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EXPERIMENTAL OSTEOARTHRITIS IN THE RABBIT

Comparison of Different Periods of Repeated Immobilization

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The objective of this study was to compare the degree of osteoarthritis caused by different periods of repeated immobilization and mobilization. Existing knowledge of the pathogenic factors causing osteoarthritis is deficient, but it is well known that long-term immobilization produces degenerative joint changes. In this experimental study it is shown that short repetitive periods of immobilization also induce osteoarthritis. The results can be summarized as follows: immobilization, periodic or continuous, over more than 30 days will lead to progressive osteoarthritis. 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. Even an immobilization period of 4 days had a cumulative effect in producing osteoarthritis. An interval of 4 weeks between immobilization periods did not prevent immobilization from causing osteoarthritis. It can be assumed that all situations which lead to the immobilization of a joint can cause osteoarthritic changes. Radiology, photography, and histology all showed some degree of degenerative changes also in the contralateral non-immobilized knee.

Key words: animal experiments; immobilization; knee; osteoarthritis

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The long-term immobilization of a joint causes degenerative articular changes similar to those seen in human osteoarthritis (OA) (Ely & Mensor 1933, Evans et al. 1960, Field & Hueston 1970, Finsterbush & Friedman 1973, 1975, Hall 1963, 1964, Langenskiöld et al. 1979, Salter & Field 1960, Sood 1971, Thaxter et al. 1965, Trias 1961). Although it is not fully understood why immobilization produces OA changes, there is evidence that capsular thickening and shortening (Videman et al. 1979, Videman & Michelsson 1977, Videman et al. 1977) and muscle contraction (Evans et al. 1960, Thaxter et al. 1965) increase compression on articular cartilage and thus cause cartilage damage and other OA changes.

The continuous immobilization of a rabbit knee in extension for a period of 7 weeks or more results in marked contracture of the joint with severe OA changes. In addition a continuous immobilization for 4 to 6 weeks produces progressive OA in the knee, but with only slightly diminished mobility (Langenskiöld et al. 1979). Although short repetitive periods of immobilization are more common in man than long-term immobilization, the importance of such periods has not been studied extensively. The purpose of this investigation was to compare the effect of different lengths of immobilization on the production of osteoarthritic changes in the rabbit knee.

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MATERIAL AND METHODS

The experimental series consisted of 79 nine-month-old rabbits of the Californian strain. The method used to immobilize the rabbits was a modification of a published technique (Langenskiöld et al. 1979). An individually shaped Orthoplast® splint was applied on the dorsal aspect of the right leg from the proximal end of the thigh to the distal end of the limb. The splint was attached to the limb by three to six turns of a Tensoplast® bandage (Figure 1). The animals were divided into four periodically immobilized groups and two control groups, immobilized continuously (Table 1 and Figure 2).

The mobility measurements were made with a goniometer before the application of the splint, after its removal, and regularly once a week during the follow-up period. The fully extended position was recorded as 0°, and full flexion as 170°. Hypertension was expressed with negative numbers.

Both knees were radiographed in a postero-anterior projection when the splint was removed, after 7 to 8 weeks of follow-up, and, if the follow-up was longer, after the rabbits were killed. In addition lateral views were taken of the dead rabbits. The osteoarthritic changes were estimated from radiographs by two workers independently using the following scale: nor-

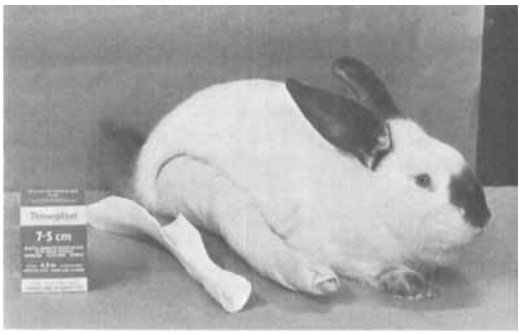

Figure 1. The immobilization method used. A rabbit with the right hind limb immobilized with the knee in extension and showing the individually shaped splint and the bandage.

Figure 2. Graphic representation of the 79 rabbits divided into six groups with different immobilization periods. The code number of the groups is explained in Table 1.

