Clustering of leukaemia and other childhood cancers in the UK provides aetiological clues

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Summary.

The evidence from studies of spatial and space-time clustering of childhood cancer in the UK is examined. Space-time clustering was found for cases of leukaemia, CNS tumour, soft tissue sarcoma and Wilms tumour. Spatial clustering was found for cases of leukaemia. The findings are interpreted as supporting an infectious aetiology, especially for leukaemia and CNS tumours.

Introduction.

This paper examines clustering of childhood cancer in the UK. The study of disease clustering can provide aetiological clues. Two different types of clustering are considered, namely space-time clustering and spatial clustering.

Space-time clustering is said to occur when excess numbers of cases are observed within small geographical locations at limited periods of time, which cannot be explained in terms of general excesses in those locations or at those times. Space-time clustering may be described as “the irregular grouping of cases of any disease simultaneously in space and time”. These irregularities might result from any number of the following situations. (1) A small number of “locations” with greatly increased incidence at short (but distinct) periods of time. (2) A large number of “locations” with moderately increased incidence at limited periods of time. (3) A small number of short (but distinct) “time periods” with greatly increased incidence at limited locations. (4) A large number of limited “time periods” with moderately increased incidence at limited locations.

Spatial clustering is defined as “the irregular grouping of cases of any disease in space”. Such an irregular distribution is a general phenomenon and is not confined to one specific small area. These irregularities could arise because there are a small number of areas with greatly increased incidence or a large number of areas with moderately increased incidence.

Materials and Methods.

A number of different statistical methods have been used to test for space-time clustering of cases of childhood cancer, including the methods due to Knox (1964) and Diggle et al (1995). The Knox (1964) method has been criticised because it relies on an arbitrary choice of boundaries to define ‘close in time’ and ‘close in space’. The more recent method of Diggle (1995) overcomes this problem.

Also, a number of different statistical methods have been used to test for spatial clustering of cases of childhood cancer (Besag and Newell, 1991; Black et al, 1996; Muirhead and Ball, 1989; Openshaw et al, 1988; Potthoff and Whittinghill, 1966a, b).

Results.

Six studies have found statistically significant evidence for space-time clustering of childhood leukaemia. For two studies (Birch et al, 2000; Gilman and Knox, 1995) the space-time clustering was based on time and place of diagnosis. For one study (Mainwaring, 1966) the space-time clustering was based on time and place of onset. For four studies (McNally et al, 2002a; Smith et al, 1976; Morris,
1990; Gilman and Knox, 1995) the space-time clustering was based on time and place of birth. For one study (Birch et al, 2000) there was also space-time clustering based on time of diagnosis and place of birth.

Also, one study has found statistically significant space-time clustering amongst central nervous system (CNS) tumours (McNally et al, 2002b), whilst another study has found significant space-time clustering amongst cases of soft tissue sarcoma and Wilms tumour (McNally et al, 2003). The space-time clustering amongst cases of CNS tumour was mainly based on time and place of diagnosis, whilst the space-time clustering amongst cases of soft tissue sarcoma and Wilms tumour was only based on time and place of birth.

Four studies from the UK have found spatial clustering amongst cases of childhood leukaemia (Black et al, 1991; Alexander et al, 1991; Besag and Newell, 1991; Openshaw and Craft, 1991).

Discussion.

The finding of space-time clustering is especially consistent with the involvement of infections in aetiology. The particular combination of time and place of birth, onset or diagnosis indicates the likely timing of exposure. For example, space-time clustering based on time and place of diagnosis would indicate that infection occurs close to diagnosis, whilst space-time clustering based on time and place of birth would indicate that infection occurs at some time distant from onset including in-utero.

The presence of spatial clustering may indicate the involvement of any environmental factor including infections. If infectious agents are associated with sustained and variable latent periods then spatial clustering, but no space-time clustering, may be observed.

The results of studies from the UK provide evidence for the involvement of infections in the aetiology of childhood cancers, particularly leukaemia and CNS tumours.

Conclusions.

Taken together, the finding of clustering amongst cases of certain childhood cancer is consistent with an infectious aetiology

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References.


