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Effects of vascular occlusion on the femoral head in growing rabbits

Temporary vascular occlusion of the femoral head in 6-week-old rabbits was produced by a closed means in a hip spica; the hips were maintained for 24 h in the position of flexion, abduction and internal rotation. All animals developed necrosis of the capital femoral epiphysis, best seen histologically at 2 weeks, and this subsequently recovered. Despite marked histological changes only one hip developed radiographic changes.

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The blood supply to the hip is precarious, particularly so early in growth (Trueta 1957, Tucker 1949, Ogden & Southwick 1973, Ogden 1974). Clinically, there have been many recorded instances when the growing hip has been rendered ischaemic: usually the cause is traumatic (Ratliff 1962), but it can develop after treatment for congenital dislocation (MacKenzie et al. 1980, Gage & Winter 1972, Gore 1974). Perthes' disease is generally thought to be the result of ischaemic necrosis, but the aetiology remains obscure (Catterall 1982). It is difficult to understand the pathology of this disorder since adequate material for study has not been available except in a few cases (Catterall et al. 1982a, 1982b).

In order to help in the understanding of Perthes' disease and necrosis of the growing hip, experimental studies have been performed in the past. Most authors have used a surgical method (Young 1966, Zahir & Freeman 1972, Sanchis et al. 1973, Kemp 1973) which has obvious disadvantages. Successful reproduction of femoral head ischaemia by closed means has been reported only infrequently (Henard & Calandruccio 1970, Navarro-Quilis & Diaz-Marta 1979). We designed a study using a closed method which was reproducible and analogous to a position used in clinical practice.

Material and methods

Six-week-old Sandy Lop rabbits weighing approximately 1000 g were used for all experiments.

(a) Perfusion studies. Perfusion studies were carried out on 18 rabbits under general anaesthetic. In the initial experiment one hip was held in a position of flexion to 90 degrees, full internal rotation and full abduction without force; the other hip remained in neutral. The aorta was exposed and cannulated proximal to its bifurcation: the inferior vena cava was also cannulated. Using a previously unreported method, a suspension of Ilford Nuclear Research Emulsion L4 was perfused into the aorta until the capillaries in the feet were filled and there was a flow of the perfusate into the vena cava. The animal was killed. The proximal femora was dissected out and prepared using the standard Spalteholz technique.

This experiment was repeated with both hips held in flexion, abduction and internal rotation in a spica applied just before perfusion. Further experiments were done on animals whose hips had been held in flexion, abduction and internal rotation in a spica for 24 h.

Finally, a double perfusion technique was carried out with one hip in flexion, abduction and internal rotation and the other in neutral. Primulin dye was added to the Nuclear Research Emulsion before perfusion. The position of the hips was then reversed and a second perfusion of Nuclear Research Emulsion now coloured with fluorescein solution was done.

(b) Effects of ischaemia of the upper femoral epiphysis for 24 hours. In the second part of the experiment 35 rabbits were used. Twenty-one of these were anaesthetized briefly and a hip spica applied to maintain both hips in the position flexion, abduction and internal rotation. This position was reliably achieved and was easy to maintain for 24 h. The animals were allowed to recover and the spica was removed after 24 h. They were killed at the following intervals: immediately, and after 1, 2, 3, 5, 7, 9, and 10 weeks. The remaining animals were used as controls and killed at the equivalent times.

All animals were given a single dose of 20 mg oxytetracycline intravenously immediately after spica application.

Radiographs of the hips were taken at regular intervals.

The femoral capital epiphysis and metaphysis were bisected in the coronal plane. One half was fixed in formalin and prepared for standard histological examination. The other half was deep frozen and thick cryostat sections were examined by ultra violet-light microscopy for tetracycline fluorescence.

