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FEATURE ARTICLE

Incubation in Preparations as a Means of Influencing Cartilage Mechanics: A Mechanical Study

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Diagram of time - penetration depth

There was an average deviation of 18% between the first and second measurements in the case of samples incubated in Zeel®, while the deviation in the case of samples incubated in the culture alone averaged 6%. (This is presented in graphic form using appropriate examples in diagrams A and B.)

Problems with the measurement method

1. Although every effort was made to use plane-parallel samples for the analysis, ideal samples cannot be obtained in practice. As a result the load distribution of the sample is uneven.

2. The surfaces of the cartilage and of the cortex are not plane-parallel either. It is difficult to calculate the deviation at individual points of measurement. Consequently part of the applied load is exerted not as a compression force but as a shear force. We can therefore expect penetration depth to be greater than with pure compression deformation. Using microscopic checks we may assume the error produced to be only very slight.

3. Cartilage, and arthritic cartilage to a particular extent, does in actual fact comprise inhomogenous tissue. As revealed especially in the histological evaluation, in addition to the separate fibers on the surface there are also large groups between the cartilage, with reduced stain and collagen fiber demasking. These structural changes correspond to the differing degrees of arthritis and are not taken into account in this study when considering the changes in mechanical properties. The wide scattering is, in our opinion, due largely to arthritis at different stages.

4. The thickness of the cartilage samples differs. Greater stiffness can be expected in the basal layer, as shown by Buist (1961) in experiments using rubber. This interference factor is intensified by the nature of the cartilage structure, which in some cases includes increased calcium salt content close to the subchondral cortex.

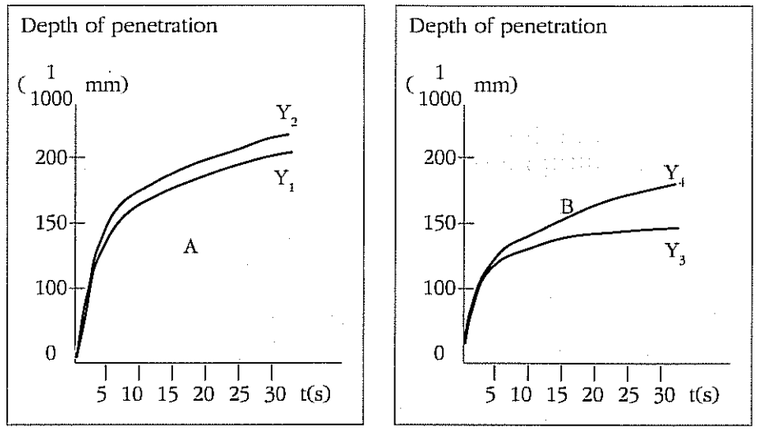

Figure 1: Depth of penetration of a ball indentation tester (5 mm 0) as a function of time.

Y_1, Y_3: Measurement on first day of test.

Y_2, Y_4: Readings on 12th day.

The curves follow the equation y = a + b • 1nx (a, b ... regression coefficients).

Diagram A: *Sample without medical preparation, average deviation 6%.*

Y_1 from placebo series sample 1 (indentation hardness H = 16.5 N/mm²).

Y_2 from placebo series sample 2 (indentation hardness H = 15.4 N/mm²).

Diagram B: *Sample incubated with Zeel®, average deviation 18%.*

Y_4 from series Zeel® sample 5 (H = 18.9 N/mm²).

Samples 1, 2 and samples 5, 6 are half samples. The higher curves of Y_2 sand Y_4 illustrate the increase in penetration depth of a ball following 12 days of incubation in culture (Y_2) and in the culture and Zeel® (Y_4).

Problems involving incubation

1. Isolation of the cylinders of cartilage extracted by punch leads to a substantially impaired cell function. The physiological interaction between the cartilage cell and the cell of the synovial membrane is interrupted. This also applies to the influence of preparations.

2. The concentration of preparation in the joint cannot be imitated with sufficient approximation. Resorption into the synovial membrane does not take place.

The following characteristics of the arthritis and its negative progression will be presented in order to establish how influential the preparation is on the consistency of the cartilage.

