SYNOVITIS OF THE HIP JOINT—AN EXPERIMENTAL MODEL IN RABBITS

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One of the sequelae to some cases of synovitis of the hip joint in young children has been coxa magna (Ferguson and Howorth 1935, McMurray 1947, Neuhauser and Wittenborg 1963, Valderrama 1963, Jacobs 1971). With this fact in mind it was decided to set up an experimental model of synovitis of the hip joint of young immature rabbits and to investigate the physiological and biomechanical disturbances so induced. For this purpose surgical talc (magnesium silicate) was chosen as a physical, non-absorbable and continuing irritant to the synovium.

MATERIALS AND METHODS

Fifty-six female rabbits, from twenty-seven to thirty-one days old, were anaesthetised with open ether. The area of the hip was shaved and cleaned with tincture of iodine. Through a posterior approach the back of the capsule of the joint was exposed. With a fine needle, surgical talc suspension in saline was injected obliquely into the joint through the lateral rotator muscle and the joint capsule, to which the former is closely applied. Injection was continued until the joint was seen to be filled. At this point an arthrographic picture of the white material visible through the capsule and constricted by the coronal ligament was apparent. Usually 0.25 millilitre was injected: occasionally a little reflux of talc solution occurred but the obliquity of the needle track largely prevented this. No further traumatic or ischaemic insult was applied to the hip and the wound was closed with one or two silk sutures in the muscle and skin. The animals were allowed full activity in their cages and were exercised every few days in a large pen. Initially some animals dragged slightly the leg that had been operated upon, but in a few days all were hopping normally.

In a further eleven animals control experiments with intra-articular saline injections (five animals), needle perforation of the capsule without injection (three animals), and sham operations with exposure of the capsule only (three animals) were also performed.
Antero-posterior radiographs at one metre were taken of each animal at frequent intervals with the hips in as neutral a position as possible as regards abduction, flexion and rotation. The medial joint space was measured by constructing a horizontal line from one lateral acetabular lip to the other and dropping perpendiculars from this line, one to the most medial point on the capital ossific nucleus and a second to the apex of the concavity of the acetabular floor, and comparing the distance between the perpendiculars on the two sides.

One animal died within a day of operation and one developed purulent arthritis of the hip. The remaining sixty-five animals were killed at intervals of three to 100 days. The appearances of the synovial membrane, fluid and cartilage were noted and photographed. The right and left heads and necks were measured in the supero-inferior and antero-posterior planes with calipers which permitted an accuracy to 0·1 millimetre (Fig. 1). No direct measurements on the acetabula could consistently be made and these measurements had to be abandoned.

**TABLE I**

**Measurement of Medial Joint Space from Radiographs**

<table>
<thead>
<tr>
<th>Time after operation (days)</th>
<th>Number of animals</th>
<th>Number with difference* in medial joint space greater than 0·3 millimetre</th>
<th>Range of difference* of medial joint space (millimetres)</th>
<th>Average difference* of medial joint space for group (millimetres)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–20</td>
<td>38</td>
<td>37</td>
<td>0·3–2·7</td>
<td>0·97</td>
</tr>
<tr>
<td>21–30</td>
<td>17</td>
<td>15</td>
<td>0·3–1·5</td>
<td>0·80</td>
</tr>
<tr>
<td>31–100</td>
<td>12</td>
<td>6</td>
<td>0·3–1·9</td>
<td>0·42</td>
</tr>
<tr>
<td>3–63 (controls)</td>
<td>11</td>
<td>0</td>
<td>0–0·2</td>
<td>0·02</td>
</tr>
</tbody>
</table>

* Compared with side not operated upon.

N.B.: The total number of measurements of medial joint space exceeds the number of animals because serial radiographs were performed and therefore one animal may appear in two or three time groupings.

The heads and acetabula were decalcified in a formic acid buffer solution for two weeks. To obtain comparable histological pictures of the two sides, drill biopsies with a Turkel biopsy needle were taken at right angles to the articular surface at defined points in the heads, necks and acetabula. These were mid-superior, mid-inferior and mid-anterior points of the head, superior mid-point of the neck, and lateral, superior and inferior points in the acetabulum. The cut sections were stained with haematoxylin and eosin and photomicrographed. All heads and acetabula were then split with a knife in the coronal plane and photographed.