Results

Perfusion studies. Single dye perfusion demonstrated that in flexion, abduction and internal rotation there was occlusion to normal perfusion of the capital femoral epiphysis (Figure 1), the capsule of the hip joint and short external rotator muscles, and that this remained constant after 24 h in the immobilised position. Double dye perfusion made clear that the previously occluded hip in flexion, abduction and internal rotation was normally perfused when the position was reversed. In three out of eight single perfusion specimens a small area of the infero-medial part of the head was perfused normally. We were not able to identify the site of obstruction to perfusion. The reproducibility of the procedure was confirmed in all studies.

Macroscopic changes. Only three femoral heads were abnormal. At 3 weeks there was in one femoral head a small depression of the superolateral surface with a heaped-up rim. In a further animal at 7 weeks the left femoral head had a small crease on the superior surface and the right femoral head was grossly flattened and small. Only this femoral head was radiographically abnormal (Figure 2).

Microscopic changes (Table 1). Infarction of the epiphysis was most marked at 2–3 weeks and then recovered rapidly (Figures 3–6). There was some variability in the extent of the changes in the femoral head of animals killed at similar times. Changes occurred throughout the epiphysis and there was no evidence of subchondral fracture.

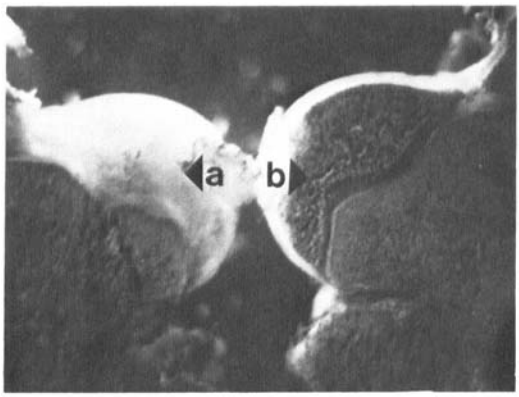

Figure 1. Single dye perfusion with Ilford Nuclear Research Emulsion.
Capital femoral epiphysis unperfused (a) when the hip was held in flexion, abduction and internal rotation, contrasted with the normally perfused contralateral epiphysis (b). Nuclear emulsion (fine grain silver bromide) turns black on exposure to UV light. The perfused parts are black, and the unperfused head is transparent. Magnification ×3.

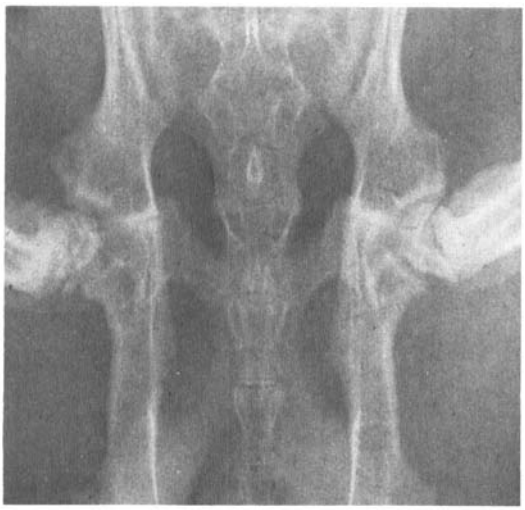

Figure 2. Radiograph of the pelvis 6 weeks after removal of the spica in the only animal with macroscopic necrosis of a femoral head; the right femoral head was small and dense.

Table 1. Summary of histological findings

Weeks after spica removal	Number of animals	Histology
0–1	6	Normal
1	2	Increased cellularity of marrow only
2	3	Established infarct involving all lamellae with granulation tissue replacing marrow elements and early appositional new bone formation
3	1	Healing infarct: lamellae mostly surrounded by new bone with vascular granulation tissue in marrow
5	3	Few areas of dead bone lying within new bone and normal bone
7	2	In one hip only unhealed infarct. Dead lamellae with little appositional new bone. Marrow elements normal. Thickened articular cartilage. Abnormal epiphysis. Metaphyseal reaction. Other specimens normal.
9	2	Normal
10	2	Normal

