Age of exposure to infections and risk of childhood leukaemia

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Building on previous suggestions,[1-3] we speculated that childhood leukaemia might be a rare manifestation of an infection that would have remained subclinical at an earlier age. Several ecological studies have produced evidence to support a hypothesis based on herd immunity, but others have not.[4] We reasoned that a better approach would be to compare cases of childhood leukaemia with controls with respect to attendance at creches, where crowding of children ensures effective transmission of infectious agents.

Subjects, methods, and results

From July 1987 to June 1991 170 cases of childhood leukaemia were diagnosed in the population of Attica (Athens and its surrounding region).[5] During the first eight months of 1992 we conducted telephone interviews with these children's parents to obtain details about their age, sex, social class (based on mother's education and number of siblings), and potential risk factors—attending a creche, birth order (which can also affect age of exposure to infections[4]), and exposure to magnetic fields. Controls were children resident in Attica who attended the outpatient clinics of the two children's teaching hospitals of the University of Athens, where all the children with leukaemia were treated. We attempted to assemble a control group similar to the expected series of cases with roughly equal distributions of sex, age, and hospital by systematically selecting every fifth child of each sex in the age ranges 0-4, 5-9, and 10-14 at each hospital. We contacted the parents of 240 children to obtain enough controls because some parents (mainly of lower social class) refused to participate.

We also conducted telephone interviews about the 13 cases of childhood leukaemia diagnosed from July 1990 to June 1992 in the University of Crete's teaching hospital, where all cases of leukaemia on the island are treated. The hospital's Paediatric Oncology Unit opened in July 1990, and earlier data were unavailable. During 1992 we contacted the parents of 20 children in the outpatient clinic to obtain controls.

We received satisfactory details for 125 of the cases of leukaemia in Attica (in four cases the parents refused to cooperate, in 12 the information was inadequate, and in 29 the parents could not be contacted) and 11 of the cases in Crete (two were rejected because of inadequate information) to give a total of 136. The 172 controls recruited in Attica and 15 recruited in Crete had attended hospital because of general paediatric problems (92 from Attica and eight from Crete), surgical and orthopaedic problems (48 and three), otolaryngological problems (19 and four), and ophthalmic problems (13 from Attica).

The table shows the distribution of cases and controls by the study variables and the relative risks of leukaemia (from multiple logistic regression analyses that also controlled for place of residence). The results for the two variables assessing exposure to magnetic fields were not significant and suggested opposite conclusions. Attendance at a creche was inversely associated with the risk of childhood leukaemia, and for early attendance (for ≥3 months during the first two years of life) the association was significant (p=0·03). The results were not appreciably affected by considering only control children with general paediatric diagnoses, changing the operational definition of early attendance, or restricting analysis to children aged ≥5. Residence in Attica or Crete did not interact with attending a creche (p=0·76, logistic regression model).

Relative risk of childhood leukaemia by selection variables and risk factors estimated from 136 cases and 187 controls

	No of cases: No of controls	Relative risk (95% confidence interval)	Two tailed p value
Selection variables			
Sex:			
Female	57:77	1	
Male	79:110	1·15 (0·71 to 1·86)	0·57
Age at diagnosis (years):			
0-4	62:62	1	
5-9	54:73	0·80 (0·47 to 1·38)	0·42
10-14	20:52	0·43 (0·22 to 0·85)	0·02
Sibship size:			
≥3	42:31	1	
2	67:123	0·52 (0·25 to 1·12)	0·09
1	27:33	0·75 (0·29 to 1·93)	0·55
Length of mother's education (years):			
1-6	47:37	1	
7-14	65:100	0·54 (0·31 to 0·95)	0·03
≥15	24:50	0·38 (0·19 to 0·76)	0·01
Risk factors			
Birth order:			
1	62:99	1	
2	50:75	1·04 (0·58 to 1·85)	0·90
≥3	24:13	1·48 (0·52 to 4·25)	0·47
Exposure to magnetic fields:			
Distance from electricity substation			
≥100 m	131:174	1	
<100 m	5:13	0·35 (0·12 to 1·08)	0·07
Distance from power lines			
≥50 m	40:55	1	
5-49 m	69:99	1·06 (0·61 to 1·84)	0·83
<5 m	27:33	1·19 (0·59 to 2·41)	0·63
Attendance at creche:			
At any time			
No	85:93	1	
Yes	51:94	0·67 (0·41 to 1·11)	0·12
In infancy*			
No	132:169	1	
Yes	4:18	0·28 (0·09 to 0·88)	0·03

*For ≥3 months in the first two years of life.

Comment

As with other studies of this topic, our study suffers from cases and controls not being ascertained simultaneously. Furthermore, although the study was meant to be population based, data for several subjects were unavailable, and controls were of higher social class than cases. Social class, however, was not strongly associated with attending a creche (35% of control mothers with 1-6 years' education, 52% of those with 7-14 years, and 58% of those with ≥15 years) and was controlled for in the analysis. Except for sex and age, and possibly social class and exposure to magnetic fields, there are no other suspected risk factors for childhood leukaemia.

Our results are compatible with previous suggestions[1-3] in indicating that early attendance at creches reduces the risk of childhood leukaemia, presumably by reducing the age of exposure to infectious agents. The association survives when alternative operational definitions of early attendance were used.

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