

# Legg-Calvé-Perthes' disease

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The etiology, radiographic classification, and treatment of Legg-Calvé-Perthes' disease remain controversial. Several recent papers focus on these issues in an effort to provide guidance in the clinical care of Perthes' disease. The research studied in this paper lends further support to the hypothesis of clotting abnormalities with vascular thrombosis, which seems to be the most likely etiology for Legg-Calvé-Perthes' disease. Several studies focus on use of magnetic resonance imaging for the early diagnosis and prognosis of Perthes' disease. A few researchers whose work is featured in this paper add information on the treatment of Perthes' disease, supporting surgical treatment for older patients with more severe disease and non-surgical treatment for younger patients with less extensive femoral head involvement. *Curr Opin Orthop* 2000,

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## Abbreviations

<b>LCP</b>	Legg-Calvé-Perthes' disease
<b>MR</b>	magnetic resonance
<b>MRI</b>	magnetic resonance imaging

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## Update on Legg-Calvé-Perthes' Disease

Legg-Calvé-Perthes' disease (LCP) remains an enigma for the pediatric orthopedist in regards to the etiology, early prognosis, and treatment. Over the past year, several papers have been published that add knowledge in these critical areas. In terms of etiology, one paper is focused on clotting abnormalities, while another is focused on insulin-like growth factor abnormalities. The bulk of recent studies focus on improving the early prognosis of LCP, largely through the use of magnetic resonance imaging (MRI). Finally, four papers focus on the orthopedic treatment of LCP in patients.

## Etiology

In Cincinnati, Gruppo *et al.* (1998) [1] provide further evidence for clotting abnormalities in a case report of three siblings with clotting abnormalities who developed LCP. The family described had three-generation transmission of factor V Leiden mutation. This mutation increases the body's ability to form clots (thrombophilia) by providing resistance to activated protein C. This may cause thrombotic venous occlusion of the bone, which can lead to intramedullary hypertension, anoxia, and ischemic bone death, as seen in LCP and some other forms of avascular necrosis. Prior work by these authors shows that 60% to 80% of children with LCP have evidence of familial increased clot formation (thrombophilia) or decreased clot breakdown (hypofibrinolysis). The authors call for increased testing of the clotting factors in children with LCP and recommend a future study of anticoagulant treatment for those patients with the worst prognoses.

This author is of the opinion that the benefits of anticoagulant therapy in LCP do not outweigh the risks. At this time, clotting abnormalities represent the most common etiology for Perthes' disease; however, further research is necessary to confirm the findings of the Cincinnati group. Researchers at Boston's Children's Hospital [2] found a lower incidence of clotting abnormalities due to LCP than did the Cincinnati group. Despite finding a statistically significant Protein C abnormality, these researchers question the association between thrombolytic tendency and LCP disease. Researchers based in Atlanta [3] studied 207 patients with LCP, using a case control study format. They found significantly low levels of both Protein C and Protein S ( $P < .001$ ); however, the incidence itself of these lower rates was less than for the Cincinnati group. Researchers located in Israel [4] found a significant 10% presence of Protein C deficiency in

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children with LCP, but they could not confirm the etiological role of thrombophilia in LCP.

The only other paper that deals with etiology of Perthes' condition is from Japan. These authors [5] investigated the known delayed bone age in LCP patients by investigating insulin-like growth factors. These researchers found that serum levels of insulin-like growth factor binding protein-3 was significantly lower in LCP patients than in normal patients used as controls. Delayed bone age, delayed skeletal maturity, and growth factor abnormalities have been previously noted in children with LCP, but the role of these (association versus causation) in the etiology of Perthes' disease remains to be identified.