**RESULTS**

**Radiographic measurement of medial joint space** (Table I)—Until the tenth day there were no significant radiological changes. From this time it was apparent that the medial joint space on the side of operation in nearly every animal was enlarged (Fig. 2). In serial radiographs on the same animal the medial joint space was seen slowly to continue to enlarge, denoting further subluxation of the head.

Twelve animals were followed for as long as thirty-one to 100 days. In six of these the medial joint space approached equality with the side not operated upon, while six maintained an enlarged medial joint space until killed (Fig. 3). In the first group the medial joint space had never increased to more than 0·7 millimetre; in the second group the range of medial joint space increase was 0·7 to 1·9 millimetres.

In some cases with pronounced subluxation there appeared to develop a slight "rounding off" of the lateral acetabular lip (Fig. 4).
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Fig. 2
Showing enlargement of the medial joint space and subluxation sixteen days after induced synovitis of the left hip joint.

Fig. 3
Same animal as in Figure 2, now thirty-six days after operation. The difference between the medial joint space on the right and left has slightly decreased but subluxation persists.

Fig. 4
Twenty-one days after induction of synovitis of left hip, showing “rounding off” of the lateral acetabular lip.
No other abnormalities or obvious specific changes in radiological density were noted in the head, neck or acetabulum.

**Hip pathology**—At defined intervals after operation animals were killed and examined immediately. The hip joints were opened and disarticulated. In all animals killed before thirty days remnants of talc were visible, denoting slow absorption or phagocytosis of the material. A slight increase of joint fluid was noted on the sides of operation and usually there was evidence of synovial thickening and redness. The ligament of the femoral head was swollen but was never found disrupted before disarticulation.

An impression was gained that usually the hip cartilage was less opalescent on the side of operation. Animals killed between ten to thirty days invariably showed an obvious enlargement to the naked eye of the osteochondral head.

### TABLE II

**Measurements of Head and Neck**

<table>
<thead>
<tr>
<th>Time between operation and killing (days)</th>
<th>Number of animals</th>
<th>Average difference* of supero-inferior diameter of head (millimetres)</th>
<th>Average difference* of antero-posterior diameter of head (millimetres)</th>
<th>Average difference* of supero-inferior diameter of neck (millimetres)</th>
<th>Average difference* of antero-posterior diameter of neck (millimetres)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-20</td>
<td>26</td>
<td>0·30</td>
<td>0·22</td>
<td>0·36</td>
<td>0·31</td>
</tr>
<tr>
<td>21-30</td>
<td>9</td>
<td>0·31</td>
<td>0·35</td>
<td>0·49</td>
<td>0·34</td>
</tr>
<tr>
<td>31-100</td>
<td>12</td>
<td>0·26</td>
<td>0·37</td>
<td>0·14</td>
<td>0·23</td>
</tr>
<tr>
<td>13-63 (controls)</td>
<td>11</td>
<td>0</td>
<td>-0·08†</td>
<td>0·03</td>
<td>-0·05†</td>
</tr>
</tbody>
</table>

* Compared with side not operated upon.  
† The side not operated upon in the control animals was minimally larger.

**Measurements of head and neck** (Table II)—Comparative measurements of the heads in identical diameters on each side were made in all cases. In rabbits killed between ten to twenty days the superior-inferior and antero-posterior head, and superior-inferior and antero-posterior neck measurements were invariably increased compared to the opposite side. In animals killed between twenty-one to thirty days all measurements on average had increased a little more. However, between thirty-one and 100 days only the antero-posterior diameter of the head had continued on average to increase. Most of the animals that were observed for longer periods (over thirty days) showed flattening of the superior aspect of the head, which probably accounts for the relative decreased difference in superior-inferior diameter. In the controls no significant differences were found between the two sides.