Table 1. Effects of immobilization

Type of immobilization		Total length of immobilization (days)	Total mobility* (median)	Remarks
Periodic immobilization				
1) 2) 3)				
Group 4- 7- 7	(n = 18)	28	160°	Some restriction of both
Group 5- 7-28	(n = 16)	35	150°	flexion and extension
Group 4-10- 4	(n = 12)	40	147.5°	Restriction of flexion
Group 12- 4-10	(n = 12)	48	138°	Restriction of extension
Continuous immobilization				
Group 35	(n = 12)	35	140°	Restriction of extension
Group 49	(n = 9)	49	68.5°	Restriction of flexion

* Eight weeks after the last immobilization period
1) Number of immobilization periods
2) Length of immobilization period in days
3) Length of the period between each immobilization in days
n = number of rabbits

mal, slight OA, moderate OA, and severe OA (Figure 8 a–d and Figure 9, Videman et al. 1977).

Macroscopic appearance was recorded for 22 rabbits by photography. Before the photography the soft tissues were carefully removed from the distal ends of the femurs and the proximal ends of the tibiae. Two workers independently assessed the photographs of the tibia and femur using the following scale: normal = 0, slight changes = 1, moderate changes = 2, and severe degenerative changes = 3. Histological sections were made of both knees of 20 rabbits with a routine histological method. This method has been described in detail earlier (Langenskiöld et al. 1979).

RESULTS

Mobility of the knee. The development of changes in mobility in group 4-7-7 is presented in Figure 3. As the number of immobilization periods increased, the mobility of the knee decreased. Three weeks after the last immobilization period mobility had reached a "steady state", the median of the flexion and extension angles being 165 and 5°, respectively.

In group 12-4-10 the first signs of restricted mobility were visible after seven to ten 4-day periods of immobilization. After the last immobilization period the median angle of flexion was 72.5°, and that of extension 5.5°; at the end of the follow-up period the corresponding medians were 165 and 26.5°, respectively (Figure 4).

The restriction of mobility in group 5-7-28 developed in the same manner as in group 4-7-7 (Figure 4). After the last period of mobilization the medians of the flexion and extension angles were 32.5 and 2.5°, respectively, and after 8 weeks of follow-up the corresponding values were 165 and 15°, respectively.

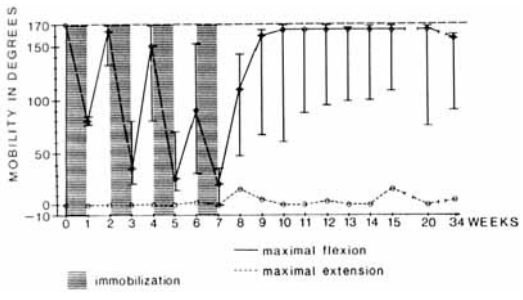

Figure 3. Development of mobility in group 4-7-7. The curves are drawn according to the medians, and the distribution symbols are upper and lower quartiles.

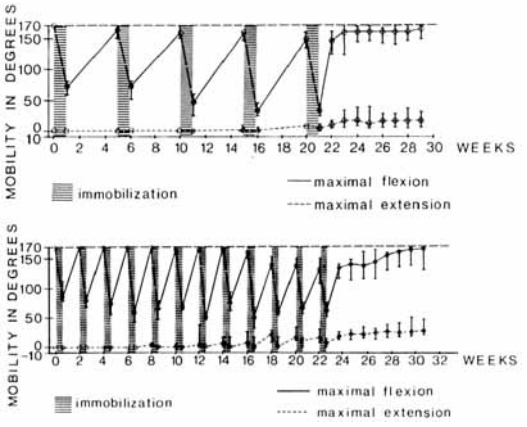

Figure 4. Development of mobility in group 5-7-28 (upper picture) and group 12-4-10 (lower picture). Medians and upper and lower quartiles.

The development of changes in flexion and extension in group 4-10-4 was generally the same as in the other three groups, but the most distinct restriction of motion was seen in this group. At the end of the last immobilization period the median angle of flexion was 20°, while full extension (= 0) was achieved. In this group there was no restriction of extension during the entire experiment, but the restriction of flexion remained marked even during the follow-up (Figure 5).