### Radiographic prognosis

The bulk of recent literature on LCP focuses on early determination of the prognosis of LCP, especially with regards to MRI. It is well known that LCP can be radiographically silent for the first 3 to 6 months. The gold standard for early diagnosis has been bone scintigraphy (bone scan). Several papers investigate the use of MRI scans for early diagnosis. Previous literature documents that standard MRI scanning may miss or overread LCP in the early stages. Sebag *et al.* [6•] performed a study using gadolinium subtraction MRI to provide early diagnosis of LCP. In this technique, an unenhanced image of the femoral head is compared to a gadolinium enhanced sequence. Conventional MRI scanner software automatically can subtract the two images and demonstrate marrow blood flow abnormalities. The authors studied 4 patients who had a recent history of hip pain or limping, using normal radiography, and compared bone scintigraphy with MRI. They were able to identify early ischemia and also early reperfusion of the femoral head using MRI. Clinical relevance of gadolinium subtraction MRI remains to be determined, but it appears to be a promising technique that may help guide treatment and improve the prognosis of children with LCP. In another study [7•], nine patients with Perthes' disease were followed at 6-month intervals with MRI scans and at 3-month intervals with plain radiography. This study used conventional MRI (not subtraction MRI). The authors found that the extent of the epiphyseal necrosis was not well demonstrated until 3 to 8 months after the first symptoms. It appears that MRI did not provide a tremendous advantage over plain radiography in the staging of LCP.

Sales de Gauzy *et al.* [8] evaluated hip subluxation in LCP, comparing MRI with plain radiographs. On plain radiographs, they measured the percentage of the bony femoral head that was uncovered beneath the bony acetabulum; however, on MRI, they measured the percentage of the larger cartilaginous femoral head that was uncovered by the cartilaginous acetabulum. In their 26

patients with Perthes' disease, they found that in about one third of the patients studied, the femoral head was well contained on the plain radiographs but was subluxated on the MRI due to thickening of the cartilaginous portion of the femoral head. However, the authors state that it is unknown if the subluxation visible on MRI scan and not shown on plain radiographs is associated with a poorer prognosis. Hochbergs *et al.* [9] evaluated 86 cases of LCP with serial MRI scans and attempted to correlate signal abnormalities in the femoral epiphysis with Catterall radiographic classification. They found that MR images showed the extent of necrosis earlier than did radiographic images. They came up with a new classification for MRI abnormalities, and also divided the images of the femoral head into four zones. This study did not include long-term follow up on patients or patient treatment; hence, the clinical utility of using MRI to determine LCP prognosis remains unproven. In 21 children who were treated for LCP, MRI was used to examine the femoral head after femoral varus osteotomy. Using MR images, the authors demonstrated earlier remodeling of the femoral head than was noted with conventional radiography after Perthes' surgery. In children with severe Perthes' involvement, the authors demonstrated early and continuous spherical remodeling of the femoral head after containment surgery. Unfortunately, this study had no control group. Most metaphyseal cysts in LCP are thought to be cartilage divided from the growth plate. Johnson *et al.* [10] present a case report of non-cartilaginous metaphyseal cysts in LCP that were detected on MRI. A biopsy of the cysts revealed no cartilaginous elements but rather granulation tissue, fat necrosis, and dense fibrous connective tissue in the cyst, with no cartilaginous elements. This case illustrated that not all metaphyseal lesions in LCP are cartilaginous or are located in the anterior metaphysis.

Retrospectively, Ismail and Macinol [11••] reviewed conventional radiographs and arthrograms from childhood to maturity in children with LCP. The Herring classification correlated best with the ultimate Stulberg grade, followed by sphericity on arthrogram and the patient age. Catterall grouping and Salter-Thompson grading did not correlate as well. These authors recommend surgical treatment for children over age six in the Herring group C as well as for those in Herring B when arthrography shows loss of sphericity. The authors' surgical treatment of choice was a 15° to 20° femoral varus osteotomy. Specchiulli and Scialpi [12••] performed a similar retrospective study with different results. 45 patients with LCP were reviewed an average of 24 years after the onset of the disease. These authors' results differed from those of Ismail and Macinol [11••], in that Specchiulli and Scialpi [12••] found a better overall predictive value for the Catterall classification than for the Herring system; however, the intraobserver reproducibility was much better with the Herring system, which

showed 80% reproducibility versus 42% reproducibility using Catterall classification. Because prognosis is the most important factor in an LCP classification scheme, this paper supports the Catterall system over the Herring classification.

