CONSEQUENCES OF AVASCULAR NECROSIS OF THE FEMORAL HEAD IN RABBITS
A Histological and Radiological Study

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Avascular necrosis of the head of the femur is found in many different conditions. Most often it occurs after injury or during growth. It has been generally accepted that vascular occlusion is its immediate cause (Trueta and Harrison 1953, Trueta 1957). This occlusion leads primarily to ischaemia of the tissues, which results in necrosis if the circulation is not restored in time. Morphological signs of tissue decay become perceptible only after some time (Rössingh and James 1969). The subsequent series of changes commonly result in deformation of the affected femoral head.

There is no agreement as to the nature of the tissue changes which ultimately lead to deformation. One long-established concept holds that deformation is a consequence of the penetration of vessels into the necrotic head. This would lead to resorption of dead bone which would only gradually be compensated for by apposition of new living bone tissue (Sherman and Phemister 1947).

According to other investigators, deformation appears in avascular parts of the femoral head (Axhausen and Bergmann 1937, Jonsäter 1953, Brown and Abrami 1964, Catto 1965b). It is supposed that the bone tissue in the necrotic femoral head is no longer able to adapt to the functional demands. Under the influence of weight-bearing this would lead to a definite pattern of stress fractures in the dead trabeculae, resulting in a typically deformed femoral head as seen radiographically. “Late segmental collapse” is the term which has been proposed for this sequence of events (Brown and Abrami 1964, Catto 1965b).

Two facts are in disagreement with these theories. In the first place generalised sclerosis of the affected femoral head, as revealed in radiographs, may actually precede deformation (Waldenström 1934, Jonsäter 1953, Hulth 1961). This observation suggests that the quantity of bone salt in the femoral head may increase before deformation occurs. In the second place, apposition of abundant quantities of new bone after revascularisation has been observed by various authors. This quantitative increase in bone mineral might be the cause of the radiographic sclerosis (Bobechko and Harris 1960, Hulth 1961, Bohr and Larsen 1965, Catto 1965b). A direct relationship between an increased quantity of bone and deformation of the femoral head is not readily apparent, however. In an attempt to obtain more information on these problems, experiments were performed in rabbits. These studies will now be reported and discussed.

MATERIAL AND METHODS
A total of sixty-three two-month-old rabbits were used. In forty-two animals the right hip joint was opened under intravenous Nembutal anaesthesia (30 milligrams per kilogram of body weight) and the ligament of the femoral head was cut. Subsequently the blood supply of the femoral head was
blocked by a nylon ligature tied around the femoral neck (operation A). In the remainder of the animals only the ligament of the femoral head was cut and the blood supply was left intact (operation B). These rabbits served as controls. After different periods of time, ranging from six hours to twenty-one weeks (Table I), the animals were killed by an intracardiac injection of approximately 10 millilitres of a 10 per cent solution of potassium chloride. Immediately after cardiac arrest the proximal parts of the right and left femora were removed and cut in a frontal plane. This material was prepared for microscopic study as follows.

**Decalcified material**—The samples were fixed for four hours in a mixture of 100 parts of 96 per cent alcohol, forty parts of undiluted neutral formalin and six parts of glacial acetic acid. Subsequently the samples were decalcified under constant agitation for six days in a mixture of 21 per cent nitric acid and a saturated alcoholic solution of picric acid. The decalcification was checked radiographically. After decalcification the specimens were dehydrated and embedded in Rallwax. At different sites in these proximal femoral ends sections 6 µ thick were cut in a direction parallel to the original cleaving plane. These sections were stained with haematoxylin and phloxin; with the silver impregnation method of Laguesse and Gomori for reticulin, combined with Mallory’s stain for collagen; with the periodic acid-Schiff method for neutral polysaccharides, and with Alcian blue for acid polysaccharides.

In complete and undamaged sections from thirty animals (fifteen animals with and fifteen animals without a ligature) the relative area of the epiphysis of the femoral head occupied by bone tissue was approximated with the aid of a morphometric technique (Weibel and Elias 1967). As a rule, four non-consecutive sections from each block were used for this purpose. By a standard photographic procedure, enlargements (× 25) of these sections were made. A grid was put over the pictures of which more than 100 intersections fell within the boundary of the osseous nucleus of the epiphysis. The ratio of the intersections overlying bone and those overlying the total area of the nucleus was taken to represent the relative area of the bone tissue and also the relative volume of bone in the epiphyseal nucleus, since the sections were presumed to be of constant and equal thickness. The reliability of this method was checked by placing the grid in ten different positions on the same photograph and determining the ratio in each case. The range of the ratios was approximately 6 per cent of the mean value.