Recovery after continuous immobilization clearly depended on the duration of the immobilization period. After 5 weeks the median angle of flexion was 53°, and that of extension –3°; after 7.5 weeks of follow-up in this group the corresponding values were 162.5 and 22.5°, respectively (Figure 6). After 7 weeks of immobili-

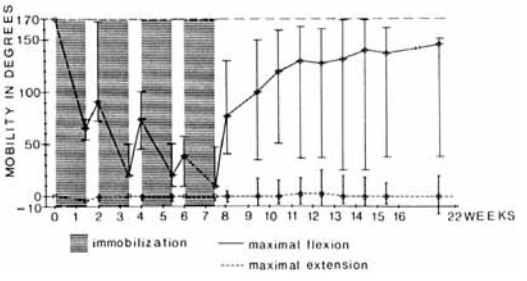

Figure 5. Development of mobility in group 4-10-4. Medians and upper and lower quartiles.

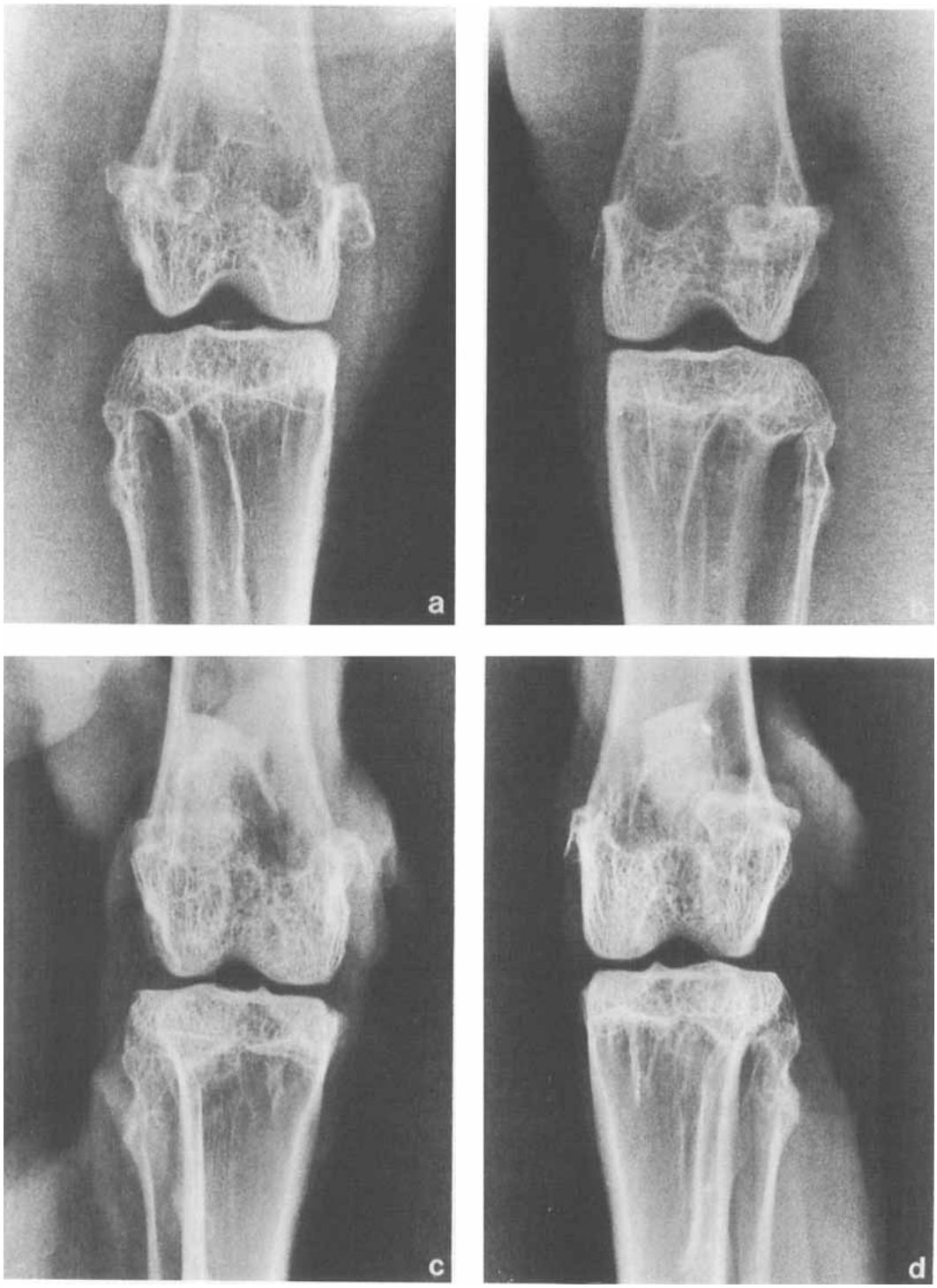

Figure 8. Radiographs of rabbit knees in group 35. Situation at the end of immobilization. a) Immobilized knee with slight osteoarthritic changes; b) Contralateral, normal knee. Situation after 8 weeks of follow-up of the same rabbit. c) Immobilized knee with moderate changes; and d) Contralateral knee with slight degenerative changes.