**Hemisections and biopsy results**—In heads and acetabula which were directly bisected in the coronal plane it was seen that their absolute enlargement was mainly due to cartilage increase (Figs. 5 and 6). The capital ossific nucleus appeared to remain the same size except in more severely deformed heads in which the nucleus also was flattened and the concavity of the acetabulum decreased (Figs. 7 and 8). Animals killed after thirty days usually showed persistent deformities (coxa magna, cervix magna and ischium magnum) but cartilage thickening was much less obvious (Figs. 9 and 10).

The histological picture provides further proof that the enlargement of the head and acetabulum is mainly due to hyperplasia of their chondral parts. The cartilage of the side of operation is approximately 25 per cent thicker, there is hyperplasia of the cellular and matrix elements, and the columns of cells appear longer in both the femoral and acetabular cartilage (Figs. 11 and 12).
DISCUSSION

In an attempt to interpret the effects of pathological insults to the hip joint appraisal of the joint's embryology, micro-anatomy and physiology may justifiably be made. Thus the acetabulum and femur are derived from chondrification of the blastema (bone precursor) and receive a contribution by chondrification of the tissue of the joint inter-zone; it is thought that the articular cartilage may originate from this joint inter-zone (Haines 1947). The blastemal cartilage remaining between the metaphysial bone and the capital epiphysis becomes the growth plate. It is important to remember that this plate runs along the supero-lateral side of the metaphysis (femoral neck) and is in continuity morphologically and functionally with the growth plate of the greater trochanter. Trueta (1957) described how, even at puberty, the infantile unity of the epiphysial plate persists as a single cartilage layer covering the whole of the neck under the epiphyses of the head and greater trochanter. Salenius and Videman (1970) showed clearly with tetracycline labelling the extent of this growth plate and the new bone formation under it. In our material the hemisections demonstrate it quite clearly (Fig. 5), and the drill biopsy taken from the superior mid-point of the neck illustrates the microscopic picture (Fig. 13). The capital bony epiphysis is a sphere and is surrounded initially by a cartilage-producing layer of cells. At a later date the latter in approximation to the growth plate disappears and the spherical layer effectively becomes a cup (Rang 1969).

McKibbin and Holdsworth (1967) showed in lambs that "the cartilage of a developing epiphysis consists of two separate moieties, there is a superficial zone which from the first
is destined to become articular cartilage and is incapable of ossification, whereas the deeper layers are concerned with the actual growth of the epiphysis and will eventually be converted totally to bone”. This reflects Haines’s embryological theory.

Cameron and Robinson (1958) demonstrated by electron-microscopy a difference in collagen fibres and cells between, on the one hand, articular cartilage, and on the other hand epiphyseal head and growth plate cartilage. Mankin (1962) by autoradiographic studies showed that in immature cartilage the site of mitotic activity is concentrated into two zones—that is, he suggested an outermost zone of proliferation of articular cartilage and a deeper zone of cells awaiting endochondral ossification. Indirect evidence for this double zone of cartilage comes from consideration of the source of nutrition of the two cartilage types. Articular cartilage receives nutrition from the synovial fluid—that is, original joint tissue is sustained by joint fluid—while the ossifiable (blastemal) cartilage in children and young animals depends on vessels in the underlying bone (McKibbin and Holdsworth 1966, Honner and Thompson 1971). It thus seems justifiable to illustrate the cartilage germinal layers in the hip joint of the pre-adolescent child as in Figure 14.

**Induced synovitis**—In the present experiments a synovitis in the hip joint was produced; this would be expected to cause 1) hyperaemia, 2) raised local temperature, and 3) venous congestion. Hyperaemia brings more nutritional products and oxygen to the area, which may encourage more rapid growth. McKibbin and Holdsworth (1966) demonstrated that increased
blood supply to cartilage can stimulate it to thicken. Raised local temperature will increase the speed of all chemical and enzymal reactions and thus accelerate cell division. Thus Richards and Stofer (1959) produced stimulation of bone growth by local heat. Venous stasis may allow greater abstraction of growth materials and therefore local enlargement of parts. Thus Hutchison and Burdeaux (1954) produced limb lengthening by venous stasis operations.