Arthritic pain

Changes in the metaplastic bone process can lead to hyperemia of the marrow and dilation of vessels. The associated compression of interosseous nerve fibers is considered the cause of arthritic pain.

Studies by Helal (1965) and Arnoldi et al. (1971) have proved the existence of venous circulatory disorders and intramedullary increases in pressure in the case of coxarthritis of the head of the femur and gonarthritis of the head of the tibia and the condyles of the femur. These studies have also provided additional evidence of the way in which such pain is caused. A number of authors, including Arlet et al. (1968) and Eberle (1971) have observed intramedullary increases in pressure in the case of idiopathic necrosis of the hip.

Permeability of the cartilage tissue

Barnett and Stockwell (1964) assumed a diminished permeability of synovia to be the cause of the degeneration of the cartilage. Basing their investigations on the diffusive properties of silver proteinates and thorium dioxides, they established that distinctions were clearly dependent on age. Accordingly, not only can an impairment of the nutrient supply be expected, but also an increase in intra-cartilageneous pressure when subjected to loads, because of the reduced possibilities for intra-articular pressure equalization as a result of diffusion.

Attrition and degeneration of the cartilage

The increase in penetration depth, i.e. the „softening" of the cartilage, raises questions about the associated increase in friction resistance and intensified attrition of the cartilage. The following aspects should be considered in this respect:

The frictional resistance of the joints increases proportionally with age, as Barnett (1966) has proved in studies of the joints of the finger ends. This change can be correlated with the reduction in synovial viscosity (Jeben, Jones, 1959). The idea that attriton of the cartilage is the decisive process in the development of arthritis is not borne out by histological observations.

There have never been any indications of the destruction of a chondrocyte on the surface. Instead a matrix layer is always apparent above the surface cells. No processes have been discovered which would provide evidence of effective cell substitution activity (Barnett, 1966).

Inadequate pressure load is a decisive factor in the degeneration of hyaline cartilage:

Kummer (1980) refers to the „traditional character" of the hyaline cartilage. He assigns a narrow tolerance range to the cartilage tissue. Excessive deformation would lead to an increase in the fibrous elements, while insufficient deformation would induce swelling of the chondrocytes, followed by ossification.

Progression or non-progression of the separation of the cartilage into fibers

Separation of the cartilage into fibers can be regularly found at numerous points in the joints, e.g., the fovea of the hip, the periphery of the knee joint, the elbow and the shoulder (Goodfellow et al. 1967). This separation of the cartilage into fiber could lead to arthritis, but this need not necessarily occur.

The absorbency of the subchondral cortex fulfills a key role. In order to establish whether increased stiffness of the underlying bone would have an effect on the cartilage, Radin et al. (1980) filled the metatarsal of a cow with methacrylate. Under these conditions increased stiffness of the surface of the joint by approximately 22-25% occured. Subsequently the joints of this animal were subjected to an alternate series of impulses, with the result that these joints, when compared with others, very soon indicated evidence of wear.

In this series of tests Radin et al. (1980) examined a number of possibilities for inducing artificial damage to the joint. They added different enzymes to the synovia, and scarified the cartilage. The required effect was produced in the form of increased stiffness of the underlying bone.

Interpreting the results of experiments

As already reported in connection with other preparations (Weh et al., 1981), increased penetration depth was also found following incubation with Zeel.

The experimental set up presents a number of problems, and thus any transferral to in-vivo conditions should be accompanied by certain reservations. Nevertheless, we believe that a reduction in the hardness of the cartilage may be assumed following in-vivo application of preparations too. In view of the way in which this experiment was set up, particular caution should be exercised when comparing one preparation with another, because the completely different points of departure for intra-articularly applied pharmaceuticals also lead us to expect different effects on the isolation of the cartilage from the complex system of the joint.

The basic work referred to above provides some interesting aspects for evaluating our own results: according to findings by Arnoldi (1971), Helal (1965) and others we may assume an increase in intramedullary pressure, and thus increased stiffness of the surface of the joint when arthritis occurs. Experimental investigations by Radin (1980) suggest that a decisive influence on the development of cartilage degeneration is exerted by a subchronic inrease in elasticity. The ability of intra-articularly applied pharmaceuticals to increase the ductility of the cartilage is based on a still unknown principle. It is possible that an increase in the capacitiy to absorb water plays a part here. At the present time our continuing investigations are concerned with clarifying these causes.

