

# The incidence and distribution of Legg–Calvé–Perthes' disease in Liverpool, 1982–95

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## Abstract

**Aims**—To determine the incidence and distribution of Legg–Calvé–Perthes' disease in Liverpool, in the period 1982–95.

**Methods**—Examination of information in a register, analysing the patients' addresses by indices of deprivation.

**Results**—A total of 122 white children were diagnosed as having Perthes' disease during the study, whereas black and minority groups form 5.8% of the population. The incidence rate in inner Liverpool had decreased to 10.5 in the period 1990–95. Simple Spearman correlations revealed an association between the disease incidence in electoral wards and deprivation. Regression analysis showed that for the period 1990–95 the most powerful effects on incidence were increases in ward deprivation since 1976, the percentage free school meals in 1986, the ward Health Index in 1981, and the percentage low birth weight in 1981.

**Conclusions**—We suggest that environmental influences may come into play some years before a child presents with pain in the hip. There may be a genetic predisposition to the disease.

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Keywords: Perthes' disease; deprivation; dysplasia; osteochondroses

Many factors appear to be involved in the development of Legg–Calvé–Perthes' disease (LCPD). Abnormalities of growth and development have led to the concept of "the predisposed child".<sup>1</sup> The patients are below average in stature, have retarded skeletal maturation, and skeletal disproportion.<sup>2,3</sup> Hall and colleagues<sup>4</sup> noted that similar disproportionate growth is found in chickens suffering from trace metal deficiency, and found low serum manganese concentrations in their patients, but this has not been confirmed.<sup>5</sup> Glueck and colleagues<sup>6</sup> reported that patients had a deficiency of antithrombin factors, but this is unproven.<sup>7</sup> Glueck and colleagues<sup>8</sup> also found depressed fibrinolysis in association with parental smoking. There is correlation with breech birth, low birth order, and older than average parents.<sup>9</sup> A multifactorial pattern of inheritance has been reported<sup>10</sup>; this concept of a genetic aetiology is supported by Burch and Nevelos.<sup>11</sup> A survey in South Africa showed a low incidence in the black compared to the white population.<sup>12</sup>

In the UK, the disease occurs more frequently in Northern Ireland,<sup>13</sup> and in north west England, where around Liverpool there are many people of Irish descent.<sup>14</sup> However, in

Liverpool we have previously favoured an environmental causation, the highest incidence being in urban areas, in families from a poorer socioeconomic background.<sup>15</sup> Hall and colleagues<sup>15</sup> reported in 1983 the highest annual incidence ever recorded: 21.1 cases per 100 000 for children aged 0–14 years who lived in inner city wards of Liverpool in the period 1976–81. The City Planning Office defined these "inner city" wards for administrative purposes.<sup>15,16</sup> In the 1998 update of the Index of Deprivation for 310 Districts in England,<sup>17</sup> Liverpool scored highest (most depressed); adjacent districts to Liverpool were also high (Knowsley is ninth and Sefton is 54th).

In the present study we have calculated the incidence rates of LCPD for the electoral wards of Liverpool City and the adjacent districts of Sefton and Knowsley from 1982 to 1995, using a case register of new patients. The objective was to determine whether there has been a change in the disease incidence since 1981, and to study further the environmental factors involved in the aetiology.

## Methods

Children from Liverpool, Sefton, and Knowsley were referred under the National Health Service to the Orthopaedic Department at Alder Hey Children's Hospital, where a Perthes' disease register has been maintained by two of the present authors since 1978. This formed the basis for the study, and has been reviewed up until 1999, but no further children have attended who were symptomatic during the study period of 1982–95. We also undertook a search of the computer records of Hospital Activity Analysis, and a manual search of registers in the operating theatres and wards, to check the completeness of the register and compile the annual list of patients. We interviewed the parents to determine the district in which the patient was born.

Incidence rates per 100 000 children aged 0–14 years were calculated for each district and the Mann–Whitney U test was used to calculate the significance of the difference in rates between the districts (table 1). For the electoral wards in the period 1982–89, the denominator was derived from ward specific numbers of children aged 14 years or below from the 1981 census. For 1990–95 the 1991 census figures were used. We have calculated the average of the ward specific rates of Perthes' disease for the three districts of Merseyside (Liverpool, Sefton, and Knowsley); Liverpool was further subdivided into inner and outer.<sup>16</sup>

The deprivation index, calculated by the Department of the Environment for each ward,<sup>17</sup> was used to correlate the rates of LCPD

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Table 1 Trends of incidence rates of LCPD per 100 000 children under 15 years by area of residence

Area	Years		
	1976-81	1982-89	1990-95
All Liverpool	16.9 (13.5-20.3) 16.3	8.5 (6.7-10.4) 9.2	8.7 (6.3-11.1) 6.9
Inner city	21.9 (16.7-27.1) 21.0*	8.0 (5.0-10.9) 9.6	10.5 (7.0-14.0) 10.6
Outer city	13.2 (9.1-17.2) 11.8	8.9 (6.3-11.6) 7.9	7.4 (4.0-10.8) 5.9
Knowsley	14.6†	14.1†	11.3 (6.7-15.9) 11.1‡
Sefton	11.9†	8.9†	4.4 (2.4-9.9) 6.0

Results expressed as mean (95% CI), followed by the median value.

