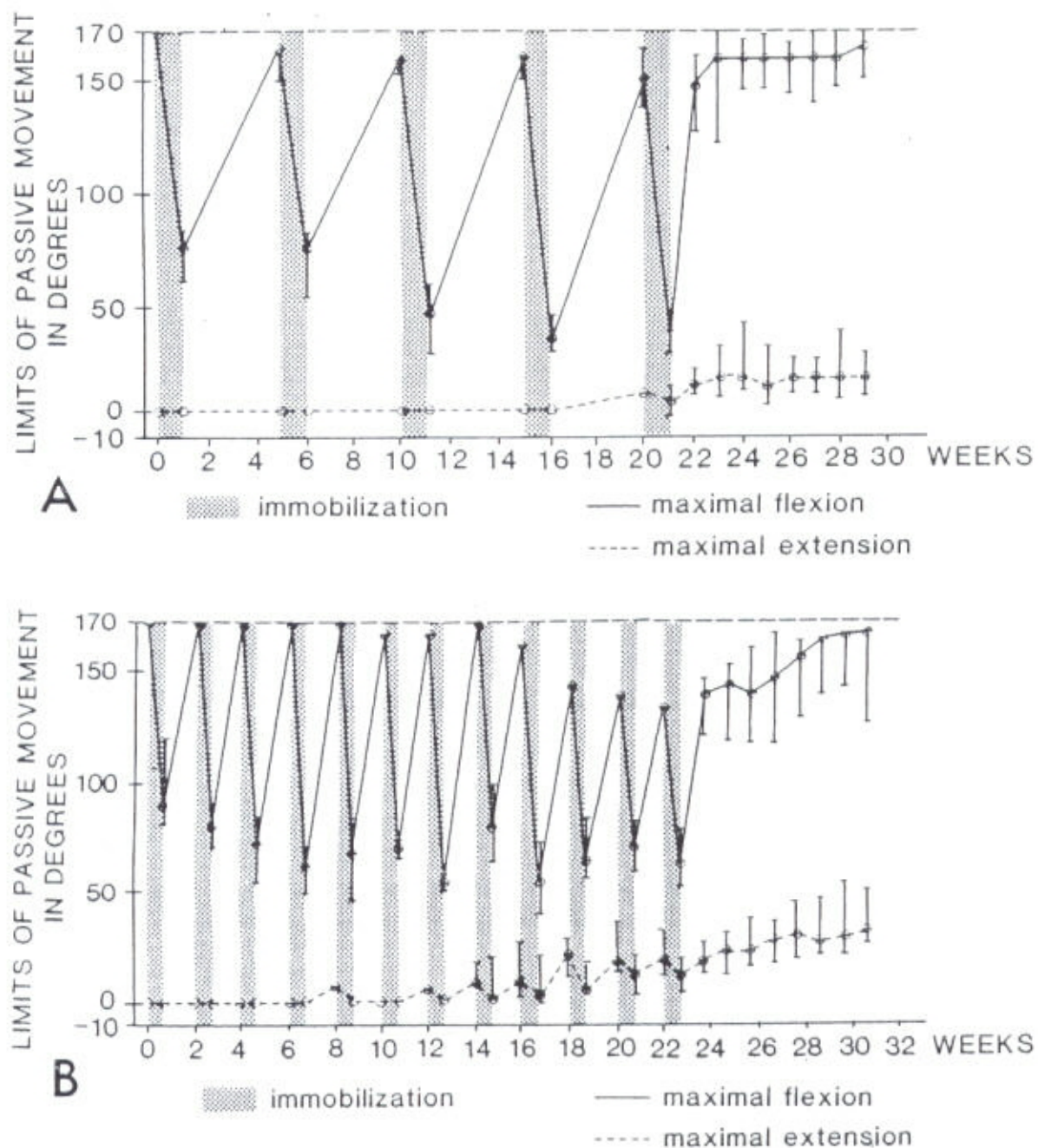


FIG. 3. Specific radioactivity of hydroxyproline (indicator for collagen synthesis rate) in the medial collateral ligament of the knee. Median curves for immobilized (●) and nonimmobilized (○) legs ($p < 0.005$).