**Undecalcified material**—In six of the forty-two animals which had a ligature around the right femoral neck, oxytetracycline (50 milligrams per kilogram of body weight) and alizarin red S (100 milligrams per kilogram of body weight) had been injected intra-abdominally respectively twenty-four hours before operation and twenty-four hours before death. This had been done to identify the sites of bone formation at that moment (Steenendijk 1964). One pair of animals was killed each at five days, at four weeks and eight weeks after the operation. The ventral parts of the proximal ends of the right and left femora were fixed in 70 per cent alcohol. After dehydration the material was embedded in methylmethacrylate. After polymerisation of the medium, sections approximately 130 µ thick were prepared with a rotary saw in a direction parallel to the original cleaving plane. The sections were ground to a thickness of 100 µ between roughened glass plates and subsequently contact microradiographs were made on Kodak 649-0 spectroscopic film, with the aid of an x-ray tube with Cu-anode, operated at 30 kilovolts and 20 milliamperes. Focus-to-film distance was 30 centimetres. Finally the sections were mounted on glass slides and the pattern of uptake of tetracycline and alizarin was studied with the fluorescence microscope.

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**Table I**

**Analysis of Material**

<table>
<thead>
<tr>
<th>Interval between operation and slaughter</th>
<th>Number of animals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Operation A</td>
</tr>
<tr>
<td>6 hours</td>
<td>2</td>
</tr>
<tr>
<td>12 hours</td>
<td>2</td>
</tr>
<tr>
<td>24 hours</td>
<td>2</td>
</tr>
<tr>
<td>3 days</td>
<td>2</td>
</tr>
<tr>
<td>5 days</td>
<td>7</td>
</tr>
<tr>
<td>10 days</td>
<td>4</td>
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<td>2 weeks</td>
<td>2</td>
</tr>
<tr>
<td>3 weeks</td>
<td>2</td>
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<td>4 weeks</td>
<td>5</td>
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<tr>
<td>6 weeks</td>
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<tr>
<td>7 weeks</td>
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<tr>
<td>8 weeks</td>
<td>4</td>
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<td>10 weeks</td>
<td>4</td>
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<tr>
<td>12 weeks</td>
<td>1</td>
</tr>
<tr>
<td>13 weeks</td>
<td>1</td>
</tr>
<tr>
<td>21 weeks</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42</strong></td>
</tr>
</tbody>
</table>
**Radiography of living animals**—Before operation and immediately before death radiographs of the pelvis of each animal were made. The rabbits were anaesthetised and care was taken to ensure that each animal was radiographed in the same position. To detect sclerosis of the femoral head on the ligated side, the density of the projections of both epiphyses on each film was compared visually, while the surrounding areas of the film were covered with black paper. In some animals, radiographs were made at intervals of two weeks after the operation in order to follow any change in the density of the femoral head that might occur.
RESULTS
HISTOLOGICAL STUDIES

From the decalcified sections it appeared that the bone marrow cavities in the untreated side as well as in the greater trochanter and the proximal diaphysis of the treated side were always filled with normal reticular haemopoietic connective tissue. Over large distances the endosteum showed a continuous layer of active osteoblasts. Osteoclasts were encountered only sporadically. The osseous trabeculae consisted of lamellar bone, containing osteocytes with spindle-shaped nuclei in fusiform lacunae (Fig. 1). After transection of the ligament of the femoral head the same picture was found.

After ligation of the femoral neck morphological changes appeared in the epiphysis. These changes could be differentiated arbitrarily into four consecutive phases, which were not sharply delineated from each other.

The first phase was characterised by tissue decay. The cells of the bone marrow and of the endosteum showed signs of disintegration as early as six hours after operation; the osteocyte nuclei were pyknotic twenty-four hours after the operation. The staining affinity of the nuclei had visibly declined after three days (Fig. 2) (Rosingh and James 1969).

The second phase was characterised by the penetration of granulation tissue into the necrotic bone marrow (Fig. 3). This tissue began to appear three days after the operation at the cranio-dorsal side of the epiphysis and it reached the marrow cavity of the ventral side after three weeks.

