Acta orthop. Scandinav. *41*, 522–530, 1970

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EXPERIMENTAL OSTEOARTHRITIS IN RABBITS

*Preliminary report**

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Received 5.ii.70

In earlier investigations, where experimental degenerative changes of the joint cartilage have been studied, these changes have been mostly induced by compression of the joint (Salter & Field 1960, Crelin & Southwick 1964, Ginsberg et al. 1968), or by incisions in the cartilage (Carlsson 1957). These methods are more to compare to acute traumas than slowly progressing degeneration. A method for inducing slowly progressing degenerative changes seems to be missing. Mitosis has never been found in osteoarthritic joint cartilage of adult animals or humans. The purpose of this investigation therefore was: (1) to devise a method for producing a slowly progressing experimental osteoarthritis in rabbits, and (2) to investigate with an autoradiographic technique if cartilage cells in osteoarthritic joint can divide by mitosis and if the so-called "cell clusters" in osteoarthritic joint cartilage are formed by mitotic cell division.

MATERIAL AND METHODS

The medial collateral ligament, the medial meniscus, and both cruciate ligaments were excised in the right knee joint of 28 adult rabbits. The non-operated left knee joints served as controls. The animals were divided in groups of four which were

* Financial support was obtained from the Swedish Medical Research Council, Grants K68-17X-2436-01 and B69-14X-2552-01, and Herman Järnhardts Stiftelse.

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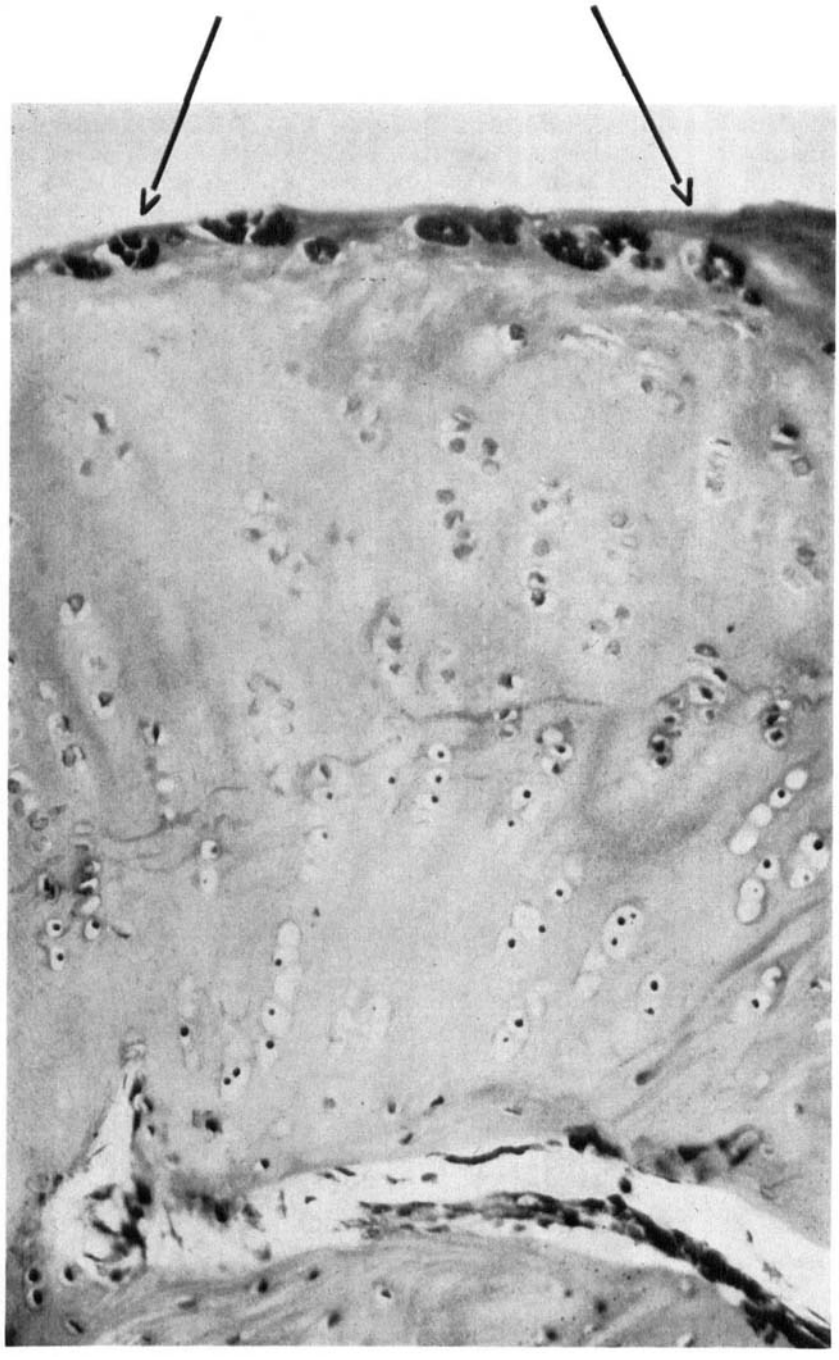
Figure 1. Cell clusters in the superficial layer of the femoral knee joint cartilage, 15 days after the operation. Haemotoxin–eosin. × *350.*