FIG. 4. Glycosaminoglycan metabolism parameters of medial collateral ligament. Means of the immobilized/contralateral knee as a function of immobilization time. (\square = specific ^{35}S -sulphate activity, indicator for synthesis rate; \blacksquare = hexosamine concentration; \bullet = uronic acid concentration.) (Modified and reproduced with permission from Videman, T., Eronen, I., Friman, C., and Langenskiöld, A.: Glycosaminoglycan metabolism of the medial meniscus, the medial collateral ligament, and the hip joint capsule caused by immobilization of the rabbit knee. *Acta Orthop. Scand.* 50:467, 1979, Fig. 2.)¹²



FIGS. 5A AND 5B. Histologic sections of rabbit knee in the frontal plane. (A) The knee immobilized for four weeks and (B) the contralateral knee. Note the thickened capsule and the marked variation of articular cartilage in the immobilized knee.

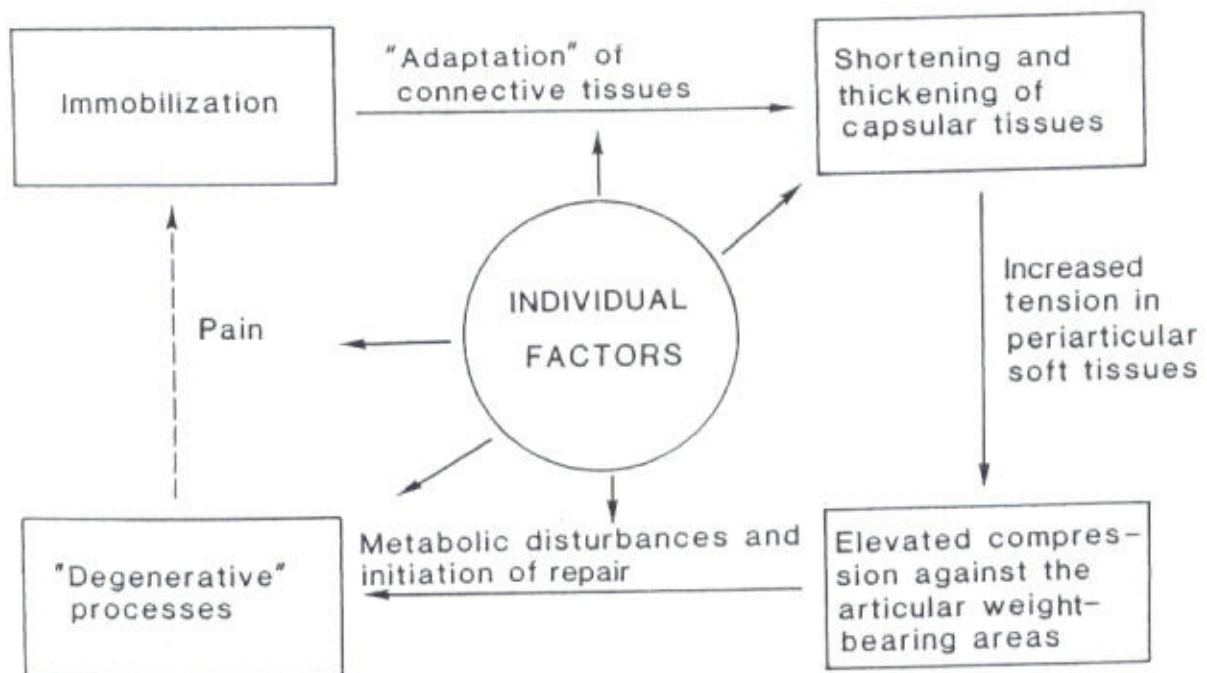
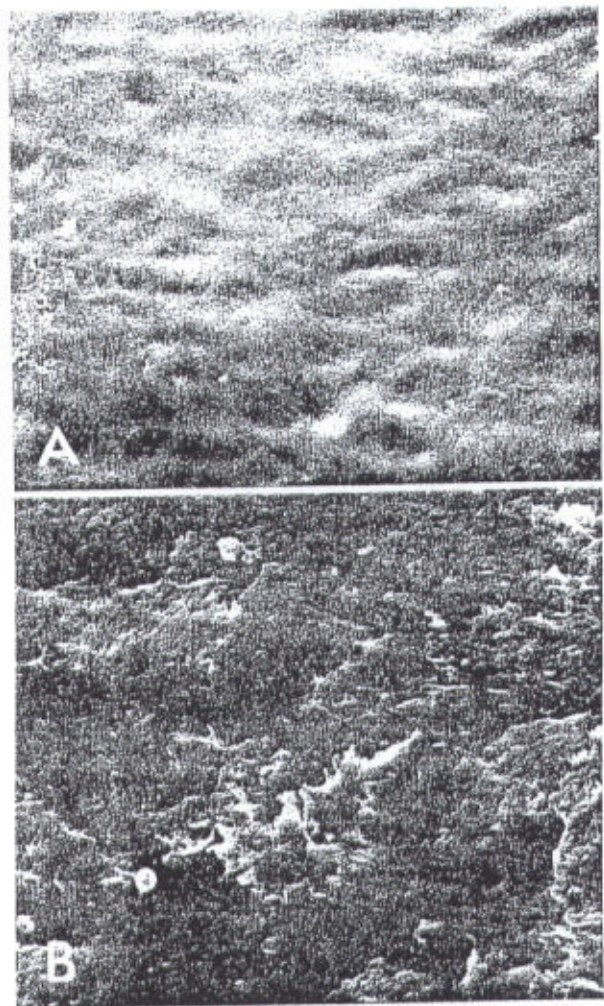