The third phase gradually developed in the granulation tissue during the first three weeks after operation. It was characterised by cellular differentiation. At some distance from the necrotic bone marrow polynuclear giant cells with a vacuolar cytoplasm appeared in the granulation tissue. The nuclei of the giant cells usually were placed in a circle around a central
vacuole. In this way "polynuclear ring-structures" arose. These ring-structures occupied most of the bone marrow cavity approximately two weeks after the operation (Figs. 4 and 5). On the osseous surfaces surrounding these marrow areas, a dense network of reticular fibres appeared and subsequently active osteoblasts were seen. At some sites these cells were grouped together and gradually became enveloped in new bone tissue. The bone tissue deposited at these sides, which sometimes extended far into the marrow cavity, had the features of immature woven bone (Ham 1965). Its matrix was more periodic acid-Schiff-positive and less eosinophile than the matrix of the dead lamellar bone and the collagen fibres were irregularly arranged. The mineral density of this new bone tissue was higher than that of the old bone, as revealed by the microradiographs (Fig. 6). The osteocytes of this woven bone displayed unmistakable features of osteoblasts, but the negative image of the Golgi-apparatus—which is characteristic of the last mentioned cells—was absent as a rule. These osteocytes were situated in large irregularly shaped lacunae and they were placed comparatively close together. The boundary between the old bone tissue and the new bone was marked by a clearly defined cement line (Figs. 7 and 8). This line had a distinct affinity for basic dyes and was not argentophile with the Laguesse technique. Moreover, it was strongly periodic acid-Schiff-positive. In the decalcified sections it was noted that many more tears were present in these cement lines than anywhere else. No tears were seen in the undecalcified sections. In the microradiographs the boundary between the old and the new bone was marked by a line which had a low mineral density. To define the exact geographical relationship between the cement line in the decalcified sections and the low density line in the microradiographs, a number of undecalcified sections were stained with the periodic acid-Schiff method. Comparison of the resulting periodic acid-Schiff-positive cement line, the uptake of tetracycline and the low density line revealed that the latter was situated between the fluorescent line and the periodic acid-Schiff-positive line. This meant that the low density line was situated at the edge of the old bone.

The fourth phase appeared for the first time between two and four weeks after the operation. In the bone marrow this phase was characterised by the disappearance of the polynuclear giant cells and the ring-structures. Simultaneously in some areas the bone marrow acquired a reparative aspect (phase 4 A). The marrow cavity was filled with closely packed and irregularly interwoven bands of collagen and in these areas oil cysts, granulocytes, fibroblasts and histiocytes were found. As a rule the bone surface was covered by inactive osteoblasts. In some areas no new bone had been deposited and the old bone extended to the surfaces of the trabeculae. Elsewhere, woven bone was present adjacent to the layer of resting osteoblasts. Usually, however, the marrow tissue in the fourth phase had a restorative character (phase 4 B). In this case it could not be distinguished from the reticular haemopoietic tissue which was present in the untreated epiphyses. In such an area the endosteam had a normal aspect and it covered living mature lamellar bone with fusiform lacunae. Some distance away from the endosteam the structure of the bone tissue gradually changed into woven bone.
which in turn was separated from the old dead bone with empty lacunae by the distinct cementing line. This structure still persisted twenty-one weeks after the operation. The changes described were seen in material from thirty-six of the forty-two animals (86 per cent) in which a ligature had been tied around the femoral neck. In this group therefore the ligature appeared to have been successful since it had resulted in ischaemia. In the remaining six animals no changes that could be regarded as having resulted from ischaemia were seen. Obviously, vascular occlusion had not been achieved.

In Figure 9 the changes found in the bone marrow of the thirty-six animals with successful ligatures have been graphically represented in chronological order. First, it can be seen that the different phases may appear simultaneously in one epiphysis. As a rule, the changes were slightly more advanced in the dorso-cranial part of the epiphysis—the site where the granulation tissue first was seen—than in the ventro-medial part, which was revascularised last. Secondly, it can be seen that no further changes occurred from four weeks after the operation. From this moment normal lamellar bone again was deposited by the endosteum.