\*Mann-Whitney U test for comparison between inner and outer Liverpool;  $p = 0.014$ .

†Crude overall rate, not based on ward specific rates.

‡Mann-Whitney U test for comparison between Knowsley and Sefton ( $p = 0.02$ ).

Table 2 District mean deprivation indices and incidence rates of LCPD per 100 000 children under 15 years in the period 1990-95

	Area		
	Liverpool	Knowsley	Sefton
Deprivation index	10.5 (8.8-12.2)	9.4 (7.4-11.3)	4.4 (2.3-6.4)
Rate of LCPD*	8.7 (6.3-11.1) <i>R</i> ( <i>p</i> value)	11.3 (6.7-15.9) <i>R</i> ( <i>p</i> value)	4.4 (2.4-9.9) <i>R</i> ( <i>p</i> value)
Spearman correlation†	0.23 ( $p = 0.28$ )	0.45 ( $p = 0.03$ )	0.11 ( $p = 0.47$ )
All causes death (SMR) males‡	118	121	83
Low birth weight (%) (1997)‡	8.1	8.5	7.8

\*Average ward specific rate.

†Correlation between deprivation index and rate of Perthes' disease.

‡The information on SMR and low birth weight is from the Public Health Common Data Set, 1998.

Table 3 Multiple regression analysis of the factors associated with the incidence of Perthes' disease in the period 1990-95

	<i>B</i>	<i>t</i>	<i>p</i> value
Change in z score for deprivation between 1976 and 1995	2.670	3.196	0.003
Percent low birth weight in 1981	3.361	2.706	0.011
Percent free school meals in 1986	-0.233	-2.356	-0.026
Health index in 1981 (z score)	-2.425	-2.016	0.054

$R^2$  44%; *df* (4, 28); *F* ratio = 5.53;  $p$  value = 0.002.

Data for ward deprivation rates were only available for Liverpool City. The table is based on 33 wards, not 78. *B* is the regression coefficient. The table indicates that the incidence of LCPD changes 2.67 units per unit change in z score.  $R^2$  represents the percentage variation explained by the variables in the model.

with ward deprivation (table 2). This index gives a deprivation index for each electoral ward based on unemployment (percentage economically active residents aged 16-59/64 who are unemployed), car ownership, home ownership, and overcrowding.

Table 3 presents an overall health index based on mortality (standardised mortality ratio), disablement (percentage classified as permanently sick or disabled), and delayed development (proportion of live births below 2500 g), which was used as a summary measure for health status. The information on standardised mortality ratio and low birth weight is from the Public Health Common Data Set, 1998. Multiple regression analysis was used in table 3 to calculate the significance of these factors in their association with ward rates of LCPD. For Merseyside as a whole we have used the Spearman correlation.

## Results

During the 14 years of the study, 122 children in Liverpool City were diagnosed as having Perthes' disease, of which 51 were in the inner city and 71 in the outer. There were 60 patients

from Knowsley and 38 from Sefton. Four patients entered in the LCPD register were excluded from the review: two had other joints involved with dysplasia and were considered to have multiple epiphyseal dysplasia; in two others, on review, the radiographs were not considered to be abnormal, transient synovitis being the diagnosis. An active search among colleagues in Liverpool leads us to believe that within the city no patients were omitted from the review. However, in Sefton and Knowsley, we have been told that an occasional patient with mild disease, possibly one or two per annum in each district, has been seen and not referred to Alder Hey. There is no reason to believe that the numbers involved in such under referral have changed over the review period. In the period 1982-89 the mean age of patients from Liverpool City was 5.8 years and 5.7 years for males and females respectively. In 1990-95 the corresponding figures were 6.3 and 6.0 years. In 1982-89 the male:female ratio was 4.2; in 1990-95 it was 5.6.

There were no children from any black or minority ethnic groups registered with LCPD, despite these groups representing 5.8% of the Liverpool population in the 1991 census. However, between 1981 and 1991 the population at risk has declined in Liverpool from 100 269 to 89 142; in Knowsley from 41 427 to 34 994; and in Sefton from 61 228 to 54 207.