Cell clusters in the superficial layer



killed respectively 5, 10, 15, 30, 60, 90, and 120 days after the operation. Routine histologic sections were taken from the tibial and femoral ends of both knee joints.

For the autoradiographic investigation, 14 adult rabbits were operated according to the method described above. Two animals were killed respectively 5, 10, 30, 60, 90, and 120 days after the operation. Four hours before sacrifice 0.2 ml physiological saline containing 20 μCi tritiated thymidine was injected in both knee joints of each animal. Autoradiograms were made with Ilford K-2 liquid emulsion on routine histological sections from both knee joints. After exposure and processing the sections were stained through the emulsion with Mayers haematoxyline.

RESULTS

Histologic Part

In this description the nomenclature suggested by Collins (1949) is used. In the *non-operated control knee joints* no pathological changes were found.

In the operated knee joints, no pathological changes were found until 15 days after the operation when the first degenerative changes, i.e. derangement of the cell arrangement and formation of cell clusters, began to appear in the superficial layer of the joint cartilage of both tibia and femur (Figure 1). After 30 days the clusters were more common, and in addition, some flaking of the superficial layer was now found (Figure 2). Ninety days after the operation, the first signs of "blistering" were more conspicuous and, moreover, degenerative changes as derangement of the cell columns in the deep layer and cracks between the columns were also found (Figure 3). After 120 days all degenerative changes were still more advanced but, in spite of this, some parts of both the tibial and femoral cartilages appeared quite normal.

At the present stage of the investigation it it not possible to describe the development of osteophytes, but 90 days after the operation, an increased amount of fibroblast-like cells were seen in the capsular attachments, and after 120 days fibrous cartilage with new bone formation was found in these areas, indicating the formation of osteophytes.

Audioradiographic Part

In the non-operated control joints, no labelled cartilage cells were found.

In the operated joints, a few labelled cartilage cells were found in the superficial layers of both the tibial and femoral joint cartilage

