Spatial, temporal and risk factor studies on the epidemiology of human and bovine cryptosporidiosis in Scotland.

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Summary

Human and animal case data from Scottish cases of *Cryptosporidium parvum* infection during the period 1999-2002 were analysed using spatio-temporal statistical techniques. Three spatial lag models were constructed. For each model there was evidence that there were both local and more distant spatial effects significant. Whilst the overall model was broadly informative, decomposing the spatial structures into COWP 1 and COWP 2 specific models confirmed differing epidemiological processes. Investigation of risk factors identified age of patient and location as risk factors for COWP1 versus COWP 2.

Introduction

Cryptosporidium parvum is a coccidian parasite which has become well established as a cause of intestinal disease in humans and animals over the last two decades, representing the third major cause of diahorreal disease worldwide (Abrahamsen and Schroeder, 1999; Fayer *et al.*, 2000; Spano and Crisanti, 2000; Jellison *et al.*, 2002). In addition to causing morbidity and mortality in livestock, this pathogen has attracted significant investigation in recent years because of its importance in terms of human illness and also because infected animals are regarded as a source of domestic water contamination (Chappell, 1999; Casemore, 2001; Gale, 2001). Central to epidemiological considerations of whether the parasite in any given case is anthroponic or zoonotic is the ability to type or subtype the organism. One system for typing *C parvum* is the use of the Cryptosporidium Outer Wall Protein (COWP) gene (e.g., Caccio *et al.*, 2000), which can be used to differentiate two types, commonly referred to as COWP 1 and COWP 2. COWP 1 is accepted as specific to humans, whereas COWP 2 affects both humans and animals; as a result COWP 1 is recently recognised as *C. hominis* (Morgan-Ryan *et al.*, 2002)

Objectives

To establish the temporal and spatial epidemiology of cryptosporidiosis in Scotland, in humans and animals, with the focus on the established COWP typing system.

Materials and methods

Human case data were accessed through the databases held by the Scottish Centre for Infection and Environmental Health (SCIEH). Animal data were similar in structure but were sourced via SCIEH, from the Scottish Agricultural Colleges' (SAC) laboratories. Spatial boundary data were obtained from EDINA Digital boundary data, from the 1991 human census, via the internet from UK Borders at the University of Edinburgh. Human population data were based on the 1991 census and retrieved, at post-code level, again via the internet from the University of Manchester. Animal population data were accessed through the Scottish Executive Environment and Rural Affairs Department. Data manipulation was carried out using Microsoft Access and Microsoft Excel. Summary statistics were calculated using Minitab statistical software. Using available data and with the prevalence of cryptosporidiosis as the dependent variable, three spatial models (all, COWP1, COWP2) were developed. In comparison of human genotypes COWP 1 and COWP 2, a multivariable logistic regression model was developed in order to identify significant factors and variables associated with the two COWP types.

Results

Three spatial models were constructed. For each model there was evidence that there were both local and more distant spatial effects significant. Whilst the overall model was broadly informative (Table 1), decomposing the spatial structures in COWP 1 and COWP 2 specific models confirmed the differing epidemiological processes highlighted by other analyses. In the case of COWP 1 the x co-ordinate was significant, with a move towards the east increasing the likelihood of COWP 1 occurrence. The more cattle per person, the less the occurrence of COWP 1; the greater the human population density the greater the occurrence of COWP 1. The spatial lag pointed towards local to moderate distance spatial processes. Cattle density was not significant. In the case of COWP 2, different factors appeared to be significant. The ratio of cattle to people was a positive risk factor and the spatial lag suggested more distant effects. Cattle density was not significant.

Table 1. Spatial model for all human cases of cryptosporidiosis regardless of COWP type reported in Scotland 1999-2002.

	Coefficient	se	z value	Pr(>|z|)
(Intercept)	-1.125e+01	2.720e-01	-41.376	< 2.00e-16
10 Km lag	1.880e+03	1.701e+02	11.049	< 2.00e-16
X co-ordinate	5.796e-06	8.866e-07	6.538	6.25e-11
Ratio of cattle to people	1.443e-01	2.609e-02	5.532	3.16e-08
Human population density	5.390e-05	1.311e-05	4.112	3.92e-05

Risk factor analysis discriminating between COWP 1 and COWP 2 in humans identified a number of factors as being significantly associated with outcome: Health Board, Sex, Age, and Year were significant at the univariable stage. It was noted that an isolate was 5.2 times more likely to be COWP 2 in 2000 compared to 1999 and 5.3 times more likely to be COWP 1 in 2002 compared to 1999. 2001 did not differ significantly from 1999. At the multivariable stage Age and Board remained significant. Grampian (GR) COWP 1 was twice as likely as COWP 2 compared to Tayside. COWP 1 was also over twice as likely in the 20-30 year olds and 30s and over compared to the under five year olds.

Discussion

There has been debate regarding the epidemiological relevance of the COWP typing system and its utility in addressing issues of public health significance and directing policy. This report provides quantitative evidence that the epidemiology of COWP 1 and 2 do differ significantly both in terms of spatial and temporal behaviour as well as in possible predisposing factors and host susceptibilities. The spatial lag models identified that spatial processes for COWP 1 were more local than for COWP 2 and that the ratio of cattle to humans was protective for COWP 1 and a risk factor for COWP 2. All of these findings bolster, in a quantitative fashion, the understanding of the natural history of the two types. In the case of COWP 1 human to human spread is likely to be less dependent on rural indicators, be more affected by population density and have local spatial structures. For COWP 2 the inverse appears to hold true. In terms of risk factors, the age predisposition of young humans to COWP 2 is suggestive of either exposure differences among age groups or an age acquired immunity to COWP 2.

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References

Abrahamsen, M.S. and Schroeder, A.A. (1999) Characterization of intercellular *Cryptosporidium parvum* gene expression. *Molecular and Biochemical Parasitology*, **104**, 141-146.

Caccio, S., Homan, W., Camilli, R., Traldi, G., Kortbeek, T and Pozio, E. (2000) A microsatellite marker reveals population heterogenicity within human and animals genotypes of *Cryptosporidium parvum*. *Parisitology*, **120**, 237-244.

Casemore, D.P. (2001) Department of the Environment, Transport and the Regions, Cryptosporidium in water supplies. UK Drinking Water Inspectorate Information.

Chappell, C.L. (1999) Annual drinking water quality reports: A new consumer awareness requirement. *Disease Prevention News*, **59**, 17, 1-6.

Fayer, R., Morgan, U. and Upton, S.J. (2000) Epidemiology of *Cryposporidium*: transmission, detection and identification. *International Journal for Parasitology*, **30**, 1305-1322.

Gale, P. (2001) Developments in microbiological risk assessment for drinking water. *Journal of Applied Microbiology*, **91**, 191-205.

Jellison, K.L., Hemond, H.F and Schauer, D.B. (2002) Sources and species of *Cryptosporidium* oocysts in the Wachusett Reservoir Watershed. *Applied and Environmental Microbiology*, **68**, 2, 569-575.

Morgan-Ryan U.M., Fall, A., Ward, L.A., Hijjawi, N., Sulaiman, I., Fayer, R., Thompson, R.C., Olson, M., Lal, A. and Xiao, L. (2002) *Cryptosporidium hominis* n. sp. (Apicomplexa: Cryptosporidiidae) from *Homo sapiens*. Journal of Eukaryotic Microbiology **6**, 433-440.

Spano, F. and Crisanti, A. (2000) *Cryptosporidium parvum*: the many secrets of a small genome. *International Journal for Parisitology*, **30**, 553-565.