FIGS. 6A AND 6B. (A) Development of limits of passive mobility in rabbits immobilized for one week, five times at four-week intervals and (B) limits of mobility in rabbits immobilized for four days, 12 times at ten-day intervals. The curves are drawn according to the medians, and the distribution symbols are upper and lower quartiles. (Modified and reproduced with permission from Videman, T.: Experimental osteoarthritis in the rabbit. Comparison of different periods of repeated immobilization. *Acta Orthop. Scand.* 53:314, 1982, Fig. 4.)¹⁰

teoarthritis. The range of motion after periodic immobilization depends more on the total immobilization time than on the duration of either the immobilization or mobilization periods (Fig. 6). Even an immobiliza-

tion period of four days has a cumulative effect in producing osteoarthritis, and an interval of four weeks between immobilization periods does not prevent osteoarthritis from developing.

FIG. 7. Scanning electron micrographs of the articular cartilage of the medial tibial condyle. (A) "Normal" rabbits living in a cage and (B) rabbits that have been running uphill for five days. (Original magnification, $\times 500$.) (Modified and reproduced with permission from Videman, T., Eronen, I., and Candolin, C.: Effects of motion load changes on tendon tissues and articular cartilage. A biochemical and scanning electron microscopic study on rabbits. Scand. J. Work Environ. Health [Suppl. 3] 5:59, 1979, Fig. 2.)¹¹



HYPOTHESIS:

Immobilization, for any reason, initiates this pathogenetic chain of musculoskeletal degeneration

FIG. 8. Hypothesis for the role of periarticular soft tissues in joint degeneration.

Incomplete immobilization causes changes in the joint capsule, including an increase in the synthesis rate of glycosaminoglycans.¹⁴ After the same period of standardized immobilization, the restriction of motion and the degree of degeneration varies markedly between animals. These differences, like the variation seen in metabolism, might be due to individual factors.

Conversely, a sudden increase in running load produces "degenerative" changes in the surface structures of joints, at least temporarily.¹³ This phenomenon has been shown in rabbit knee joints by scanning electron microscopy after five-day periods of treadmill running¹¹ (Fig. 7). It has been impossible, however, to produce osteoarthritic joint changes in prolonged running experiments,⁴ probably because of the adaptation phenomenon and possible limiting factors (for example, cardiovascular characteristics) which, to some extent, prevent overuse.

Degenerative changes during immobilization can be partly inhibited by traction^{13,15} or continuous passive motion.^{6,7}

SPECULATIONS

Pain often causes involuntary joint immobilization in patients and even interferes with attempts to overcome the effects of immobilization. The ultimate result can be disuse of the musculoskeletal system and the possible beginning of a vicious cycle (Fig. 8). Certainly this hypothesis addresses only one possible mechanism for the development of osteoarthritis.

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