It was noted that during the first four weeks after the operation the trabeculae in the revascularised areas became thicker in an irregular manner by the deposition of large quantities of woven bone (Figs. 10 and 11). The bone mass appeared to increase especially during the period of cellular differentiation (phase 3), whereas the space occupied by the bone marrow concomitantly decreased. In an attempt to put this finding on a quantitative basis the relative areas occupied by bone were determined by the morphometric method described. This was done in material from thirty animals at different times after the operation; the results were expressed as the ratio:

\[
\frac{\text{relative area of bone on operated side}}{\text{relative area of bone on untreated side}}
\]

and they are represented graphically in Figure 12.
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Statistical treatment of the results strongly supports the view that the quantity of bone tissue in the revascularised epiphyses increased at the expense of the marrow volume during the first four weeks after the operation. Subsequently the relative amount of bone tissue decreased again. The quantity of dead bone and the number of tetracycline lines decreased from four weeks after the operation and many resorption cavities were formed in the trabeculae. During the period of relative increase of bone tissue as well as afterwards osteoclasts were seen only sporadically in the revascularised epiphyses.

Finally, it should be mentioned that amorphous deposition of calcified material in the marrow cavities was never seen.

RADIOLOGICAL OBSERVATIONS

Radiographs of the animals taken just before death were independently judged by two of the authors (Rosingh and Steendijk). A total of forty pictures were considered to be of sufficient quality to be used for comparison of the densities of the left and right femoral head epiphyses. One of the examiners (Rosingh) was acquainted with the results of the morphometric study. In the animals in which the ligature had been successful, this examiner found no difference in the densities within the first three weeks after the operation. From that time, the density of the ligated epiphysis appeared to be higher than that of the other side in seven out of eleven cases; in the other four cases the densities appeared to be equal. No difference in density was found in the twenty-one animals from the control group (Figs. 13 and 14; Table II). The results of the other examiner (Steendijk), who was completely unbiased because he had no foreknowledge of the results of the morphometric study, corresponded in thirty-seven out of the forty cases (Table II). Two of the pictures on which the examiners disagreed were from animals killed four weeks after a successful ligature; the bone-volume ratios were 1.36 and 1.16 respectively. The third animal was killed eight weeks after a control operation and had a bone-volume ratio of 1.09.

Although this radiographic investigation was only performed visually and therefore was not quantitative, the close agreement between the results of the two examiners and the fact that differences in density between the left and the right side were almost exclusively found in pictures taken more than three weeks after the operation and in animals which had a successful ligature, are at least highly suggestive of an objective difference in the densities of the left and right epiphyses in this period. Therefore this study appeared to corroborate the results of the morphometric investigation.

DISCUSSION

The results show that ligation of the femoral head of young rabbits leads to avascular necrosis, followed by the ingrowth of granulation tissue into the marrow cavities and—at a few weeks—to the deposition of new bone on the old necrotic bone, which causes an increase of the total bone mass at the expense of the marrow spaces. The presence of an excessive amount of bone, as observed histologically, coincides with an increase in radiographic density.
Two types of bone were involved in new bone formation. The first bone to be deposited was of the immature or woven type (Ham 1965); it was attached to the old necrotic bone by means of a pronounced cement line. At a later stage mature, lamellar bone was deposited. Ultimately the original bone-marrow ratio was restored by the action of osteoclasts. This reversion to the normal bone-marrow ratio in the last phase implies that quantitatively a restoration had been achieved, but that qualitatively the new situation differed from the pre-operative situation on two points: the bone trabeculae now partly consisted of woven bone, and cement lines were present within the trabeculae. The question is relevant whether these structural changes have a bearing on the mechanical qualities of the femoral head. As regards the mechanical qualities of woven bone no specific facts are known. Morphologically woven bone has characteristics in common with bone and cartilage. With lamellar bone it shares the disposition to calcification, the non-chondroid character of its cells and its irregular ground

![Fig. 10](image1)

Low power view of the epiphysis of the femoral head four weeks after vascular occlusion. (Haematoxylin and phloxin, × 8.) Figure 10—Treated side. Figure 11—Control side. A marked difference is seen between the operated side where heavy irregular trabeculae surround small marrow cavities and the untreated side, where slender trabeculae lie between large marrow cavities.