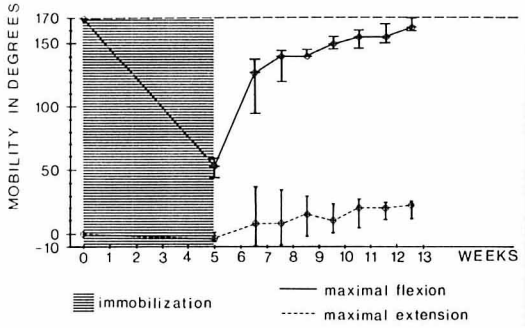

Figure 6. Development of mobility in group 35. Medians and upper and lower quartiles.

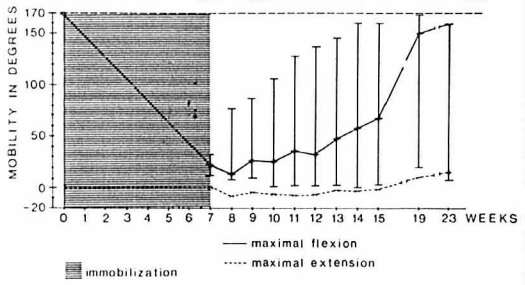

Figure 7. Development of mobility in group 49. Medians and upper and lower quartiles.

Figure 9. Radiograph of a rabbit knee in group 5-7-28. The situation at the end of follow-up showing severe osteoarthritic changes in the knee joint.

zation, the medians of the flexion and extension angles were 21.5 and 0°, respectively, and after 8 weeks of follow-up a restriction of flexion was still evident (flexion angle 67°, extension angle –1.5°) (Figure 7). After continuous immobilization the development of mobility did not reach a "steady state" during 8 weeks of follow-up.

The results of the different immobilization periods can be summarized as follows: Mobility decreased as the total length of immobilization increased, and the type of restriction varied according to the type of immobilization.

Radiological assessments. The radiological results are presented in Figures 8–10. They show that the osteoarthritic changes progressed during the follow-up period. The stage of OA correlated with the total duration of immobilization and the length of the intervals between the immobilization periods. The same type of slight changes also occurred on the contralateral non-immobilized side. To summarize, OA was assessed as slight at the end of immobilization and as moderate after 8 weeks of follow-up.

Gross appearance. The assessments from the photographs of the femur and tibia are presented in Figures 11–13. The degenerative changes were the most marked in group 5-7-28 and the least noticeable in group 4-7-7. No correlation was found between macroscopic appearance and the total duration of immobilization combined with the length of follow-up. The OA changes found in the non-immobilized knee were nearer "normal" than "slight".

Histological findings. No clear differences in the histological picture were found between the groups. A thickening of the joint capsule and the collateral ligaments was evident in all the groups.