## Treatment

Three of the last four papers deal with the treatment of LCP. Lahdes-Vasama *et al.* [13] compared a group of 22 hips of patients with LCP who were all treated with femoral varus osteotomy regardless of the stage of the disease, with a group of 34 patients (historical controls) who underwent treatment with a non-containment ischial-bearing caliper (Thomas splint). Lahdes-Vasama *et al.* noted no difference in outcome in children who were in Salter Group A, but in patients whose hips had more than 50% head involvement (Salter Group B), the surgical method resulted in slightly better coverage and sphericity of the femoral head than did treatment with the Thomas splint. Follow up of patients in the splint group averaged 18 years versus 15 years' follow up of patients who were treated surgically. This study adds to the increasing evidence that operative treatment seems to benefit the more severely involved children with LCP. Dimitriou *et al.* [14] performed shelf arthroplasty on 14 hips of 12 children with severe LCP. All children were over 9 years of age. In 4 years of follow up, these children showed good clinical outcome. The authors noted that at the last follow up, the children were pain free, walked without a limp, and had a negative Trendelenburg sign; moving was painless and all hips were improved. The authors did state that abduction and flexion in 6 hips of patients was slightly reduced. This study fails to mention the exact range of motion in children and also fails to place children into Stulberg classification; thus, long-term results cannot be predicted. These authors also did not use a control group. The final paper, by Koyama *et al.* [15], discusses 13 patients (14 hips), each of whom underwent a modified Chiari osteotomy performed for late arthrosis after LCP. Median age of the patients at the time of surgical treatment was 33, with an average of 6 years' follow up. These authors found that the hip score improved substantially from 76 presurgery to 91 postsurgery. These authors recommended this procedure for patients with early arthrosis, early acetabular dysplasia, and pain with good range of motion.

The most significant study on LCP, from the Texas Scottish Rite Hospital, remains in progress [16]. This multi-center study involves children age 6 and older (chronological age) with LCP. The preliminary results indicate that children who are Herring Group A patients do not benefit from surgery (either femoral or Salter osteotomy). Herring Group B patients with a *bone age* greater than 6 years old, and all Herring Group C patients regardless of bone age, do show a statistically significant improvement with surgical intervention (femoral or

Salter osteotomy) [16]. The Herring study does not provide data on children younger than 6 years of age.

## Current treatment recommendations

Observation is indicated for children with LCP who maintain good hip motion and are Herring group A patients, or are Herring Group B patients with a bone age of less than 6 years. When symptoms flare, activity restriction (bed or couch rest), along with physical therapy stretching and traction may be indicated. Six to 12 weeks of Petrie casts placed on patients under anesthesia (with or without medial soft tissue release) may be indicated for symptoms of persistent hip stiffness in young patients. Children who are Herring Group B patients and who have a *bone age* of less than 6 years, and all Herring Group C patients with a chronological age of 6 years or older, should be considered for surgical containment regardless of their bone age. Because the Herring study shows a positive surgical effect down to age 6 in Group C patients, it is likely that some children younger than 6 years of age with severe LCP may benefit from surgery. However, the treatment of most children who have LCP and are younger than 6 years of age can be managed nonsurgically.

## Conclusions

The recent studies discussed in this paper have increased the knowledge of LCP etiology, imaging, and treatment. The most promising new research in LCP etiology comes from clotting factor abnormalities, which remain a hotly contested subject. Identifying clotting abnormalities in patients with LCP may help identify both patients and families who are at risk for other thrombotic disorders, such as pulmonary embolism, stroke, and ischemic heart disease. Until further collaborative evidence is obtained, treatment of clotting abnormalities does not appear indicated at this time. New techniques in MRIs, such as subtraction imaging, may help in establishing early prognosis and also may help to dictate treatment. Finally, early results from the multi-center LCP study [16] indicate that most children who are classed with Herring Group A and Herring Group B, who also have a *bone age* of 6 years or less, do well with observation and limited non-surgical treatment. For those children with Herring Group B and a bone age of 6 years or more, and those children with Herring Group C and a chronological age of 6 years or more, the changes observed through radiography appear to do better with surgical containment.

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