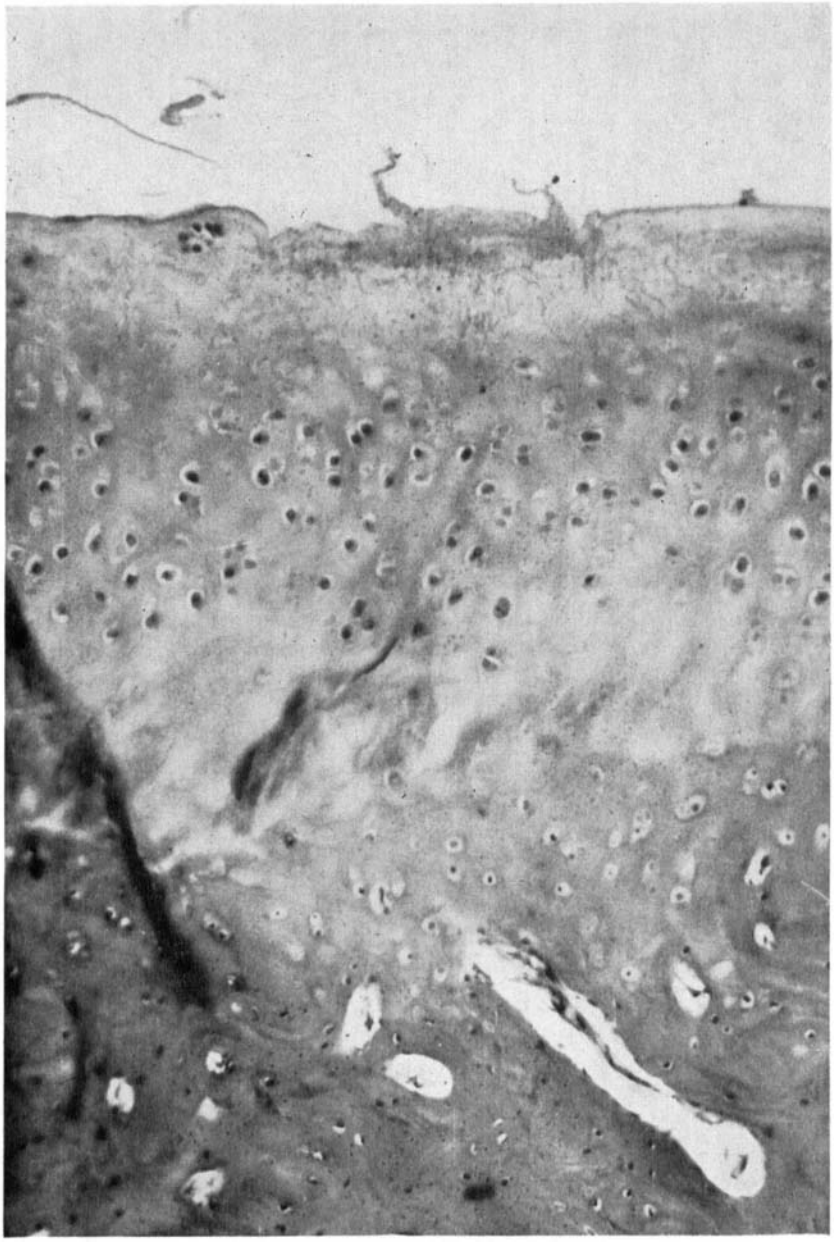


Figure 2. Flaking of the superficial layer of the femoral knee joint cartilage, 30 days after the operation. Haematoxin-eosin. × 280.

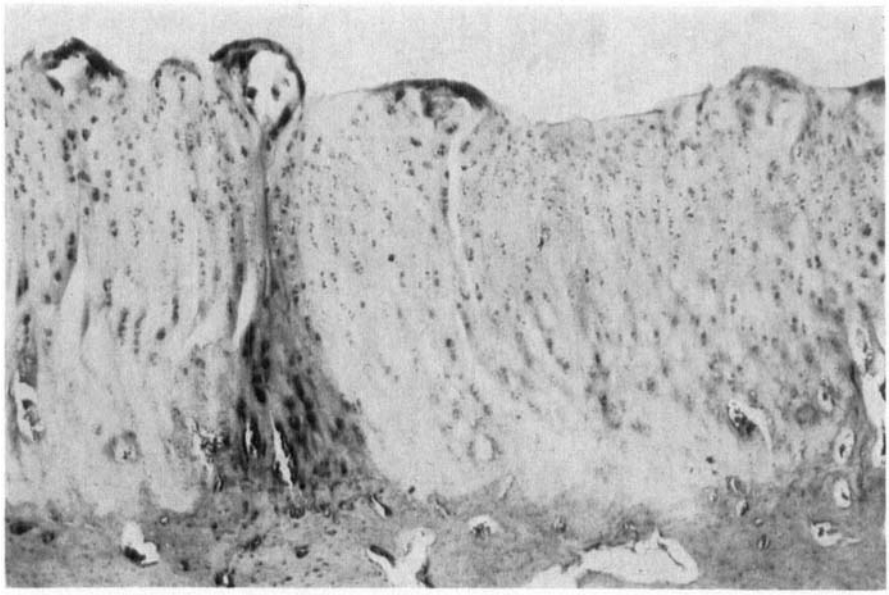


Figure 3. Blistering of the cartilage together with derangement of the cell columns and cracks in the deep layer of the tibial knee joint cartilage, 2 months after the operation. Haematoxin-eosin. × 70.

of one animal already five days after the operation. After 5–30 days, labelled single cells were found in increasing amounts in both the superficial and transitional layers. After 60–120 days labelled single cells were also found in the deep layers in all animals.

Labelled cells appeared in the cell clusters as soon as these were found, i.e. 15 days after the operation in the superficial layer (Figure 4) and after 120 days even in the deep transitional layers (Figures 5 and 6).

DISCUSSION

Degenerative changes of the cartilage, induced by this method, develop much more slowly than those more acutely induced by the methods described by Salter, Crelin, or Carlsson. The morphological changes induced are of the same type as those found in human osteoarthritis (Collins 1949). Therefore, this method seems to be suitable for experimental model investigation on osteoarthritis.