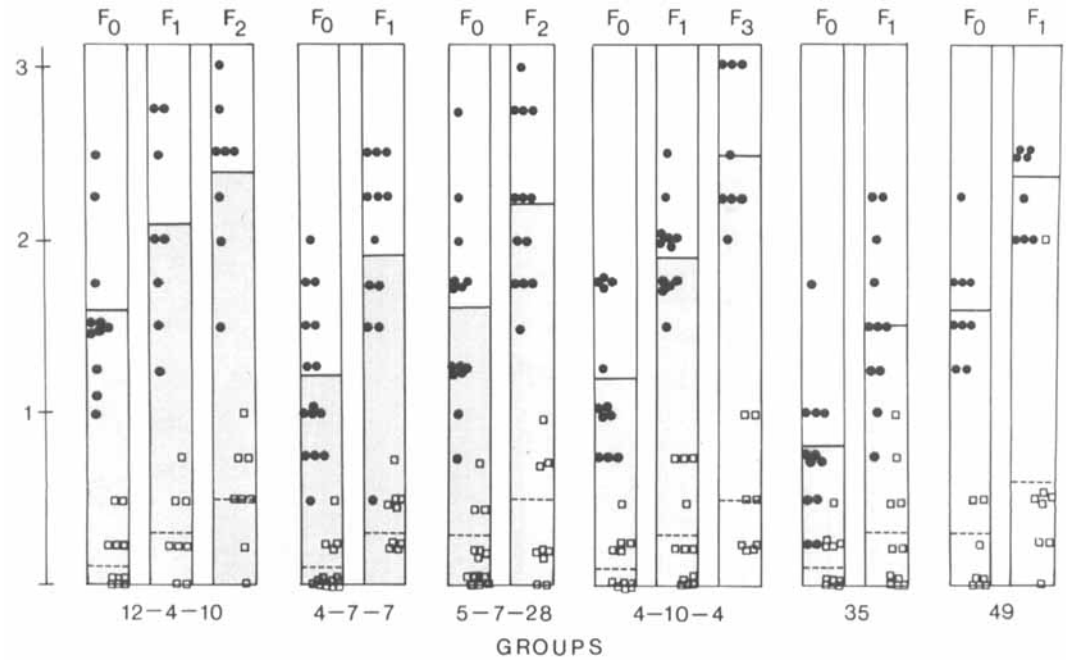

Figure 10. Assessment of the osteoarthritic changes found in radiographs of the different immobilization groups. 1 = slight OA, 2 = moderate OA, and 3 = severe OA, F_0 = at the end of immobilization, F_2 = after 8 weeks of follow-up, F_2 = after 22 weeks of follow-up, F_3 = after 32 weeks of follow-up. Solid lines indicate the means and ● symbols the assessments of the immobilized leg. The dotted lines are means and □ symbols the assessments of the non-immobilized knee.

Fibrillation, irregular proliferation, variation in thickness and regional disappearance of articular cartilage were also seen in most of the histological sections taken from the immobilized knees.

Cysts and sclerosis were found regularly in the subcortical areas of the bone. Osteophytes were common in the immobilized knees, except in group 4-7-7, and in some sections eburnation and osteoporosis were also seen.

In the contralateral non-immobilized knee a thickening of the joint capsule, fibrillation, clefts in the articular cartilage, and also small

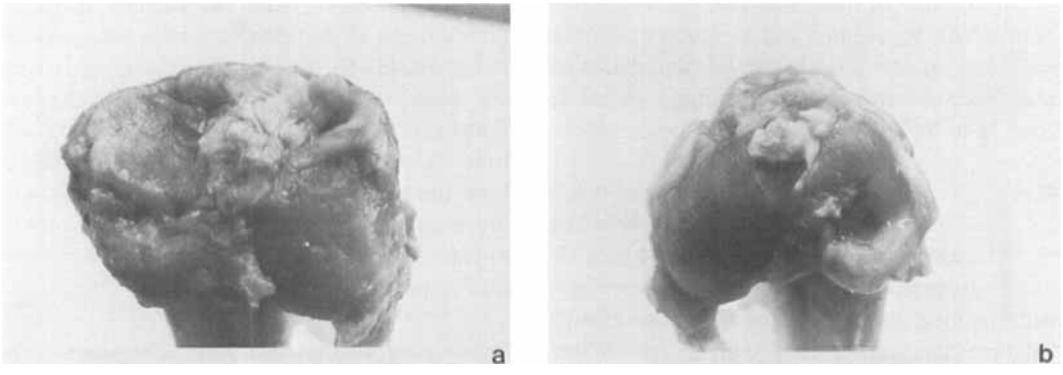

Figure 11. Photographs of the proximal ends of both tibia of a rabbit in group 4-10-4. On the immobilized side (a) the degenerative changes are moderate to severe, and the changes in the contralateral non-immobilized knee (b) are assessed as slight.