The incidence of the LCPD per 100 000 for all Liverpool children aged 0-14 has decreased from 16.9 in the period 1976-81 to 8.7 in 1990-95 (table 1). There is a significant difference between the incidence in 1976-81 and incidence in the periods 1982-89 and 1990-95, but no difference between the later two periods, as indicated by the confidence intervals for the three districts. In 1976-81 the rate in inner Liverpool was 21.0, significantly different from the rate for outer city children of 11.8. We have not found a change in the incidence rates in Knowsley and Sefton between 1976-81 and those for the periods 1982-89 and 1990-95. However in the period 1990-95 there was a significant difference in the rate of 11.1 for Knowsley and that for the more affluent district of Sefton of 6.0. We do not have adequate information for the two earlier periods to permit proper statistical analysis.

The ward maps (figs 1 and 2) show that in 1990-95 (fig 2), high incidence wards were found both near the city centre and also at the periphery. This compares with the distribution in the period 1976-81,<sup>15</sup> when higher rates were noted in the downtown area of Liverpool, adjacent to the River Mersey (fig 1).

Table 2 presents the mean deprivation index and Perthes' rate for all of Liverpool and for Sefton and Knowsley based on the most recent data. Sefton has both the lowest average deprivation index and rate of LCPD in Merseyside. For Merseyside as a whole, there was a statistically significant positive correlation between rates of deprivation and LCPD (Spearman  $r = 0.36$ ;  $p = 0.001$ ).

In 1981 nearly 7% of babies born in Liverpool were low birth weight (less than

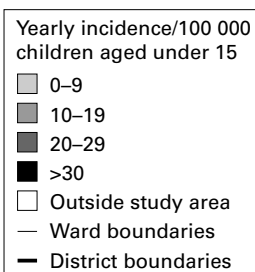
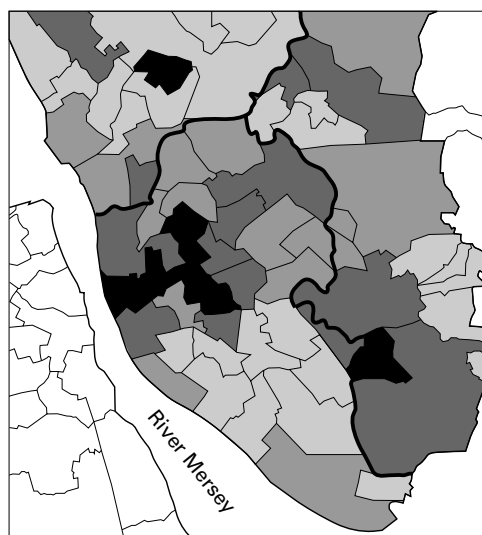


Figure 1 Average incidence of Perthes' disease per 100 000 children aged 14 years and under, in the electoral wards of Liverpool and adjacent area of Merseyside, in the period 1976-81 (redrawn from Hall et al, with permission<sup>15</sup>).

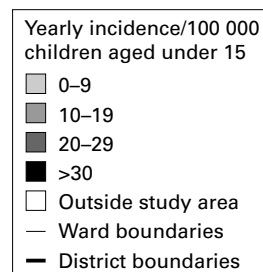
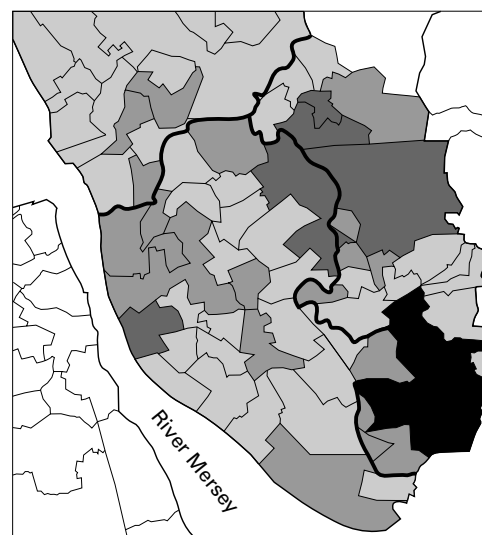


Figure 2 Average incidence of Perthes' disease per 100 000 children aged 14 years and under, in Liverpool in the period 1990-95.

2500 g); the average percentage of children receiving free school meals was 50%; and the average unemployment was 27%. The 1990-95 rate for LCPD in Liverpool as a whole was statistically significantly correlated with the percentage of low birth weight babies in 1981 (Spearman  $r = 0.47$ ,  $p = 0.007$ ). The overall health index was weakly related to the LCPD rate (Spearman  $r = 0.32$ ,  $p = 0.07$ ); but neither the percentage unemployed nor the percentage of children on free school dinners were related to rates of LCPD.