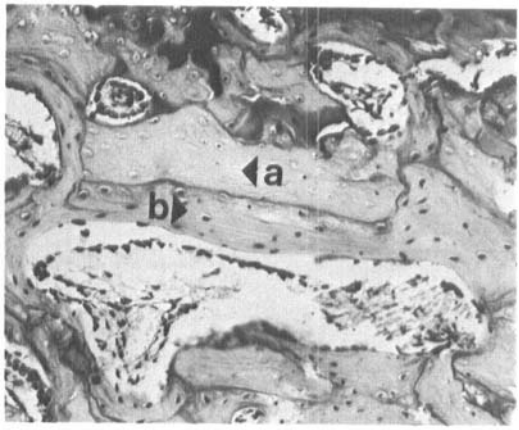

Figure 4. Histology of capital femoral epiphysis 2 weeks after spica removal showing areas of dead bone (a) and appositional new bone (b). Haematoxylin and neutral red (×80.)

Articular cartilage. No structural abnormality of the articular cartilage was seen. In a number of spica-treated hips and controls the thickness of the articular cartilage was compared using a scale inserted in the eyepiece. In the 12 control animals the thickness was remarkably constant with a mean of 536±40 μm. In the 21 spica-treated animals the mean thickness was 674±138 μm. The difference between these two means was significant.

Tetracycline studies. In all spica-treated animals there was absence of tetracycline fluorescence in the capital femoral epiphysis as compared to the fluorescence seen in control animals under U.V. light microscopy.

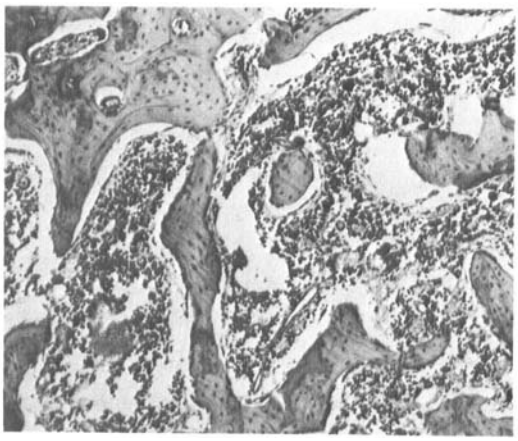

Figure 3. Histology of capital femoral epiphysis immediately after spica removal showing normal appearances. Haematoxylin and neutral red (×40).

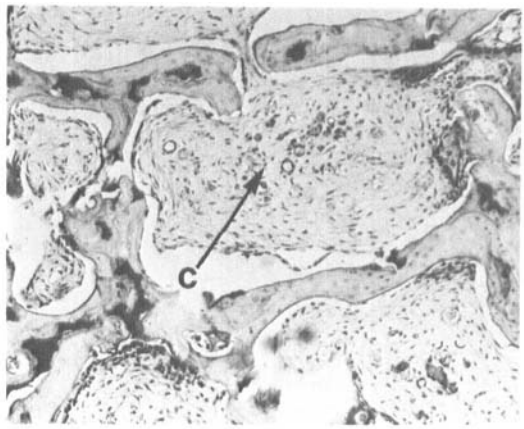

Figure 5. Histology of capital femoral epiphysis 3 weeks after spica removal showing in addition to the dead lamellae and appositional new bone a vascular granulation tissue (c) filling the narrow spaces. Haematoxylin and neutral red (×40).

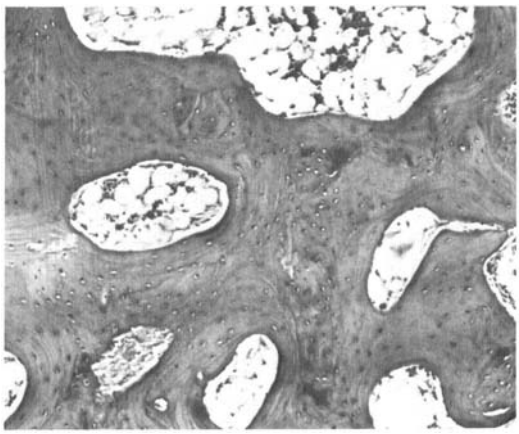

Figure 6. Histology of capital femoral epiphysis 10 weeks after spica removal showing mature lamellae and normal marrow. Haematoxylin and Eosin (×40).