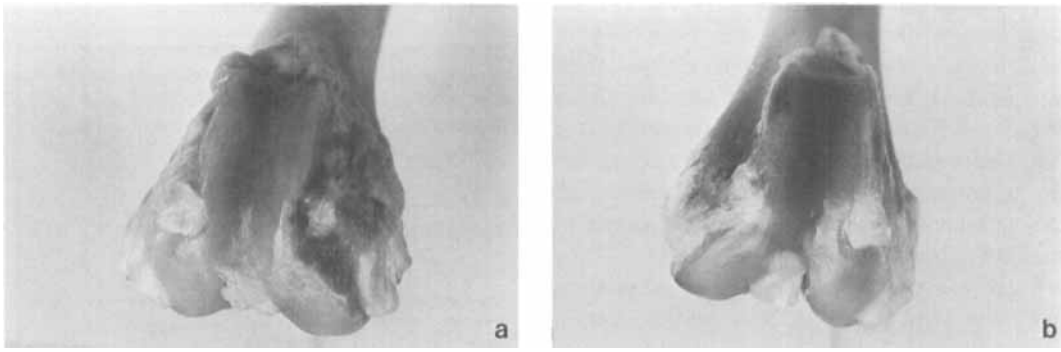

Figure 12. Photographs of the distal ends of both femora of a rabbit in group 35. The immobilized knee (a) shows slight to moderate degenerative changes and the contralateral side (b) is normal.

osteophytes were sometimes found. When compared with the immobilized leg, the changes were, however, slight.

DISCUSSION

Existing knowledge of the pathogenic factors producing OA is deficient. The importance of immobilization on the pathogenic chain has already been pointed out (Langenskiöld et al.

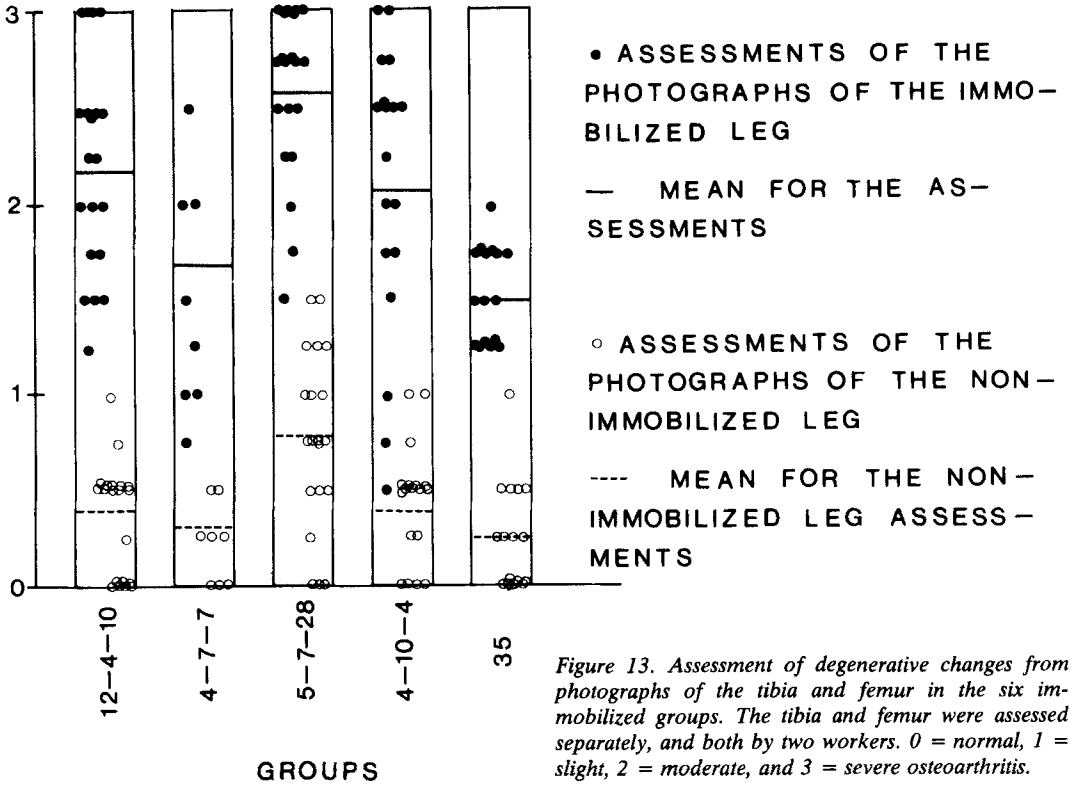

Figure 13. Assessment of degenerative changes from photographs of the tibia and femur in the six immobilized groups. The tibia and femur were assessed separately, and both by two workers. 0 = normal, 1 = slight, 2 = moderate, and 3 = severe osteoarthritis.

1979, Videman & Michelsson 1977). On the basis of experimental results and clinical experience, it can be assumed that all conditions which lead to the immobilization of a joint can cause disturbances in the articular cartilage and lead to OA. Such conditions in human life are, for example, traumata and inflammatory processes, both of which are commonly followed by periods of immobilization of various lengths.