Bearing in mind the aforementioned extensive areas of potential cartilage development in the immature hip, we submit that synovitis in the present experiment on rabbits' hips has caused enlargement of the cartilaginous parts of the acetabulum, femoral head and neck (ischium magnum, coxa magna and cervix magna). This result is similar to that obtained by Hoaglund (1967) who produced articular cartilage thickening in the knees of puppies by inducing chronic synovitis with repeated blood injections.

In this experiment the absence of enlargement of the medial joint space in the first week indicates no direct displacement effect of the injection on the femoral head but must imply subsequent pathological changes in the joint.

The hip is a very stable joint: the almost spherical head is deeply placed in a nearly hemispherical socket, the surrounding capsule, ligaments and muscles are strong, and these and the atmospheric pressure contribute to congruity of its surfaces.

In the rabbits' hips no large effusion under high pressure was noted. The soft tissues in the fossa acetabuli were swollen, but one must question the ability of such an inflammatory swelling with the relatively low pressure involved to subluxate the hip.

If both the acetabular and femoral head cartilage rapidly thickened it is easy to see that incongruity would arise and subluxation must ensue (the large ball cannot fit the small cup) as was found in these experiments.

Strobinia, Colonna, Brodey and Leinbach (1956) showed that a force of 154 kilograms—3·2 kgf/square centimetre cross-section—is required to produce arrest of the upper tibial growth plate in calves. It is suggested that the pressures involved with cell division and hypertrophy in hip joint cartilage following synovitis produce forces of this magnitude. Therefore the effect of swollen joint soft tissue and joint effusion pressure becomes insignificant in relation to subluxation in the present experiment.

In Tables I and II it is seen that enlargement of the medial joint space on the side of operation is over three times that of the head (0·30 millimetre head superior-inferior difference compared with 0·97 millimetre medial joint space difference at the tenth to twentieth day). Consequently, small changes of head diameter (presumably also of acetabular capacity) produce correspondingly significant degrees of subluxation.

The "rounding off" of the lateral lip of the acetabulum in the subluxated hips of some rabbits is presumably due to abnormal pressure effects on this region by the large displaced head.
If this experimental work could be extrapolated to young children with hip synovitis, one might perhaps speculate that coxa magna, which is usually considered to be enlargement of the osseous head of the femur, may be preceded by cartilaginous hypertrophy with the subsequent ossification of this cartilage model. It is also important to note that arthrographic studies of hips of children with Legg-Calvé-Perthes' syndrome have actually revealed the presence of an enlargement of the osteocartilaginous femoral head already in the initial stages of the condition (Axer and Schiller 1972).

In the above experiment there were six rabbits in which the radiographic medial joint space after first increasing in size decreased again. These rabbits had only moderate (less than 0-7 millimetre) enlargement of the medial joint space in the first place. Thus after subluxation, it seems that remodelling occurred and joint congruity was re-established. If a similar situation obtains in children with so-called transient synovitis it is easy to see why most cases have a satisfactory outcome. However, if subluxation and joint incongruity persist, the abnormal anatomical circumstances might produce their own pathological sequelae.

SUMMARY
1. Synovitis was induced in the hip joints of fifty-six rabbits by the intra-articular injection of surgical talc. The opposite hip joint and eleven suitable “sham” operations served as controls.
2. The results in the hips injected with talc were as follows. Widening of the medial joint space and sometimes acetabular changes were seen; enlargement of the femoral head and neck in two planes was found, with, in most cases, flattening of the superior aspect of the head; there was thickening of the joint cartilage and sometimes deformity of the capital epiphysis; thickening of the cartilage was the main cause of the coxa magna, cervix magna and ischium magnum.
3. The embryology, micro-anatomy and development of the hip joint is reviewed and attention is drawn to the configuration of the layers of germinal cartilage cells. The effect of an induced synovitis in producing hyperplasia of the joint cartilage, incongruity of the articulating surfaces and subsequent subluxation is discussed.
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REFERENCES