Multiple regression analysis was used to summarise the effects of various measures of social deprivation and health on the ward specific rates of LCPD within Liverpool in 1990-95. Various models were run to explore the impact of key measures of deprivation on incidence. The most robust model ( $R^2$  44%; F ratio 5.5;  $p = 0.002$ ) consisted of a measure of the change in deprivation from 1976 to 1995 (LCPD rates were higher where deprivation had increased), the percentage of neonates having low birth weight in 1981 (rates of LCPD were highest where the prevalence of low birth weight was highest), the proportion of free school meals in 1986, and a low health index in the electoral ward (table 3). The 1996 ward deprivation indices and ward specific rates of low birth weight did not contribute specifically to the model.

## Discussion

This study has shown that the incidence rate of LCPD for children in all of Liverpool diminished after the period 1976-81. However, between 1982-89 and 1990-95 any change is not statistically significant. In the nearby districts of Sefton and Knowsley we found no statistical evidence of any decline. There is no reason to believe that the diagnostic criteria used during the present work have been more stringent than those used by Hall and colleagues, who reported on the period 1976-81.<sup>15</sup> However, we agree with Moberg and Rehnburg,<sup>18</sup> who reported an incidence of 8.5 from Sweden, and said that it should more properly be termed the "minimal incidence", as some children do not present to a physician during the active stages of the disease. While the children presenting in 1990-95 were slightly older than in 1982-90, we do not believe this had an effect on the incidence data. Although mild cases of LCPD in Sefton and Knowsley may not have been seen at Alder Hey, we do not believe that such under reporting has varied over the years.

While the population studied in the present work has disparate origins, many people have a common ancestry in Ireland, and Kealey and Cosgrove reported a high incidence of 11.6 in the north of that country.<sup>13</sup> Moreover, the present work reveals a lack of LCPD in black children, as noted previously in South Africa.<sup>12</sup> These findings point to a genetic predisposition.

## TRENDS WITH TIME

The present work shows that within Liverpool the overall rate of LCPD has fallen from 16.9 to 8.7 over some 19 years. This may be explained by an improved standard of living within the city. Much of the population is now living in improved housing. Between 1971 and 1991 there was a decline in the average number of people per household from 3.04 to 2.44.<sup>19</sup>

## TRENDS WITH DEPRIVATION

In 1976–81 there was a significantly increased rate of LCPD in children of inner city wards (table 1) compared to those in the outer city. Moreover, the children of Knowsley are more deprived than those in Sefton and we have found a diminished incidence of LCPD in the latter, more affluent district (table 1). The disease incidence correlates with contemporaneous deprivation indices using Spearman correlation. Although Peic<sup>20</sup> in Dortmund related peak incidence to periods of economic depression, there has been little recent European support for the concept that urban life and associated deprivation increased the incidence. Hall and Barker<sup>21</sup> found no correlation with urbanisation in Yorkshire, but this is a low incidence county. Their results are in accord with the high incidence rates reported in the population of rural west India.<sup>22</sup> In Northern Ireland, Kealey and colleagues<sup>13</sup> found a similar incidence in urban and rural areas, deprivation being common in the latter. However, the ward correlation with deprivation reported here cannot be explained on differences in water supply nor in the atmosphere external to the home or workplace.

This study has shown that even within a relatively poor area such as Liverpool, measures of deprivation at the ward level, such as low birth weights or the percentage of free school meals predict the incidence of LCPD. Furthermore, the results presented in table 3 lead us to conclude that in 1990–95, children living in wards where deprivation had been increasing relative to the other wards were more likely to develop LCPD. This was the case for children in wards where the prevalence of low birth weight was high in 1981, the prevalence of free school meals was high in 1986, and the general health index for adults was poor. It is not possible in this analysis to draw causal relations between individual measures. However, the strong links with measures which indicate deprivation earlier in the life of the children with LCPD, lead us to speculate that the aetiology may be determined by environmental factors acting some years prior to the disease onset.

There is good evidence that the diet of children in the north of England is poorer in a qualitative sense than elsewhere in the UK where rates of LCPD are lower.<sup>23</sup> This does not

prove a dietary link, as we have no good data to show that those children who develop LCPD had poorer diets at conception or in early life. It is unlikely that vitamin C deficiency is important as a sole aetiological factor, as there is no lack of this in the high incidence areas of Karnataka.<sup>22</sup> However, if the disease onset is determined earlier in life, dietary or serological studies of the affected child at the time of diagnosis may yield negative or misleading information. Moreover, if the onset of LCPD is influenced by dietary deficiency in infancy, supplementation of the patient might be expected to have little effect on the outcome.

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