There was a wide variation in the assessments and measurements of mobility despite careful control of the efficiency of splintage. The explanation for this variation must be partly due to differences between the rabbits. There was a comparably wide variation in biochemical changes resulting from immobilization (Eronen et al. 1978, Videman et al. 1979).

After immobilization in the present study, mobility increased although the radiographic stage of OA progressed, and the significance of both of these methods for estimating the degree of disease should be re-evaluated.

In this experiment, 4-day immobilization periods had a cumulative effect in producing OA. On the other hand, a mobilization period of 28 days did not prevent the effect of immobilization, but it seems that when the total duration of immobilization (either continuous or periodic) exceeds 30 to 40 days, progressive OA occurs in the rabbit knee.

In earlier biochemical studies (Eronen et al. 1978, Videman et al. 1979), changes were also found in the contralateral non-immobilized leg. In the present study the macroscopic appearance and radiographic OA grade also indicated small degenerative changes in the non-immobilized leg. Whether local mechanical stress from moving around on three legs or humoral factors were responsible remains to be determined.

We suggest that periodic immobilization provides a useful, non-traumatic method for studies on therapy and the pathogenesis of developing osteoarthritis.

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REFERENCES

Ely, L. W. & Mensor, M. C. (1933) Studies of the immobilization of normal joints. *Surg. Gynecol. Obstet.* **57**, 212–215.

Eronen, I., Videman, T., Friman, C. & Michelsson, J.-E. (1978) Glycosaminoglycan metabolism in experimental osteoarthrosis caused by immobilization. *Acta Orthop. Scand.* **49**, 329–334.

Evans, E. B., Eggers, G. W. N., Bulter, J. K. & Blumel, J. (1960) Experimental immobilization and remobilization of rat knee joints. *J. Bone Joint Surg.* **42**-A, 737–758.

Field, P. L. & Hueston, J. T. (1970) Articular cartilage loss in longstanding immobilization of interphalangeal joints. *Br. J. Plast. Surg.* **23**, 186–191.

Finsterbush, A. & Friedman, B. (1973) Early changes in immobilized rabbits knee joints: A light and electron microscopic study. *Clin. Orthop.* **92**, 305–319.

Finsterbush, A. & Friedman, B. (1975) Reversibility of joint changes produced by immobilization in rabbits. *Clin. Orthop.* **111**, 290–298.

Hall, M. C. (1963) Cartilage changes after experimental immobilization of the knee joint of the young rat. *J. Bone Joint Surg.* **45**-A, 36–44.

Hall, M. C. (1964) Articular changes in the knee of the adult rat after prolonged immobilization in extension. *Clin. Orthop.* **34**, 184–195.

Langenskiöld, A., Michelsson, J.-E. & Videman, T. (1979) Osteoarthritis of the knee in rabbits produced by immobilization: Attempts to achieve a reproducible model for studies on pathogenesis and therapy. *Acta Orthop. Scand.* **50**, 1–14.

Salter, R. B. & Field, P. (1960) The effect of continuous compression on living articular cartilage: An experimental investigation. *J. Bone Joint Surg.* **42**-A, 31–49.

Sood, S. C. (1971) A study of the effects of experimental immobilization on rabbit articular cartilage. *J. Anat. (Lond.)* **108**, 497–507.

Thaxter, T. H., Mann, R. A. & Anderson, C. E. (1965) Degeneration of immobilized knee joints in rats: Histological and autoradiographic study. *J. Bone Joint Surg.* **47**-A, 567–585.

Trias, A. (1961) Effects of persistent pressure on the articular cartilage: An experimental study. *J. Bone Joint Surg.* **43**-B, 376–386.

Videman, R., Eronen, I., Friman, C. & Langenskiöld, A. (1979) Glycosaminoglycan metabolism of the medial meniscus, the medial collateral ligament and the hip joint capsule in experimental osteoarthritis caused by immobilization of the rabbit knee. *Acta Orthop. Scand.* **50**, 465–470.

Videman, T. & Michelsson, J.-E. (1977) Inhibition of development of experimental osteoarthritis by distraction during immobilization *IRCS Med. Sci.* **5**, 139.

Videman, T., Michelsson, J.-E. & Langenskiöld, A. (1977) The development of radiographic changes in experimental osteoarthritis provoked by immobilization of the knee in rabbits. *IRCS Med. Sci.* **5**, 62.

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