As mitosis has never been found in articular cartilage of adult animals or humans (Mankin 1963), there has been some doubt about

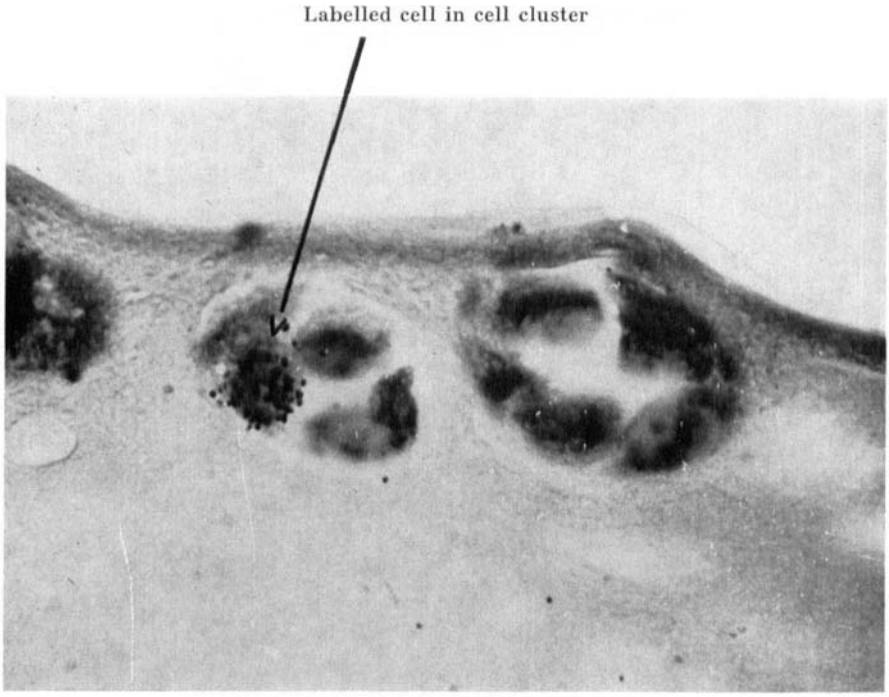


Figure 4. Labelled cell in a cell cluster in the superficial cartilage layer of the femoral knee joint cartilage, 15 days after the operation. Haematoxin-eosin. × 800.

the "cell clusters" seen in osteoarthritic cartilage. Crelin & Southwick (1964) have been able to demonstrate a few mitoses in the cartilage of compressed joints after treating the animals with colchicine, but also an amitotic division has been suggested (Mankin 1963).

Only cells in the premitotic, DNA-replicating, phase can be labelled with tritiated thymidine. This labelling is a reliable mark that the labelled cell is going to divide by mitosis in the near future. Thus, the result of this investigation shows that mitosis is induced in the joint cartilage of adult animals at the same time as degenerative changes similar to those of osteoarthritis. As labelled cells are also found inside the clusters, it seems probable that the clusters are formed by mitotic cell division.

SUMMARY

A method is described by which it is possible to elaborate a slowly progressing experimental osteoarthritis in the cartilage in knee joints