The following questions regarding the effects of preparations should be discussed in subsequent analyses:

1. Is the immediate lessening of pain that subjects regularly report following intra-articular injections the result of an increase in the cartilage's cushioning capacity?

2. Can we expect increased storage of fluids in the cartilage to improve permeability and thus enhance the supply of nutrients to the chondrocytes?

3. Can the ossification or fibrosation processses be slowed down as a result of the increased cushioning capacity of the cartilage?

If positive answers to these questions can be obtained, this would offer a decisive new basis for the application of medical preparations in the therapy of arthritis from a biochemical aspect.

Summary

Changes in the mechanical behaviour of the cartilage under the influence of medical preparations are largely unknown. These investigations examined the influence of an intra-articularly applied pharmaceutical on the hardness of the cartilage. A substantial increase in the penetration depth was revealed, and the possible causes submitted for discussion. The importance of these physical components for the effects of therapy is presented.

Incubation in Preparations as a Means of Influencing Cartilage Mechanics: A Mechanical Study

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Introduction

Functioning of the cartilage is restricted by degenerative arthropathies. Although it is claimed that pharmaceuticals, when administered intra-articularly, have a positive effect on the mechanics of the joint, as far as we know no studies have been carried out into the changes in physical parameters under the influence of these so-called „arthritis therapeutica".

In a previous study we examined changes in the mechanical behaviour of cartilage tissue following incubation in Arteparon®, Diprosone®, Dona® 200S and Neyarthros® (Weh, Dahmen, Fröschle. 1981). The medical preparations used were chosen from a range offering a variety of different action mechanisms.

The choice of pharmaceuticals does not imply any evaluation of the pharmaceuticals used. This particular study uses the same experimental procedure to present the effects of Zeel®.

Experimental set up

Samples of cartilage from the joints of patients requiring an endoprosthetic replacement joint were examined to determine indentation hardness prior to and following incubation in a culture and a pharmaceutical.

Cylinders of cortex cartilage with a height of 1.3 - 3.8 mm were prepared using a punch with a diameter of 7 mm. These were accurately separated into two equal quantities. One half received a small quantity of culture and was packed under sterile conditions in plastic foil for the purposes of measurement. The tests were conducted using a special device for testing hardness in order to establish elastic ductility. The tests were conducted at the Materials Testing Laboratory of the Technische Hochschule Hamburg. The depth of penetration of a ball with a diameter of 5 mm was measured as a function of time. The load imposed was 49.03 N at an initial load of 9.81 N. The indentation hardness was determined using the 30 second value, from

$$H = \frac{1}{dx} \times \frac{F}{h}$$

(H = indentation hardness, d = diameter of indentation, F = effective force, h = depth of penetration).

A pressure of D = 1.27 N/mm2 was obtained.

The remaining samples were placed in a culture (25 ml Hank's isotonic solution) and were incubated for 12 days following application of Zeel®, 2.2 ml. The culture and pharmaceutical were changed at 3 day intervals.

Simultaneous cartilage incubation without any medical preparation was carried out as a placebo series.

Following completion of the incubation period, tests were conducted on the second set of samples to determine their indentation hardness.

These readings were compared with the final results of the placebo series and with the readings obtained prior to incubation.

Results

In the case of the samples incubated with Zeel®, the increase in the depth of penetration between the first and second measurements averaged 18 %, while penetration depth increased by an average of 6 % in the case of samples incubated in the culture only (see Fig. 1).

Number of samples	Initial average indentation hardness N/mm²	Final average indentation hardness N/mm²
1	13.3	11.0
2	22.1	18.9
3	14.1	11.8
4	14.8	14.4
5	16.5	15.1
6	22.3	14.5

Average reading for the initial measurement:

H_1 = 17.4 N/mm²

Average reading for the final measurement:

H_2 = 14.3 N/mm²

(obtained in each case from 6 samples)

Table 1: Results of the measurements of hardness of 6 samples incubated with Zeel®.

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