![Fig. 11](image2)

![Fig. 12](image3)

Morphometrically determined bone-volume ratios in the femoral head epiphysis on the operated and the untreated side of animals with (●) and without (○) a successful ligature, plotted against time. The ratios for animals with a successful ligature belonging to one experimental period which as a group were significantly larger (at the 5 per cent level) than the ratios in the control group are marked ○.
substance. In other respects woven bone resembles cartilage: its cellular lacunae are large and close together; when it calcifies woven bone exhibits the same changes in the polysaccharide pattern of its matrix as cartilage (van den Hooff, van Nie and Buitenweg 1966); in the third place the matrices of both woven bone and cartilage contain collagen in a random and non-compact arrangement. As a consequence of this last property more room is available for mineral deposition in calcifying cartilage as well as in woven bone. This factor may explain the higher radiographic density of woven bone compared with lamellar bone.

The strength of lamellar bone depends on its highly ordered ultrastructural organisation (Currey 1962). Because the matrix of woven bone is far less ordered, Currey’s considerations are not valid and therefore the supposition seems warranted that woven bone is weaker, although direct measurements of its strength are not feasible. As far as the cement lines are concerned, the low mineral density and the occurrence of tears in the course of histological processing are highly suggestive of a local mechanical weakness. It is in these lines that the collagen fibres of the new living bone are linked to the collagen fibres of the old (necrotic) bone. In the course of wound healing in soft tissues it was observed on an ultrastructural level that at the wound margin the newly formed collagen fibrils became interspersed between the old ones (van den Hooff, unpublished results). There was no direct continuity between old and young fibrils; so it is possible that such a margin presents an area of lessened resistance. Apart from the presence of bone salts, a similar situation prevails at the cement line. The periodic acid-Schiff-positive (neutral) carbohydrates present at the cement lines may be of functional significance. According to some authors (van den Hooff 1963) periodic acid-Schiff-reactive connective components may play a role in maintaining tissue stability. It is therefore suggested that the periodic acid-Schiff-reactive substance present at the cement lines is somehow involved in increasing the integrity of the bone at sites which are weak because of the
discontinuity of the collagen fibrils. So it seems likely that the mechanical strength of the femoral head is impaired when the pre-operative bone-marrow ratio has been re-established after revascularisation and excessive bone formation. According to this point of view the disappearance of sclerosis is a decisive factor in weakening, because woven bone, which is mechanically inferior, has taken the place of superior, though necrotic, lamellar bone.

A practical question is if and to what extent the considerations given above are relevant to processes following avascular necrosis of the human femoral head. Little is known about the processes which lead to excessive bone formation and consequently to radiographic sclerosis. It has been observed that in autologous cancellous bone transplants necrotic haemopoietic bone marrow, which is also present in the necrotic femoral head, stimulates revascularisation and new bone formation (Barth 1893, Trueta 1963, Burwell 1964, 1966).

**TABLE II**

**Assessment by Two Independent Observers (R and S) of Radiographs of the Pelvis in Forty Living Animals for Sclerosis of the Femoral Head Epiphysis**

<table>
<thead>
<tr>
<th>Duration of experiment</th>
<th>Successful ligature</th>
<th>Animals</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Increased density</td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td>(R)</td>
<td>(S)</td>
<td>(R)</td>
</tr>
<tr>
<td>0-2 weeks</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3-6 weeks</td>
<td>8</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>7-21 weeks</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Histological study of femoral heads removed after fractures of the neck has shown that radiological sclerosis is caused by new formation of bone (Bobechko and Harris 1960, Hulth 1961, Bohr and Larsen 1965, Catto 1965a, b). Whether this is also true for Perthes’ disease cannot be ascertained because of the lack of sufficient histological details. The above-mentioned observations from the literature and the results of the present study, however, suggest that sclerosis of the femoral head in the course of Perthes’ disease may also be caused by an excessive formation of new bone following revascularisation. The implication of an endocrine disturbance does not seem to be necessary (Ljunggren 1967).

Since deformation is an important feature in human pathology, the question comes up whether woven bone and pronounced cement lines are present after revascularisation of the necrotic femoral head or in autologous bone transplants. No explicit findings are given in the literature. However, careful study of the many micrographs presented by Hulth (1961), Bohr and Larsen (1965) and Catto (1965a, b) leaves no room for doubt that in the human femoral head woven bone is formed after revascularisation. This is attached to dead bone by means of a pronounced cement line. This observation supports the view that in man also revascularisation of a necrotic femoral head may be accompanied by the formation of an excess of mechanically inferior woven bone, which moreover is insufficiently attached to the dead, but mechanically superior, lamellar bone.