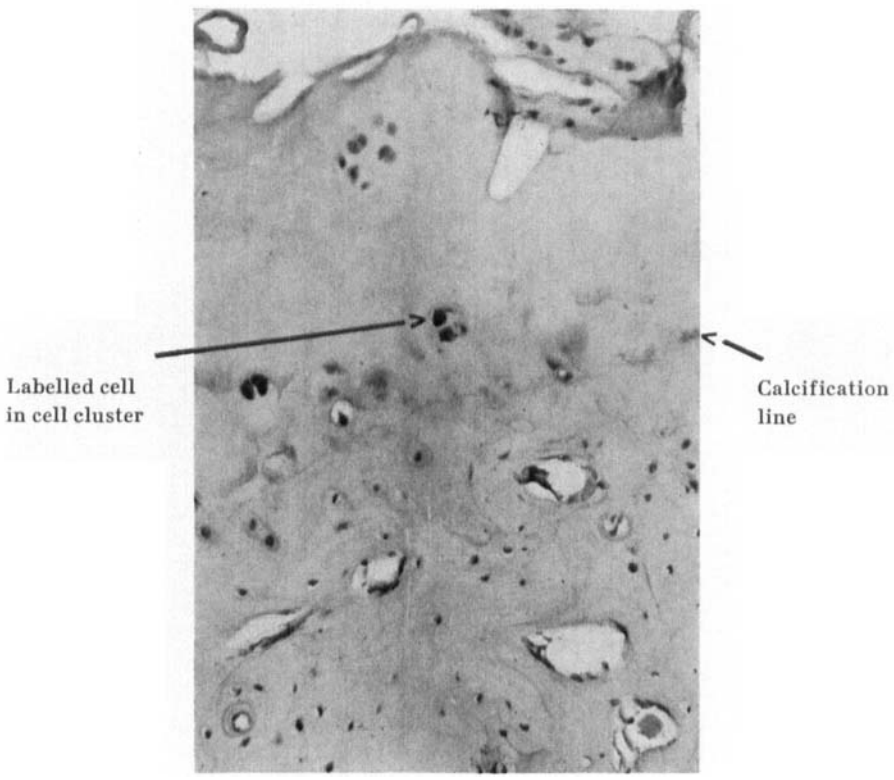


Figure 5. One labelled cell in a cell cluster in the deep cartilage layer of the femoral knee joint cartilage, 3 months after the operation. Haematoxin-eosin. × 300.

of adult rabbits. By using this method and autoradiography with tritiated thymidine, it has been possible to show that mitotic cell division is induced in cartilage cells in osteoarthritic joints.

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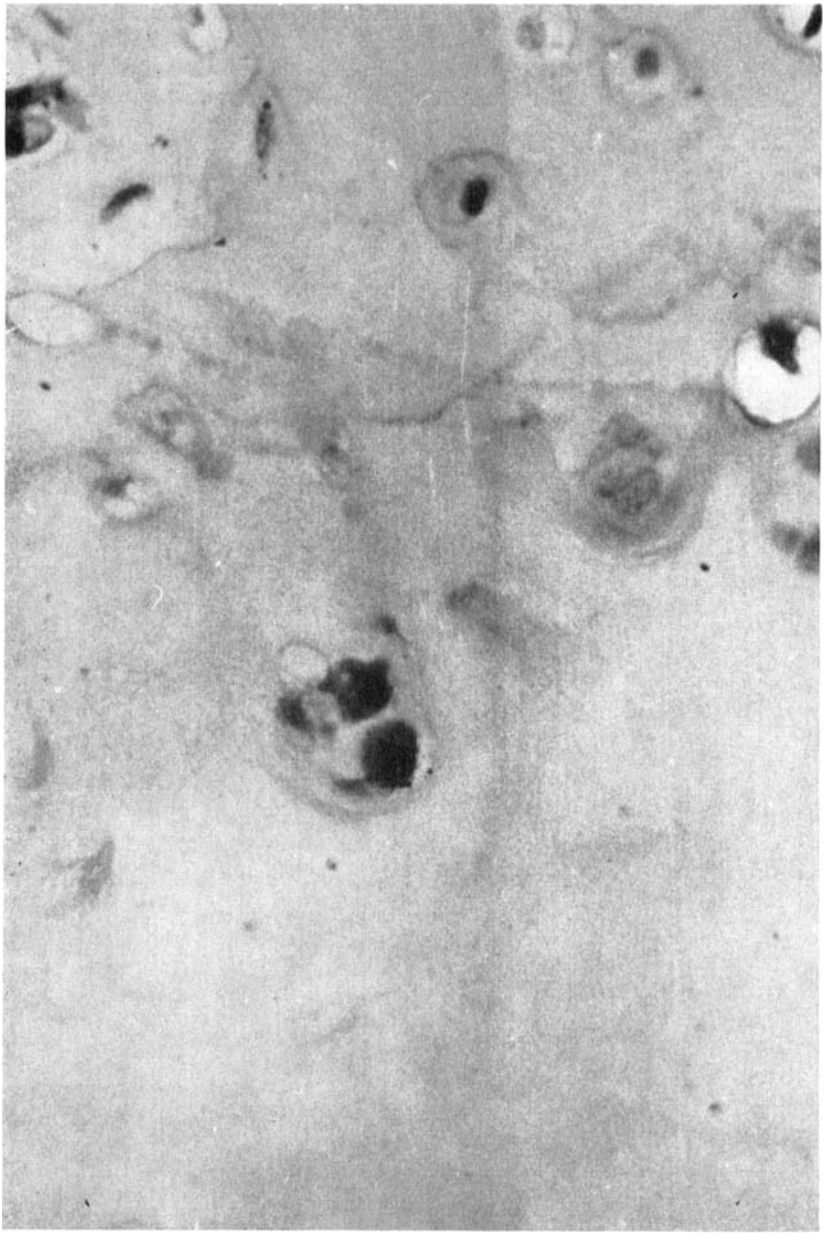

Figure 6. The same as in Figure 5 but in a higher magnification. Haematoxin-eosin × 800.

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