Discussion

Lemoine (1957) described the normal vascular anatomy of the upper femoral epiphysis in the rabbit and showed that surgical division of the large metaphyseal branch of the anterior circumflex artery caused osteonecrosis. He compared the radiographic changes to those seen in human juvenile osteochondritis. He was able to demonstrate that revascularization occurred but that some residual deformity remained. Zahir & Freeman (1972) and Sanchis et al. (1973) produced necrosis of the capital femoral epiphysis in the dog, but found that in order to produce changes like those seen in Perthes' disease consecutive interruptions of the blood supply were required. Kemp (1973) by tamponading the hip joint produced histological and radiographic changes. The disadvantage of these methods is that an open procedure is required, which directly interferes with the blood supply in and around the hip joint. Following these open procedures recovery is slower and some residual deformity remains. In contrast in this closed model recovery was rapid and there was no residual deformity with the exception of one specimen.

Other workers (Zahir & Freeman 1972, Sanchis et al. 1973, Rang 1974) have produced changes in the structure and marked thickening of the articular cartilage. We found no structural change but there was some thickening of the articular cartilage. The implication is that a severe ischaemic result and failure to revascularise is required to produce change in the structure of the articular cartilage; our model does not reproduce the described features of Perthes' disease, which would appear to be more than just ischaemia. In only one hip were radiographic features of necrosis apparent. This can be contrasted with the marked histological changes seen in the 2 and 3 week specimens in which there were no radiographic abnormalities.

Navarro-Quilis & Diaz-Marta (1979) were able to produce perfusion defects but not ossification changes in rabbits using a closed method of hip positioning. Henard & Calandruccio (1970) employed a position in puppies which included extension and was very abnormal; using this, they produced ossification changes. By contrast, we used a position at the limit of normal and did produce an infarct. Schoenecker et al. (1978) found that frog-leg abduction and forced internal rotation of the hip in dogs drastically reduced circulation in the femoral head. They proposed that excessive mechanical pressure on the immature femoral head was directly causing ischaemia.

Others have proposed extracapsular obstruction to blood flow, in extreme positions of immobilisation of the hips. Trueta (1957) in a series of perfusion experiments in children demonstrated that from the ages of 4 to 7 years the circulation to the capital femoral epiphysis was from the lateral epiphyseal vessels. Ogden (1974) using human cadaver dissections showed that all the blood supply to the capital femoral epiphysis around the age of 3 years was from the medial circumflex artery. At positional extremes he found that perfusion through this artery was occluded and that relief of occlusion allowed normal perfusion to occur. We found, in our perfusion studies, that in the position used, in addition to ischaemia of the femoral head, there was ischaemia of the capsule and short rotators. This supports the view of an extracapsular obstruction to blood flow to the femoral head in extreme positions of immobilisation of the hips.

In the treatment of congenital dislocation of the hip, the position of immobilisation has been found to have a direct bearing on the incidence of avascular necrosis. Buchanan et al. (1981)

recommend that the "human" position is used; and that the "frog" and also the Lange (maximum abduction and maximum flexion) are no longer used. Westin et al. (1976) found that the incriminating common denominator in total avascular necrosis was the use of the "frog" position.

Our rabbit experiments confirm that occlusion to perfusion of the growing femoral head may occur when hip positions at the extreme of the normal range are maintained in a spica, perhaps correlated with femoral head necrosis following closed treatment for congenital dislocation of the hip (MacKenzie et al. 1950).

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