The decline of sclerosis—that is, the decrease in the total amount of bone to the prenecrotic amount—involves a mechanical weakening due to the presence of inferior woven bone, a weakening which may explain collapse and deformation.

**Statistical Analysis of Bone-Volume Ratios**

Two groups of rabbits were considered: a group of fifteen animals with a successful ligature and a group of fifteen animals without a successful ligature (the control group). At
eight different times after the operation some of the rabbits of both groups were killed and the bone-volume ratios in the femoral head epiphyses of the operated and the untreated side were determined. The results are graphically represented in Figure 12.

To investigate whether systematic differences between both groups could be discerned at the different times, the following statistical analysis was performed. It was assumed that the bone-volume ratios of the animals in the control group were identically distributed, independent of the different times. This assumption is corroborated by the observations (Fig. 12). The bone-volume ratios of the animals with a successful ligature and killed at a certain time after operation were compared with the bone-volume ratios of all animals in the control group. For each of the eight periods the null hypothesis

\[ H_0: \text{there is no systematic difference between animals with a successful ligature and animals without a successful ligature} \]

was tested against the alternative hypothesis

\[ H_1: \text{animals with a successful ligature have systematically larger bone-volume ratios than animals without a successful ligature.} \]

Since normality assumptions of the bone-volume ratios did not seem justified, the non-parametric two-sample test of Wilcoxon (Mann-Whitney) was used to test \( H_0 \) against \( H_1 \). In each case exact one-sided tail probabilities (\( p \)-values) were computed and a one-sided test was performed at the 5 per cent level of significance. The results of the statistical analysis are listed below (Table III). Thus the tests indicate that the bone-volume ratios of animals

<table>
<thead>
<tr>
<th>Time after operation</th>
<th>Tail probability (( p )-value)</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 day</td>
<td>0.59</td>
<td>( H_0 ) not rejected</td>
</tr>
<tr>
<td>3 days</td>
<td>0.41</td>
<td>( H_0 ) not rejected</td>
</tr>
<tr>
<td>3 weeks</td>
<td>0.007</td>
<td>( H_0 ) rejected in favour of ( H_1 )</td>
</tr>
<tr>
<td>4 weeks</td>
<td>0.001</td>
<td>( H_0 ) rejected in favour of ( H_1 )</td>
</tr>
<tr>
<td>6 weeks</td>
<td>0.007</td>
<td>( H_0 ) rejected in favour of ( H_1 )</td>
</tr>
<tr>
<td>8 weeks</td>
<td>0.31</td>
<td>( H_0 ) not rejected</td>
</tr>
<tr>
<td>10 weeks</td>
<td>0.044</td>
<td>( H_0 ) rejected in favour of ( H_1 )</td>
</tr>
<tr>
<td>12 weeks</td>
<td>0.37</td>
<td>( H_0 ) not rejected</td>
</tr>
</tbody>
</table>

with a successful ligature are systematically larger than the bone-volume ratios of animals without a successful ligature at three, four, six and ten weeks after the operation, although at ten weeks after the operation the result is barely significant at the 5 per cent level.

**SUMMARY**

1. In two-month-old rabbits the femoral heads were made necrotic by transecting the ligament of the femoral head and applying a ligature around the femoral neck. The animals were killed at different periods, from six hours to twenty-one weeks after the operation. The changes in the femoral heads were studied histologically, microradiographically and radiographically.

2. In the first three weeks the necrotic bone marrow was penetrated by granulation tissue in which cellular differentiation gradually developed. Subsequently large quantities of new bone were deposited on the dead trabeculae. This led to an increase in the bone volume at the expense of the marrow volume: this increase coincided with an increase in the radiographic density.
(sclerosis) of the femoral head. The new bone tissue was attached to the necrotic trabeculae by a specific cement line and showed the features of woven bone. At a later stage lamellar bone was deposited. From six weeks on a normal bone-marrow ratio was gradually restored with concomitant radiographic loss of sclerosis.

3. It is suggested that mechanical weakening of the femoral head is the consequence of this late post-operative restoration of the normal pre-operative bone-to-marrow ratio, the new bone trabeculae being mechanically inferior because of the presence of woven bone and cement lines. This weakness may initiate collapse and deformation of the revascularised femoral head.

REFERENCES


